Prevention and Management of Frailty

Edited by
Haewon Byeon and Jaewon Nah

MDPI

Prevention and Management of Frailty

Prevention and Management of Frailty

Editors

Haewon Byeon
Jaewon Nah

MDPI

Editors

Haewon Byeon
Inje University
Korea

Jaewon Nah
Honam University
Korea

This is a reprint of articles from the Special Issue published online in the open access journal *International Journal of Environmental Research and Public Health* (ISSN 1660-4601) (available at: https://www.mdpi.com/journal/ijerph/special_issues/Prevet_Frailty).

For citation purposes, cite each article independently as indicated on the article page online and as indicated below:

LastName, A.A.; LastName, B.B.; LastName, C.C. Article Title. *Journal Name* **Year**, *Volume Number*, Page Range.

Contents

Review

Meta-Analysis on the Effects of Transcranial Direct Current Stimulation on Naming of Elderly with Primary Progressive Aphasia

Haewon Byeon

Department of Speech Language Pathology, School of Public Health, Honam University, 417, Eodeung-daero, Gwangsan-gu, Gwangju 62399, Korea; bhwpuma@naver.com; Tel.: +82-10-7404-6969

Abstract: *Purpose*: This study aimed to conduct a qualitative evaluation by synthesizing previous studies on the effect of transcranial direct current stimulation (tDCS) on primary progressive aphasia (PPA)'s naming ability and prove the effects of tDCS mediation on PPA naming using meta-analysis. *Methods*: This study searched literature published from January 2000 to July 2019 using four academic databases (i.e., PubMed, Web of Science, MEDLINE, and Cochrane Library). The final seven publications were systematically evaluated and meta-analysis was conducted for two papers. The effect size was estimated by a standard mean difference (SMD) using Hedge's g, and the significance of effect size was confirmed using the 95% confidence interval. *Results*: The results of seven previous studies' quality assessments ranged from 15 to 26, which were rated above adequate. The results of the meta-analysis showed that the effect size was 0.82 (95% CI: 0.16–1.47), which was a significant 'large effect'. *Conclusions*: This meta-analysis proved that tDCS intervention significantly improved the naming performance of PPA. Future studies must confirm the effects of tDCS on naming intervention by using meta-analysis including many RCT studies.

Keywords: brain stimulation; dementia; meta-analysis; naming; primary progressive aphasia; qualitative evaluation

1. Introduction

Naming is widely used as a representative screening test for determining communication disorders around the world. Naming is divided into confrontation naming and generative naming [1]. The confrontation naming requires the complex coordination of visual stimuli, object recognition, linguistic system, vocabulary system, and phonological production system and it is affected by the function of the temporal lobe [1]. If the brain area associated with word recall is damaged, the confrontation naming function will be compromised [2,3].

On the other hand, generative naming is an evaluation that produces words in a specific category during a given time [4]. It is composed of semantic fluency, which expresses words associated with a presented category (e.g., animal) voluntarily, and phonemic fluency, which speaks given phonemes (e.g., words beginning with 'k') voluntarily [5]. Generation naming, unlike confrontation naming requiring the role of the temporal lobe, is affected by the frontal lobe's executive function, which searches for information and yields words using presented clues [6]. In particular, confrontation naming drew attention as an indicator for detecting neurolingual disorders as soon as possible and measuring the recovery of them because naming is the communication problem that commonly remains until the last recovery stage for patients with fluent aphasia and those with nonfluent aphasia [7]. It has been used as the most representative test for determining the communication problems of patients with neurolingual disorders [7].

Recent studies have reported that naming is one of the most prominent language problems due to dementia [8,9]. Although the degeneration of naming abilities occurs at a different stage depending on dementia types [10], it is a common language deficit of most dementia patients and naming issues are observed from the incipient stage [11]. Particularly, primary progressive aphasia (PPA), a type of dementia, is a neurological dysphasia associated with temporal lobe atrophy and it is different from other dementia types (e.g., Alzheimer's disease) in the aspect that a language defect occurs ahead of a cognitive ability defect [12]. PPA draws attention because of language disorders such as naming, advance gradually, unlike the aphasia, a neurogenic language disorder. In other words, PPA gradually loses naming abilities such as verbal fluency while maintaining other communication abilities such as articulation ability. Therefore, naming is an important indicator in identifying and intervening PPA in the early stage and many researchers have been interested in this topic due to this reason [13].

On the other hand, the safety of brain stimulation such as tDCS, which stimulates the brain using electricity, has been proved and it has been widely used in the clinical coalface [14]. tDCS is brain stimulation stimulating a large area, unlike repetitive transcranial magnetic stimulation (rTMS) stimulating a small area intensively [15]. It has many advantages: It is inexpensive compared to rTMS, is portable because it is light, and does not require a specific posture in the course of treatment [15].

Many studies have proved the effectiveness of tDCS since 2010, and meta-studies are actively conducted in recent years to establish the basis of tDCS [16–18]. In the early stages of development, tDCS was used mainly in the fields of exercise rehabilitation and mental health (e.g., schizophrenia and depression) [17]. However, the use of tDCS tended to increase in recent years as a tool for the linguistic mediation of patients with a neurological impairment such as aphasia and dementia [18]. However, since the research trends to date are mainly limited to the fields of exercise rehabilitation and mental health, more studies are needed to prove the effectiveness of tDCS on dementia.

Up to date, the effects of tDCS on cognition and linguistic abilities are still controversial [19] and, above all, no common implications have been drawn to improve the language ability of PPA. Therefore, it is needed to prove the therapeutic effect of PPA scientifically. This study aimed to conduct a qualitative evaluation by synthesizing previous studies on the effect of tDCS mediation on PPA's naming ability and prove the effects of tDCS mediation on PPA naming using meta-analysis.

2. Methods

This study carried out systematic analysis and meta-analysis in the process of research question selection, systematic literature search and selection, quality evaluation of literature, data extraction and coding, data analysis, and result report preparation.

2.1. Literature Search

This study searched literature published from January 2000 to July 2019 using four academic databases (i.e., PubMed, Web of Science, MEDLINE, and Cochrane Library). The search terms included 'Dementia', 'Primary progressive aphasia', 'Neurodegenerative diseases', 'Transcranial direct current stimulation', 'tDCS', 'Naming', 'Generative naming', 'Naming ability', 'Confrontational naming', 'Responsive naming', 'Semantic fluency', 'Verbal fluency', 'Phonemic fluency', 'Executive function', 'Cognitive rehabilitation', 'Cognitive training', 'Language recovery', and 'Language therapy'.

2.2. Literature Selection

The literature was selected based on the Patient–Intervention–Comparison–Outcome–Study design (PICOS) [20] of the PRISMA protocol. The selection and exclusion of the searched literature were conducted by three researchers independently. When there is a discrepancy in selection and exclusion, the three researchers discussed whether the publication should be included in or excluded from the systematic review or now. The inclusion criteria of this study were (1) studies conducted on PPA, (2) studies confirming the effects of tDCS, (3) experimental studies, and (4) studies published in

English. This study excluded qualitative studies, unpublished publications including dissertations, and articles published in other languages such as French, German, and Chinese.

This study found 132 publications in total. In the first step, 31 duplicated publications were excluded by comparing titles and abstracts. Moreover, 53 publications not related to the study topic were excluded. In the second step, the full texts of the remaining 48 publications were carefully examined and 41 publications were excluded. The excluded studies were non-experimental studies (n = 12), those without original full text (n = 3), those not evaluating dementia (n = 17), and those with inaccurate outcomes (n = 9). As a result, the final seven publications were systematically evaluated and meta-analysis was conducted for two papers, which we could extract representative values. The flow diagram of this study is shown in Figure 1.
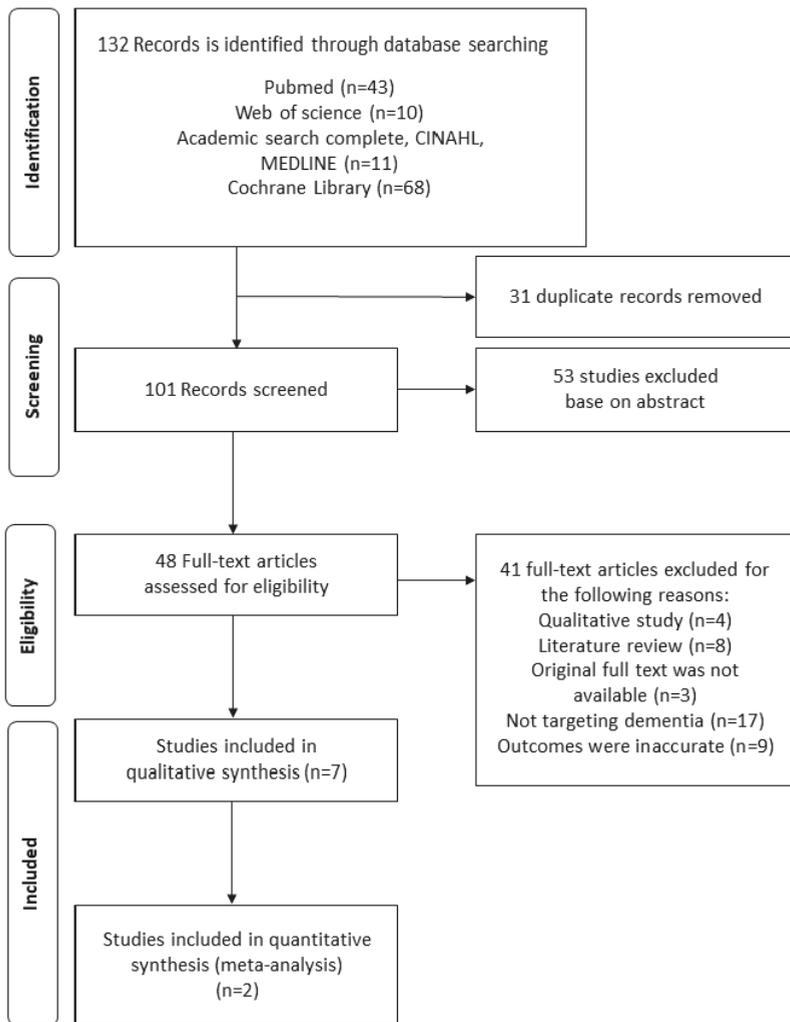
Figure 1. The flow diagram of this study.

2.3. Quality Assessment

This study used "Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields [21]" for quality assessment. This evaluation tool measured scores using a three-point scale (Yes = 2, Partial = 1, No = 0, N/A) and summed the scores of 14 evaluation items. The total score was converted into a percentage value and divided into strong (>80%), good (70–80%), adequate (50–69%), and limited (<50%) to examine the overall quality of studies [22]. The quality assessment of studies was performed by two researchers independently. If there is a discrepancy in the quality assessment item of a specific study, the final score was determined by discussion.

2.4. Meta-Analysis

This study extracted the analysis data of the selected publications and conducted meta-analyses for publications that could be statistically integrated using R version 3.4.2 (Foundation for Statistical Computing, Vienna, Austria). The representative values used for the analysis were estimated by calculating the difference between the treatment group's mean and the control group's mean and the mean differences normalized by standard deviations. The mean differences normalized by standard deviations were calculated according to Equation (1).

$$\sqrt{S1_{pre}^2 + S1_{post}^2 - \left(2 \times Corr \times S1_{pre} \times S1_{post}\right)} \tag{1}$$

The effect size was estimated by a standard mean difference (SMD) using Hedge's g, and the significance of effect size was confirmed using the 95% confidence interval. The calculated effect size was interpreted as 'small effect' when it was smaller than 0.32, 'middle effect' when it was between 0.33 and 0.55, and 'big effect' when it was 0.56 or higher. Publication bias could not be estimated because target publications were less than 10.

3. Results

3.1. Quality Assessment Results

The quality assessment results of this study are presented in Table 1. The results of seven previous studies' quality assessments ranged from 15 to 26, which were rated above adequate. All seven studies systematically presented the 'objective of study', 'research design', and 'conclusion' suitable for each item. Six studies, except one study [23], described the procedure of random allocation in the methodology section. While conducting studies, three studies [24–26] blinded researchers and four studies [24,26–28] blinded subjects. Six studies [23–28], except for [29], described the measurement methods and evaluation tools in detail. However, only one study [25] conducted a power test before starting the experiment. Additionally, only two studies controlled confounding variables [24,28].

Table 1. Results of the publication's quality assessment.

Criteria / Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Wang, et al. 2013 [29]	+	+	±	+	N/A	N/A	N/A	+	−	−	+	±	±	+	15
Cotelli, et al. 2014b [24]	+	+	+	+	±	+	+	+	±	+	+	+	+	+	26
Tsapkini, et al. 2014 [27]	+	+	±	+	±	−	+	+	±	+	+	±	+	+	22
Hung, et al. 2017 [23]	+	+	±	+	−	N/A	N/A	+	±	+	±	±	+	+	18
McConathey, et al. 2017 [28]	+	+	+	+	±	−	+	+	±	+	+	+	+	+	24
Ficek, et al. 2018 [25]	+	+	±	+	±	+	+	+	+	+	+	±	+	+	25
Tsapkini, et al. 2018 [26]	+	+	±	±	±	+	+	+	±	±	+	±	+	+	22

+ = 2, ± = 1, − = 0.

3.2. Effects of tDCS on Improving the Naming Ability for PPA

The effects of tDCS on improving the naming ability for PPA were analyzed and the results are presented in Table 2. Ficek et al. (2018) [25] examined the combined effects of tDCS and speech therapy

on 24 patients with PPA using letter accuracy. Their results showed that letter accuracy improved for the tDCS group and the placebo stimulation group but the improvement of the tDCS group was significantly larger. Hung et al. (2017) [23] evaluated the accuracy of naming by combining semantic feature training and tDCS intervention for patients with PPA and those with alzheimer's disease (AD). Hung et al. (2017) [23] tested the intervention effect by dividing the results of the compounded intervention into trained items and untrained items. It was found that the trained items had higher accuracy than the untrained items after tDCS intervention and the effect was maintained until the follow-up period. Tsapkini et al. (2014) [27] evaluated the compound effects of spelling intervention and tDCS for six patients with PPA. In the untrained spelling item, the group which received tDCS and spelling intervention maintained the improved ability longer than the group which received placebo stimulation and spelling intervention. Tsapkini et al. (2018) also examined the combined effects of tDCS and naming/spelling intervention on 36 patients with PPA and reported that the trained items of the tDCS group were significantly improved immediately after the intervention. The difference between the trained words and the untrained words increased for the tDCS group and the placebo stimulation group as time goes on.

Int. J. Environ. Res. Public Health **2020**, 17, 1095

Table 2. The effects of tDCS on naming improvement for PPA.

Study and Design	Participants	Stimulated Region	Intervention tDCS	Sham tDCS	Session	Assessment	Outcomes
Ficek et al. (2018) [25] Blinding & Crossover & RCT Design	PPA (n = 24) tDCS (n = 12) : age = 65.2 ± 7.0 Sham (n = 12) : age = 69.1 ± 5.6	Left inferior frontal gyrus	Anodal 2 mA 20 min	30 s	15 sessions (daily)	Letter accuracy (Written naming)	Both tDCS and sham groups improved the letter accuracy of trained words
Hung et al. (2017) [23] pre-post design	PPA (n = 4) & AD (n = 1) : age = 66.6±8.56)	Left temporoparietal region	Anodal 1.5 mA 20 min	30 s	10 sessions (2 weeks)	Naming : six semantic items (trained and untrained items)	After tDCS intervention, trained items were maintain longer than untrained items.
Cotelli et al. (2014b) [24] Blinding & RCT design	PPA (n = 16) AtDCS (n = 8) : age = 63.4 ± 6.8 Placebo tDCS (n = 8) : age = 70.4 ± 6.8	Left dorsolateral prefrontal cortex	Anodal 2 mA 25 min	10 s	10 sessions (2 weeks)	Languistic abilities : Aachen Aphasia Tes (AAT)	Naming accuracy of the AtDCS group increased selectively during the pre–after intervention period.
McConathey et al. (2017) [28] Blinding & Crossover & RCT design	PPA (n = 15) : age = 68.71 ± 6.97 tDCS (n = 7, analysis n = 4), Sham (n = 8, analysis n = 3)	Left prefrontal region	Anodal 1.5 mA 20 min	30 s	10 sessions (2 weeks)	Semantic process : BNT, PPT, Category Fluency tests	Those with lower base scores have improved significantly since the actual tDCS compared to those with higher base scores.
Wang et al. (2013) [29] A1-B1-A2-B2	PPA (n = 1) : age = 67	Left posterior perisylvian region, left Broca's area	B1–B2 Anodal 1.2 mA 20 min	A1–A2 30 s	5 days (A1–A2) 5 days (B1–B2)	Psycolinguistic Assessment in Chinese Aphasia (PACA)	After the B1 intervention, the scores of the four PACA sub items increased significantly.
Tsapkini et al. (2014) [27] Blinding & Crossover & RCT design	PPA(n = 6)	Left inferior frontal gyrus	1–2 mA 20 min	30 s	15 sessions	Number of correctly spelled word-prompts associated with each phoneme	Significant improvement has been maintained through the follow-up period under the tDCS.
Tsapkini et al. (2018) [26] Blinding & Crossover & RCT	PPA (n = 36) 1. tDCS (n = 20, crossover n = 15) 2. Sham (n = 16, crossover n = 15)	Left inferior frontal gyrus	2 mA 20 min	30 s	15 sessions (5 sessions per week)	Letter accuracy : trained & untrained items	Trained items were significantly improved immediately after tDCS intervention.

6

3.3. Meta-analysis for the Effects of tDCS Intervention on the Naming Performance of Patients with PPA

SMD about the effects of tDCS intervention on naming performance was analyzed (Figure 2). The results showed that the effect size was 0.82 (95% CI: 0.16–1.47), which was a significant 'large effect'.
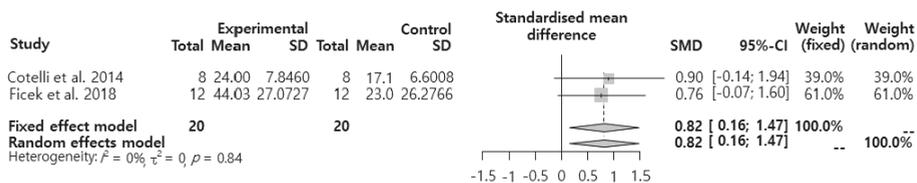
Figure 2. Effects of transcranial direct current stimulation (tDCS) intervention on patients with primary progressive aphasia (PPA's) naming performance.

4. Discussion

This study conducted systematic reviews and meta-analysis to establish the scientific basis regarding the effect of tDCS on PPA's naming ability based on literature published from January 2000 to May 2019. This study evaluated the quality of seven studies and found that, even though most of them were designed as RCT studies and blinded either researchers or subjects, only one study [25] conducted power analysis and only two studies controlled confounding variables [24,28]. Since the sample size bias has the possibility to distort the results of studies, it is recommended to carry out RCT studies that estimate sample size and control confounding variables before designing studies in the future.

This study conducted pre- and post-meta-analysis and found that tDCS intervention had a significant effect on improving PPA's naming ability. PPA is a degenerative disease that causes linguistic problems such as naming ahead of cognitive problems such as orientation and visuospatial abilities [12,25,30]. The problem of naming ability is clearly observed from the incipient stage [12]. PPA may be classified as speech logopenic progressive aphasia, semantic dementia, or progressive nonfluent aphasia [31]. Naming ability decreases in patients with PPA regardless of PPA types [32]. PPA shows the deficiency of linguistic ability primarily and tDCS may have a significant effect on the PPA's naming performance.

It is known that tDCS promotes and inhibits the spontaneous activity of the cranial nerve by stimulating with minute DC current through the scalp and making the DC reach the cerebral cortex [33]. In other words, tDCS stimulates the brain with a weak current below 2 mA to regulate the resting membrane potential voltage and induces changes in the spontaneous discharge rate of nerve cells and the activation of N-methyl-D-aspartic acid (NMDA) receptor [33]. However, how tDCS improves naming is not clearly known because the effectiveness of tDCS began to be evaluated in very recent years and there are no large-scale and long-term follow-up studies that evaluated the effects of tDCS on the improvement of naming [34]. Nevertheless, the results of this meta-analysis show that tDCS had a significant effect on improving PPA's naming performance suggested tDCS could be an effective language mediator of PPA. Long-term follow-up studies will be needed to identify the effects of tDCS fully.

The importance of this study was that this study established the scientific foundation to evaluate the effects of tDCS on the naming ability of PPA. The limitations of this study are as follows. First, although this study collected and analyzed literature through various academic databases, this study only evaluated publications written in English and excluded papers written in other languages such as French and Chinese. Second, this study could not conduct a bias test because meta-analysis only analyzed two studies and there was a limit in proving the results. If the sample is small, the variance and standard deviation of individual studies become relatively large, which affects the confidence interval of the overall effect size and increases type II error. However, it is believed that the bias due to

the small sample size was negligible because this study confirmed that the effects of tDCS intervention on PPA's naming performance were a significant 'big effect'. In the future, meta-analysis containing more samples is required.

5. Conclusions

This meta-analysis proved that tDCS intervention significantly improved the naming performance of PPA. However, the results should be generalized very carefully because the meta-analysis was conducted on only a few samples. Therefore, future studies must confirm the effects of tDCS on naming intervention by using meta-analysis using many RCT studies.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Laine, M.; Martin, N. *Anomia: Theoretical and Clinical Aspects*; Psychology Press: Hove, UK, 2006.
2. Manning, L.; Warrington, E.K. Two routes to naming: A case study. *Neuropsychologia* **1996**, *34*, 809–817. [CrossRef]
3. Glosser, G.; Donofrio, N. Differences between nouns and verbs after anterior temporal lobectomy. *Neuropsychology* **2001**, *15*, 39–47. [CrossRef] [PubMed]
4. Ross, T.P. The reliability of cluster and switch scores for the Controlled Oral Word Association Test. *Arch. Clin. Neuropsychol.* **2003**, *18*, 153–164. [CrossRef] [PubMed]
5. Laws, K.R.; Adlington, R.L.; Gale, T.M.; Moreno-Martínez, F.J.; Sartori, G. A meta-analytic review of category naming in Alzheimer's disease. *Neuropsychologia* **2007**, *45*, 2674–2682. [CrossRef] [PubMed]
6. Klumpp, H.; Deldin, P. Review of brain functioning in depression for semantic processing and verbal fluency. *Int. J. Psychophysiol.* **2010**, *75*, 77–85. [CrossRef] [PubMed]
7. Coppens, P. *Aphasia and Related Neurogenic Communication Disorders*; Jones & Bartlett Publishers: Burlington, VT, USA, 2016.
8. Jokel, R.; Graham, N.L.; Rochon, E.; Leonard, C. Word retrieval therapies in primary progressive aphasia. *Aphasiology* **2014**, *28*, 1038–1068. [CrossRef]
9. Tak, S.; Hong, S.H. Face-name memory in Alzheimer's disease. *Geriatr. Nurs.* **2014**, *35*, 290–394. [CrossRef]
10. Hodges, J.R.; Erzinçlioğlu, S.; Patterson, K. Evolution of cognitive deficits and conversion to dementia in patients with mild cognitive impairment: A very-long-term follow-up study. *Dement. Geriatr. Cogn. Disord.* **2006**, *21*, 380–391. [CrossRef]
11. Vogel, A.; Gade, A.; Stokholm, J.; Waldemar, G. Semantic memory impairment in the earliest phases of Alzheimer's disease. *Dement. Geriatr. Cogn. Disord.* **2005**, *19*, 75–81. [CrossRef]
12. Crinion, J.T. Transcranial direct current stimulation as a novel method for enhancing aphasia treatment effects. *Eur. Psychol.* **2016**, *21*, 65–77. [CrossRef]
13. Helm-Estabrooks, N.; Albert, M.L. *Manual of Aphasia and Aphasia Therapy*; Pro-Ed Publishing: Austin, TX, USA, 2004.
14. Bikson, M.; Grossman, P.; Thomas, C.; Zannou, A.L.; Jiang, J.; Adnan, T.; Mourdoukoutas, A.P.; Kronberg, G.; Truong, D.; Boggio, P.; et al. Safety of transcranial direct current stimulation: Evidence based update 2016. *Brain Stimul.* **2016**, *9*, 641–661. [CrossRef] [PubMed]
15. Shaw, M.T.; Kasschau, M.; Dobbs, B.; Pawlak, N.; Pau, W.; Sherman, K.; Bikson, M.; Datta, A.; Charvet, L.E. Remotely supervised transcranial direct current stimulation: An update on safety and tolerability. *J. Vis. Exp.* **2017**, *128*, e56211. [CrossRef] [PubMed]
16. Jacobson, L.; Koslowsky, M.; Lavidor, M. tDCS polarity effects in motor and cognitive domains: A meta-analytical review. *Exp. Brain Res.* **2012**, *216*, 1–10. [CrossRef] [PubMed]
17. Shiozawa, P.; Fregni, F.; Benseñor, I.M.; Lotufo, P.A.; Berlim, M.T.; Daskalakis, J.Z.; Cordeiro, Q.; Brunoni, A.R. Transcranial direct current stimulation for major depression: An updated systematic review and meta-analysis. *Int. J. Neuropsychopharmacol.* **2014**, *17*, 1443–1452. [CrossRef] [PubMed]

18. Elsner, B.; Kugler, J.; Pohl, M.; Mehrholz, J. Transcranial direct current stimulation (tDCS) for improving aphasia in patients with aphasia after stroke. *Cochrane Database Syst. Rev.* **2015**, *5*. [CrossRef] [PubMed]

19. Horvath, J.C.; Forte, J.D.; Carter, O. Quantitative review finds no evidence of cognitive effects in healthy populations from single-session transcranial direct current stimulation (tDCS). *Brain Stimul.* **2015**, *8*, 535–550. [CrossRef] [PubMed]

20. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D.G. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Ann. Intern. Med.* **2009**, *151*, 264–269. [CrossRef]

21. Kmet, L.M.; Lee, R.; Cook, L.S. *Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields*; Alberta Heritage Foundation for Medical Research: Edmonton, AB, Canada, 2004.

22. Lee, L.; Packer, T.L.; Tang, S.H.; Girdler, S. Self-management education programs for age-related macular degeneration: A systematic review. *Australas. J. Ageing* **2008**, *27*, 170–176. [CrossRef]

23. Hung, J.; Bauer, A.; Grossman, M.; Hamilton, R.H.; Coslett, H.B.; Reilly, J. Semantic feature training in combination with transcranial direct current stimulation (tDCS) for progressive anomia. *Front. Hum. Neurosci.* **2017**, *11*, 253. [CrossRef]

24. Cotelli, M.; Manenti, R.; Petesi, M.; Brambilla, M.; Cosseddu, M.; Zanetti, O.; Miniussi, C.; Padovani, A.; Borroni, B. Treatment of primary progressive aphasias by transcranial direct current stimulation combined with language training. *J. Alzheimers Dis.* **2014**, *39*, 799–808. [CrossRef]

25. Ficek, B.N.; Wang, Z.; Zhao, Y.; Webster, K.T.; Desmond, J.E.; Hillis, A.E.; Frangakis, C.; Vasconcellos Faria, A.; Caffo, B.; Tsapkini, K. The effect of tDCS on functional connectivity in primary progressive aphasia. *Neuroimage Clin.* **2018**, *19*, 703–715. [CrossRef] [PubMed]

26. Tsapkini, K.; Webster, K.T.; Ficek, B.N.; Desmond, J.E.; Onyike, C.U.; Rapp, B.; Frangakis, C.E.; Hillis, A.E. Electrical brain stimulation in different variants of primary progressive aphasia: A randomized clinical trial. *Alzheimers Dement.* **2018**, *4*, 461–472. [CrossRef] [PubMed]

27. Tsapkini, K.; Frangakis, C.; Gomez, Y.; Davis, C.; Hillis, A.E. Augmentation of spelling therapy with transcranial direct current stimulation in primary progressive aphasia: Preliminary results and challenges. *Aphasiology* **2014**, *28*, 1112–1130. [CrossRef]

28. McConathey, E.M.; White, N.C.; Gervits, F.; Ash, S.; Coslett, H.; Grossman, M.; Hamilton, R.H. Baseline performance predicts tDCS-mediated improvements in language symptoms in primary progressive aphasia. *Front. Hum. Neurosci.* **2017**, *11*, 347. [CrossRef] [PubMed]

29. Wang, J.; Wu, D.; Chen, Y.; Yuan, Y.; Zhang, M. Effects of transcranial direct current stimulation on language improvement and cortical activation in nonfluent variant primary progressive aphasia. *Neurosci. Lett.* **2013**, *549*, 29–33. [CrossRef]

30. Rohrer, J.D.; Knight, W.D.; Warren, J.E.; Fox, N.C.; Rossor, M.N.; Warren, J.D. Word-finding difficulty: A clinical analysis of the progressive aphasias. *Brain* **2008**, *131*, 8–38. [CrossRef]

31. Hardiman, O.; Doherty, C.P.; Elamin, M.; Bede, P. *Neurodegenerative Disorders*; Springer: Berlin/Heidelberg, Germany, 2011.

32. Budd, M.A.; Kortte, K.; Cloutman, L.; Newhart, M.; Gottesman, R.F.; Davis, C.; Heidler-Gary, J.; Seay, M.W.; Hillis, A.E. The nature of naming errors in primary progressive aphasia versus acute post-stroke aphasia. *Neuropsychology* **2010**, *24*, 581–589. [CrossRef]

33. Medeiros, L.F.; de Souza, I.C.; Vidor, L.P.; de Souza, A.; Deitos, A.; Volz, M.S.; Fregni, F.; Caumo, W.; Torres, I.L. Neurobiological effects of transcranial direct current stimulation: A review. *Front. Psychiatry* **2012**, *3*, 110. [CrossRef]

34. Kim, J.W.; Lee, J. Application of transcranial direct current stimulation in psychiatry. *J. Korean Neuropsychiatr. Assoc.* **2016**, *55*, 158–167. [CrossRef]

Review

Machine Learning Approaches for the Frailty Screening: A Narrative Review

Eduarda Oliosi [1,2], Federico Guede-Fernández [1,2] and Ana Londral [1,3,*]

1   Value for Health CoLAB, 1150-190 Lisboa, Portugal; mariaeduardaoliosi@icloud.com (E.O.);
    federico.guede@vohcolab.org (F.G.-F.)
2   LIBPhys (Laboratory for Instrumentation, Biomedical Engineering and Radiation Physics), NOVA School of
    Science and Technology, NOVA University of Lisbon, 2829-516 Caparica, Portugal
3   Comprehensive Health Research Center, NOVA Medical School, NOVA University of Lisbon,
    1150-082 Lisboa, Portugal
*   Correspondence: ana.londral@vohcolab.org

Abstract: Frailty characterizes a state of impairments that increases the risk of adverse health outcomes such as physical limitation, lower quality of life, and premature death. Frailty prevention, early screening, and management of potential existing conditions are essential and impact the elderly population positively and on society. Advanced machine learning (ML) processing methods are one of healthcare's fastest developing scientific and technical areas. Although research studies are being conducted in a controlled environment, their translation into the real world (clinical setting, which is often dynamic) is challenging. This paper presents a narrative review of the procedures for the frailty screening applied to the innovative tools, focusing on indicators and ML approaches. It results in six selected studies. Support vector machine was the most often used ML method. These methods apparently can identify several risk factors to predict pre-frail or frailty. Even so, there are some limitations (e.g., quality data), but they have enormous potential to detect frailty early.

Keywords: frailty; indicators; screening; artificial intelligence; healthcare

1. Introduction

With the growing aging population worldwide, an important subject matter is "frailty" (or fragility) which is closely age-related [1]. Living longer can lead to a longer period of frailty with increased demand for care [2]. The proportion of the elderly is expected to be approximately 30% of the population by 2060, in Europe [3]. Moreover, aging expenditures are projected to increase by 1.5 percentage points of GDP, from 26.8% in 2013 to 28.3%, in 2060 [4]. Frailty is a broad term used to denote a complex clinical condition [5,6] that can be defined as a medical syndrome caused by multisystem dysregulation and contributors. In addition, it is characterized by loss of health reserves (e.g., physical fitness), reduced physiologic function, and impaired homeostasis, which increases an individual's vulnerability, resulting in risk for early dependency, morbidity, and/or death when exposed to stressors. In summary, the frailty syndrome involves the main domains: physical, psychological, social, cognitive, and environmental [6–11]. Moreover, frailty characterizes a state of impairments that increase the risk of negative health outcomes such as physical limitation, falls, fractures, disability, morbidity, dependence, hospitalization, institutionalization, lower quality of life, and premature death [4,12–15].

Barriers to implementing frailty screening in clinical settings still exist as a lack of consensus on the assessment tool best suited to each domain and undetermined cost-effectiveness [16]. Moreover, it is imperative to note that the frailty assessment tools can provide different data regarding the incidence of frailty [17]. The identification of frailty might seem an ideal way to identify the elderly who need additional healthcare support services. In a recent review, Liotta and colleagues (2018), from a public health perspective,

stressed that it is vital to identify factors that contribute to successful health and social care interventions and to the health systems' sustainability [18]. Nevertheless, there is a lack of substantial research evidence to support this strategy and to identify the most effective tools to detect frailty [10]. In addition, there is no consensus about the key components and assessment of frailty [19].

In a systematic review, Sutton and colleagues (2016) identified 38 multi-component frailty assessment tools where, surprisingly, only 5% (2/38) of the frailty assessment tools had evidence of reliability and validity that was within statistically significant parameters and of fair–excellent methodological quality: the Frailty Index—Comprehensive Geriatric Assessment and the Tilburg Frailty Indicator [20]. In addition, a score or set of criteria was used, developed, and validated to identify frailty. The most common frailty instruments used in research and clinical practice are the Fried frailty phenotype (FP), which is based on five items (slow walking speed, weak grip strength, low physical activity, unintended weight loss, and exhaustion), minimum of three of five criteria for classifying as frailty [21–23]. Nevertheless, there is insufficient evidence to determine the best tool for use in research and clinical practice [20].

According to an umbrella review, despite these broadly used conventional methods, few frailty measures seem to be valid, reliable, diagnostically accurate, and virtuous predictive abilities. Moreover, they reported that the Frailty Index (and gait speed) emerged as the most useful in routine care and community settings [24]. The traditional measurements of frailty have potential limitations and challenges: for example, single measures of physical performance (such as timed-get-up-and-go) or a set of physical features (such as FP) are clinically suitable and validated to predict poor outcomes in older adults. Nevertheless, they have shown low consistency, accuracy, reliability, and inter-rater understanding. Moreover, these measures require specialized equipment (e.g., dynamometer to grip strength), not always clinically viable (e.g., for patients with dementia), and also require a manual evaluation process (e.g., timed-get-up-and-go) that is subject to operator error due to the need for training beyond time to administer [25]. Furthermore, the prevalence of frailty varies across settings and adopted tests, making it difficult to scale to the population level [21,22,25,26]. In this view, an alternative is exploring approaches to screening frailty from routinely collected data (e.g., medical claims, prescriptions, administrative data, and individual records) [25].

The presented work is part of the Frailcare.AI project. Its primary objective is to develop intelligent tools that aim to improve pathways for the identification of fragility in senior citizens in the Portuguese population. This paper aims to review tools and clinical indicators for identifying early frailty and supply evidence for developing innovative tools and artificial intelligence (AI) technologies to support frailty care. This review provides recent evidence for the assessment and screening of frailty. It reviews the existing tools and clinical indicators for complex frailty, focusing on measures extracted from healthcare datasets. We seek to improve knowledge and application opportunities for machine learning (ML). This intelligent screening tool relies on an approach that includes ML methods.

1.1. Background

ML methods can adapt conventional frailty screening methods validated in previous studies. While AI is a subfield of computer science dedicated to providing computers with intelligent problem-solving capabilities, including planning, reasoning, perception, or learning (i.e., AI aims to mimic human intelligence and behavior through systems), ML, a subfield of AI, provides algorithms that build mathematical models based on sampled data. These models map input data to desired outputs. Inputs can be images and an arbitrary sequence of numerical or categorical data. The inputs are also known as features [27–30].

The AI resource includes advanced algorithms and methods that do not even process quantitative data. Consequently, comparing ML to traditional statistical methods

makes it coherent. Conventional statistical models focus on discovering interactions and confidence intervals between data points and outcomes; comparatively, ML approaches seek to reach high prediction accuracy, placing less emphasis on whether it is possible to interpret the model. Prediction is critical in ML to generate otherwise unavailable data. Moreover, ML is often better fitting for significant input variables (e.g., time series from biosignals), and the traditional analysis with statistical models is intended for data with tens of input columns [28].

1.1.1. Decision Trees

Decision tree (DT) classification is broadly used for different classification tasks (for example, pattern recognition). DTs make their decisions from the root, all the way up to the branches. The DT approach essentially partitions the space into subspaces by computing the decision boundaries for each node, and it continues adding inputs to the tree nodes until no further improvement can be made to the prediction results. The leaf nodes in the decision tree are labeled according to the groups in the classification problem [31,32].

1.1.2. K-Nearest Neighbours

K-nearest neighbor (KNN) is among the generally used classification approaches. Its algorithm does not create any model through learning strategies. Its training is based on sorting the class labels of the training dataset together with the feature vectors for each record. The accuracy of this model is comparable to more complicated classifiers [31,33].

1.1.3. Support Vector Machine

Support vector machine (SVM) is a supervised classification algorithm; in supervised learning, the models are trained based on given examples, containing inputs and desired outputs provided by an expert (e.g., physical therapist). The SVM has been applied to many real-world classification problems because of its effectiveness, such as pattern recognition for text classification and bioinformatics systems. SVMs are robust to overfitting and have a prominent generalization capability, as well as being good at handling complex, nonlinear scenarios and tending not to overfit. Moreover, SVM is robust to bias and variance of data and results in accurate predictions for either binary or multiclass classifications. As such, SVM has been broadly used in health research, for example, to identify imaging biomarkers of neurological and psychiatric disease, cancer diagnosis, and early detection of Alzheimer's, among others [29,31–34].

1.1.4. Artificial Neural Networks

As a brain's neurons, the artificial neural networks (ANN or NN) are a class of nonlinear statistical algorithms modeled, able to process information. Thus, this approach is defined by how the components of the network are linked and the weights of these connections. This learning process constructs derived parameters as linear combinations of the input parameters and then further models the outcome as a nonlinear constructions of these derived parameters. Although they are excellent at handling many inputs, they are rather computationally costly [32].

1.1.5. Random Forest

The random forest (RF) consists of many decision trees that operate as an ensemble. Each tree provides a class prediction, and the prediction with the most votes turns into the overall model prediction. Therefore, this method is a random forest consisting of a set of individual decision trees; hence, individual errors of the trees are decreased. RF results in a good performance on imbalanced datasets while handling missing values well. These models are not substantially affected by outliers in data. Such decision trees are designed to have a low correlation to each other to encourage range among the trees. Moreover, RFs

use the rules of bootstrapping and aggregating to build trees based on several subsets of the training data using different subsets of features [21,35].

1.1.6. Extreme Gradient Boosting

Extreme gradient boosting (XGBoost) is a supervised machine learning model. This method builds a robust model created on weaker models that are short decision trees. The XGBoost works on building a new weak model designed to predict the residual values between the ground truth and the robust model. These weak models are then added to the overall robust model. The predictions of the models are added simultaneously to make the final prediction. The main benefits are execution speed and model performance. These models use boosting, an ensemble method where each tree or model corrects errors made by earlier trees. XGBoost requires minimal feature engineering, allowing steps such as normalizations and scaling to be omitted, and outliers have little impact [21,35,36].

2. Methods

Search Strategy and Data Extraction

Studies were sought using general (Web of Science and Google Scholar) and healthcare (PubMed and The Lancet) databases. Two independent reviewers reviewed all the titles and abstracts in the first selection step. Three keywords were used without period restriction: Frailty screening, as this was the focus of this review, artificial intelligence (AI), and machine learning because ML was considered a subarea of AI. The study inclusion criteria were (i) it described frailty screening tools; (ii) the population was presented with pre-frail or frail conditions/concepts; (iii) studies about frailty indicators, validity studies, articles on frailty screening (frailty assessment, detection, or prediction), and contained significant determinants of frailty; (iv) or if they had a combination of all these criteria. The exclusion criteria were (i) frailty studies about intervention or prevalence; (ii) frailty screening through the inertial sensors; (iii) non-peer-reviewed and academic studies; (iv) all types of reviews (e.g., umbrella and systematic) or case reports or non-English language. There is no existing restriction to frailty screening assessment tools.

3. Results

The selection process produced six studies relevant to the aim of this review. Table 1 provides an overview of the selected studies in the frailty screening for ML methods. In general, all studies classified frailty with only one tool, such as the Rockwood Clinical Frailty Scale (CFS) [36], electronic Frailty Index (eFI) [31]; frailty phenotype (FP) [37]; electronic Frailty Score (eFS) [5]; and an exception that utilized a combination of tools [21], which included FRS-26-ICD (frailty drawn from ICD-10 Clinical Modification), ECI (The Elixhauser Comorbidity Index (ECI), high-risk medications (10 risk classification, Beers Criteria, 2019), sociodemographic characteristics, healthcare, and insurance utilization. Another exception used a set of predictors variables, including clinical and socioeconomic aspects, and six target variables (mortality, disability, urgent hospitalization, fracture, preventable hospitalization, and accessing the emergency department with red code) [38].

ML algorithms have been used to predict frailty-derived indicators based on health-related data. The eFI, which is based on the deficit accumulation approach, was predicted using several ML algorithms such as DT, KNN, and SVM [31]. They analyzed the data of 592 patients and the best performance was obtained with SVM, the accuracy was 93.5%, sensitivity 97.8%, and specificity 89.1%. The SVM algorithm requires 70 input variables and they remarked that SVM may prove less feasible in clinical scenarios where rule-based models, such as DT models, may be more interpretable to clinicians but the results in terms of accuracy are the poorest (42.4%) with DT models.

Aponte-Hao, in 2021, proposed to use ML algorithms to predict the CFS score based on two-year electronic medical records (EMR). The CFS ranges from one to nine, with one having the label of "very fit" and nine labeled "terminally ill" (the highest degree of frailty);

the frailty was predicted using a dichotomized indicator into frail or not frail with a cut-off of five from the original physician-rated CFS score. After the removal of features with low variance or high correlation, they reduced the total number of features from 5466 to 75. They used DT, LR, SVM, NB, NN, KNN, RF, and XGBoost models, and the XGBoost was the model with the best results of the eight models which were developed; it achieved the highest sensitivity (78.14%) and specificity (74.41%), but the F1-score was not shown when they used the best threshold that was achieved by using the most optimal thresholds determined using ROC curves [36].

An ML-based tool for stratification of FP based on one-year hospital discharge data was developed and validated (Pogam 2022). They created a clinical knowledge-driven eFS calculated as the number of deficient organs/systems among 18 critical ones identified from the ICD-10 diagnoses coded in the year before FP assessment. In addition, for eFS development and internal validation, they linked individual records of the cohort database to inpatient discharge data for an 11-year period. The best-performing model for predicting the dichotomized FP was the LR model with four predictors: age and sex at FP assessment, time since last discharge, and the eFS. The eFS score was associated with all adverse health outcomes of interest (death, prolonged length of hospital stay, number of hospitalizations, and nursing home admission within 12 months after FP assessment). They also conducted an external validation which confirmed that the eFS was a significant predictor of the 13 adverse outcomes [5].

Six frailty conditions (mortality, urgent hospitalization, disability, fracture, and emergency admission) were predicted with ML models (Tarekegn 2020). These models were assessed with a dataset that contains 1,095,612 subjects and 64 variables (58 input and 6 output variables). They resolved the imbalanced nature of the data through a resampling process and they performed a comparative study between the different ML algorithms: ANN, genetic programming (GP), SVM, DT, and RF. The obtained results show that the prediction performance of ML models significantly varies from problem to problem in terms of different evaluation metrics. The mortality prediction outcome showed higher performance with ANN (F1-score 0.79) and SVM (F1-score 0.78) than predicting the other outcomes. On average, over the six problems, the DT classifier showed the lowest accuracy, while other models (GP, LR, RF, ANN, and SVM) performed better. All models showed lower accuracy in predicting an event of an emergency admission with a red code than predicting fracture and disability. In predicting urgent hospitalization, only SVM achieved better performance (F1-score 0.76) [38].

ML models were also developed for predicting 30-day unplanned readmissions for elderly patients by integrating variables such as frailty and comorbidities (Mohanty 2022). The models were developed with data from 68,152 patients, consisting of 18,840 readmissions and 109,741 non-readmissions and containing 458 variables that were used for the prediction of readmission. The ML models compared were RF, XGBoost, CatBoost, and logistic regression, and a stacking classifier CatBoost outperformed the other models with an AUROC of 79% and F1 score of 71%. They performed an in-depth study of the model explainability by assessing the feature importance by means of the SHAP methods [21].

Moreover, a deep learning approach was followed to classify pre-frail/frail vs. non-frail older adults using heart rate response to physical activity [37]. They compared resting-state heart rate characteristics with heart rate monitoring without controlling for physical activities, the objective of the study. They assessed the performance of ML and deep learning models such as LSTM. The obtained results showed that LSTM outperformed other approaches. These results were obtained with a reduced sample size of 88 patients. This work shows that heart rate dynamics classification using LSTM deep learning models without any feature engineering may provide an accurate and objective marker for frailty screening [37].

Table 1. Selected studies using the machine learning methods.

First Author and Year	Sample Size and Age	Methods	Type of Data	Instrument (s)	Main Outcomes
Ambagtsheer 2020 [31]	592; ≥75	SVM; DT; KNN	Administrative records	Electronic Frailty Index	Arthritis; diabetes; hypertension; osteoporosis; vision issues; PAS score; Cornell scale; VBC; PBC; WC.
Aponte-Hao 2021 [36]	5466; ≥65	ENLR; SVM; KNN; NB; DT; RF; XGBoost; ANN	Electronic medical record	Rockwood Clinical Frailty Scale	Older; female; less likely to have no known CD.
Eskandari 2022 [37]	88; ≥65	LR; MLP; XGBoost; LSTM	Time-series ECG	Frailty Phenotype	HR dynamics.
Le Pogam 2022 [5]	469 int valid; 54,815 ext valid; 71.6 (mean)	BS-LR; Lasso-LR; RF; SVM	IR Lc65+ CHUV	Electronic frailty score	Older; female.
Mohanty 2022 [21]	76,000; ≥50	LR; RF; XGBoost; CatBoost; SC	electronic record data	Demo; FRS-26-ICD; ECI; H-RM; HIU	Prior readmissions; discharge to a rehabilitation facility; length of stay; comorbidities; frailty indicators (30-day readmission).
Tarekegn 2020 [38]	1,095,612; ≥65	ANN; GP; SVM; RF; LR; DT	administrative records	a set of variables (64)	Age (all problems); CI (mortality); number of urgent hospitalizations, femur and neck fracture (fracture problem); mental disease, polyprescription and disease of the circulatory system (urgent hospitalization and preventable hospitalization); CI and number of urgent hospitalizations (emergency admission with red code).

Abbreviations: ANN: Artificial neural network; BS-LR: Best-Subsets; CatBoost: Category boost; CD: Chronic diseases; CI: Charlson Index; Demo: Demographic; DT: Decision tree; ECG: Electrocardiogram; ECI: The Elixhauser Comorbidity Index; EMR: Electronic medical records; ENLR: Elastic net logistic regression; Ext valid: External validation; FRS-26-ICD: The Frailty Risk Score 26 drawn from ICD-10 Clinical Modification (ICD-10-CM); ICD-10-CM: International Statistical Classification of Diseases and Related Problems 10th revision; GP: Genetic programming; HIU: Healthcare and insurance utilization; HR: Heart rate; HR-M: High-risk medications (Beers Criteria: 2019); German Modification; Int valid: Internal validation; IR Lc65+ CHUV: Individual Records Lc65+ cohort database data from Lausanne University Hospital (CHUV); KNN: K-nearest neighbors; Lasso-LR: Lasso-penalized logistic regression; LR: Logistic regression; LSTM: Long short-term memory; MLP: Multilayer perceptron; NB: Naïve Bayes; PAS Score: Psychogeriatric Assessment Scales; PBC: Physical Behavior Checklist; RF: Random forest; SC: Stacking classifier; SVM: Support vector machine; VBC: Verbal Behavior Checklist; WC: Wandering checklist; XGBoost: Extreme gradient boosting.

4. Discussion

This paper presents a literature review of screening tools and clinical indicators for identifying early frailty and provides evidence for developing innovative tools through the focus on artificial intelligence. To our knowledge, this is the first narrative review summarizing and discussing frailty and ML for frailty screening. However, previous related research has been published on the relevance of the role in osteoporosis of AI models to model the risk of fragility fracture [32]. The selected studies were delivered between 2020 and 2022.

As mentioned earlier, the condition of frailty involves many domains that are not always easily identified, as well as the differences between them (e.g., cognitive, and physical domains). There are various instruments and identification criteria, thus hindering an accurate evaluation. Therefore, approaches that encompass all (or most) of these domains become relevant since they seem to have relevance in the early identification of the frail condition. Thus, ML is a promising approach, supported by recent studies.

The main findings of this study are that older age, females, clinical conditions (such as arthritis, hypertension, osteoporosis, and diabetes), high use of healthcare utilization, and adverse health outcomes (such as fractures, prolonged length of hospital stay, and number of hospitalizations) were the most significant predictive variables for the screening outcomes in frail persons. Previous studies reported that frailty was the most important predictor of rehospitalization and the second most important predictor of mortality in patients with cardiovascular disease [39]. Not surprisingly, the sociodemographic questions revealed importance. According to other studies, sociodemographic variables, namely, age and gender, are significant features [16,40]. Furthermore, in another recent study, age was the most important variable in predicting 90-day mortality and the second-most important variable for 30-day mortality [41].

The unsupervised learning methods are often used to process large databases, such as EMRs or large patient cohorts. Then, they can also cluster patients (subdividing them into groups) and characterize outliers or other essential features. Online electronic diagnosis systems are increasingly used by the population and healthcare professionals to a lesser extent. Most symptom checkers are ruled-based systems based on simple (conventional methods) decision trees. Therefore, ML is increasingly applied to EMRs in various health fields because they contain large, heterogeneous datasets that can be used to train disease detection or classification approaches using the supervised learning method [29].

Regarding algorithms, SVM was the most often applied ML method for frailty screening [5,31,36,38]. SVMs are competent in finding the best possible separation of different categories by familiarizing the weights of polynomial functions. ML models are typically trained using EMR or national cohorts. However, they require challenges to be applied effectively to information: the quantity and quality of the data. For example, deep neural networks commonly require massive training sets. Therefore, poor-quality training data (e.g., missing values) from EMRs will reduce the model's overall quality [29]. Thus, ML has already shown clinically practical applications in frailty screening. It has the potential to support specialists in clinical and foster personalized health. Combined databases have the tremendous potential to provide sufficient data [29] because AI "feeds" on data. The more and better-quality data it accesses, the more it can excel at tasks. Some advanced algorithms need annotated data to ensure that those can learn. These annotated data depend on the health professionals. Relying on the algorithm utilized, they could require lots of annotated data. Thus, the dedicated contribution of "data annotators" is critical for the benefit of implementing AI in healthcare systems, as well as established standard methods to report data [28]. As is the case, Aponte Hao and colleagues include the RECORD Statement [42], promoting quality and transparency [36].

The accomplishment of AI and its place in clinical practice and healthcare depends on whether it can infiltrate the boundaries of an evidence-based approach, the lack of policies, and the lack of enthusiasm of health professionals to use it. On the other hand, the demand

for AI to be implemented into everyday health professions is increasing among researchers, policymakers, clinical professionals, patients, hospitals, and developers. Therefore, it is essential to an integrated and appropriate multidisciplinary approach [28].

Some limitations regarding the data quality that impact the results should be noted. Although it is a validated tool for screening frailty, the CFS could not be advantageous to AI, because of the dichotomization, which fails to capture the severity of diseases, i.e., a person classified with pre-frail could be classified in the same category as a person with severe frailty. Therefore, an alternative could be to evaluate CFS as a continuous variable, bringing the distribution underlying the distribution of classes closer to the distribution of classes, then generating decision limits for the transformation back to the ordinal CFS to evaluate performance [36]. As well as in the CFS, the FRS-26 also be prone to bias in the quality of data and incapacitation of capturing the severity of symptoms [21]. In addition, the eFP, which could not classify frailty adequately, is often thought to reduce frailty to physical deficiencies and ignore mental and cognitive health problems [5]. In another study, they also merged pre-frail and fragile groups into a single group due to the limited number of fragile participants, and the size of the data (time series) was transformed to improve quality [37]. Moreover, other potential limitations include extensive missing data and test data being relatively small [31].

The accuracy of AI-generated results is highly dependent on the quality of the input data. Whether frailty is identified via the ML methods, very-high-quality data must be utilized if identification is ultimately proven accurate [31,41]. Further, efforts devoted to increasing the quality of the input data, such as standardized codes rather than free text and regular attention to data cleansing, may substantially improve the accuracy of the result obtained. The limited availability of high-quality data for training correctly labeled in medical claims, lack of detailed physiologic information, and indicators of the severity of comorbidities are inconsistently assigned, leading to a training set with underprivileged reproducibility and no "ground truth" to learn associations [28].

The heterogeneity of models makes it difficult to understand how accurate these methods might be in clinical practice or how reproducible they are in various clinical environments. The successful application of AI within the healthcare sphere does not remove the requirement for maintaining the quality of databases; instead, it is dependent on such activities. Another limitation is the studies using the codes ICD-10. The codes do not fully capture disease severity and might also miss out on essential elements of frailty such as weakness, polypharmacy, and need for support in everyday living. In addition, the potential variation in documentation and coding of diagnoses could contribute to measurement error (e.g., routine diagnosis and documentation of conditions such as delirium vary between clinicians and/or hospitals) [26].

In the future, with rapidly advanced wearables and monitoring technologies, we suggest researching other available frailty indicators—for example, using biosignals for postural control, gait assessment, and home-based frailty assessment. These types of data are also easily adapted to AI. They could be practical and feasible, such as falls prevention, an essential issue for frailty screening [15,33,43–48].

5. Conclusions

This review explores the tools and clinical indicators for frailty assessment and screening, through AI-based innovative tools. These existing tools, and clinical indicators for complex frailty, focusing on measures extracted from healthcare datasets were reviewed. The typical "health-professionally dependent" approaches for frailty screening could be adapted for technology-based approaches, such as eFI. The potential of AI techniques was explored; according to our findings, these methods can be used to identify risk factors to predict pre-frail or frailty. Thus, they facilitate the process to find the best treatment strategies for a person as well as frailty screening at the public health level. We suggest that databases collected from different populations be shared for improving the AI-based models.

This narrative review described the complex condition of frailty involving multi factor and summarized the indicators and the tools that were most used in the recent literature, as well as the AI models and the accuracies—making it easier for the developer and clinical to infer important data/variables for screening frailty. This review aims not to compare methods but to investigate the evidence for frailty screening. It was possible to conclude that the potential for ML to focus on frailty is immense, and offers an overabundance of new opportunities [29].

Author Contributions: E.O. and F.G.-F. drafted the text and selected the articles to be revised. E.O., F.G.-F. and A.L. were involved in the concept of the review. A.L. critically revised and edited the final report. All authors have read and approved the final version of the manuscript.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Collaborators, G.A. Global, regional, and national burden of diseases and injuries for adults 70 years and older: Systematic analysis for the Global Burden of Disease 2019 Study. *BMJ* **2022**, *376*, e068208. [CrossRef]
2. Alves, S.; Teixeira, L.; Ribeiro, O.; Paúl, C. Examining Frailty Phenotype Dimensions in the Oldest Old. *Front. Psychol.* **2020**, *11*, 434. [CrossRef] [PubMed]
3. Pujos-Guillot, E.; Pétéra, M.; Jacquemin, J.; Centeno, D.; Lyan, B.; Montoliu, I.; Madej, D.; Pietruszka, B.; Fabbri, C.; Santoro, A.; et al. Identification of Pre-frailty Sub-Phenotypes in Elderly Using Metabolomics. *Front. Physiol.* **2019**, *9*, 1903. [CrossRef] [PubMed]
4. Kouroubali, A.; Kondylakis, H.; Logothetidis, F.; Katehakis, D.G. Developing an AI-Enabled Integrated Care Platform for Frailty. *Healthcare* **2022**, *10*, 443. [CrossRef]
5. Pogam, M.A.L.; Seematter-Bagnoud, L.; Niemi, T.; Assouline, D.; Gross, N.; Trächsel, B.; Rousson, V.; Peytremann-Bridevaux, I.; Burnand, B.; Santos-Eggimann, B. Development and validation of a knowledge-based score to predict Fried's frailty phenotype across multiple settings using one-year hospital discharge data: The electronic frailty score. *EClinicalMedicine* **2022**, *44*, 101260. [CrossRef] [PubMed]
6. Singh, M.; Stewart, R.; White, H. Importance of frailty in patients with cardiovascular disease. *Eur. Heart J.* **2014**, *35*, 1726–1731. [CrossRef]
7. Duppen, D.; der Elst, M.C.J.V.; Dury, S.; Lambotte, D.; Donder, L.D. The Social Environment's Relationship with Frailty: Evidence From Existing Studies. *J. Appl. Gerontol.* **2019**, *38*, 3–26. [CrossRef]
8. Morley, J.E.; Vellas, B.; van Kan, G.A.; Anker, S.D.; Bauer, J.M.; Bernabei, R.; Cesari, M.; Chumlea, W.; Doehner, W.; Evans, J.; et al. Frailty Consensus: A Call to Action. *J. Am. Med. Dir. Assoc.* **2013**, *14*, 392–397. [CrossRef]
9. Uchmanowicz, I.; Nessler, J.; Gobbens, R.; Gackowski, A.; Kurpas, D.; Straburzynska-Migaj, E.; Kałuzna-Oleksy, M.; Jankowska, E.A. Coexisting Frailty With Heart Failure. *Front. Physiol.* **2019**, *10*, 791. [CrossRef]
10. Dent, E.; Martin, F.C.; Bergman, H.; Woo, J.; Romero-Ortuno, R.; Walston, J.D. Management of frailty: Opportunities, challenges, and future directions. *Lancet* **2019**, *394*, 1376–1386. [CrossRef]
11. Oviedo-Briones, M.; Laso, Á.R.; Carnicero, J.A.; Cesari, M.; Grodzicki, T.; Gryglewska, B.; Sinclair, A.; Landi, F.; Vellas, B.; Checa-López, M.; et al. A Comparison of Frailty Assessment Instruments in Different Clinical and Social Care Settings: The Frailtools Project. *J. Am. Med. Dir. Assoc.* **2021**, *22*, 607.e7–607.e12. [CrossRef] [PubMed]
12. Gobbens, R.J.; Boersma, P.; Uchmanowicz, I.; Santiago, L.M. The Tilburg Frailty Indicator (TFI): New Evidence for Its Validity. *Clin. Interv. Aging* **2020**, *15*, 265–274. [CrossRef] [PubMed]
13. Soong, J.T.Y.; Ng, S.H.X.; Tan, K.X.Q.; Kaubryte, J.; Hopper, A. Variation in coded frailty syndromes in secondary care administrative data: An international retrospective exploratory study. *BMJ Open* **2022**, *12*, e052735. [CrossRef] [PubMed]
14. Woo, J.; Leung, J.; Morley, J.E. Comparison of Frailty Indicators Based on Clinical Phenotype and the Multiple Deficit Approach in Predicting Mortality and Physical Limitation. *J. Am. Geriatr. Soc.* **2012**, *60*, 1478–1486. [CrossRef]
15. Vermeiren, S.; Vella-Azzopardi, R.; Beckwée, D.; Habbig, A.K.; Scafoglieri, A.; Jansen, B.; Bautmans, I.; Bautmans, I.; Verté, D.; Beyer, I.; et al. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. *J. Am. Med. Dir. Assoc.* **2016**, *17*, 1163.e1–1163.e17. [CrossRef]

16. Boreskie, K.F.; Hay, J.L.; Boreskie, P.E.; Arora, R.C.; Duhamel, T.A. Frailty-aware care: Giving value to frailty assessment across different healthcare settings. *BMC Geriatr.* **2022**, *22*, 13. [CrossRef]

17. Teixeira-Santos, L.; Bobrowicz-Campos, E.; Parola, V.; Coelho, A.; Gil, I.; de Lurdes Almeida, M.; Apóstolo, J.L. What Is the Relationship between Lifestyle and Frailty Status? Data from the Portuguese Multicentre Descriptive Study. *Nurs. Rep.* **2022**, *12*, 39–49. [CrossRef]

18. Liotta, G.; Ussai, S.; Illario, M.; O'Caoimh, R.; Cano, A.; Holland, C.; Roller-Winsberger, R.; Capanna, A.; Grecuccio, C.; Ferraro, M.; et al. Frailty as the Future Core Business of Public Health: Report of the Activities of the A3 Action Group of the European Innovation Partnership on Active and Healthy aging (EIP on AHA). *Int. J. Environ. Res. Public Health* **2018**, *15*, 2843. [CrossRef]

19. Salminen, M.; Viljanen, A.; Eloranta, S.; Viikari, P.; Wuorela, M.; Vahlberg, T.; Isoaho, R.; Kivelä, S.L.; Korhonen, P.; Irjala, K.; et al. Frailty and mortality: An 18-year follow-up study among Finnish community-dwelling older people. *Aging Clin. Exp. Res.* **2020**, *32*, 2013–2019. [CrossRef]

20. Sutton, J.L.; Gould, R.L.; Daley, S.; Coulson, M.C.; Ward, E.V.; Butler, A.M.; Nunn, S.P.; Howard, R.J. Psychometric properties of multicomponent tools designed to assess frailty in older adults: A systematic review. *BMC Geriatr.* **2016**, *16*, 55. [CrossRef]

21. Mohanty, S.D.; Lekan, D.; McCoy, T.P.; Jenkins, M.; Manda, P. Machine learning for predicting readmission risk among the frail: Explainable AI for healthcare. *Patterns* **2022**, *3*, 100395. [CrossRef] [PubMed]

22. Op het Veld, L.P.; van Rossum, E.; Kempen, G.I.; de Vet, H.C.; Hajema, K.; Beurskens, A.J. Fried phenotype of frailty: Cross-sectional comparison of three frailty stages on various health domains. *BMC Geriatr.* **2015**, *15*, 77. [CrossRef] [PubMed]

23. Dolenc, E.; Rotar-Pavlič, D. Frailty assessment scales for the elderly and their application in primary care: A systematic literature review. *Slov. J. Public Health* **2019**, *58*, 91–100. [CrossRef] [PubMed]

24. Apóstolo, J.; Cooke, R.; Bobrowicz-Campos, E.; Santana, S.; Marcucci, M.; Cano, A.; Vollenbroek-Hutten, M.; Germini, F.; Holland, C. Predicting risk and outcomes for frail older adults: An umbrella review of frailty screening tools. *JBI Database Syst. Rev. Implement. Rep.* **2017**, *15*, 1154–1208. [CrossRef]

25. Soong, J.T.Y. Frailty measurement in routinely collected data: Challenges and benefits. *Lancet Healthy Longev.* **2021**, *2*, e117–e118. [CrossRef]

26. Gilbert, T.; Neuburger, J.; Kraindler, J.; Keeble, E.; Smith, P.; Ariti, C.; Arora, S.; Street, A.; Parker, S.; Roberts, H.C.; et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: An observational study. *Lancet* **2018**, *391*, 1775–1782. [CrossRef]

27. Challen, R.; Denny, J.; Pitt, M.; Gompels, L.; Edwards, T.; Tsaneva-Atanasova, K. Artificial intelligence, bias and clinical safety. *BMJ Qual. Saf.* **2019**, *28*, 231–237. [CrossRef] [PubMed]

28. Meskó, B.; Görög, M. A short guide for medical professionals in the era of artificial intelligence. *NPJ Digit. Med.* **2020**, *3*, 126. [CrossRef]

29. Hügle, M.; Omoumi, P.; van Laar, J.M.; Boedecker, J.; Hügle, T. Applied machine learning and artificial intelligence in rheumatology. *Rheumatol. Adv. Pract.* **2020**, *4*, rkaa005. [CrossRef]

30. Yu, K.H.; Beam, A.L.; Kohane, I.S. Artificial intelligence in healthcare. *Nat. Biomed. Eng.* **2018**, *2*, 719–731. [CrossRef]

31. Ambagtsheer, R.; Shafiabady, N.; Dent, E.; Seiboth, C.; Beilby, J. The application of artificial intelligence (AI) techniques to identify frailty within a residential aged care administrative data set. *Int. J. Med. Inform.* **2020**, *136*, 104094. [CrossRef] [PubMed]

32. Ferizi, U.; Honig, S.; Chang, G. Artificial intelligence, osteoporosis and fragility fractures. *Curr. Opin. Rheumatol.* **2019**, *31*, 368–375. [CrossRef] [PubMed]

33. Akbari, G.; Nikkhoo, M.; Wang, L.; Chen, C.P.C.; Han, D.S.; Lin, Y.H.; Chen, H.B.; Cheng, C.H. Frailty Level Classification of the Community Elderly Using Microsoft Kinect-Based Skeleton Pose: A Machine Learning Approach. *Sensors* **2021**, *21*, 4017. [CrossRef]

34. Jiang, F.; Jiang, Y.; Zhi, H.; Dong, Y.; Li, H.; Ma, S.; Wang, Y.; Dong, Q.; Shen, H.; Wang, Y. Artificial intelligence in healthcare: Past, present and future. *Stroke Vasc. Neurol.* **2017**, *2*, 230–243. [CrossRef] [PubMed]

35. Kilic, A. Artificial Intelligence and Machine Learning in Cardiovascular Health Care. *Ann. Thorac. Surg.* **2020**, *109*, 1323–1329. [CrossRef] [PubMed]

36. Aponte-Hao, S.; Wong, S.T.; Thandi, M.; Ronksley, P.; McBrien, K.; Lee, J.; Grandy, M.; Mangin, D.; Katz, A.; Singer, A.; et al. Machine learning for identification of frailty in Canadian primary care practices. *Int. J. Popul. Data Sci.* **2021**, *6*, 1650. [CrossRef]

37. Eskandari-Nojehdehi, M.; Parvaneh, S.; Ehsani, H.; Fain, M.; Toosizadeh, N. Frailty Identification using Heart Rate Dynamics: A Deep Learning Approach. *IEEE J. Biomed. Health Inform.* **2022**, *26*, 3409–3417. [CrossRef]

38. Tarekegn, A.; Ricceri, F.; Costa, G.; Ferracin, E.; Giacobini, M. Predictive Modeling for Frailty Conditions in Elderly People: Machine Learning Approaches. *JMIR Med. Inform.* **2020**, *8*, e16678. [CrossRef]

39. Goyal, P.; Yum, B.; Navid, P.; Chen, L.; Kim, D.H.; Roh, J.; Jaeger, B.C.; Levitan, E.B. Frailty and Post-hospitalization Outcomes in Patients With Heart Failure With Preserved Ejection Fraction. *Am. J. Cardiol.* **2021**, *148*, 84–93. 2021.02.019. [CrossRef]

40. Feng, Z.; Lugtenberg, M.; Franse, C.; Fang, X.; Hu, S.; Jin, C.; Raat, H. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: A systematic review of longitudinal studies. *PLoS ONE* **2017**, *12*, e0178383. [CrossRef]

41. Ju, C.; Zhou, J.; Lee, S.; Tan, M.S.; Liu, T.; Bazoukis, G.; Jeevaratnam, K.; Chan, E.W.Y.; Wong, I.C.K.; Wei, L.; et al. Derivation of an electronic frailty index for predicting short-term mortality in heart failure: A machine learning approach. *ESC Heart Fail.* **2021**, *8*, 2837–2845. [CrossRef] [PubMed]

42. Benchimol, E.I.; Smeeth, L.; Guttmann, A.; Harron, K.; Moher, D.; Petersen, I.; Sørensen, H.T.; von Elm, E.; Langan, S.M. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Med.* **2015**, *12*, e1001885. [CrossRef] [PubMed]

43. Zak, M.; Sikorski, T.; Wasik, M.; Courteix, D.; Dutheil, F.; Brola, W. Frailty Syndrome—Fall Risk and Rehabilitation Management Aided by Virtual Reality (VR) Technology Solutions: A Narrative Review of the Current Literature. *Int. J. Environ. Res. Public Health* **2022**, *19*, 2985. [CrossRef] [PubMed]

44. Ganea, R.; Paraschiv-Ionescu, A.; Salarian, A.; Bula, C.; Martin, E.; Rochat, S.; Hoskovec, C.; Piot-Ziegler, C.; Aminian, K. Kinematics and dynamic complexity of postural transitions in frail elderly subjects. In Proceedings of the 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Paris, France, 29–31 August 2007; pp. 6117–6120. [CrossRef]

45. Simpson, L.; Maharaj, M.M.; Mobbs, R.J. The role of wearables in spinal posture analysis: A systematic review. *BMC Musculoskelet. Disord.* **2019**, *20*, 55. [CrossRef] [PubMed]

46. Chang, Y.C.; Lin, C.C.; Lin, P.H.; Chen, C.C.; Lee, R.G.; Huang, J.S.; Tsai, T.H. eFurniture for home-based frailty detection using artificial neural networks and wireless sensors. *Med. Eng. Phys.* **2013**, *35*, 263–268. [CrossRef]

47. Yacchirema, D.; de Puga, J.S.; Palau, C.; Esteve, M. Fall detection system for elderly people using IoT and Big Data. *Procedia Comput. Sci.* **2018**, *130*, 603–610. [CrossRef]

48. Bian, C.; Ye, B.; Chu, C.H.; McGilton, K.S.; Mihailidis, A. Technology for home-based frailty assessment and prediction: A systematic review. *Gerontechnology* **2020**, *19*, 1–13. [CrossRef]

Article

Is the Random Forest Algorithm Suitable for Predicting Parkinson's Disease with Mild Cognitive Impairment out of Parkinson's Disease with Normal Cognition?

Haewon Byeon

Department of Speech Language Pathology, School of Public Health, Honam University, Gwangju 62399, Korea; bhwpuma@naver.com

Abstract: Because it is possible to delay the progression of dementia if it is detected and treated in an early stage, identifying mild cognitive impairment (MCI) is an important primary goal of dementia treatment. The objectives of this study were to develop a random forest-based Parkinson's disease with mild cognitive impairment (PD-MCI) prediction model considering health behaviors, environmental factors, medical history, physical functions, depression, and cognitive functions using the Parkinson's Dementia Clinical Epidemiology Data (a national survey conducted by the Korea Centers for Disease Control and Prevention) and to compare the prediction accuracy of our model with those of decision tree and multiple logistic regression models. We analyzed 96 subjects (PD-MCI = 45; Parkinson's disease with normal cognition (PD-NC) = 51 subjects). The prediction accuracy of the model was calculated using the overall accuracy, sensitivity, and specificity. Based on the random forest analysis, the major risk factors of PD-MCI were, in descending order of magnitude, Clinical Dementia Rating (CDR) sum of boxes, Untitled Parkinson's Disease Rating (UPDRS) motor score, the Korean Mini Mental State Examination (K-MMSE) total score, and the K- Korean Montreal Cognitive Assessment (K-MoCA) total score. The random forest method achieved a higher sensitivity than the decision tree model. Thus, it is advisable to develop a protocol to easily identify early stage PDD based on the PD-MCI prediction model developed in this study, in order to establish individualized monitoring to track high-risk groups.

Keywords: cognitive function; data mining; Parkinson's disease with mild cognitive impairment; random forest; neuropsychological test

1. Introduction

Over the past decade, the field of geriatrics has experienced emerging interest in Parkinson's disease with mild cognitive impairment (PD-MCI) [1–4]. The Sydney cohort study [5], the most highly representative epidemiology study on the subject, examined 136 patients diagnosed with Parkinson's disease (PD) over 20 years. The study reported that 84% of PD patients had cognitive impairment, and 50% of them progressed to PD dementia (PDD). Likewise, PD is often accompanied by cognitive dysfunction in addition to dyskinesia [2].

The mild cognitive impairment (MCI) stage is the earliest at which we can detect dementia [6]. Because it is possible to delay the progression of dementia when it is detected and treated in an early stage, identifying MCI is an important primary goal of dementia treatment [6]. PD-MCI is frequently found in patients with PD [7,8]. However, the sociodemographic and neuropsychological characteristics of PD-MCI are less well-known than those of MCI and vascular mild cognitive impairment (vascular-MCI) [7,8]. The distinctive neuropsychological characteristics found in early stage

PD-MCI are caused by executive function damage due to prefrontal hypofunction or malfunction [9]. However, it is difficult to distinguish PD-MCI from MCI or vascular-MCI, because they show similar symptoms [10]. Additionally, people with PD experience a slowly deteriorating cognitive deficit and impaired motor function, which can be mistaken for cognitive frailty as part of the normal aging process. As a result, it is difficult to diagnose early stage PD. MCI can be diagnosed based on interviewing, cognitive function evaluation via a standardized neuropsychological test, and brain imaging such as magnetic resonance imaging (MRI). It is possible to diagnose cerebrovascular diseases or to analyze brain atrophy using brain imaging. However, this is unsuitable for early PD diagnosis, because brain atrophy can be confirmed visually only at a very advanced stage. Therefore, neuropsychological testing that also tests cognitive function has been used as an effective screening test for diagnosing MCI [11].

Recent studies have pointed to the necessity of considering mental health, such as depression, while diagnosing MCI [12,13]. In particular, the development pattern and risk factors of cognitive impairment are known to vary according to race. Therefore, it is necessary to develop an MCI prediction model reflecting the characteristics of the neuropsychological indices and lifestyles of the elderly in South Korea; however, South Korea has less systematic epidemiological data on cognitive impairment in the elderly than other countries such as the United States and European countries. In South Korea, previous community-based epidemiological studies on PD have been conducted on patients living in a single city [14]. However, there has been no study to develop a prediction model based on a nationwide epidemiological survey. Moreover, most of the previous studies [15,16] evaluating the neuropsychological characteristics of patients with PD have used regression models. Regression models are effective in exploring the neuropsychological characteristics of individual risk factors but are limited in analyzing multiple risk factors simultaneously. It is also difficult to prioritize risk factors with regression models. Linear regression models in particular require several assumptions, including linearity, equal variance, and a normal distribution, but disease data have been known to violate these assumptions.

In recent years, the medical field has applied data mining to predict the risk of diseases and vulnerable groups [16,17]. Data mining is a type of big data analysis that examines the relationships and rules within a dataset to extract valuable information [18]. The health science field has traditionally used tree-based methods such as Classification and Regression Tree (CART) as data mining methods for disease prediction [19]. Decision trees carry the risk of overfitting, and the accuracy of decision trees can vary greatly depending on the training data (input variables). Random forests, a data mining method developed in 2001, were designed to overcome these limitations. Random forests generate multiple decision trees by conducting random sampling on the same dataset and combining them to predict the target variable. Therefore, the accuracy of random forests is higher than that of decision trees [20,21]. Moreover, random forests can be used to explore the relationship between explanatory variables and diseases when many (types of) explanatory variables are applied to a random forest model [22]. In addition, the prediction power of random forests outperforms the bagging model [22].

Several previous studies [23–25] have reported on Parkinson's dementia predictors using biomarkers such as cerebrospinal fluid (CSF) and electroencephalogram (EEG) data. However, we are unaware of any study that identifies the predictors of PD-MCI for patients with PD and normal cognition (PD-NC), taking into account sociodemographic factors, lifestyles, depression, and neuropsychological characteristics. The objectives of this study were to develop a random forest-based PD-MCI prediction model considering health behaviors, environmental factors, medical history, physical functions, depression, and cognitive functions by using the Parkinson's Dementia Clinical Epidemiology Data (a national survey conducted by the Korea Centers for Disease Control and Prevention), and to compare its prediction of accuracy with those of decision tree and multiple logistic regression models.

2. Methods

2.1. Data Source

This study was conducted using the Parkinson's Dementia Clinical Epidemiology Data obtained from the National Biobank of Korea, the Center for Disease Control and Prevention, the Republic of Korea (no. KBN-2019-005). We obtained the approval of the Research Ethics Review Board, the National Biobank of Korea (no. KBN-2019-005), and the data use approval of the Korea Centers for Disease Control and Prevention (no. KBN-2019-1327). The National Biobank of Korea was established in 2008 with the approval of the Ministry of Health and Welfare and is managed by the Korea Centers for Disease Control and Prevention for the emerging necessity of managing bio-data systematically at a national level. The ultimate goal of the National Biobank of Korea is to promote biomedical research and public health. Please refer to Lee et al. [26] for the specific activities of the National Biobank of Korea, including its quality control programs.

The Parkinson's Dementia Clinical Epidemiology Data used in this study were collected under the supervision of the Korea Centers for Disease Control and Prevention at 14 tertiary care organizations (university hospitals) from January to December 2015. Health surveys, including health behavior questions, were conducted using computer-assisted personal interviews. The data are composed of sociodemographic factors (e.g., gender), environmental factors (e.g., exposure to pesticides), health behaviors (e.g., smoking), disease history (e.g., hypertension), exercise characteristics related to PD (e.g., tremor), sleep behavior disorders (e.g., rapid eye movement (REM)), and neuropsychological characteristics (e.g., cognitive function). PD-MCI was diagnosed by neuropsychologists according to the criteria of the International Working Group on MCI [27].

2.2. Subjects

Observational studies frequently utilize secondary data and these studies are more likely to experience data imbalance while comparing patients and healthy subjects [28]. Propensity score matching (PSM) was used to minimize selection bias and resolve the imbalance of case-control [29]. This study found an imbalance between PD-NC and PD-MCI. In order to solve this issue, this study used PSM, balancing between populations using the nearest neighbor matching by controlling the age of the case-control group [30]. Moreover, this study excluded individuals (subjects) that did not match in both groups in common to ensure good data balance. Before matching, there were 274 subjects (PD-MCI = 223; PD-NC = 51), and, after conducting PSM, it was matched to 96 subjects (PD-MCI = 45, PD-NC = 51; Figure 1). This study finally analyzed 96 subjects.
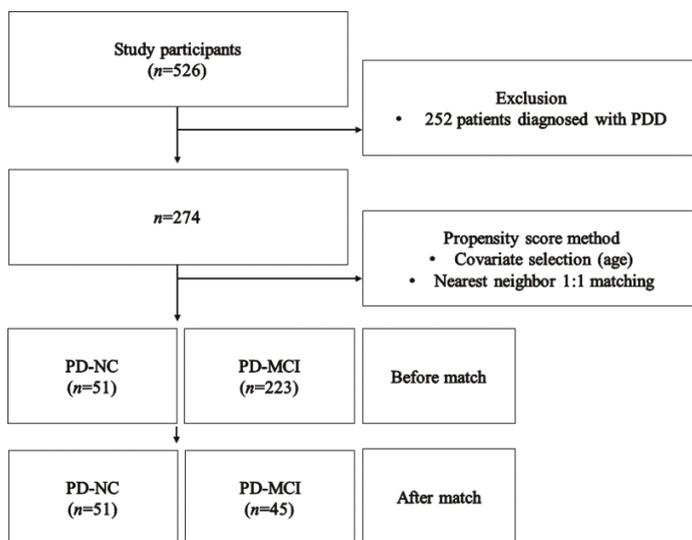
Figure 1. Framework of study.

2.3. Measurement

The outcome variable is defined as the prevalence of PD-MCI classified by medical diagnosis. The explanatory variables included age (60–74 years old or ≥75 years old), gender (male or female), education (middle school graduate and below, or high school graduate and above), handedness (left hand, right hand, or both hands), family dementia history (yes or no), family PD history (yes or no), pack-years (non-smoking, 1–20, 21–40, 41–60, or ≥61 pack-years), coffee-drinking (yes or no), mean coffee intake per day (no, ≤1, 2–3, or ≥4 cups), coffee drinking period (no, ≤5, 6–9, or ≥10 years), pesticide exposure (never, currently not exposed but exposed previously, or currently exposed to pesticide), disease history (carbon monoxide poisoning, manganese poisoning, encephalitis, traumatic brain injury, stroke, alcoholism, diabetes, hypertension, hyperlipidemia, and/or atrial fibrillation), PD related motor signs (tremor, akinesia/bradykinesia, postural instability, and/or late motor complications), REM, sleep behavior disorders, neuropsychological characteristics such as those outlined in the Korean Mini Mental State Examination (K-MMSE) [31], Korean Montreal Cognitive Assessment (K-MoCA) [32], Geriatric Depression Score (GDS) [33], global Clinical Dementia Rating (CDR) score [34], Korean Instrumental Activities of Daily Living (K-IADL) score [35], Untitled Parkinson's Disease Rating (UPDRS) total score [36], UPDRS motor score [37], Hoehn and Yahr staging (H&Y staging) [38], and the Schwab and England Activities of Daily Living scale (Schwab and England ADL) [39]. These variables are defined in Table 1.

Table 1. Measurement and definition of variables.

Variable.	Measurement	Characteristics
Sociodemographic factors	Gender	Male or female
	Education	Middle school graduate and below or high school graduate and above
	Mainly used hand	Left hand, right hand, or both hands
	Family dementia history	Yes or no
	Family PD history	Yes or no
	Pack-years	Non-smoking, 1–20, 21–40, or ≥41 pack-years
Health behaviors	Coffee-drinking	Yes or no
	Mean coffee intake per day (cups/day)	No, ≤1, 2–3, or ≥4 cups
	Coffee drinking period (year)	No, ≤5, 6–9, or ≥10 years
	Exposure to pesticide	Never, currently not exposed but exposed previously, or currently exposed to pesticide
Environmental factors	Carbon monoxide poisoning	Yes or no
Disease history	Manganese poisoning	Yes or no
	Traumatic brain injury	Yes or no
	Stroke	Yes or no
	Diabetes	Yes or no
	Hypertension	Yes or no
	Hyperlipidemia	Yes or no
	Atrial fibrillation	Yes or no
	Tremor	Yes or no
Exercise characteristics related to PD (PD related motor signs)	Rigidity	Yes or no
	Bradykinesia	Yes or no
	Postural instability	Yes or no
	Rapid eye movement (REM) and sleep behavior disorders (RBD)	Yes or no
Sleep behavior disorders	Total score of K-MMSE	Continuous variable
Neuropsychological characteristics	Total score of K-MoCA	
	CDR global score	
	CDR sum of boxes	
	K-IADL	
	Total score of UPDRS	Continuous variable
	Motor score of UPDRS	
	H&Y staging (Hoehn and Yahr staging)	
	Schwab and England ADL	

Pack-years: Cumulative amount of smoking, based on one pack of smoking per day. For example, 30 pack-years means smoking one pack of cigarettes per day for 30 years or two packs of cigarettes per day for 15 years. CDR—Clinical Dementia Rating; K-IADL—Korean Instrumental Activities of Daily Living; UDPRS—Untitled Parkinson's Disease Rating; ADL—Schwab and England Activities of Daily Living scale.

2.4. Development and Evaluation of Prediction Models

The prediction model was developed using a random forest algorithm, and the results of the developed prediction model were compared with those of a decision tree based on multiple logistic regression and a classification and regression tree. The prediction accuracy of the model was calculated using the recognition rate.

Random forests are ensemble classifiers that randomly learn multiple decision trees. The random forest method consists of a training step that constructs several decision trees, and a test step that classifies or predicts an outcome variable based on an input vector. The ensemble form of random forest training data can be expressed as Forest F = {f1, ..., fn} (Figure 2). The distributions obtained from the decision trees of each forest were first averaged by T (the number of the decision trees) and then classification was conducted. The predictors of each sample were combined by using the mean for continuous target variables and the majority vote for categorical target variables.

$$L(p) = \frac{1}{T} \sum_{t=1}^{T} P_t(b|I,\ p) \tag{1}$$
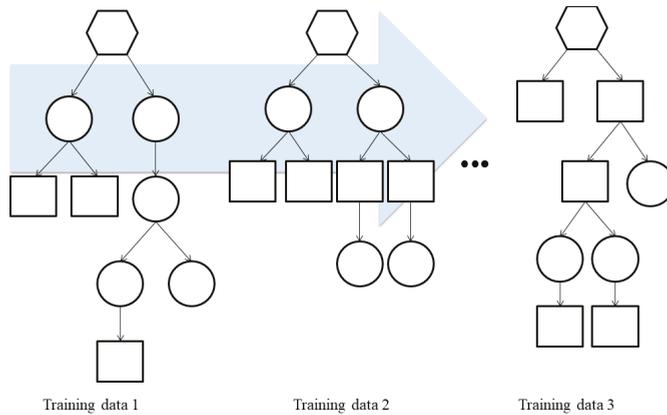
Figure 2. Ensemble classifiers that combines many single decision trees.

Random forest is similar to the bagging technique, because both approaches combine decision trees generated from multiple bootstrap samples using the majority vote principle in order to increase stability. However, they are different, because the former uses a few explanatory variables that were randomly selected from each bootstrap sample.

This study presented a partial dependence plot and variable importance to show the prediction power of the main explanatory variables. The variable importance indicates the effect of an explanatory variable on the accuracy of a model. Therefore, when an explanatory variable improves the performance of a model, the importance of the variable increases. A partial dependence plot shows the changes in response variables according to the continuous change of each explanatory variable. The contribution of a dependent variable to an independent variable is expressed as a function of a variable. The function of partial dependence is presented in Equation (2).

$$\left(\frac{p_1(x, x_{ic})}{p_0(x, x_{ic})} \right) \tag{2}$$

RF can be free from overfitting theoretically, and is not affected by noise or outliers much [20]. Moreover, it can generate high accuracy results by reducing generalization errors [20]. However, RF is more likely to have an elbow point, which means a steep drop in slope with more trees. Moreover, there is a higher probability that each tree will be more complex when an unimportant explanatory variable is selected. Therefore, this study improved the accuracy of the model by considering the number of mtry, the number of candidate explanatory variables, in advance.

The prediction performance of a model was validated while considering the overall accuracy, sensitivity, and specificity together. Sensitivity means the prediction accuracy of PD-MCI, while specificity indicates that of PD-NC. As the objective of this study was to develop a model that can predict PD-MCI, this study considered overall prediction accuracy and sensitivity as the most important factors for evaluating prediction performance. When the overall prediction accuracies and sensitivities of the two models were identical, their specificities were compared. This study first established a random forest model and then compared the results and the accuracies of models obtained from multiple logistic regression and CART. In this case, forward selection based on standard likelihood ratio tests was used to select variables in the multiple logistic regression analysis. All of the statistical analyses were conducted using the "RandomForest" package of R-version-3.6.1 (Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. General Characteristics of the Subjects

The General characteristics of the subjects are presented in Table 2. Of the 96 subjects (after match), 47.9% were male, 52.1% were female, 38.5% had a high school or above level of education, 8.0% had a family history of PD, and 6.8% had a family history of Alzheimer's dementia. Additionally, 5.7%, 2.3%, 23.2%, and 40.0% of the subjects had a history of head injury (e.g., traumatic brain injury), stroke, diabetes, and hypertension, respectively.

Table 2. General characteristics of the subjects, *n* (%).

Characteristics	After Match		
	PD-MCI (*n* = 45)	PD-NC (*n* = 51)	Total (*n* = 96)
Gender			
Male	24 (53.3)	22 (43.1)	46 (47.9)
Female	21 (46.7)	29 (56.9)	50 (52.1)
Education			
Middle school graduate and below	27 (60.0)	32 (62.7)	59 (61.5)
High school graduate and above	18 (40.0)	19 (37.3)	37 (38.5)
Mainly used hand			
Right hand	44 (97.8)	47 (92.2)	91 (94.8)
Left hand	1 (2.2)	1 (2.0)	2 (2.1)
Both hands	0	3 (5.9)	3 (3.1)
Family PD history			
No	36 (92.3)	33 (91.7)	69 (92.0)
Yes	3 (7.7)	3 (8.3)	6 (8.0)
Family dementia history			
No	36 (94.7)	32 (91.4)	68 (93.2)
Yes	2 (5.3)	3 (8.6)	5 (6.8)
Pack year (Smoking)			
1–20	6 (13.3)	3 (5.9)	9 (9.4)
21–40	3 (6.7)	2 (3.9)	5 (5.2)
41+	36 (80.0)	46 (90.2)	82 (85.4)
Coffee-drinking			
No	15 (33.3)	19 (37.3)	34 (35.4)
Yes	30 (66.7)	32 (62.7)	57 (64.6)
Carbon monoxide poisoning			
No	42 (97.7)	38 (86.4)	80 (92.0)
Yes	1 (2.3)	6 (13.6)	7 (8.0)
Traumatic brain injury			
No	40 (93.0)	42 (95.5)	82 (94.3)
Yes	3 (7.0)	2 (4.5)	5 (5.7)
Stroke			
No	41 (95.3)	44 (100)	85 (97.7)
Yes	2 (4.7)	0	2 (2.3)
Diabetes			
No	36 (80.0)	37 (74.4)	73 (76.8)
Yes	9 (20.0)	13 (26.0)	22 (23.2)
Hypertension			
No	32 (71.1)	25 (50.0)	57 (60.0)
Yes	13 (28.9)	25 (50.0)	38 (40.0)
Hyperlipidemia			
No	41 (91.1)	43 (86.0)	84 (88.4)
Yes	4 (8.9)	7 (14.0)	11 (11.6)
Atrial fibrillation			
No	44 (97.8)	47 (94.0)	91 (95.8)
Yes	1 (2.2)	3 (6.0)	4 (4.2)
Tremor			
No	14 (33.3)	8 (17.4)	22 (25.0)
Yes	28 (66.7)	38 (82.6)	66 (75.0)

Table 2. *Cont.*

Characteristics	After Match		
	PD-MCI (*n* = 45)	PD-NC (*n* = 51)	Total (*n* = 96)
Rigidity			
No	3 (7.0)	8 (17.0)	11 (12.2)
Yes	40 (93.0)	39 (83.0)	79 (87.8)
Bradykinesia			
No	2 (4.7)	6 (12.8)	8 (8.9)
Yes	41 (95.3)	41 (87.2)	82 (91.1)
Postural instability			
No	22 (55.0)	28 (60.9)	50 (58.1)
Yes	18 (45.0)	18 (39.1)	36 (41.9)
REM sleep behavior disorders			
No	29 (67.4)	27 (56.3)	56 (61.5)
Yes	14 (32.6)	21 (43.7)	35 (38.5)
Depression (GDS)			
No	22 (62.9)	22 (75.9)	44 (68.8)
Yes	13 (37.1)	7 (24.1)	20 (31.3)
K-MMSE, mean ± SD	25.8 ± 2.7	25.4 ± 4.7	25.6 ± 3.9
K-MoCA, mean ± SD	20.6 ± 4.0	20.5 ± 6.2	20.5 ± 5.3
Global CDR score, mean ± SD	0.5 ± 0.2	0.5 ± 0.6	0.5 ± 0.4
Sum of boxes in CDR, mean ± SD	1.4 ± 1.4	0.8 ± 1.3	1.2 ± 1.4
K-IADL, mean ± SD	1.0 ± 2.6	0.7 ± 1.0	0.8 ± 2.0
Total UPDRS, mean ± SD	34.9 ± 18.9	29.9 ± 13.1	33.0 ± 16.9
Motor UPDRS, mean ± SD	22.6 ± 11.6	17.9 ± 8.6	20.0 ± 10.3
H&Y staging score, mean ± SD	2.1 ± 0.8	1.8 ± 0.6	2.0 ± 0.7
Schwab and England ADL, mean ± SD	80.0 ± 16.0	87.7 ± 8.1	83.6 ± 13.3

REM sleep behavior disorders—rapid eye movement sleep behavior disorders; PD-MCI—Parkinson's Disease with Mild Cognitive Impairment; PD-NC—Parkinson's Disease with Normal Cognition; K-MMSE—Korean Mini Mental State Examination; K-MoCA—Korean Montreal Cognitive Assessment; CDR—Clinical Dementia Rating; K-IADL—Korean Instrumental Activities of Daily Living; UPDRS—Untitled Parkinson's Disease Rating; H&Y staging—Hoehn and Yahr staging; Schwab and England ADL—Schwab and England Activities of Daily Living scale.

3.2. Major Risk Factors of Random Forest-Based PD-MCI Prediction Model

A PD-MCI prediction model was established using random forests, and the results are presented in Figure 3. Some of the random forest models estimated major risk factors using decreased in the GINI coefficient. The major risk factors of PD-MCI were, in descending order of magnitude, CDR sum of boxes, UPDRS motor score, the K-MMSE total score, and the K-MoCA total score. Among these factors, the UPDRS motor score was the most important predictor of PD-MCI. In contrast, the importance of atrial fibrillation and stroke was zero.
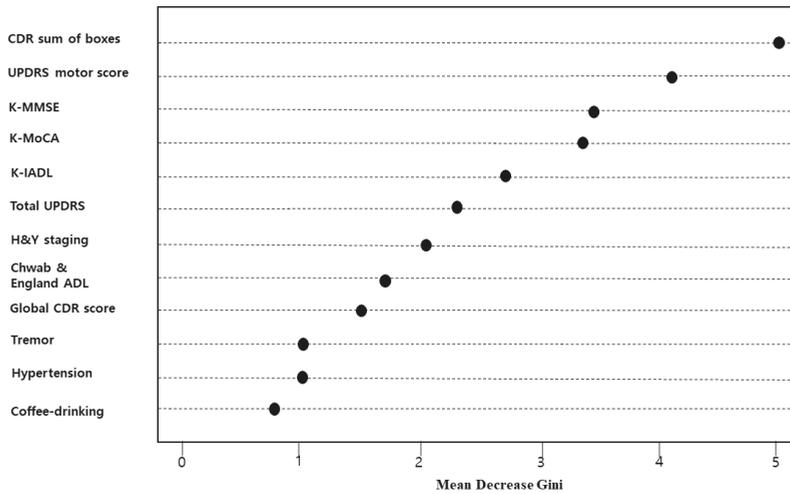
Figure 3. Variable importance in a random forest model (showing only the top 12 factors).

The partial dependence plot regarding the CDR sum of boxes, the most important variable in the predictive model, is presented in Figure 4. The results showed that, when other factors were constant, the risk of PD-MCI increased with a higher CDR sum of boxes (Figure 4).
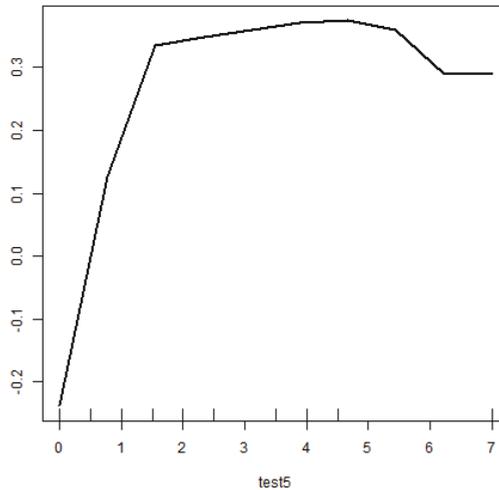
Figure 4. Partial dependence plot (CDR sum of boxes).

3.3. Comparison of the Accuracy of the Developed Prediction Models

This study changed the mtry values (numbers), presenting the number of explanatory variables to be used in the decision tree constituting RF, from 5 to 15, and selected the value with the smallest error of Out-Of-Bag. The changes in the error of Out-Of-Bag are presented in Table 3. The optimal mtry to be applied in this study was 5, showing the lowest error rate (34.4%).

Table 3. Error of out-of-bag.

Numbers of mtry	Error of Out-of-Bag
5	0.344
6	0.375
7	0.396
8	0.375
9	0.396
10	0.365
11	0.385
12	0.375
13	0.375
14	0.375
15	0.375

When ntree, the number of tree generation, and mtry were set as 500 and 5, respectively, the final RF model of this study had an overall accuracy of 65.6%, a sensitivity of 70.6%, and a specificity of 60.0% (Table 4). On the other hand, the overall accuracy of CART was calculated as 67.7%, higher than that of RF, but the sensitivity of it was the lowest (51.1%). In Figure 4, the black line indicates the changes in each error rate against 500 bootstrap samples. Figure 5 shows that the changes in error rate become relatively stable after the number of bootstrap samples exceeded 150.

Table 4. Comparison of accuracies developed prediction models, %.

Model	Overall Accuracy	Sensitivity	Specificity
Multiple logistic regression	NA	NA	NA
Decision tree	67.7	51.1	82.4
Random Forest	65.6	70.6	60.0

NA—not available.
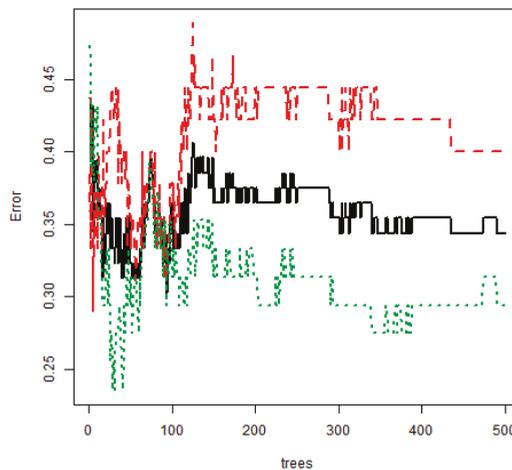
Figure 5. Out-of-bag error rate curve (random forest model). Black line—overall accuracy; red line—sensitivity; Green line—specificity.

4. Discussion

Diagnosing early stage PD-MCI is important in the health sciences, because it can delay the cognitive decline associated with PDD. Previous studies [22,40] have reported that the impairment of the executive function is a major cognitive feature of PDD. However, it is challenging to distinguish PD-MCI from PD-NC solely based on executive function. Therefore, we explored the major differential indicators of PD-MCI, taking into account sociodemographic variables, health habits, PD related motor and non-motor symptoms, cognitive tests, and neuropsychological tests. We developed a PD-MIC prediction model based on random forests, and confirmed that the CDR sum of boxes, UPDRS motor score, K-MMSE total score, and the K-MoCA total score were major predictors of PD-MCI. Among all of the neuropsychological screening tests, the CDR sum of boxes was the most important predictor for distinguishing PD-MCI from PD-NC. Therefore, when a neuropsychological test is performed to diagnose PD-MCI in patients with PD, the CDR (sum of boxes) scoring should be conducted first over other cognitive-language screening tests so as to achieve higher sensitivity.

Previous studies [41,42] examining the sociodemographic and emotional characteristics of PDD reported that depression is the main characteristic of PDD. For example, Aarsland et al. (2007) [41] evaluated 537 patients with PDD and observed that 58% of the patients had depression. However, in the present study, depression was not an important indicator for predicting PD-MCI. This might differ from previous studies [41,42], because previous studies compared healthy elderly individuals versus those with PD-MCI, while the present study only examined people with PD. In other words, depression is potentially not a major differential indicator in this study, because both PD and PD-MCI have high depression rates (31.3%). As only a few studies have tried to distinguish PD-MCI from PD-NC considering neuropsychological characteristics, health habits, and depression, more observation studies on PD-MCI are needed in order to verify the major predictors of PD-MCI.

Another meaningful finding of this study is that the sensitivity of random forests is higher than that of the decision tree model. These results agree with the results of previous studies predicting MCI [6] or cardiovascular disease in the elderly using random forests [43]. The prediction accuracy of random forests is higher than that of regression models or decision trees, because random forests are based on the bagging algorithm, which generates diverse decision trees using 500 bootstrap samples. As outliers can form decision tree nodes, the effects of the parameters that determine nodes are substantial, and, consequently, carry a risk of overfitting [44]. In contrast, random forests based on the bagging algorithm can prevent overfitting, because they reduce variance while maintaining tree bias. Moreover, random forests achieve a higher prediction accuracy than decision trees [45]. In addition, one advantage of random forests is their reduction of variance compared with the bagging model, which is achieved by decreasing the correlation between trees [43]. Random forests show a particularly better prediction accuracy than bagging models when there are many input variables [43]. Therefore, when selecting the key independent variables from a dataset containing many independent variables, such as the disease data used in this study, or developing prediction models on big data, random forests provide a higher accuracy than decision tree or multiple logistic regression models.

The merit of this study was the development of an MCI prediction model using examination data from a national survey. The limitations of this study are the following: (1) The number of study subjects was small. (2) The obsessive-compulsive symptoms commonly observed in patients with PD were not examined. (3) The prediction model did not include a biomarker, such as CFS. (4) This study adjusted the balance of the number of subjects between the groups by using age-matched PSM to solve the problem of unbalanced data. However, as a result of the PSM, a number of samples were excluded from the analysis, and the same size decreased. As a result, the overall accuracy, sensitivity, and specificity of the multiple logistic regression analysis were not calculated. Moreover, the age used for matching could not be used as an explanatory variable in the predictive model. Future studies will require more advanced techniques that can reduce the probability of overfitting to minimize imbalance, in addition to PSM. (5) Subjects taking PD medications (e.g., dopaminergics) were not

evaluated. As PD medication particularly affects the expression of cognitive and behavioral symptoms, future studies should consider whether or not a subject takes medication.

5. Conclusions

It is necessary to develop a protocol that can easily identify early stage PDD in order to establish individualized monitoring for tracking high-risk groups based on the PD-MCI prediction model developed in this study. Moreover, to further increase the prediction accuracy of the present method, a random forest model using weighted voting is warranted. In addition, the development of multi-modal data-based machine learning models that include biomarkers and brain imaging test indicators, as well as sociodemographic factors, health habits, and neuropsychiatric indicators, is needed.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Broeders, M.; De Bie, R.M.A.; Velseboer, D.C.; Speelman, J.D.; Muslimovic, D.; Schmand, B. Evolution of mild cognitive impairment in Parkinson disease. *Neurology* **2013**, *81*, 346–352. [CrossRef]
2. Goldman, J.G.; Aggarwal, N.T.; Schroeder, C.D. Mild cognitive impairment: An update in Parkinson's disease and lessons learned from Alzheimer's disease. *Neurodegener. Dis. Manag.* **2015**, *5*, 425–443. [CrossRef]
3. Ciafone, J.; Little, B.; Thomas, A.J.; Gallagher, P. The Neuropsychological Profile of Mild Cognitive Impairment in Lewy Body Dementias. *J. Int. Neuropsychol. Soc.* **2020**, *26*, 210–225. [CrossRef]
4. Nicoletti, A.; Luca, A.; Baschi, R.; Cicero, C.E.; Mostile, G.; Davì, M.; Pilati, L.; Restivo, V.; Zappia, M.; Monastero, R. Incidence of Mild Cognitive Impairment and Dementia in Parkinson's Disease: The Parkinson's Disease Cognitive Impairment Study. *Front. Aging. Neurosci.* **2019**, *11*, 21. [CrossRef] [PubMed]
5. Hely, M.A.; Reid, W.G.; Adena, M.A.; Halliday, G.M.; Morris, J.G. The Sydney multicenter study of Parkinson's disease: The inevitability of dementia at 20 years. *Mov. Disord.* **2008**, *23*, 837–844. [CrossRef] [PubMed]
6. Byeon, H. A prediction model for mild cognitive impairment using random forests. *IJACSA* **2015**, *6*, 8–12. [CrossRef]
7. Geda, Y.E.; Roberts, R.O.; Knopman, D.S.; Petersen, R.C.; Christianson, T.J.; Pankratz, V.S.; Smith, G.E.; Boeve, B.F.; Ivnik, R.J.; Tangalos, E.G.; et al. Prevalence of neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging: Population-based study. *Arch. Gen. Psychiatry* **2008**, *65*, 1193–1198. [CrossRef] [PubMed]
8. Langa, K.M.; Levine, D.A. The diagnosis and management of mild cognitive impairment: A clinical review. *JAMA* **2014**, *312*, 2551–2561. [CrossRef]
9. Bott, N.T.; Johnson, E.T.; Schuff, N.; Galifianakis, N.; Subas, T.; Pollock, J.; Pressman, P.; Kramer, J.H.; Possin, K.L. Sensitive measures of executive dysfunction in non-demented Parkinson's disease. *Parkinsonism Relat. Disord.* **2014**, *20*, 1430–1433. [CrossRef]
10. Sudo, F.K.; Alves, C.E.O.; Alves, G.S.; Ericeira-Valente, L.; Tiel, C.; Moreira, D.M.; Laks, J.; Engelhardt, E. White matter hyperintensities, executive function and global cognitive performance in vascular mild cognitive impairment. *Arq. Neuropsiquiatr.* **2013**, *71*, 431–436. [CrossRef]
11. Petersen, R.C. Early diagnosis of Alzheimer's disease: Is MCI too late? *Curr. Alzheimer. Res.* **2009**, *6*, 324–330. [CrossRef] [PubMed]
12. Gabryelewicz, T.; Styczynska, M.; Luczywek, E.; Barczak, A.; Pfeffer, A.; Androsiuk, W.; Chodakowska-Zebrowska, M.; Wasiak, B.; Peplonska, B.; Barcikowska, M. The rate of conversion of mild cognitive impairment to dementia: Predictive role of depression. *Int. J. Geriatr. Psychiatry* **2007**, *22*, 563–567. [CrossRef] [PubMed]
13. Lang, M.; Rosselli, M.; Greig, M.T.; Torres, V.L.; Vélez-Uribe, I.; Arruda, F.; Barker, W.W.; Garcia, P.; Loewenstein, D.A.; Curiel, R.E.; et al. Depression and the Diagnosis of MCI in a Culturally Diverse Sample in the United States. *Arch. Clin. Neuropsychol.* **2019**. [CrossRef] [PubMed]

14. Koh, S.B.; Kwon, D.Y.; Lee, J.M.; Han, J.K.; Kim, B.J.; Park, M.K.; Park, K.W.; Lee, D.H. Prevalence of Parkinsonism in Ansan-city. *J. Korean Neurol. Assoc.* **2003**, *21*, 498–501.

15. Kim, H.M.; Nazor, C.; Zabetian, C.P.; Quinn, J.F.; Chung, K.A.; Hiller, A.L.; Shu, CH.; Leverenz, J.B.; Montine, T.J.; Edwards, K.L.; et al. Prediction of cognitive progression in Parkinson's disease using three cognitive screening measures. *Clin. Parkinsonism Relat. Disord.* **2019**, *1*, 91–97. [CrossRef]

16. Barnish, M.; Daley, D.J.; Deane, K.H.; Clark, A.B.; Gray, R.J.; Horton, S.M.; Butterfint, Z.R.; Myint, P.K. Cognitive profile and determinants of poor cognition in people without dementia in Parkinson's disease. *Med. J. Islam. Repub. Iran* **2019**, *33*, 1.

17. Byeon, H. Predicting the Swallow-Related Quality of Life of the Elderly Living in a Local Community Using Support Vector Machine. *Int. J. Environ. Res. Public Health* **2019**, *16*, 4269. [CrossRef]

18. Joloudari, J.H.; Hassannataj Joloudari, E.; Saadatfar, H.; GhasemiGol, M.; Razavi, S.M.; Mosavi, A.; Nabipour, N.; Shamshirband, S.; Nadai, L. Coronary Artery Disease Diagnosis; Ranking the Significant Features Using a Random Trees Model. *Int. J. Environ. Res. Public Health* **2020**, *17*, 731. [CrossRef]

19. Byeon, H. Development of Depression Prediction Models for Caregivers of Patients with Dementia Using Decision Tree Learning Algorithm. *Int. J. Gerontol.* **2019**, *13*, 314–319.

20. Chen, J.; Li, Q.; Wang, H.; Deng, M. A machine learning ensemble approach based on random forest and radial basis function neural network for risk evaluation of regional flood disaster: A case study of the Yangtze River Delta, China. *Int. J. Environ. Res. Public Health* **2020**, *17*, 49. [CrossRef]

21. Byeon, H. Developing a random forest classifier for predicting the depression and managing the health of caregivers supporting patients with Alzheimer's Disease. *Technol. Health Care* **2019**, *27*, 531–544. [CrossRef] [PubMed]

22. Byeon, H.; Jin, H.; Cho, S. Development of Parkinson's disease dementia prediction model based on verbal memory, visuospatial memory, and executive function. *J. Med. Imaging Health Inform.* **2017**, *7*, 1517–1521. [CrossRef]

23. Zhang, J.; Sokal, I.; Peskind, E.R.; Quinn, J.F.; Jankovic, J.; Kenney, C.; Chung, K.A.; Millard, S.P.; Nutt, J.G.; Montine, T.J. CSF multianalyte profile distinguishes Alzheimer and Parkinson diseases. *Am. J. Clin. Pathol.* **2008**, *129*, 526–529. [CrossRef] [PubMed]

24. Chaturvedi, M.; Hatz, F.; Gschwandtner, U.; Bogaarts, J.G.; Meyer, A.; Fuhr, P.; Roth, V. Quantitative EEG (QEEG) measures differentiate Parkinson's disease (PD) patients from healthy controls (HC). *Front. Aging Neurosci.* **2017**, *9*, 3. [CrossRef] [PubMed]

25. Chaturvedi, M.; Bogaarts, J.; Hatz, F.; Gschwandtner, U.; Cozac, V.; Meyer, A.; Liepelt, I.; Babiloni, C.; Fuhr, P.; Roth, V. Distinguishing Parkinson's Disease Dementia (PDD) patients from Parkinson's Disease (PD) patients using EEG frequency and connectivity measures. *Clin. Neurophysiol.* **2018**, *129*, e92. [CrossRef]

26. Lee, J.E.; Kim, J.H.; Hong, E.J.; Yoo, H.S.; Nam, H.Y.; Park, O. National Biobank of Korea: Quality control programs of collected-human biospecimens. *Osong. Public Health Res. Perspect.* **2012**, *3*, 185–189. [CrossRef]

27. Winblad, B.; Palmer, K.; Kivipelto, M.; Jelic, V.; Fratiglioni, L.; Wahlund, L.O.; Nordberg, A.; Bäckman, L.; Albert, M.; Almkvist, O.; et al. Mild cognitive impairment–beyond controversies, towards a consensus: Report of the International Working Group on Mild Cognitive Impairment. *J. Intern. Med.* **2004**, *256*, 240–246. [CrossRef]

28. Byeon, H. The risk factors of laryngeal pathology in Korean adults using a decision tree model. *J. Voice* **2015**, *29*, 59–64. [CrossRef]

29. Ghavami, P. *Big Data Analytics Methods: Analytics Techniques in Data Mining, Deep Learning and Natural Language Processing*; Walter de Gruyter: Berlin, Germany, 2019.

30. Zhang, Z.; Kim, H.J.; Lonjon, G.; Zhu, Y. Balance diagnostics after propensity score matching. *Ann. Transl. Med.* **2019**, *7*, 16. [CrossRef]

31. Kang, Y.; Na, D.L.; Hahn, S. A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients. *J. Korean Neurol. Assoc.* **1997**, *15*, 300.

32. Kang, Y.; Park, J.; Yu, K.H.; Lee, B.C. The validity of the Korean-Montreal Cognitive Assessment (K-MoCA) as a screening test for both MCI and VCI. In Proceedings of the 20th Annual Rotman Research Institute Conference, Toronto, ON, Canada, 22–26 March 2010. [CrossRef]

33. Cho, M.J.; Bae, J.N.; Suh, G.H.; Hahm, B.J.; Kim, J.K.; Lee, D.W.; Kang, M.H. Validation of geriatric depression scale, Korean version (GDS) in the assessment of DSM-III-R major depression. *J. Korean Neuropsychiatr. Assoc.* **1999**, *38*, 48–63.

34. Choi, S.H.; Na, D.L.; Lee, B.H.; Hahm, D.S.; Jeong, J.H.; Yoon, S.J.; Yoo, K.H.; Ha, C.K.; Han, I.W. Estimating the validity of the Korean version of expanded clinical dementia rating (CDR) scale. *J. Korean Neurol. Assoc.* **2001**, *19*, 585–591.

35. Kang, S.J.; Choi, S.H.; Lee, B.H.; Kwon, J.C.; Na, D.L.; Han, S.H. The reliability and validity of the Korean Instrumental Activities of Daily Living (K-IADL). *J. Korean Neurol. Assoc.* **2002**, *20*, 8–14.

36. Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The unified Parkinson's disease rating scale (UPDRS): Status and recommendations. *Mov. Disord.* **2003**, *18*, 738–750. [CrossRef] [PubMed]

37. Richards, M.; Marder, K.; Cote, L.; Mayeux, R. Interrater reliability of the Unified Parkinson's Disease Rating Scale motor examination. *Mov. Disord.* **1994**, *9*, 89–91. [CrossRef] [PubMed]

38. Hoehn, M.M.; Yahr, M.D. Parkinsonism: Onset, progression and mortality. *Neurology* **1967**, *17*, 427–442. [CrossRef]

39. Gillingham, F.J.; Donaldson, M.C. Schwab and England Activities of Daily Living. In *Third Symposium of Parkinson's Disease*; E&S Livingstone: Edinburgh, UK, 1969.

40. Woods, S.P.; Tröster, A.I. Prodromal frontal/executive dysfunction predicts incident dementia in Parkinson's disease. *J. Int. Neuropsychol. Soc.* **2003**, *9*, 17–24. [CrossRef]

41. Aarsland, D.; Brønnick, K.; Ehrt, U.; De Deyn, P.P.; Tekin, S.; Emre, M.; Cummings, J.L. Neuropsychiatric symptoms in patients with Parkinson's disease and dementia: Frequency, profile and associated care giver stress. *J. Neurol. Neurosurg. Psychiatry* **2007**, *78*, 36–42. [CrossRef]

42. Prell, T.; Witte, O.W.; Grosskreutz, J. Biomarkers for dementia, fatigue, and depression in Parkinson's disease. *Front. Neurol.* **2019**, *10*, 195. [CrossRef]

43. Byeon, H. Developing a model to predict the occurrence of the cardiocerebrovascular disease for the Korean elderly using the random forests algorithm. *IJACSA* **2018**, *9*, 494–499.

44. Larose, D.T. *Discovering Knowledge in Data: An Introduction to Data Mining*; John Wiley & Sons: Hoboken, NJ, USA, 2014.

45. Lunetta, K.L.; Hayward, L.B.; Segal, J.; Van Eerdewegh, P. Screening large-scale association study data: Exploiting interactions using random forests. *BMC Genet.* **2004**, *5*, 32. [CrossRef] [PubMed]

Article

Motoric Cognitive Risk Syndrome Using Three-Item Recall Test and Its Associations with Fall-Related Outcomes: The Korean Frailty and Aging Cohort Study

Hayoung Shim [1], Miji Kim [2,*] and Chang Won Won [3,*]

[1]   Department of Biomedical Science and Technology, Graduate School, Kyung Hee University, Seoul 02447, Korea; hayoung0517@khu.ac.kr
[2]   Department of Biomedical Science and Technology, College of Medicine, East-West Medical Research Institute, Kyung Hee University, Seoul 02447, Korea
[3]   Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul 02447, Korea
*   Correspondence: mijiak@khu.ac.kr (M.K.); chunwon62@naver.com (C.W.W.);
    Tel.: +82-2-958-2840 (M.K.); +82-2-958-8700 (C.W.W.);
    Fax: +82-2-958-2836 (M.K.); +82-2-958-8699 (C.W.W.)

Abstract: Motoric cognitive risk (MCR) syndrome is originally defined as the presence of subjective cognitive complaints (SCCs) and slow gait (SG). MCR is well known to be useful for predicting adverse health outcomes, including falls and dementia. However, around four out of five older Korean adults reported SCCs, thereby, it may not be discriminative to define MCR in Korea. We adopted the three-item recall (3IR) test, instead of SCCs, to define MCR. This cross-sectional analysis included 2133 community-dwelling older adults aged 70–84 years, without dementia or any dependence in activities of daily living from the Korean Frailty and Aging Cohort Study. The newly attempted criteria of MCR using 3IR were met by 105 participants (4.9%). MCR using 3IR showed synergistic effects on fall-related outcomes, whereas the conventional definition of MCR using SCCs was not superior to SG only. MCR using 3IR was associated with falls (odds ratio [OR]: 1.92; 95% confidence interval (CI): 1.16–3.16), recurrent falls (OR: 2.19; 95% CI: 1.12–4.32), falls with injury (OR: 1.98; 95% CI: 1.22–3.22), falls with fracture (OR: 2.51; 95% CI: 1.09–5.79), fear of falling (OR: 3.00; 95% CI: 1.83–4.92), and low activities-specific balance confidence (OR: 3.13; 95% CI: 1.57–6.25). We found that MCR using 3IR could be useful in predicting fall-related outcomes in a cultural background reporting more SCCs, such as Korea.

1. Introduction

Substantial links have been reported between cognition and gait, and the combination of these two factors has been conceptualized by motoric cognitive risk (MCR) syndrome [1,2]. Compared to each component alone, MCR has stronger predictive validity for adverse health outcomes, such as dementia, falls, disability, and death [3–5].

MCR was originally defined as the presence of subjective cognitive complaints (SCCs) and slow gait speed, without dementia and any dependence in activities of daily living [3]. Of these criteria, most studies have defined slow gait as below one standard deviation of the usual gait speed established in each cohort according to age and sex [6]. To the contrary, many previous studies flexibly adapted

various criterion of SCCs to suit their research environments, i.e., from standardized questionnaires regarding general cognitive performance, from one simple self-rating question regarding memory function, from cut-off scores used in several objective cognitive function tests, or from informant reports on subjects' cognitive problems [5,6]. The various criteria of SCCs in previous studies might have influenced the inconsistent results [6]. In particular, there were different results on the association between MCR and subtypes of dementia. Verghese et al., reported that MCR was strongly associated with vascular dementia (VaD), but not with Alzheimer's disease (AD), when identifying SCCs using comprehensive objective assessments [3]. By contrast, in some studies using self-rating questions on memory [7,8], MCR was associated with increasedrisk of AD [9].

MCR is expected to be useful for various settings because the assessments of each component, presence of SCCs and gait speed, are relatively convenient [9]. However, several studies have reported limitations of SCCs that may be influenced to a greater extent by depression, personality, or cultural differences, than actual cognitive performance [10–12]. Similarly, MCR, which includes SCCs among the criteria, was associated with anxio-depressive disorders, depression [13] and personality, particularly neuroticism [14]. Furthermore, a number of studies have reported disparities between SCCs and objective cognitive function, with robust evidence that depressive symptoms seemed to have the greatest influence on SCCs [12].

Moreover, several studies reported that older Korean adults may have a cultural tendency to report SCCs more frequently [15,16]. The prevalence of SCCs in community-dwelling older adults in Korea was 77.7% [16]. SCCs may not be discriminative in Korea. The tendency of high reporting of SCC in older Korean adults may stem from culturally based factors, such as high prevalence of depressive symptoms [15,17,18].

MCR was found to predict adverse health outcomes [4]. Particularly, MCR is well known to be associated with falls and their recurrence, or post-fall fractures [19–21]. Therefore, we aimed to explore another criterion for the cognitive aspects of MCR, based on fall-related outcomes. As most previous studies have identified SCCs in memory [22], we introduced three-item recall (3IR) test, instead of SCCs, for defining MCR. 3IR test is a simple and well validated objective memory test. We investigated the associations between MCR and comprehensive fall-related outcomes by comparing the new MCR using 3IR, and original MCR using SCCs.

2. Materials and Methods

2.1. Study Population

The Korean Frailty and Aging Cohort Study (KFACS) is an ongoing prospective cohort study to investigate the frailty status of older Korean adults [23]. The KFACS recruited 3014 community-dwelling older adults aged 70–84 years from 10 nationwide centers, including rural, suburban, and urban areas, in a 2-year comprehensive baseline survey. Among the participants of the KFACS, those who were dependent in any of the basic activities of daily living (ADL) ($n = 69$), self-reported a diagnosis of dementia ($n = 11$), or scored < 24 points in the Mini-Mental State Examination (MMSE; $n = 641$) [24], and had a history of Parkinson's disease ($n = 1$) or hemiplegia ($n = 6$), were excluded from the present study. In addition, those who had missing 3IR test scores ($n = 48$), a question about SCCs ($n = 6$), and fall-related outcomes ($n = 51$) and covariates ($n = 48$), were excluded. On the result, a total of 2133 older adults were selected for the present study (Figure 1). The Clinical Research Ethics Committee of Kyung Hee University Hospital approved the KFACS protocol (Institutional Review Board [IRB] number: 2015-12-103). The present study was exempt from the requirement for IRB approval by the Clinical Research Ethics Committee of the Kyung Hee University Medical Center (IRB No.: 2020–03–073).
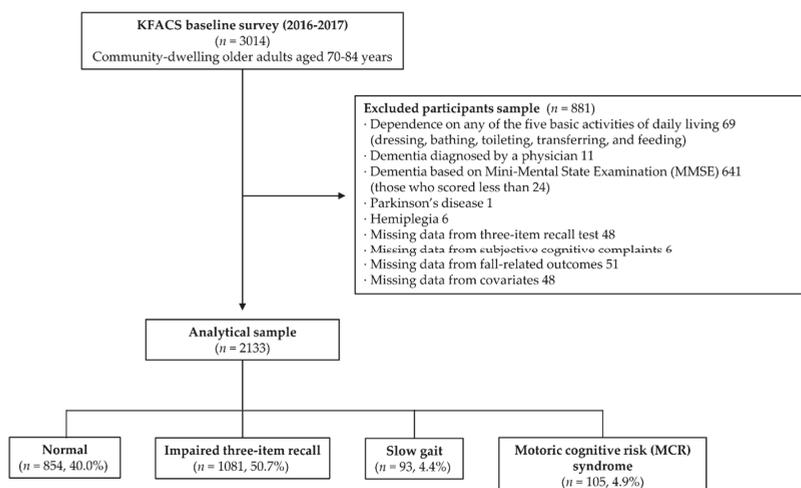
Figure 1. Flow chart of the study population.

2.2. Definitions of Motoric Cognitive Risk (MCR) Syndrome

2.2.1. Original MCR using Subjective Cognitive Complaints (SCCs)

A single question extracted from the Korean Version of Short Form Geriatric Depression Scale (SGDS-K) was used to ascertain SCCs: "Do you feel you have more problems with memory than most?" [25,26]. A positive response, "yes", to this question was defined as indicating the presence of SCCs [4,19,27]. Slow gait was defined as one standard deviation (SD) or below the age- and sex-specific mean values established in the KFACS [16]. The participants were asked to walk a 7 m distance, with initial acceleration and terminal deceleration sections of 1.5 m in their normal pace, and gait speed was calculated at the speed (m/s) of walking 4 m, the middle section of 7 m, using an automatic machine (Gaitspeedometer, Dyphi, Daejeon, Korea).

2.2.2. New MCR using three-item recall (3IR)

The 3IR test of MMSE was administered to identify the deficits in memory function [28]. The examiner named three unrelated objects clearly and slowly, then asked the participant to name all three of them. The examiner repeated the words up to three times until the participant learned all of them, if possible. A few minutes later, the participant was asked to recall the three words as much as possible, without any hint. Scores were calculated from 0 (incorrect) to 1 (correct) for each item, where higher score indicates better ability. The sum of the 3IR tests was used to determine cognitive aspects of MCR. A score < 3 was considered to indicate deficits in memory recall [29]. Slow gait (SG) was still defined as one or more standard deviation (SDs) or below the age- and sex-specific mean values established in the KFACS [16].

2.3. Definitions of Fall-Related Outcomes

We collected the following six types of fall-related information using a standardized questionnaire: experience of a fall in the past 1 year, recurrent falls, falls with injury, falls with fracture, fear of falling, and low activities-specific balance confidence.

Experience of falls, recurrent falls, and falls with injury or fracture during the past 1 year were investigated. A fall was defined as an event that resulted in a person coming to rest unintentionally on the ground, not as a result of a major intrinsic event (such as stroke or syncope) or overwhelming hazard [30]. In addition, falls caused by acute medical events, such as sudden onset of paralysis and

epileptic seizure, or excess alcohol intake, were excluded [31]. Recurrent falls were defined as two or more falls in the past 12 months. Falls with injury were defined as those where the participants reported sprains, bruises, lacerations, and fractures after falls. When a participant reported fracture as a consequence of a fall, it was defined as fall with fracture.

Fear of falling (FoF) was assessed using a question presented with five response choices: "Are you usually afraid that you may fall?" If participants answered "considerably" or "very much," they were considered to have a FoF. Participants who responded "not at all," "a little," or "don't know" were considered to have no FoF [32].

Activities-specific balance confidence (ABC) was administered using a 16-item ABC scale in which participants rated their balance confidence when doing specific activities [33]. Scores ranged from 0 (no confidence) to 100 (complete confidence). A higher score indicated greater confidence, and the total score was calculated as the average of 16 items. Low ABC was defined as ABC scale score ≤ 58.13 [34].

2.4. Measurements

All participants were interviewed based on standardized surveys for collecting information, and were examined using health assessments. The trained investigators obtained sociodemographic and lifestyle information: education level, type of residence, living conditions, marital status and whether they receive social security aid, smoking status, alcohol intake, and physical activity level. Low physical activity was defined as < 494.64 kcal/week for men and < 283.50 kcal/week for women, using the International Physical Activity Questionnaire (IPAQ), values of which correspond to the lowest quintile (20%) of the total consumed energy established in a general population study of Korean older adults [35]. We inquired about the general health and medical history of each participant: body mass index (BMI), number of drugs taken daily, and medical conditions. Diseases were self-reported diagnoses by a physician, and comorbidities were defined as two or more of the following diseases: hypertension, diabetes mellitus, dyslipidemia, myocardial infarction, congestive heart failure, angina pectoris, cerebrovascular disease, peripheral vascular disease, osteoarthritis, rheumatoid arthritis, osteoporosis, asthma, and chronic obstructive pulmonary disease. Visual impairment was determined when the maximum value of left and right vision was < 0.3 [36]. Hearing impairment was identified as the minimum of the average value of left and right hearing exceeding 40 dB [37]. Instrumental activities of daily living (IADL) disability was determined when participants did not answer "completely independent" for one or more of the 10 activities using the Korea Instrumental Activities of Daily Living Scale (K-IADL) [38]. Nutritional status was determined using the Korean version of the short-from Mini-Nutritional Assessment (MNA-SF) [39]. Global cognitive function was assessed using the MMSE in the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (MMSE-KC) [40]. Depressive symptoms were assessed using the SGDS-K [41]. Participants were asked whether they perceived their health status as poor, fair, good, very good or excellent; "poor" or "fair" responses to the question were defined as fair/poor self-perceived health. Quality of life was evaluated using EuroQol five-demension scale (EQ-5D) [42]. Participants took the following physical function tests: handgrip strength, usual-pace gait speed, timed up and go (TUG) test [43], and short physical performance battery (SPPB) [44].

2.5. Statistical Analyses

Descriptive statistic analyses were conducted to compare the participants' characteristics according to MCR status. The Chi-square test or Fisher's exact tests was used for categorical variables, with adjusted standardized residuals as appropriate. In addition, after employing Levene's test to determine homogeneity of variances, one-way analysis of variance (ANOVA) with Bonferroni post hoc test, or Welch's ANOVA with Games–Howell post hoc tests, for continuous variables were conducted. Participants were divided into four groups for each definition: (1) MCR using SCCs: normal, SCCs only, SG only, and MCR using SCCs; (2) MCR using 3IR: normal, impaired 3IR only, SCCs only, SG only, MCR using 3IR. Multiple logistic regression analyses were performed to investigate the associations

between MCR status and fall-related factors. We adjusted confounding factors by dividing the models into four steps. First, we adjusted for the recruited center and sociodemographic factors in Model 1: the recruited center, age, sex, low educational level, residence area, living alone, without partner, and social security aid recipient. Second, we further adjusted for lifestyle-related factors in Model 2: current smoker, alcohol consumption ($\geq$ 2 to 3 times/week) and low physical activity level. Third, further adjustments were conducted regarding general health and medical conditions in Model 3: BMI, number of drugs taken daily, number of diseases, urinary incontinence, visual impairment, hearing impairment, poor nutritional status, and IADL disability. In the final model, Model 4 adjusted for the same factors as Model 3, with the addition of psychological factors: depressive symptoms and fair/poor self-reported health. All analyses were performed using SPSS (ver. 25.0; IBM Corp., Armonk, NY, USA). In all analyses, two-sided $p < 0.05$ was taken to indicate statistical significance.

3. Results

3.1. Descriptive Characteristics of the Study Population

Characteristics of participants according to new MCR status using 3IR are shown in Table 1. Sociodemographic factors including sex, education level, residence area, living alone, without partner, and status of receiving social securities, were significantly different between groups ($p < 0.05$). However, the age of the participants was not significantly different between the groups. Participants with MCR using 3IR showed significantly lower physical activity level than the normal group ($p < 0.001$). Moreover, compared to the normal group, the MCR using 3IR group was taking more medicines per day, and had more diseases, especially diabetes (all $p < 0.01$). The disabilities on any of the IADL were significantly different among the groups ($p = 0.01$). With regard to psychological factors, the MMSE score was the highest in the normal group and the lowest in the MCR using 3IR group ($p < 0.001$). Individuals with SG only or MCR using 3IR were more likely to rate their health status as poor and to have depressive symptoms than other groups (all $p < 0.001$). In all physical function tests, including handgrip strength, usual gait speed, TUG and SPPB, new MCR using 3IR showed poorer performance compared to the normal or impaired 3IR group ($p < 0.001$). Meanwhile, characteristics of participants according to original MCR status using SCCs are shown in Table S1.

Of the total of 2133 older adults in this cohort study, 105 (4.9%) met the newly developed MCR criteria using 3IR, of whom 55.6% had impaired 3IR and 9.2% had SG (Figure 2). Of the participants, 134 (6.3%) had MCR defined conventionally using SCCs, and SCCs were present in 81.0% of the all participants. A total of 943 participants (44.2%) had both impaired 3IR and SCCs.
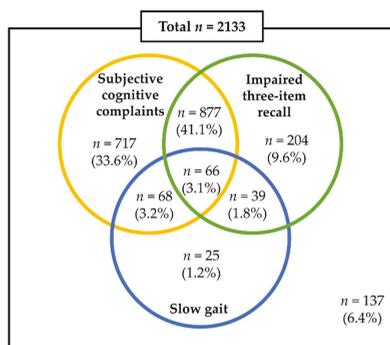
Figure 2. Venn diagram for the criteria and their overlaps.

The prevalence of fall-related outcomes according to MCR status using 3IR are presented in Figure 3. The MCR group using 3IR showed the highest prevalence of falls, recurrent falls, and falls

with injury among the groups (all *p* < 0.0063). The prevalence of falls with fracture was lowest in the impaired 3IR only group, and highest in the MCR using 3IR group (all *p* < 0.0063). FoF and low ABC were significantly different among the groups (all *p* < 0.0063), with higher prevalence in the SG only or MCR using 3IR group.

	Experience of falls		Recurrent falls		Falls with injury		Falls with fracture		Fear of falling		Low activities-specific balance confidence	
■ Normal	141	(16.5)	52	(6.1)	150	(17.6)	29	(3.4)	220	(25.8)	69	(8.1)
■ Impaired 3-item recall	164	(15.2)	50	(4.6)	178	(16.5)	23	(2.1)*	257	(23.8)*	74	(6.8)*
■ Slow gait	21	(22.6)	11	(11.8)	25	(26.9)	7	(7.5)	48	(51.6)*	27	(29.0)*
■ MCR using 3IR	29	(27.6)*	15	(14.3)*	32	(30.5)*	10	(9.5)*	56	(53.3)*	25	(23.8)*
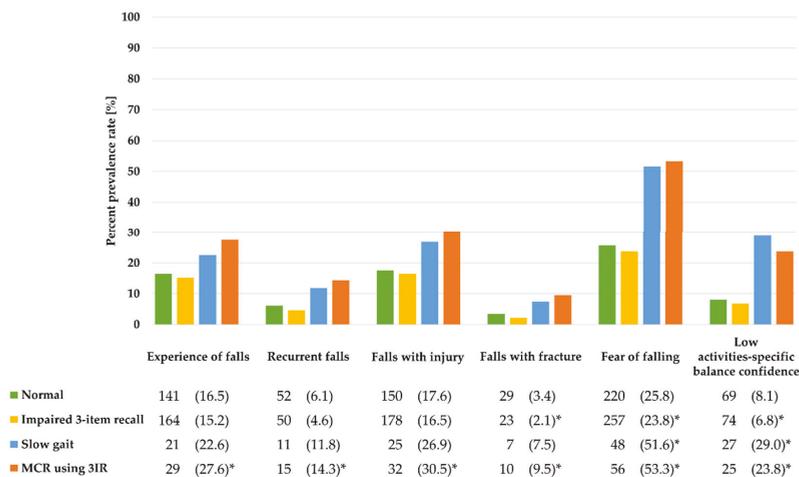
Figure 3. The prevalence of fall-related outcomes according to MCR status using 3IR. The numbers and percentages of outcomes are presented as *n* (%). * *p* < 0.0063.

3.2. Associations of MCR using 3IR or MCR using SCCs with Fall-Related Outcomes

Multiple logistic regression analyses were performed to investigate the associations between MCR and fall-related outcomes. Those for MCR using 3IR are shown in Table 2, and those of MCR using SCCs are presented in Table 3. Compared with the individual component of MCR using 3IR alone (i.e., impaired 3IR only and SG only), MCR using 3IR was only significantly associated with experience of falls in the past 1 year (OR: 1.92, 95% CI: 1.16–3.16), recurrent falls (OR: 2.19, 95% CI: 1.12–4.32), falls with injury (OR: 1.98, 95% CI: 1.22–3.22) and falls with fracture (OR: 2.51, 95% CI: 1.09–5.79) after considering all confounding factors. Moreover, the group with SG only (OR: 2.22, 95% CI: 1.31–3.75) and MCR using 3IR (OR: 3.00, 95% CI: 1.83–4.92) showed a significant association with FoF after adjusting for all confounders. With regard to low ABC, a significant association was observed in the groups with SG only (OR: 2.99, 95% CI: 1.47–6.12) and MCR using 3IR (OR: 3.13, 95% CI: 1.57–6.25) after adjustment for all confounding factors. MCR using 3IR showed synergistic effects on all fall-related outcomes (Table 2).

By contrast, MCR using SCCs was not associated with experience of falls, recurrent falls, falls with injury or falls with fracture (*p* > 0.05), while SG only was significantly associated with experience of falls (OR: 1.87, 95% CI: 1.01–3.45), recurrent falls (OR: 2.27, 95% CI: 1.04–4.96), and falls with injury (OR: 1.87, 95% CI: 1.02–3.42). In addition, both SG only (OR: 3.72, 95% CI: 1.86–7.43) and MCR using SCCs (OR: 2.04, 95% CI: 1.26–3.30) showed a significant association with FoF. Moreover, SG only (OR: 2.72, 95% CI: 1.24–6.00) and MCR using SCCs (OR: 2.75, 95% CI: 1.37–5.50) were associated with low ABC. However, the impact of SG only on most fall-related outcomes was stronger than that of MCR using SCCs.

Table 1. Characteristics of the participants according to motoric cognitive risk (MCR) syndrome status using three-item recall (3IR).

Characteristics	Overall	Normal (without Impaired 3IR and Slow Gait)	Impaired 3IR only	Slow Gait only	MCR Using 3IR	p Value
	(n = 2133)	(n = 854)	(n = 1081)	(n = 93)	(n = 105)	
Sociodemographic factors						
Age (years)	75.6 ± 3.8	75.4 ± 3.9	75.7 ± 3.8	75.2 ± 3.8	75.8 ± 4.0	0.350
Female sex	1032 (48.4)	468 (54.8) *	476 (44.0) *	48 (51.6)	40 (38.1)	<0.001
Education (years)	9.7 ± 4.7	9.6 ± 4.7 [b]	10.1 ± 4.5 [d]	7.7 ± 5.3 [b,d]	9.0 ± 4.6	<0.001
Residence						0.008
Urban	652 (30.6)	287 (33.6)	311 (28.8)	25 (26.9)	29 (27.6)	
Suburban	976 (45.8)	374 (43.8)	523 (48.4)	34 (36.6)	45 (42.9)	
Rural	505 (23.7)	193 (22.6)	247 (22.8) *	34 (36.6)	31 (29.5)	
Living alone	423 (19.8)	178 (20.8)	193 (17.9)	26 (28.0)	26 (24.8)	0.034
Marital status (without partner)	614 (28.8)	259 (30.3)	283 (26.2)	37 (39.8)	35 (33.3)	0.011
Basic livelihood security and/or medical care aid recipient	149 (7.0)	61 (7.1)	61 (5.6)	16 (17.2) *	11 (10.5)	<0.001
Lifestyle-related factors						
Current smoker	121 (5.7)	43 (5.0)	65 (6.0)	5 (5.4)	8 (7.6)	0.650
Alcohol consumption(≥2 to 3 times/week)	405 (19.0)	150 (17.6)	222 (20.5)	13 (14.0)	20 (19.0)	0.228
Low physical activity	169 (7.9)	54 (6.3) *	75 (6.9)	20 (21.5) *	20 (19.0) *	<0.001
General health and medical conditions						
BMI (kg/m²)	24.5 ± 3.0	24.6 ± 3.0	24.4 ± 2.9 [d]	25.1 ± 3.0 [d]	24.8 ± 3.6	0.061
<18.5	34 (1.6)	10 (1.2)	21 (1.9)	0 (0.0)	3 (2.9) *	0.257
18.5–24.9	1213 (56.9)	479 (56.1)	630 (58.3)	48 (51.6)	56 (53.3)	
≥25	886 (41.5)	395 (42.7)	430 (39.8)	45 (48.4)	46 (43.8)	
Number of drugs taken daily	3.4 ± 2.9	3.3 ± 2.8 [b,c]	3.3 ± 2.9 [d,e]	4.7 ± 3.8 [b,d]	4.2 ± 3.0 [c,e]	<0.001
Number of diseases	1.7 ± 1.2	1.7 ± 1.2 [c]	1.6 ± 1.2 [e]	1.9 ± 1.2	2.0 ± 1.3 [c,e]	0.004
Hypertension	1211 (56.8)	476 (55.7)	611 (56.5)	55 (59.1)	69 (65.7)	0.258
Diabetes	458 (21.5)	160 (18.7)	236 (21.8)	23 (24.7)	39 (37.1) *	<0.001
Dyslipidemia	718 (33.7)	304 (35.6)	353 (32.7)	27 (29.0)	34 (32.4)	0.408
Urinary incontinence	65 (3.0)	29 (3.4)	29 (2.7)	5 (5.4)	2 (1.9)	0.390
Visual impairment	39 (1.8)	14 (1.6)	18 (1.7)	4 (4.3)	3 (2.9)	0.230
Hearing impairment	325 (15.2)	126 (14.8)	166 (15.4)	15 (16.1)	18 (17.1)	0.915
Poor nutritional status (MNA screening score ≤11)	144 (6.8)	56 (6.6)	69 (6.4)	11 (11.8)	8 (7.6)	0.239
IADL disability	246 (11.5)	109 (12.8)	107 (9.9) *	19 (20.4) *	11 (10.5) *	0.010

Table 1. *Cont.*

Characteristics	Overall	Normal (without Impaired 3IR and Slow Gait)	Impaired 3IR only	Slow Gait only	MCR Using 3IR	p Value
	(n = 2133)	(n = 854)	(n = 1081)	(n = 93)	(n = 105)	
Psychological factors						
General cognitive function (MMSE score)	27.0 ± 1.7	27.8 ± 1.7 [a,c]	26.4 ± 1.4 [a,d]	27.6 ± 2.0 [d,f]	26.0 ± 1.4 [c,f]	**<0.001**
Fair/poor self-perceived health	533 (25.0)	201 (23.5)	244 (22.6)	45 (48.4) *	43 (41.0) *	**<0.001**
Depressive symptoms (GDS score ≥ 6)	383 (18.0)	141 (16.5)	179 (16.6)	31 (33.3) *	32 (30.5) *	**<0.001**
Quality of life (EQ-5D score)	0.899 ± 0.117	0.903 ± 0.113 [b,c]	0.909 ± 0.111 [d,e]	0.824 ± 0.155 [b,d]	0.830 ± 0.132 [c,e]	**0.007**
Physical functions						
Handgrip strength (kg)	27.4 ± 7.5	27.0 ± 7.4 [a]	27.9 ± 7.6 [a]	25.9 ± 7.6	26.7 ± 6.9	**<0.001**
Usual walking speed (m/s)	1.14 ± 0.24	1.19 ± 0.21 [b,c]	1.17 ± 0.22 [d,e]	0.78 ± 0.13 [b,d]	0.78 ± 0.13 [c,e]	**<0.001**
Timed get up and go test (s) [†]	10.0 ± 2.2	9.6 ± 2.0 [b,c]	9.7 ± 1.8 [d,e]	12.5 ± 3.4 [b,d]	12.5 ± 3.1 [c,e]	**<0.001**
SPPB score [†]	11.1 ± 1.3	11.2 ± 1.1 [b,c]	11.2 ± 1.1 [d,e]	10.1 ± 2.0 [b,d]	9.9 ± 1.9 [c,e]	**<0.001**
MCR syndrome Using three-item recall test						
Impaired three-item recall	1186 (55.6)	0 (0)	1081 (100)	0 (0)	105 (100)	**<0.001**
Slow gait	198 (9.3)	0 (0)	0 (0)	93 (100)	105 (100)	**<0.001**

Notes: Values are mean ± SD, *n* (%). *Abbreviations*: SD = Standard deviation; BMI = Body Mass Index; IADL = Instrumental Activities of Daily Living; MNA = Mini Nutritional Assessment; GDS = Geriatric Depression Scale; SPPB = Short Physical Performance Battery; MCR = Motoric Cognitive Risk; MMSE = Mini Mental State Examination. [a] Comparison between normal group and impaired 3IR only group; [b] comparison between normal group and slow gait only group; [c] comparison between normal group and MCR using 3IR group; [d] comparison between impaired 3IR only group and slow gait only group; [e] comparison between impaired 3IR only group and MCR using 3IR group; [f] comparison between slow gait only group and MCR using 3IR group. with Bonferroni post hoc test or Welch's ANOVA with Games-Howell post hoc test for continuous variables. *P* < 0.05 indicated in bold. * Significance with *P* < 0.05 divided by the number of rows × columns, with post hoc test of chi-square tests. [§] Sample size. [†] Some missing data. [‡] *P*-values were calculated using the Chi-square test or Fisher's exact test for categorical variables and one-way ANOVA.

Table 2. Associations between motoric cognitive risk (MCR) syndrome using three-item recall (3IR) and the fall-related outcomes (*n* = 2133).

Dependent Variables	Odds Ratio (95% Confidence Interval) (*p*-Value)								
	Normal (without Impaired 3IR and Slow Gait)	Impaired 3IR only	*p*	Slow Gait only	*p*	MCR Using 3IR	*p*		
Experience of falls in the past 1 year									
Model 1	Ref.	0.971 (0.754, 1.251)	0.820	1.406 (0.823, 2.402)	0.212	2.157 (1.282, 2.255)	0.002		
Model 2		0.969 (0.753, 1.248)	0.809	1.349 (0.784, 2.320)	0.279	2.098 (1.288, 3.416)	0.003		
Model 3		0.972 (0.753, 1.254)	0.827	1.257 (0.725, 2.179)	0.414	2.080 (1.271, 3.404)	0.004		
Model 4		0.959 (0.742, 1.239)	0.748	1.166 (0.667, 2.038)	0.590	1.915 (1.160, 3.160)	0.011		
Recurrent falls (≥ twice)									
Model 1	Ref.	0.789 (0.523, 1.189)	0.257	1.881 (0.921, 3.840)	0.083	2.745 (1.446, 5.213)	0.002		
Model 2		0.785 (0.521, 1.184)	0.248	1.686 (0.811, 3.505)	0.162	2.503 (1.302, 4.811)	0.006		
Model 3		0.809 (0.535, 1.223)	0.315	1.563 (0.745, 3.280)	0.237	2.581 (1.329, 5.012)	0.005		
Model 4		0.778 (0.513, 1.180)	0.237	1.361 (0.642, 2.889)	0.422	2.194 (1.115, 4.318)	0.023		
Falls with injury									
Model 1	Ref.	0.980 (0.766, 1.252)	0.869	1.647 (0.992, 2.735)	0.054	2.207 (1.380, 3.530)	0.001		
Model 2		0.977 (0.764, 1.250)	0.856	1.585 (0.949, 2.648)	0.079	2.151 (1.340, 3.454)	0.002		
Model 3		0.980 (0.765, 1.255)	0.871	1.493 (0.888, 2.511)	0.131	2.141 (1.328, 3.452)	0.002		
Model 4		0.967 (0.754, 1.240)	0.790	1.392 (0.821, 2.360)	0.219	1.982 (1.220, 3.220)	0.006		
Falls with fracture									
Model 1	Ref.	0.660 (0.373, 1.165)	0.660	2.442 (0.996, 5.987)	0.051	3.133 (1.404, 6.988)	0.005		
Model 2		0.659 (0.373, 1.164)	0.151	1.967 (0.780, 4.961)	0.152	2.764 (1.224, 6.237)	0.014		
Model 3		0.662 (0.372, 1.180)	0.162	1.727 (0.671, 4.444)	0.257	2.722 (1.185, 6.251)	0.018		
Model 4		0.648 (0.363, 1.157)	0.143	1.593 (0.608, 4.171)	0.343	2.508 (1.086, 5.791)	0.031		
Fear of falling									
Model 1	Ref.	0.969 (0.769, 1.221)	0.789	3.090 (1.901, 5.023)	<0.001	3.851 (2.409, 6.157)	<0.001		
Model 2		0.967 (0.767, 1.218)	0.776	2.885 (1.764, 4.720)	<0.001	3.664 (2.283, 5.878)	<0.001		
Model 3		0.981 (0.776, 1.241)	0.875	2.604 (1.575, 4.305)	<0.001	3.407 (2.111, 5.497)	<0.001		
Model 4		0.954 (0.751, 1.212)	0.700	2.218 (1.314, 3.746)	0.003	3.000 (1.830, 4.917)	<0.001		

Table 2. *Cont.*

Dependent Variables	Normal (without Impaired 3IR and Slow Gait)	Odds Ratio (95% Confidence Interval) (p-Value)					
		Impaired 3IR only	p	Slow Gait only	p	MCR Using 3IR	p
Low activities-specific balance confidence							
Model 1	Ref.	1.037 (0.713, 1.508)	0.849	5.403 (2.960, 9.863)	**<0.001**	5.269 (2.881, 9.639)	**<0.001**
Model 2		1.010 (0.692, 1.474)	0.957	4.358 (2.335, 8.135)	**<0.001**	4.609 (2.477, 8.576)	**<0.001**
Model 3		1.087 (0.733, 1.613)	0.678	4.094 (2.087, 8.032)	**<0.001**	4.320 (2.268, 8.230)	**<0.001**
Model 4		0.978 (0.648, 1.478)	0.917	2.994 (1.467, 6.108)	**0.003**	3.134 (1.571, 6.253)	**0.001**

Notes: Model 1: Adjusted for recruited center and sociodemographic factors; age, sex, low education level, residence (urban/suburban/rural), living alone, without partner, receiving basic livelihood security and/or medical care aid. Model 2: Further adjustment on Model 1 for lifestyle-related factors; current smoker, alcohol consumption, low physical activity. Model 3: Further adjustment on Model 2 for general health and medical conditions; body mass index (underweight/normal/obese), number of drugs taken daily, number of diseases (self-reported doctor diagnosis of hypertension, diabetes mellitus, dyslipidemia, myocardial infarction, congestive heart failure, angina pectoris, cerebrovascular disease, peripheral vascular disease, osteoarthritis, rheumatoid arthritis, osteoporosis, asthma, and chronic obstructive pulmonary disease), urinary incontinence, visual impairment, hearing impairment, poor nutritional status, number of difficulties in instrumental activities of daily living (IADL). Model 4: Further adjustment on Model 4 for psychological factors; depressive symptoms, fair/poor self-reported health status. *p* < 0.05 indicated in bold.

Table 3. Associations between motoric cognitive risk (MCR) syndrome using subjective cognitive complaints (SCCs) and the fall-related outcomes (*n* = 2133).

Dependent Variables	Normal (without SCCs and Slow Gait)	Odds Ratio (95% Confidence Interval) (p-Value)					
		SCCs only	p	Slow Gait only	p	MCR Using SCCs	p
Experience of falls in the past 1 year							
Model 1	Ref.	0.705 (0.519, 0.959)	**0.026**	2.047 (1.133, 3.699)	**0.018**	1.080 (0.647, 1.801)	0.769
Model 2		0.711 (0.523, 0.967)	**0.029**	1.989 (1.095, 3.612)	**0.024**	1.061 (0.634, 1.774)	0.823
Model 3		0.770 (0.562, 1.055)	0.103	1.955 (1.066, 3.586)	**0.030**	1.123 (0.667, 1.888)	0.663
Model 4		0.902 (0.650, 1.253)	0.540	1.865 (1.008, 3.452)	**0.047**	1.254 (0.740, 2.126)	0.400
Recurrent falls (≥ twice)							
Model 1	Ref.	0.531 (0.336, 0.840)	**0.007**	2.631 (1.255, 5.517)	**0.010**	1.165 (0.574, 2.367)	0.672
Model 2		0.550 (0.346, 0.872)	**0.011**	2.430 (1.145, 5.156)	**0.021**	1.106 (0.539, 2.271)	0.784
Model 3		0.609 (0.378, 0.979)	**0.041**	2.411 (1.113, 5.220)	**0.026**	1.214 (0.586, 2.513)	0.601
Model 4		0.790 (0.479, 1.304)	0.356	2.269 (1.038, 4.958)	**0.040**	1.410 (0.672, 2.960)	0.364

Table 3. *Cont.*

Dependent Variables	Normal (without SCCs and Slow Gait)	Odds Ratio (95% Confidence Interval) (*p*-Value)					
		SCCs only	*p*	Slow Gait only	*p*	MCR Using SCCs	*p*
Falls with injury							
Model 1	Ref.	0.709 (0.526, 0.955)	**0.024**	2.021 (1.127, 3.622)	**0.018**	1.258 (0.776, 2.040)	0.352
Model 2		0.716 (0.531, 0.965)	**0.028**	1.961 (1.089, 3.533)	**0.025**	1.241 (0.763, 2.047)	0.384
Model 3		0.766 (0.565, 1.040)	0.088	1.950 (1.073, 3.541)	**0.028**	1.299 (0.794, 2.123)	0.297
Model 4		0.897 (0.652, 1.235)	0.505	1.864 (1.018, 3.416)	**0.044**	1.454 (0.882, 2.396)	0.142
Falls with fracture							
Model 1	Ref.	0.969 (0.473, 1.983)	0.931	7.533 (2.893, 19.614)	**<0.001**	1.682 (0.580, 4.874)	0.338
Model 2		0.998 (0.485, 2.051)	0.995	6.678 (2.528, 17.638)	**<0.001**	1.449 (0.493, 4.254)	0.500
Model 3		1.193 (0.561, 2.534)	0.647	8.001 (2.898, 22.094)	**<0.001**	1.479 (0.491, 4.458)	0.487
Model 4		1.491 (0.679, 3.273)	0.319	7.738 (2.766, 21.651)	**<0.001**	1.763 (0.575, 5.410)	0.321
Fear of falling							
Model 1	Ref.	0.566 (0.428, 0.747)	**<0.001**	4.245 (2.223, 8.103)	**<0.001**	1.712 (1.088, 2.696)	**0.020**
Model 2		0.569 (0.431, 0.752)	**<0.001**	4.047 (2.107, 7.773)	**<0.001**	1.632 (1.033, 2.580)	**0.036**
Model 3		0.644 (0.484, 0.857)	**0.003**	3.756 (1.945, 7.252)	**<0.001**	1.701 (1.068, 2.709)	**0.025**
Model 4		0.874 (0.644, 1.185)	0.385	3.719(1.861, 7.432)	**<0.001**	2.040 (1.260, 3.301)	**0.004**
Low activities-specific balance confidence							
Model 1	Ref.	0.414 (0.276, 0.621)	**<0.001**	3.951 (2.019, 7.733)	**<0.001**	2.198 (1.211, 3.990)	**0.010**
Model 2		0.434 (0.288, 0.654)	**<0.001**	3.449 (1.727, 6.890)	**<0.001**	1.952 (1.056, 3.610)	**0.033**
Model 3		0.561 (0.362, 0.870)	**0.010**	3.520 (1.683, 7.362)	**0.001**	2.215 (1.153, 4.254)	**0.017**
Model 4		0.829 (0.517, 1.331)	0.437	2.722 (1.235, 6.001)	**0.013**	2.748 (1.374, 5.495)	**0.004**

Notes: Model 1: Adjusted for recruited center and sociodemographic factors; age, sex, low education level, residence (urban/suburban/rural), living alone, without partner, receiving basic livelihood security and/or medical care aid. Model 2: Further adjustment on Model 1 for lifestyle-related factors; current smoker, alcohol consumption, low physical activity. Model 3: Further adjustment on Model 2 for general health and medical conditions; body mass index (underweight/normal/obese), number of drugs taken daily, number of diseases (self-reported doctor diagnosis of hypertension, diabetes mellitus, dyslipidemia, myocardial infarction, congestive heart failure, angina pectoris, cerebrovascular disease, peripheral vascular disease, osteoporosis, rheumatoid arthritis, osteoporosis, asthma, and chronic obstructive pulmonary disease), urinary incontinence, visual impairment, hearing impairment, poor nutritional status, number of difficulties in instrumental activities of daily living (IADL). Model 4: Further adjustment on Model 4 for psychological factors; depressive symptoms, fair/poor self-reported health status. *P* < 0.05 indicated in bold.

4. Discussion

In this cohort study with 70–84 year-old community-dwelling older adults, the prevalence of the new MCR using 3IR was 4.9% (105/2133), and that of MCR using SCCs was 6.3% (134/2133), which is consistent with other previous studies [6]. The prevalence of MCR using SCCs in the present study was lower than that of our previous study (8.0%) [16]. Such a gap might be due to the different exclusion criteria of the studied populations, especially additional exclusion of dementia based on MMSE score (< 24). The overlap between the newly developed criteria, impaired 3IR, and the conventional criteria of SCCs was 44.2%, which simply assesses subjects' memory status, but differs in the method of identifying memory deficits. Our main finding is that MCR using 3IR was associated with all fall-related outcomes, including experience of falls, recurrent falls, falls with injury, falls with fracture, FoF, and low ABC, with synergistic effects of its components. By contrast, MCR using SCCs was not associated with falls, recurrent falls, and falls with injury or fracture, and SG only showed a stronger association with most fall-related outcomes.

The idea of a newly attempted MCR using 3IR was developed from our previous findings that SCCs, widely used to define MCR, had a considerably high prevalence rate (77.7%) in older Korean adults, and that the effect of SCCs on cognitive impairment was not additive to SG [16]. Elderly Koreans tend to report more SCCs [15] as well as depressive symptoms [17,45] compared to Western countries. This tendency may be influenced by cultural factors [46]. Several previous studies had shown that SCCs might be more closely associated with depressive symptoms than actual cognitive function [47–49]. Therefore, we intended to compensate for the limitations of SCCs for older Korean adults by establishing another criterion for the cognitive aspects of MCR.

We adopted the 3IR test of MMSE instead of SCCs for definition of MCR based on the following reasons. First, most previous studies identified SCCs using memory-related items [22]. Therefore, we intended to find another tool to represent the subjects' memory function. Second, the 3IR test is one of the components of MMSE, which has been widely used and validated in many clinical practices and community settings to screen for dementia [24]. Third, some studies have reported that the 3IR was one of the best discriminators among the subscales of MMSE for screening dementia [50]. Fourth, the 3IR test is simple and easy to conduct, which is in line with the usefulness of MCR in various clinical practice settings [9]. In addition, the 3IR test is also a part of the Mini-Cog test, which has high sensitivity and specificity for detecting AD and related dementia in community settings [51]. The Mini-Cog test may not be greatly affected by cultural differences [29]. In our study, the cut-off score to define impaired 3IR (< 3) was based on the first step of the Mini-Cog test, in which participants with a score less than 3 either required an additional step (score 1–2) or were diagnosed as demented (score 0) [29].

In the present study, we examined the associations of MCR using a 3IR test with various fall-related outcomes, and compared the results to those of original MCR using SCCs. Callisaya et al. reported that MCR was associated with increased risk of any falls and multiple falls (≥ 2 falls) based on five Western cohort studies, reporting stronger predictive capability of MCR than its individual components [19]. Similarly, in a study in New Zealand comparing the fall risks of Māori and non-Māori populations, MCR and its components were significantly associated with increased fall risks, with synergistic effects of the components in the non-Māori group. However, these associations were not observed in the Māori group [21]. In a French cohort study, subjects with MCR were at higher risk of having experienced falls, recurrent falls, and post-fall fractures, but not those with each component of MCR [20]. Our findings, in terms of the associations of MCR with fall-related outcomes, are consistent with these three previous studies. In our study, MCR using 3IR showed synergistic effects of individual components of MCR compared to MCR using SCCs.

By contrast, in the associations of MCR using SCCs and its components with fall-related outcomes, SG only had a stronger association than MCR using SCCs, and SCCs only showed protective associations with some fall-related outcomes. These protective associations of SCCs only with most fall-related outcomes, however, became nonsignificant after adjusting for psychological factors,

including depressive symptoms and self-reported health status. This change may have been due to the influence of depression or self-rating questionnaire methods on SCCs. Several studies have reported associations between SCCs and depression or self-perceived health [48,52]. In addition, Carrasco et al. reported that the quantity or quality of memory complaints was an important issue for interpreting results, as the self-perceived state of health or mood may be the only factor influencing SCCs, particularly in subjects with fewer complaints [48], which may just be due to normal aging. Therefore, further studies are suggested to examine the effects of psychological factors to further investigate the concept of MCR.

Overall, the associations between MCR, regardless of its definition, and the fall-related outcomes showed specific features in this study. The pattern of the main results was different between each definition of MCR. MCR using 3IR showed a significant association with both fall history retrospectively collected, and self-evaluation of current fear or balance confidence, and SG only showed a significant association only with self-evaluated outcomes. In contrast to this pattern, MCR using SCCs showed a significant association with the self-rated outcomes, and did not show significance in the retrospective fall history. We suspected that these features might be related to the effects of psychological factors on both SCCs and MCR using SCCs [53].

This study had some limitations. First, the causal relationships between MCR, regardless of definition, and fall-related outcomes could not be determined because of the cross-sectional study design. Second, information on some fall-related outcomes was collected retrospectively, which may cause recall bias. Third, the subjects were relatively healthy because they were ambulatory older adults in the community. In addition, the participants were recruited in a research setting. Therefore, our findings may not be generalizable to other settings. Despite these limitations, our findings are important because we included a large, nationally representative sample of older Korean adults, and took into consideration various robust confounders.

5. Conclusions

MCR using 3IR was associated with fall-related outcomes, with synergistic effects of the individual components. However, SG only showed stronger effects on most fall-related outcomes than MCR using SCCs. SCCs was susceptible to psychological factors, such as depressive symptoms.

References

1. Montero-Odasso, M.; Verghese, J.; Beauchet, O.; Hausdorff, J.M. Gait and cognition: A complementary approach to understanding brain function and the risk of falling. *J. Am. Geriatr. Soc.* **2012**, *60*, 2127–2136. [CrossRef] [PubMed]

2. Cohen, J.A.; Verghese, J.; Zwerling, J.L. Cognition and gait in older people. *Maturitas* **2016**, *93*, 73–77. [CrossRef] [PubMed]

3. Verghese, J.; Wang, C.; Lipton, R.B.; Holtzer, R. Motoric cognitive risk syndrome and the risk of dementia. *J. Gerontol. A Biol. Sci. Med. Sci.* **2013**, *68*, 412–418. [CrossRef] [PubMed]

4. Chhetri, J.K.; Chan, P.; Vellas, B.; Cesari, M. Motoric Cognitive Risk Syndrome: Predictor of Dementia and Age-Related Negative Outcomes. *Front. Med.* **2017**, *4*, 166. [CrossRef]

5. Sekhon, H.; Allali, G.; Launay, C.P.; Barden, J.; Szturm, T.; Liu-Ambrose, T.; Chester, V.L.; Wong, C.H.; Beauchet, O.; Canadian Gait, C. Motoric cognitive risk syndrome, incident cognitive impairment and morphological brain abnormalities: Systematic review and meta-analysis. *Maturitas* **2019**, *123*, 45–54. [CrossRef]

6. Meiner, Z.; Ayers, E.; Verghese, J. Motoric Cognitive Risk Syndrome: A Risk Factor for Cognitive Impairment and Dementia in Different Populations. *Annals Geriatr. Med. Res.* **2020**, *24*, 3–14. [CrossRef]

7. Bennett, D.A.; Schneider, J.A.; Buchman, A.S.; Barnes, L.L.; Boyle, P.A.; Wilson, R.S. Overview and findings from the rush Memory and Aging Project. *Curr. Alzheimer Res.* **2012**, *9*, 646–663. [CrossRef]

8. Bennett, D.A.; Schneider, J.A.; Arvanitakis, Z.; Wilson, R.S. Overview and findings from the religious orders study. *Curr. Alzheimer Res.* **2012**, *9*, 628–645. [CrossRef]

9. Verghese, J.; Annweiler, C.; Ayers, E.; Barzilai, N.; Beauchet, O.; Bennett, D.A.; Bridenbaugh, S.A.; Buchman, A.S.; Callisaya, M.L.; Camicioli, R. Motoric cognitive risk syndrome: Multicountry prevalence and dementia risk. *Neurology* **2014**, *83*, 718–726. [CrossRef]

10. Caramelli, P.; Beato, R.G. Subjective memory complaints and cognitive performance in a sample of healthy elderly. *Dement. Neuropsychol.* **2008**, *2*, 42. [CrossRef]

11. Reid, L.M.; MacLullich, A.M. Subjective memory complaints and cognitive impairment in older people. *Dement. Geriatr. Cognit. Dis.* **2006**, *22*, 471–485. [CrossRef]

12. Burmester, B.; Leathem, J.; Merrick, P. Subjective Cognitive Complaints and Objective Cognitive Function in Aging: A Systematic Review and Meta-Analysis of Recent Cross-Sectional Findings. *Neuropsychol. Rev.* **2016**, *26*, 376–393. [CrossRef]

13. Sekhon, H.; Allali, G.; Beauchet, O. The association of anxio-depressive disorders and depression with motoric cognitive risk syndrome: Results from the baseline assessment of the Canadian longitudinal study on aging. *Geroscience* **2019**, *41*, 409–418. [CrossRef]

14. Sanders, K.M.; Stuart, A.L.; Scott, D.; Kotowicz, M.A.; Nicholson, G.C. Validity of 12-Month Falls Recall in Community-Dwelling Older Women Participating in a Clinical Trial. *Int. J. Endocrinol.* **2015**, *2015*, 210527. [CrossRef]

15. Park, M.H.; Min, J.Y.; Min, H.Y.; Lee, H.J.; Lee, D.H.; Song, M.S. Subjective memory complaints and clinical characteristics in elderly Koreans: A questionnaire survey. *Int. J. Nurs. Stud.* **2007**, *44*, 1400–1405. [CrossRef]

16. Shim, H.; Kim, M.; Won, C.W. Motoric cognitive risk syndrome is associated with processing speed and executive function, but not delayed free recall memory: The Korean frailty and aging cohort study (KFACS). *Arch. Gerontol. Geriatr.* **2020**, *87*, 103990. [CrossRef]

17. Park, J.H.; Kim, K.W.; Kim, M.H.; Kim, M.D.; Kim, B.J.; Kim, S.K.; Kim, J.L.; Moon, S.W.; Bae, J.N.; Woo, J.I.; et al. A nationwide survey on the prevalence and risk factors of late life depression in South Korea. *J. Affect. Disord* **2012**, *138*, 34–40. [CrossRef]

18. Park, J.H.; Lee, J.J.; Lee, S.B.; Huh, Y.; Choi, E.A.; Youn, J.C.; Jhoo, J.H.; Kim, J.S.; Woo, J.I.; Kim, K.W. Prevalence of major depressive disorder and minor depressive disorder in an elderly Korean population: Results from the Korean Longitudinal Study on Health and Aging (KLoSHA). *J. Affect. Dis.* **2010**, *125*, 234–240. [CrossRef]

19. Callisaya, M.L.; Ayers, E.; Barzilai, N.; Ferrucci, L.; Guralnik, J.M.; Lipton, R.B.; Otahal, P.; Srikanth, V.K.; Verghese, J. Motoric Cognitive Risk Syndrome and Falls Risk: A Multi-Center Study. *J. Alzheimers Dis.* **2016**, *53*, 1043–1052. [CrossRef]

20. Beauchet, O.; Sekhon, H.; Schott, A.M.; Rolland, Y.; Muir-Hunter, S.; Markle-Reid, M.; Gagne, H.; Allali, G. Motoric Cognitive Risk Syndrome and Risk for Falls, Their Recurrence, and Postfall Fractures: Results From a Prospective Observational Population-Based Cohort Study. *J. Am. Med. Dir. Assoc.* **2019**, *20*, 1268–1273. [CrossRef]

21. Lord, S.; Moyes, S.; Teh, R.; Port, W.; Muru-Lanning, M.; Bacon, C.J.; Wilkinson, T.; Kerse, N. Gait, cognition and falls over 5 years, and motoric cognitive risk in New Zealand octogenarians: Te Puawaitanga o Nga Tapuwae Kia Ora Tonu, LiLACS NZ. *BMC Geriatr.* **2020**, *20*, 43. [CrossRef]

22. Semba, R.D.; Tian, Q.; Carlson, M.C.; Xue, Q.L.; Ferrucci, L. Motoric cognitive risk syndrome: Integration of two early harbingers of dementia in older adults. *Ageing Res. Rev.* **2020**, *58*, 101022. [CrossRef]

23. Won, C.W.; Lee, S.; Kim, J.; Chon, D.; Kim, S.; Kim, C.O.; Kim, M.K.; Cho, B.; Choi, K.M.; Roh, E.; et al. Korean frailty and aging cohort study (KFACS): Cohort profile. *BMJ Open* **2020**, *10*, e035573. [CrossRef]
24. Creavin, S.T.; Wisniewski, S.; Noel-Storr, A.H.; Trevelyan, C.M.; Hampton, T.; Rayment, D.; Thom, V.M.; Nash, K.J.; Elhamoui, H.; Milligan, R.; et al. Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *Cochrane Database Syst. Rev.* **2016**. [CrossRef]
25. Yesavage, J.A. Geriatric depression scale. *Psychopharmacol. Bull.* **1988**, *24*, 709–711.
26. Bae, J.N.; Cho, M.J. Development of the Korean version of the Geriatric Depression Scale and its short form among elderly psychiatric patients. *J. Psychosom. Res.* **2004**, *57*, 297–305. [CrossRef]
27. Doi, T.; Verghese, J.; Shimada, H.; Makizako, H.; Tsutsumimoto, K.; Hotta, R.; Nakakubo, S.; Suzuki, T. Motoric Cognitive Risk Syndrome: Prevalence and Risk Factors in Japanese Seniors. *J. Am. Med. Dir. Assoc.* **2015**, *16*, 1103.e21–1103.e25. [CrossRef]
28. Lee, J.H.; Lee, K.U.; Lee, D.Y.; Kim, K.W.; Jhoo, J.H.; Kim, J.H.; Lee, K.H.; Kim, S.Y.; Han, S.H.; Woo, J.I. Development of the Korean Version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K): Clinical and Neuropsychological Assessment Batteries. *J. Gerontol. Ser. B* **2002**, *57*, P47–P53. [CrossRef]
29. Borson, S.; Scanlan, J.; Brush, M.; Vitaliano, P.; Dokmak, A. The mini-cog: A cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int. J. Geriatr. Psychiatry* **2000**, *15*, 1021–1027. [CrossRef]
30. Tinetti, M.E.; Speechley, M.; Ginter, S.F. Risk factors for falls among elderly persons living in the community. *N. Eng. J. Med.* **1988**, *319*, 1701–1707. [CrossRef]
31. Close, J.; Ellis, M.; Hooper, R.; Glucksman, E.; Jackson, S.; Swift, C. Prevention of falls in the elderly trial (PROFET): A randomised controlled trial. *Lancet* **1999**, *353*, 93–97. [CrossRef]
32. Uemura, K.; Shimada, H.; Makizako, H.; Doi, T.; Tsutsumimoto, K.; Lee, S.; Umegaki, H.; Kuzuya, M.; Suzuki, T. Effects of Mild Cognitive Impairment on the Development of Fear of Falling in Older Adults: A Prospective Cohort Study. *J. Am. Med. Dir. Assoc.* **2015**, *16*, 1104.e9–1104.e13. [CrossRef] [PubMed]
33. Powell, L.E.; Myers, A.M. The activities-specific balance confidence (ABC) scale. *J. Gerontol. Ser. A Biolog. Sci. Med. Sci.* **1995**, *50*, M28–M34. [CrossRef] [PubMed]
34. Moiz, J.A.; Bansal, V.; Noohu, M.M.; Gaur, S.N.; Hussain, M.E.; Anwer, S.; Alghadir, A. Activities-specific balance confidence scale for predicting future falls in Indian older adults. *Clin. Interv. Aging* **2017**, *12*, 645–651. [CrossRef] [PubMed]
35. Son, J.; Kim, S.; Won, C.; Choi, H.; Kim, B.; Park, M. Physical frailty predicts medical expenses in community-dwelling, elderly patients: Three-year prospective findings from living profiles of older people surveys in Korea. *Eur. Geriatr. Med.* **2015**, *6*, 412–416. [CrossRef]
36. Stevens, G.A.; White, R.A.; Flaxman, S.R.; Price, H.; Jonas, J.B.; Keeffe, J.; Leasher, J.; Naidoo, K.; Pesudovs, K.; Resnikoff, S.; et al. Global prevalence of vision impairment and blindness: Magnitude and temporal trends, 1990-2010. *Ophthalmology* **2013**, *120*, 2377–2384. [CrossRef]
37. Yoo, M.; Kim, S.; Kim, B.S.; Yoo, J.; Lee, S.; Jang, H.C.; Cho, B.L.; Son, S.J.; Lee, J.H.; Park, Y.S.; et al. Moderate hearing loss is related with social frailty in a community-dwelling older adults: The Korean Frailty and Aging Cohort Study (KFACS). *Arch. Gerontol. Geriatr.* **2019**, *83*, 126–130. [CrossRef]
38. Won, C.W. Korea Activities of Daily Living Scale and Korea Instrumental Activities of Daily Living Scale. *J. Korean Geriatr. Soc.* **2002**, *6*, 1–10.
39. Rubenstein, L.Z.; Harker, J.O.; Salvà, A.; Guigoz, Y.; Vellas, B. Screening for undernutrition in geriatric practice: Developing the short-form mini-nutritional assessment (MNA-SF). *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2001**, *56*, M366–M372. [CrossRef]
40. Lee, D.Y.; Lee, K.U.; Lee, J.H.; Kim, K.W.; Jhoo, J.H.; Youn, J.C.; Kim, S.Y.; Woo, S.I.; Woo, J.I. A normative study of the mini-mental state examination in the Korean elderly. *J. Korean Neuropsychiatr. Assoc.* **2002**, *41*, 508.
41. Lee, S.C.; Kim, W.H.; Chang, S.M.; Kim, B.S.; Lee, D.W.; Bae, J.N.; Cho, M.J. The use of the Korean version of Short Form Geriatric Depression Scale (SGDS-K) in the community dwelling elderly in Korea. *J. Korean Geriatr. Psychiatry* **2013**, *17*, 37.
42. Jo, M.-W.; Yun, S.-C.; Lee, S.-I. Estimating quality weights for EQ-5D health states with the time trade-off method in South Korea. *Value Health* **2008**, *11*, 1186–1189. [CrossRef] [PubMed]
43. Shumway-Cook, A.; Brauer, S.; Woollacott, M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Phys. Ther.* **2000**, *80*, 896–903. [PubMed]

44. Guralnik, J.M.; Simonsick, E.M.; Ferrucci, L.; Glynn, R.J.; Berkman, L.F.; Blazer, D.G.; Scherr, P.A.; Wallace, R.B. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *J. Gerontol.* **1994**, *49*, M85–M94. [CrossRef]
45. Jang, Y.; Small, B.J.; Haley, W.E. Cross-cultural comparability of the Geriatric Depression Scale: Comparison between older Koreans and older Americans. *Aging Ment. Health* **2001**, *5*, 31–37. [CrossRef]
46. Lee, J.J.; Kim, K.W.; Kim, T.H.; Park, J.H.; Lee, S.B.; Park, J.W.; McQuoid, D.R.; Steffens, D.C. Cross-cultural considerations in administering the center for epidemiologic studies depression scale. *Gerontology* **2011**, *57*, 455–461. [CrossRef]
47. Chin, J.; Oh, K.J.; Seo, S.W.; Na, D.L. Are depressive symptomatology and self-focused attention associated with subjective memory impairment in older adults? *Int. Psychogeriatr.* **2014**, *26*, 573–580. [CrossRef]
48. Schweizer, S.; Kievit, R.A.; Emery, T.; Cam, C.A.N.; Henson, R.N. Symptoms of depression in a large healthy population cohort are related to subjective memory complaints and memory performance in negative contexts. *Psychol. Med.* **2018**, *48*, 104–114. [CrossRef]
49. Slavin, M.J.; Brodaty, H.; Kochan, N.A.; Crawford, J.D.; Trollor, J.N.; Draper, B.; Sachdev, P.S. Prevalence and predictors of "subjective cognitive complaints" in the Sydney Memory and Ageing Study. *Am. J. Geriatr. Psychiatry* **2010**, *18*, 701–710. [CrossRef]
50. Loewenstein, D.A.; Barker, W.W.; Harwood, D.G.; Luis, C.; Acevedo, A.; Rodriguez, I.; Duara, R. Utility of a modified mini-mental state examination with extended delayed recall in screening for mild cognitive impairment and dementia among community dwelling elders. *Int. J. Geriatr. Psychiatry* **2000**, *15*, 434–440. [CrossRef]
51. Fage, B.A.; Chan, C.C.; Gill, S.S.; Noel-Storr, A.H.; Herrmann, N.; Smailagic, N.; Nikolaou, V.; Seitz, D.P. Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a community setting. *Cochrane Database Syst. Rev.* **2015**. [CrossRef] [PubMed]
52. Montejo Carrasco, P.; Montenegro-Pena, M.; Lopez-Higes, R.; Estrada, E.; Prada Crespo, D.; Montejo Rubio, C.; Garcia Azorin, D. Subjective Memory Complaints in healthy older adults: Fewer complaints associated with depression and perceived health, more complaints also associated with lower memory performance. *Arch. Gerontol. Geriatr.* **2017**, *70*, 28–37. [CrossRef] [PubMed]
53. Payette, M.C.; Belanger, C.; Leveille, V.; Grenier, S. Fall-Related Psychological Concerns and Anxiety among Community-Dwelling Older Adults: Systematic Review and Meta-Analysis. *PLoS ONE* **2016**, *11*, e0152848. [CrossRef] [PubMed]

Article

Association between Mixing Ability of Masticatory Functions Measured Using Color-Changing Chewing Gum and Frailty among Japanese Older Adults: The Kyoto–Kameoka Study

Daiki Watanabe [1,2,*], **Tsukasa Yoshida** [1,2,3,4], **Keiichi Yokoyama** [2,3], **Yasuko Yoshinaka** [5],
Yuya Watanabe [1,3,6], **Takeshi Kikutani** [7], **Mitsuyoshi Yoshida** [8], **Yosuke Yamada** [1,2,3],
Misaka Kimura [2,3,9,*] **and Kyoto-Kameoka Study Group** [1]

[1] National Institute of Health and Nutrition, National Institutes of Biomedical Innovation,
Health and Nutrition, Tokyo 162-8636, Japan; t-yoshida@nibiohn.go.jp (T.Y.);
yuwatana@mail.doshisha.ac.jp (Y.W.); yamaday@nibiohn.go.jp (Y.Y.)
[2] Institute for Active Health, Kyoto University of Advanced Science, Kyoto 621-8555, Japan;
physiol.yokoyama@gmail.com
[3] Laboratory of Applied Health Sciences, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan
[4] Senior Citizen's Welfare Section, Kameoka City Government, Kyoto 621-8501, Japan
[5] Center for Faculty Development, Kyoto University of Advanced Science, Kyoto 621-8555, Japan;
yoshinaka.yasuko@kuas.ac.jp
[6] Faculty of Health and Sports Science, Doshisha University, Kyoto 610-0394, Japan
[7] Division of Rehabilitation for Speech and Swallowing Disorders, Nippon Dental University,
Tokyo 184-0011, Japan; kikutani@tokyo.ndu.ac.jp
[8] Department of Advanced Prosthodontics, Hiroshima University Graduate School of Biomedical & Health
Sciences, Hiroshima 739-0046, Japan; mitsu@hiroshima-u.ac.jp
[9] Department of Nursing, Doshisha Women's College of Liberal Arts, Kyoto 610-0395, Japan
*   Correspondence: d2watanabe@nibiohn.go.jp (D.W.); kimura.misaka@kuas.ac.jp (M.K.)

Abstract: The relationship between mixing ability of masticatory functions and frailty has not been well evaluated. This study investigated the prevalence of physical and comprehensive frailty and its association with mixing ability in 1106 older adults aged ≥65 years who underwent physical examination as part of the Japanese Kyoto–Kameoka Study. Mixing ability was assessed using color-changing chewing gum (1–5 points, 5 representing the best mixing ability). Participants were divided into four groups (5 points, 4 points, 3 points, and 1 or 2 points). The modified Japanese versions of the Cardiovascular Health Study (mJ-CHS) criteria and the validated Kihon Checklist (KCL) were used to assess physical and comprehensive frailty, respectively. Multivariate logistic regression was used to evaluate the association between frailty and mixing ability. The prevalence of physical and comprehensive frailty was 11.8% and 27.9%, respectively. After adjusting for confounders, the odds ratios of physical and comprehensive frailty comparing the highest to the lowest chewing gum score groups were 3.64 (95% confidence interval (CI): 1.62 to 8.18; *p* for trend = 0.001) and 2.09 (95% CI: 1.09 to 4.03; *p* for trend = 0.009), respectively. Mixing-ability tests involving chewing gum may be an indicator associated with both physical and comprehensive frailty.

Keywords: mixing ability; color-changing chewing gum; frailty; older adults; cross-sectional study

1. Introduction

Frailty is a condition in which multiple physiological systems decline in function owing to a loss of homeostasis in response to stress [1,2] and is considered a worldwide public health problem

among older adults [3]. Two major concepts of frailty exist in the literature: the Fried phenotype (FP) model, which defines frailty based on five criteria (physical frailty) [1,4,5], and the health deficits model (e.g., the Rockwood Frailty Index), which defines frailty as a multidimensional clinical geriatric syndrome (comprehensive frailty) [2,4,6,7]. The Kihon Checklist (KCL) is considered a valid tool for assessment of comprehensive frailty as a multidimensional clinical geriatric syndrome and is widely used in Japan and other countries [4,8–10]. Overall, frailty is associated with increased risk of death [8,11,12], disability [8,13], and burden of disease using disability-adjusted life years [14] in older adults. Accordingly, there is a need to establish objective, simple tools for the evaluation of frailty, with concepts rooted in both conceptual models.

The prevalence of oral disease among older adults is high, and the number of people with poor masticatory functions increases with age [15]. Decline in masticatory functions limits food choices and reduces the enjoyment of eating, making it difficult to secure sufficient food intake to maintain physiological function, which, in turn, leads to malnutrition [16,17]. An association between poor masticatory functions and frailty is thus likely [18,19]. In fact, a number of previous studies have reported that masticatory functions are positively associated with grip strength [20,21] and gait speed [20], indicating that it could be used to assess physical function in older adults.

Previous epidemiological studies have investigated masticatory functions with self-reported measures, primarily questionnaire-based [22], which have also assessed the number of natural teeth of participants and denture use [23]. Objective methods of evaluating masticatory functions, likely to provide more accurate results, often require specialist technology and skill [17]. Recent studies have confirmed the validity of mixing-ability assessment using color-changing chewing gum in terms of the number of teeth [24], tongue motor function, tongue pressure [25], and chew count [26] and found that gum chewing can objectively measure masticatory performance without the requirement for specialist technology or skill. Previous studies have reported that poor oral health including a lower mixing ability is associated with physical [18,19,24,27] and comprehensive frailty [28,29]. However, those previous studies have focused only on frailty, and the association of mixing ability with the subdomains of each assessment tool for frailty has not been well evaluated. In particular, although one subdomain of the comprehensive frailty defined by KCL includes oral function, sensitivity analyses that examine the relationship between mixing ability and each domain of frailty are also needed. This study aimed to investigate the association between objective mixing ability of masticatory functions and physical and comprehensive frailty using two validated frailty assessment tools in a community-based cohort study of older adults. In addition, we also examined the association between mixing ability and the subdomains of each assessment tool for frailty. Although the term "frailty" appears simple, the definition of frailty varies between studies [30]. Therefore, the association between mixing ability and frailty defined using a multiple assessment tool should be evaluated because there are many such tools in existence, with greater heterogeneity in their classification and predictive abilities.

2. Materials and Methods

2.1. Study Design and Population

The Kyoto–Kameoka Study is a cohort study of older residents of Kameoka City, Kyoto Prefecture, aged ≥65 years, which conducted the Needs in the Sphere of Daily Life survey (baseline survey), including the KCL, on 13,294 residents on July 29, 2011 [31–35]. The Health and Nutrition Status Survey (additional survey) was conducted as a follow-up to the original surveys, and 8319 residents submitted valid responses. For our study, we randomly selected 10 from 21 areas that make up Kameoka City and sent postcards to 4831 residents inviting them to undergo a physical checkup [31]. Of those residents, 1379 participants underwent a physical checkup examination as part of the Kyoto–Kameoka Study during March or April 2012. Written informed consent was obtained from all the participants before data acquisition. Health-related information, including medical history, socioeconomic status,

smoking status and alcohol consumption, and physical activity, was extracted from the baseline and additional surveys.

The participants of the present study were respondents for whom baseline data were available (*n* = 1379), excluding those with incomplete responses to the modified Japanese version of the Cardiovascular Health Study (mJ-CHS) criteria (*n* = 75) or the KCL (*n* = 124) and those with missing color-changing chewing gum data (*n* = 74). Ultimately, 1106 participants were included in this study.

This study was approved by the ethics review boards of the Kyoto Prefectural University of Medicine (No. RBMR-E-363), Kyoto University of Advanced Science (No. 20-1), and the National Institute of Health and Nutrition (No. NIHN187-3). The study was carried out in accordance with the principles of the Declaration of Helsinki.

2.2. Frailty Definitions

We assessed physical and comprehensive frailty according to the mJ-CHS criteria and the KCL [30]. The J-CHS criteria, based on the CHS, modified for validity in Japanese individuals [9], are based on the FP model and include five elements of shrinking, exhaustion, low activity, slowness, and weakness. We evaluated physical frailty according to the mJ-CHS criteria, which are based on the J-CHS criteria with one question substituted for a question evaluating low activity: (I) Have you lost 2–3 kg or more in weight over the past 6 months without trying? If a participant responded "Yes" to this question, this was defined as "weight loss." (II) Do you engage in sports, exercise, or keep-fit activities (other than walking?) If a participant responded "No" to this question, this was defined as "low activity." (III) During the past two weeks, have you felt tired for no reason? If a participant responded "Yes" to this question, this was defined as "exhaustion." (IV) If a participant's grip strength was <26 kg for men and <18 kg for women, this was defined as "weakness." (V) If a participant's normal gait speed was <1.0 m/s, this was defined as "slow gait speed." Individuals were defined as frailty if they met three out of five of the frailty reference criteria [9]. According to a prospective cohort study, FP-model-based physical frailty can also predict disability risk among older adults [36].

Grip strength was measured with a Smedley Hand Dynamometer (Grip-D TKK5101, Takei Scientific Instruments, Niigata, Japan). Measurements were taken twice for each hand, and the mean of the highest value for each hand was used. To evaluate each participant's habitual gait speed, they were instructed to walk a 10-m distance at a comfortable pace. The time taken to walk a 6-m distance, excluding the first 2 m after acceleration and the final 2 m before deceleration, was measured with a digital stopwatch. Gait speed was calculated as distance divided by walking time.

The KCL is a self-administered questionnaire consisting of 25 questions in seven subdomains, covering instrumental activities of daily living (IADL), physical function, nutritional status, oral function, social status, cognitive status, and depression, which provide a comprehensive assessment of frailty. The KCL's assessment principle thus resembles the health deficit model proposed by Rookwood et al. [6,7]. Every problem with activity or function received a point, and the higher the total score, the greater the difficulty in daily functioning, ranging from 0 (no frailty) to 25 (high frailty), with comprehensive frailty defined as a score of 7 or above [4,32–35]. The cutoff points of the KCL subdomains are the following: IADL disability, physical, nutrition, oral, social, cognitive, and depression defined as the IADL disability domain ≥10 points on 20 items including shopping; the physical inactivity domain ≥3 points on 5 items including walk continuously and history of fall; the malnutrition domain = 2 points on 2 items including physique; the oral dysfunction domain ≥2 points on 3 items including dry mouth and poor mastication; the socialization domain ≥1 point on 2 items including frequency of going out less; the memory domain ≥1 point on 3 items including memory loss; and the mood domain ≥2 points on 5 items including fulfilment and helpless [37]. In a prospective cohort study, KCL score was associated with increased risk of death or long-term care insurance certification within the next 3 years [8]. Additionally, we investigated the association between the subdomains evaluated using the mJ-CHS criteria and KCL [37] and mixing ability.

2.3. Measurement of Mixing Ability

Mixing ability was assessed using color-changing chewing gum (Xylitol Masticatory Performance Evaluating Gum, Lotte, Tokyo, Japan) [17,24–26,28,29,38,39]. This chewing gum contained 7 kcal energy, 2.3 g carbohydrate (0 g sugar), and 1.7 g xylitol (70 mm × 20 mm × 1 mm, 3.0 g). It contained ingredients that did not adhere to teeth or dentures as well as red, yellow, and blue dyes that change color when mixed with saliva and chewed. The red dyes are sensitive to pH changes, turning red under neutral or alkaline conditions. The unchewed gum contains citric acid, which maintains it in an acid environment (low pH) and is yellowish-green in color. When chewed and mixed with saliva, the internal pH of the gum changes from acidic to neutral or alkaline, turning it red. Therefore, a higher number of chews was associated with red colored gum, which indicated better mixing ability. This test principally evaluates the mixing ability of masticatory functions.

The study staff provided participants with detailed information on the chewing gum and explained the experimental protocol, instructing all participants to chew the gum as many times as possible in a 60-s period. They told participants to spit out the chewed gum into a piece of white tissue paper as soon as the measurement period was over and immediately compared it with the color chart on the packaging. If one of the study staff was unsure how to classify the color of the gum, they discussed it with other study staff before determining the color and assessing mixing ability. If the chewed gum contained more than one color (had not been thoroughly chewed), the study staff reduced the mixing ability score by 1 point. Mixing ability measured using color-changing chewing gum was graded in a range from 1 point (yellowish-green; the poorest mixing ability) to 5 points (red; the best mixing ability). Visual determination of chewing gum color was previously validated by comparison with chromaticity of colorimetry measurements [39].

2.4. Statistical Analysis

Given the small number of participants who scored 1 or 2 points, mixing ability measured using color-changing chewing gum was categorized into four groups: 5 points, *n* = 320; 4 points, *n* = 563; 3 points, *n* = 163; and 1 + 2 points, *n* = 60. Descriptive statistics representing continuous variables were expressed as mean (standard deviation), and groups were compared by analysis of variance (ANOVA). Categorical variables were expressed as counts and percentages, and between-group differences were assessed using the χ^2 test. Missing values for covariates were supplemented with values from five data sets created by multiple imputation to perform multivariate imputation by chained equation (MICE) [40]. All missing values were assumed to be missing at random.

The prevalence of frailty in the four color-changing chewing gum score groups was measured as a case count with corresponding percentages. To adjust for potential confounders, we used multivariate logistic analysis including a number of baseline covariates. Multivariate analysis was performed using the following three models: Model 1 was adjusted for age, sex, and geographical area. Model 2 comprised covariates from model 1 with the addition of variables considered related to frailty, including body mass index (BMI), family structure, economic status, number of medications prescribed, history of hypertension, cerebral stroke, heart disease and dyslipidemia, alcohol intake, smoking, and physical activity. These covariates were selected based on the literature [22,32–34]. Model 3 comprised variables from model 2 with the addition of oral health-related variables such as use of dentures and daily teeth brushing. The results of these analyses were expressed as odds ratios (ORs) and 95% confidence intervals (95% CIs), with the ORs calculated with reference to the group with the best mixing ability. Additionally, we also examined the relationship between the subdomains of the mJ-CHS criteria and the KCL and mixing ability in a similar manner.

A two-sided *p* value < 0.05 was considered significant. All analyses were conducted using JMP Pro for Windows (SAS Institute, Inc., Cary, NC, USA) or R software 3.4.3 (R Core Team, Vienna, Austria).

3. Results

Participants with the lowest color-changing chewing gum score (the worst mixing ability) were older and had a higher rate of denture use (Table 1). This group also had a lower mean BMI, included fewer alcohol drinkers and people who brushed their teeth daily, had lower mean grip strength, and slower mean gait speed.

Table 1. Baseline characteristics of the study participants according to the color-changing chewing gum score [a].

	Color-Changing Chewing Gum Score								*p*-Value
	5 (*n* = 320)		4 (*n* = 563)		3 (*n* = 163)		1 + 2 (*n* = 60)		
Age (years) [b]	72.2	(5.2)	73.2	(5.1)	75.1	(5.6)	76.7	(5.9)	**<0.001**
Women (*n* (%)) [c]	152	(47.5)	282	(50.1)	94	(57.7)	30	(50.0)	0.208
BMI (kg/m^2) [b]	23.4	(2.9)	22.8	(3.0)	22.8	(2.8)	22.2	(3.6)	**0.011**
Alcohol drinker (*n* (%)) [c]	237	(74.1)	386	(68.6)	107	(65.6)	34	(56.7)	**0.029**
Current smoker (*n* (%)) [c]	26	(8.1)	48	(8.5)	7	(4.3)	5	(8.3)	0.350
MVPA (*n* (%)) [c]	164	(51.3)	311	(55.2)	80	(49.1)	28	(46.7)	0.326
Grip strength (kg) [b]	29.1	(8.7)	27.7	(7.6)	25.5	(8.2)	24.0	(7.8)	**<0.001**
Gait speed (m/s) [b]	1.3	(0.2)	1.3	(0.2)	1.2	(0.2)	1.1	(0.2)	**<0.001**
Living alone (*n* (%)) [c]	34	(10.6)	49	(8.7)	22	(13.5)	7	(11.7)	0.317
HSE (*n* (%)) [c]	124	(38.8)	221	(39.3)	49	(30.1)	19	(31.7)	0.129
Education ≥13 y (*n* (%)) [c]	91	(28.4)	153	(27.2)	30	(18.4)	16	(26.7)	**0.049**
Denture use (*n* (%)) [c]	159	(49.7)	330	(58.6)	118	(72.4)	43	(71.7)	**<0.001**
Daily teeth brushing (*n* (%)) [c]	311	(97.2)	525	(93.3)	151	(92.6)	46	(76.7)	**<0.001**
No medication (*n* (%)) [c]	74	(23.1)	114	(20.3)	21	(12.9)	14	(23.3)	0.058
Hypertension (*n* (%)) [c]	130	(40.6)	238	(42.3)	68	(41.7)	15	(25.0)	0.080
Stroke (*n* (%)) [c]	6	(1.9)	17	(3.0)	5	(3.1)	5	(8.3)	0.063
Heart disease (*n* (%)) [c]	29	(9.1)	65	(11.6)	20	(12.3)	5	(8.3)	0.557
Diabetes (*n* (%)) [c]	26	(8.1)	62	(11.0)	14	(8.6)	5	(8.3)	0.498
Hyperlipidemia (*n* (%)) [c]	39	(12.2)	72	(12.8)	20	(12.3)	7	(11.7)	0.990

Abbreviations: BMI = body mass index; HSE = high socioeconomic status; MVPA = moderate to vigorous physical activity; [a] Bolded *p*-values were statistically significant (*p* < 0.05). Participants with missing data underwent multiple imputation: alcohol status (*n* = 7); smoking status (*n* = 12); physical activity (*n* = 66); family structure (*n* = 41); socioeconomic status (*n* = 37); education attainment (*n* = 82); denture use (*n* = 12); brush teeth everyday (*n* = 4); and medications (*n* = 48). [b] Continuous variables are presented as mean (standard deviation) and were examined using the analysis of variance (ANOVA). [c] Categorical variables are presented as counts (%) and were examined using the χ^2 test.

The prevalence of both physical and comprehensive frailty was higher in groups with lower color-changing chewing gum scores, where it was 11.8% and 27.9%, respectively (Table 2). After adjusting for confounders, the ORs of physical and comprehensive frailty comparing the highest to the lowest chewing gum scores groups were 3.64 (95% CI: 1.62 to 8.18; *p* for trend = 0.001) and 2.09 (95% CI: 1.09 to 4.03; *p* for trend = 0.009), respectively. Groups with lower color-changing chewing gum scores had a higher prevalence of slow gait speed, weakness, exhaustion, low activity, and weight loss (Table 3). Even after adjusting for confounding factors, groups with lower color-changing chewing gum scores had a higher prevalence of weakness (weak grip strength), although there was no association with other factors. In addition, we demonstrated that groups with lower color-changing chewing gum scores had higher prevalence of oral frailty and depression, evaluated using the KCL subdomains (Table 4).

Table 2. Multivariable adjusted odds ratios and 95% confidence intervals of the prevalence of physical and comprehensive frailty according to the color-changing chewing gum score [a].

	Color-Changing Chewing Gum Score				
	5 (n = 320)	4 (n = 563)	3 (n = 163)	1 + 2 (n = 60)	p for Trend [b]
Physical					
Case (n (%))	22 (6.9)	60 (10.7)	29 (17.8)	19 (31.7)	
Model 1 [c]	1.00 (Ref)	1.44 (0.85 to 2.44)	2.01 (1.08 to 3.73)	3.97 (1.90 to 8.29)	<0.001
Model 2 [d]	1.00 (Ref)	1.47 (0.85 to 2.55)	1.95 (1.02 to 3.72)	3.96 (1.79 to 8.74)	<0.001
Model 3 [e]	1.00 (Ref)	1.44 (0.83 to 2.51)	1.94 (1.01 to 3.74)	3.64 (1.62 to 8.18)	**0.001**
Comprehensive					
Case (n (%))	65 (20.3)	154 (27.4)	61 (37.4)	29 (48.3)	
Model 1 [c]	1.00 (Ref)	1.40 (1.00 to 1.98)	1.86 (1.19 to 2.89)	2.52 (1.37 to 4.61)	<0.001
Model 2 [d]	1.00 (Ref)	1.43 (1.00 to 2.06)	1.70 (1.07 to 2.70)	2.27 (1.19 to 4.33)	<0.001
Model 3 [e]	1.00 (Ref)	1.39 (0.97 to 2.01)	1.65 (1.03 to 2.64)	2.09 (1.09 to 4.03)	**0.009**

Abbreviation: [a] All values were counts (%) or relative odds ratio (95% confidence interval). All estimates are derived from multivariable logistic regression models. Fried phenotype model-based physical frailty is defined according to the Japanese version of the Cardiovascular Health Study criteria. The Kihon Checklist-based comprehensive frailty is defined as a score of 7 or above; [b] Linear trend *p*-values are calculated with the likelihood ratio test using ordinal variable (color-changing chewing gum score) values. Bolded *p*-values are statistically significant (*p* < 0.05); [c] Model 1 was adjusted for age (continuous), sex (woman or man), and population density (≥1000 or <1000 people/km²); [d] Model 2 included variables from model 1 as well as adjustment for BMI (continuous), physical activity (yes or no), smoking status (never smoker, past smoker, or current smoker), alcohol status (drinker or nondrinker), educational attainment (<9, 10–12, or ≥13 years), medications prescribed (continuous), living alone (yes or no), socioeconomic status (high or low), and history of disease (hypertension, diabetes, dyslipidemia, heart disease, and stroke; yes or no); [e] Model 3 included variables from model 2 plus adjustment for denture use (yes or no) and daily teeth brushing (yes or no).

Table 3. Multivariable adjusted odds ratios and 95% confidence intervals of the prevalence of each component of the modified Japanese versions of the Cardiovascular Health Study criteria according to the score of color-changing chewing gum [a].

	Color-Changing Chewing Gum Score				
	5 (n = 320)	4 (n = 563)	3 (n = 163)	1 + 2 (n = 60)	p for Trend [b]
Slow gait speed					
Case (n (%))	31 (9.7)	53 (9.4)	22 (13.5)	13 (21.7)	
Model 1 [c]	1.00 (Ref)	0.86 (0.53 to 1.41)	0.94 (0.50 to 1.76)	1.41 (0.64 to 3.07)	0.571
Model 2 [d]	1.00 (Ref)	0.84 (0.50 to 1.39)	0.88 (0.46 to 1.68)	1.23 (0.54 to 2.80)	0.846
Model 3 [e]	1.00 (Ref)	0.86 (0.52 to 1.44)	0.91 (0.47 to 1.76)	1.35 (0.58 to 3.14)	0.691

Table 3. *Cont.*

	Color-Changing Chewing Gum Score				
	5 (*n* = 320)	4 (*n* = 563)	3 (*n* = 163)	1 + 2 (*n* = 60)	*p* for Trend [b]
Weakness					
Case (*n* (%))	20 (6.3)	49 (8.7)	28 (17.2)	20 (33.3)	
Model 1 [c]	1.00 (Ref)	1.20 (0.68 to 2.11)	1.91 (1.00 to 3.64)	4.37 (2.04 to 9.38)	**<0.001**
Model 2 [d]	1.00 (Ref)	1.20 (0.66 to 2.16)	1.73 (0.88 to 3.38)	4.10 (1.82 to 9.27)	**<0.001**
Model 3 [e]	1.00 (Ref)	1.14 (0.63 to 2.07)	1.66 (0.84 to 3.30)	3.59 (1.57 to 8.21)	**0.002**
Exhaustion					
Case (*n* (%))	81 (25.2)	144 (25.6)	59 (36.0)	22 (36.7)	
Model 1 [c]	1.00 (Ref)	0.99 (0.72 to 2.41)	1.41 (0.92 to 2.16)	1.32 (0.72 to 1.37)	0.129
Model 2 [d]	1.00 (Ref)	0.96 (0.69 to 1.34)	1.31 (0.84 to 2.03)	1.14 (0.61 to 2.14)	0.327
Model 3 [e]	1.00 (Ref)	0.96 (0.69 to 1.35)	1.33 (0.85 to 2.08)	1.12 (0.59 to 2.12)	0.329
Low activity					
Case (*n* (%))	181 (56.4)	299 (53.1)	98 (59.8)	43 (71.7)	
Model 1 [c]	1.00 (Ref)	0.87 (0.65 to 1.15)	1.19 (0.80 to 1.77)	1.73 (0.93 to 3.22)	0.060
Model 2 [d]	1.00 (Ref)	0.85 (0.62 to 1.15)	1.21 (0.78 to 1.87)	1.64 (0.84 to 3.21)	0.180
Model 3 [e]	1.00 (Ref)	0.79 (0.58 to 1.08)	1.10 (0.70 to 1.70)	1.38 (0.70 to 2.72)	0.483
Weight loss					
Case (*n* (%))	38 (11.8)	87 (15.5)	28 (17.1)	15 (25.0)	
Model 1 [c]	1.00 (Ref)	1.30 (0.85 to 1.97)	1.41 (0.80 to 2.48)	1.98 (0.94 to 4.16)	0.127
Model 2 [d]	1.00 (Ref)	1.20 (0.78 to 1.84)	1.33 (0.75 to 2.37)	1.85 (0.85 to 3.99)	0.114
Model 3 [e]	1.00 (Ref)	1.20 (0.78 to 1.84)	1.34 (0.75 to 2.39)	1.82 (0.83 to 4.02)	0.128

Abbreviation: [a] All values were counts (%) or relative odds ratio (95% confidence interval). All estimates are derived from multivariable logistic regression models; [b] Linear trend *p*-values are calculated with the likelihood ratio test using ordinal variable (color-changing chewing gum score) values. Bolded *p*-values are statistically significant (*p* < 0.05); [c] Model 1 was adjusted for age (continuous), sex (woman or man), and population density (≥1000 or <1000 people/km²); [d] Model 2 included variables from model 1 as well as adjustment for BMI (continuous), physical activity (yes or no), smoking status (never smoker, past smoker, or current smoker), alcohol status (drinker or nondrinker), educational attainment (<9, 10–12, or ≥13 years), medications prescribed (continuous), living alone (yes or no), socioeconomic status (high or low), and history of disease (hypertension, diabetes, dyslipidemia, heart disease, and stroke; yes or no); [e] Model 3 included variables from model 2 plus adjustment for denture use (yes or no) and daily teeth brushing (yes or no).

Table 4. Multivariable adjusted odds ratios and 95% confidence intervals of the prevalence of each component of the KCL according to the score of color-changing chewing gum [a].

	Color-Changing Chewing Gum Score				
	5 (n = 320)	4 (n = 563)	3 (n = 163)	1 + 2 (n = 60)	p for Trend [b]
IADL disability					
Case (n (%))	8 (2.5)	34 (6.0)	7 (4.3)	4 (6.7)	
Model 1 [c]	1.00 (Ref)	2.22 (1.00 to 4.96)	0.94 (0.30 to 2.99)	1.30 (0.32 to 5.27)	0.986
Model 2 [d]	1.00 (Ref)	2.35 (1.02 to 5.40)	0.84 (0.25 to 2.82)	1.23 (0.28 to 5.49)	0.900
Model 3 [e]	1.00 (Ref)	2.35 (1.02 to 5.44)	0.84 (0.25 to 2.85)	1.25 (0.27 to 5.80)	0.898
Physical					
Case (n (%))	42 (13.1)	90 (16.0)	32 (19.5)	8 (13.3)	
Model 1 [c]	1.00 (Ref)	1.19 (0.78 to 1.81)	1.19 (0.69 to 2.05)	0.66 (0.28 to 1.57)	0.787
Model 2 [d]	1.00 (Ref)	1.20 (0.77 to 1.87)	1.15 (0.65 to 2.03)	0.63 (0.25 to 1.56)	0.711
Model 3 [e]	1.00 (Ref)	1.20 (0.77 to 1.87)	1.19 (0.67 to 2.11)	0.61 (0.24 to 1.55)	0.729
Nutrition					
Case (n (%))	2 (0.6)	13 (2.3)	2 (1.2)	4 (6.7)	
Model 1 [c]	1.00 (Ref)	3.85 (0.85 to 17.32)	1.71 (0.23 to 12.50)	6.03 (0.94 to 38.59)	0.174
Model 2 [d]	1.00 (Ref)	5.50 (0.94 to 32.29)	1.80 (0.19 to 17.56)	3.18 (0.35 to 28.61)	0.663
Model 3 [e]	1.00 (Ref)	6.72 (1.06 to 42.82)	2.94 (0.27 to 31.73)	4.06 (0.39 to 41.73)	0.486
Oral					
Case (n (%))	56 (17.5)	116 (20.6)	50 (30.5)	26 (43.3)	
Model 1 [c]	1.00 (Ref)	1.23 (0.85 to 1.76)	1.80 (1.13 to 2.86)	2.91 (1.59 to 5.35)	**<0.001**
Model 2 [d]	1.00 (Ref)	1.17 (0.81 to 1.71)	1.69 (1.05 to 2.72)	2.56 (1.36 to 4.82)	**0.001**
Model 3 [e]	1.00 (Ref)	1.09 (0.74 to 1.59)	1.47 (0.91 to 2.398)	2.20 (1.15 to 4.19)	**0.011**
Social					
Case (n (%))	11 (3.4)	28 (5.0)	15 (9.2)	5 (8.3)	
Model 1 [c]	1.00 (Ref)	1.37 (0.67 to 2.82)	2.19 (0.95 to 5.06)	1.80 (0.58 to 5.60)	0.094
Model 2 [d]	1.00 (Ref)	1.37 (0.65 to 2.88)	2.11 (0.88 to 5.03)	1.69 (0.52 to 5.51)	0.138
Model 3 [e]	1.00 (Ref)	1.32 (0.62 to 2.80)	2.02 (0.83 to 4.89)	1.51 (0.45 to 5.10)	0.202

Table 4. *Cont.*

	Color-Changing Chewing Gum Score				p for Trend [b]
	5 (n = 320)	4 (n = 563)	3 (n = 163)	1 + 2 (n = 60)	
Cognitive					
Case (n (%))	104 (32.4)	183 (32.5)	53 (32.3)	17 (28.3)	
Model 1 [c]	1.00 (Ref)	1.03 (0.76 to 1.38)	0.96 (0.63 to 1.46)	0.73 (0.39 to 1.36)	0.465
Model 2 [d]	1.00 (Ref)	1.01 (0.74 to 1.37)	0.89 (0.58 to 1.36)	0.66 (0.35 to 1.24)	0.252
Model 3 [e]	1.00 (Ref)	0.99 (0.72 to 1.34)	0.86 (0.56 to 1.33)	0.62 (0.32 to 1.18)	0.183
Depression					
Case (n (%))	66 (20.6)	123 (21.9)	52 (31.7)	22 (36.7)	
Model 1 [c]	1.00 (Ref)	1.07 (0.76 to 1.51)	1.57 (1.00 to 2.45)	1.69 (1.12 to 3.15)	**0.004**
Model 2 [d]	1.00 (Ref)	1.06 (0.74 to 1.51)	1.48 (0.93 to 2.35)	1.59 (1.05 to 2.90)	**0.019**
Model 3 [e]	1.00 (Ref)	1.02 (0.71 to 1.47)	1.45 (0.91 to 2.32)	1.58 (1.04 to 2.90)	**0.024**

Abbreviations: IADL = instrumental activities of daily living; KCL = Kihon Checklist; [a] All values were counts (%) or relative odds ratio (95% confidence interval). All estimates are derived from multivariable logistic regression models; [b] Linear trend *p*-values are calculated with the likelihood ratio test using ordinal variable (color-changing chewing gum score) values. Bolded *p*-values are statistically significant ($p < 0.05$); [c] Model 1 was adjusted for age (continuous), sex (woman or man), and population density (≥1000 or <1000 people/km^2); [d] Model 2 included variables from model 1 as well as adjustment for BMI (continuous), physical activity (yes or no), smoking status (never smoker, past smoker, or current smoker), alcohol status (drinker or nondrinker), educational attainment (<9, 10–12, or ≥13 years), medications prescribed (continuous), living alone (yes or no), socioeconomic status (high or low), and history of disease (hypertension, diabetes, dyslipidemia, heart disease, and stroke; yes or no); [e] Model 3 included variables from model 2 plus adjustment for denture use (yes or no) and daily teeth brushing (yes or no).

4. Discussion

In this study, we investigated the association between the mixing ability of masticatory functions and the prevalence of frailty in a population-based cohort of older adults. Even after adjusting for confounding factors, we found that mixing ability was associated with physical and comprehensive frailty. To our knowledge, this is the first study to demonstrate an association between measured mixing ability using color-changing chewing gum, the prevalence of physical and comprehensive frailty, and each domain of frailty. These findings suggest that objectively measured mixing ability may be an indicator associated with both physical and comprehensive frailty.

We evaluated physical frailty using the mJ-CHS criteria based on the proposed phenotype model by Fried et al. and comprehensive frailty using the KCL based on the proposed health deficit model by Rockwood et al. In this study, the prevalence of physical and comprehensive frailty was 11.8% and 27.9%, respectively. In a previous study, the reported prevalence of physical frailty assessed according to the J-CHS criteria in 16,251 community-dwelling older Japanese adults (mean age 75.1 years) was 11.2% [9]. We have previously reported that the prevalence of comprehensive frailty assessed according to the KCL (baseline survey) in a population of 13,294 older adults (mean age 74.5 years), from which our study group was drawn, was 30.8% for men and 33.3% for women [35]. There was thus no significant difference between physical and comprehensive frailty prevalence in our study population (mean age 73.4 years) and the populations investigated in larger studies. Accordingly, as our results reflect similar prevalence of frailty to that reported in previous studies, comparisons with these studies involve little bias and are therefore valid. In addition, we evaluated physical frailty according to the mJ-CHS criteria with one substitute question to evaluate low activity because we did not ask the participants the same question items as in the J-CHS criteria, but these differences do not seem to be a problem.

In this study, we also investigated the associations between mixing ability and physical and comprehensive frailty assessed using two different models. We found that objective mixing ability was associated with the prevalence of FP-model-based physical frailty, defined with parameters such as grip strength and gait speed. A decline in masticatory functions could be associated with physical performance because it limits food choices and reduces the enjoyment of eating, making it difficult to secure sufficient food intake to maintain physiological function and leading to malnutrition [16,17]. In a study of older adults, the mixing ability evaluated using color-changing chewing gum was associated with physical frailty [24] and sarcopenia [38], and these previous studies support our results. This suggests that mixing ability might be a surrogate marker reflecting the physical performance of older adults. Although further research is needed to understand underlying mechanisms and to establish the causal relationships on associations between mixing ability and frailty, markers of poor oral health could be useful indicators of frailty and valuable additions to health-screening assessments used in older people [27].

In addition, our results showed that, even after adjustment for oral health-related variables, e.g., denture use and daily teeth brushing, objectively measured mixing ability was associated with the prevalence of physical frailty as well as multifaceted comprehensive frailty, including in psychological, cognitive, social, and other domains. Previous prospective [28] and cross-sectional studies [29] have reported that a lower mixing ability is associated with comprehensive frailty, and these previous studies support our results. However, those previous studies have focused only on comprehensive frailty, and the association of mixing ability with the subdomains of assessment tool for frailty has not been well evaluated. Previous studies have reported that a lower masticatory ability is associated with higher depression and anxiety scores [17,41]. Our results indicate that the prevalence of depression defined using the KCL subdomain was higher in lower mixing ability individuals, and these previous studies support our results. Previous studies comparing comprehensive frailty with physical frailty have found that comprehensive frailty is a more accurate predictor of the risk of death [11,12]. This is because the index of comprehensive frailty is suggested to exhibit a positive linear correlation with age, reflecting biological aging [42]. Nevertheless, physical frailty is reportedly associated with increased

risk of death and disability [43]. These findings suggest that assessing frailty in terms of multiple aspects may enable more accurate identification of high-risk groups. Our results suggest that measured mixing ability, using color-changing chewing gum, may be a useful tool for identifying groups at high risk of death or disability due to frailty.

One of the strengths of this study was that prevalence of frailty was assessed using two different validated methods based on established models of frailty [5–7]. Because we were able to investigate the association between objective mixing ability and the prevalence of frailty in a larger cohort of community-dwelling older adults compared with those of previous studies [24,29], our results may also be more widely generalizable.

However, this study has several methodological limitations. First, this was a cross-sectional study. Poor oral health is associated with numerous chronic diseases in addition to frailty, and oral diseases, such as periodontitis and tooth loss, are associated with social factors and lifestyle habits [44]. This means that neither a temporal nor a direct causal relationship can be inferred as underlying our observed association between mixing ability of masticatory functions and the prevalence of frailty. Second, although we selected our study participants from among Kameoka City residents by cluster random sampling, only 28.5% underwent a physical checkup examination. These participants may thus have been more health-aware than the general population of older adults, opening our study to the possibility of selection bias. Third, our study included participants with a history of diabetes, dyslipidemia, heart disease, and stroke. These limitations may interfere with the generalization of the results. However, our results were similar after excluding participants with these diseases. Finally, systematic error because of self-reporting could not be completely excluded from the results. Self-reported data in areas such as education, income, smoking, and medical history may thus have been affected by recall bias. In addition, although previous study has reported the reliability and validity of a quantitative color scale to evaluate mixing ability using color-changing chewing gum [39], we could not evaluate the inter-rater variability. The chewing gum color may be influenced by both masticatory performance and saliva amount. Although we took numerous implicit confounding factors into account, bias because of unmeasured confounding factors associated with masticatory performance and saliva amount could not be completely eliminated. However, as we did use multivariate analysis to adjust our results for known associated factors such as social and economic status, we were able to minimize the effect of confounders. Our results thus suggested that color-changing chewing gum might be an indicator associated with both physical and comprehensive frailty.

Considering the increasing interest in identifying frailty older people, color-changing chewing gum has an objective, easy, and solid methodology to evaluate simultaneously physical and comprehensive frailty suitable for the assessment of frailty, although the definition of frailty varies between studies [30]. If a self-administered questionnaire is used to assess physical and comprehensive frailty, participants may need be asked to answer the many questions contained in the questionnaires. Moreover, the questionnaire may be affected by self-reporting bias and cognitive function. Therefore, color-changing chewing gum can be used for the objective measurement of mixing ability without the need for specialist technology or skill and may thus be a useful early indicator of frailty in older adults.

5. Conclusions

The mixing ability of older adults as objectively measured using color-changing chewing gum was associated with the prevalence of both physical and comprehensive frailty. Given the rapidly increasing prevalence of frailty worldwide, its early discovery is important both for enabling people to stay healthy in old age and for limiting the burden of healthcare-related costs. Color-changing chewing gum may be useful indicators associated with both physical and comprehensive frailty in clinical practice and public health research.

Author Contributions: Conceptualization, D.W., T.Y., Y.Y., and M.K.; methodology, D.W., T.Y., Y.Y., and M.K.; software, D.W. and T.Y.; validation, T.Y., Y.W., and Y.Y.; formal analysis, D.W. and T.Y.; investigation, T.Y., K.Y., Y.Y., Y.W., T.K., M.Y., Y.Y., and M.K.; resources, Y.Y. and M.K.; writing—original draft preparation, D.W. and

References

1. Hoogendijk, E.O.; Afilalo, J.; Ensrud, K.E.; Kowal, P.; Onder, G.; Fried, L.P. Frailty: Implications for clinical practice and public health. *Lancet* **2019**, *394*, 1365–1375. [CrossRef]

2. Clegg, A.; Young, J.; Iliffe, S.; Rikkert, M.O.; Rockwood, K. Frailty in elderly people. *Lancet* **2013**, *381*, 752–762. [CrossRef]

3. Morley, J.E.; Vellas, B.; van Kan, G.A.; Anker, S.D.; Bauer, J.M.; Bernabei, R.; Cesari, M.; Chumlea, W.C.; Doehner, W.; Evans, J.; et al. Frailty consensus: A call to action. *J. Am. Med. Dir. Assoc.* **2013**, *14*, 392–397. [CrossRef] [PubMed]

4. Ambagtsheer, R.C.; Visvanathan, R.; Dent, E.; Yu, S.; Schultz, T.J.; Beilby, J.M.D. Commonly used screening instruments to identify frailty among community-dwelling older people in a general practice (primary care) setting: A study of diagnostic test accuracy. *J. Gerontol. A. Biol. Sci. Med. Sci.* **2020**, *75*, 1134–1142. [CrossRef]

5. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, 146–156. [CrossRef]

6. Rockwood, K.; Mitnitski, A. Frailty in relation to the accumulation of deficits. *J. Gerontol. A Biol. Sci. Med. Sci.* **2007**, *62*, 722–727. [CrossRef]

7. Mitnitski, A.B.; Mogilner, A.J.; Rockwood, K. Accumulation of deficits as a proxy measure of aging. *Sci. World J.* **2001**, *1*, 323–336. [CrossRef]

8. Satake, S.; Shimokata, H.; Senda, K.; Kondo, I.; Toba, K. Validity of Total Kihon Checklist Score for Predicting the Incidence of 3-Year Dependency and Mortality in a Community-Dwelling Older Population. *J. Am. Med. Dir. Assoc.* **2017**, *18*, 551–556. [CrossRef]

9. Satake, S.; Shimada, H.; Yamada, M.; Kim, H.; Yoshida, H.; Gondo, Y.; Matsubayashi, K.; Matsushita, E.; Kuzuya, M.; Kozaki, K.; et al. Prevalence of frailty among community-dwellers and outpatients in Japan as defined by the Japanese version of the Cardiovascular Health Study criteria. *Geriatr. Gerontol. Int.* **2017**, *17*, 2629–2634. [CrossRef]

10. Satake, S.; Senda, K.; Hong, Y.J.; Miura, H.; Endo, H.; Sakurai, T.; Kondo, I.; Toba, K. Validity of the Kihon Checklist for assessing frailty status. *Geriatr. Gerontol. Int.* **2016**, *16*, 709–715. [CrossRef]

11. Rockwood, K.; Andrew, M.; Mitnitski, A. A comparison of two approaches to measuring frailty in elderly people. *J. Gerontol. A Biol. Sci. Med. Sci.* **2007**, *62*, 738–743. [CrossRef] [PubMed]

12. Kulminski, A.M.; Ukraintseva, S.V.; Kulminskaya, I.V.; Arbeev, K.G.; Land, K.; Yashin, A.I. Cumulative deficits better characterize susceptibility to death in elderly people than phenotypic frailty: Lessons from the Cardiovascular Health Study. *J. Am. Geriatr. Soc.* **2008**, *56*, 898–903. [CrossRef] [PubMed]

13. Roppolo, M.; Mulasso, A.; Gobbens, R.J.; Mosso, C.O.; Rabaglietti, E. A comparison between uni- and multidimensional frailty measures: Prevalence, functional status, and relationships with disability. *Clin. Interv. Aging* **2015**, *10*, 1669–1678. [CrossRef] [PubMed]

14. O'Donovan, M.R.; Sezgin, D.; Liew, A.; O'Caoimh, R. Burden of disease, disability-adjusted life years and frailty prevalence. *QJM* **2019**, *112*, 261–267. [CrossRef] [PubMed]

15. Petersen, P.E.; Yamamoto, T. Improving the oral health of older people: The approach of the WHO Global Oral Health Programme. *Community Dent. Oral Epidemiol.* **2005**, *33*, 81–92. [CrossRef]

16. Ritchie, C.S.; Joshipura, K.; Hung, H.C.; Douglass, C.W. Nutrition as a mediator in the relation between oral and systemic disease: Associations between specific measures of adult oral health and nutrition outcomes. *Crit. Rev. Oral Biol. Med.* **2002**, *13*, 291–300. [CrossRef]

17. Okada, K.; Enoki, H.; Izawa, S.; Iguchi, A.; Kuzuya, M. Association between masticatory performance and anthropometric measurements and nutritional status in the elderly. *Geriatr. Gerontol. Int.* **2010**, *10*, 56–63. [CrossRef]

18. de Andrade, F.B.; Lebrao, M.L.; Santos, J.L.; Duarte, Y.A. Relationship between oral health and frailty in community-dwelling elderly individuals in Brazil. *J. Am. Geriatr. Soc.* **2013**, *61*, 809–814. [CrossRef]

19. Castrejon-Perez, R.C.; Jimenez-Corona, A.; Bernabe, E.; Villa-Romero, A.R.; Arrive, E.; Dartigues, J.F.; Gutierrez-Robledo, L.M.; Borges-Yanez, S.A. Oral Disease and 3-Year Incidence of Frailty in Mexican Older Adults. *J. Gerontol. A Biol. Sci. Med. Sci.* **2017**, *72*, 951–957. [CrossRef]

20. Kamdem, B.; Seematter-Bagnoud, L.; Botrugno, F.; Santos-Eggimann, B. Relationship between oral health and Fried's frailty criteria in community-dwelling older persons. *BMC Geriatr.* **2017**, *17*, 174. [CrossRef]

21. Takata, Y.; Ansai, T.; Awano, S.; Hamasaki, T.; Yoshitake, Y.; Kimura, Y.; Sonoki, K.; Wakisaka, M.; Fukuhara, M.; Takehara, T. Relationship of physical fitness to chewing in an 80-year-old population. *Oral Dis.* **2004**, *10*, 44–49. [CrossRef] [PubMed]

22. Nakanishi, N.; Fukuda, H.; Takatorige, T.; Tatara, K. Relationship between self-assessed masticatory disability and 9-year mortality in a cohort of community-residing elderly people. *J. Am. Geriatr. Soc.* **2005**, *53*, 54–58. [CrossRef] [PubMed]

23. Shimazaki, Y.; Soh, I.; Saito, T.; Yamashita, Y.; Koga, T.; Miyazaki, H.; Takehara, T. Influence of dentition status on physical disability, mental impairment, and mortality in institutionalized elderly people. *J. Dent. Res.* **2001**, *80*, 340–345. [CrossRef] [PubMed]

24. Iwasaki, M.; Kimura, Y.; Sasiwongsaroj, K.; Kettratad-Pruksapong, M.; Suksudaj, S.; Ishimoto, Y.; Chang, N.Y.; Sakamoto, R.; Matsubayashi, K.; Songpaisan, Y.; et al. Association between objectively measured chewing ability and frailty: A cross-sectional study in central Thailand. *Geriatr. Gerontol. Int.* **2018**, *18*, 860–866. [CrossRef] [PubMed]

25. Komagamine, Y.; Kanazawa, M.; Yamada, A.; Minakuchi, S. Association between tongue and lip motor functions and mixing ability in complete denture wearers. *Aging Clin. Exp. Res.* **2019**, *31*, 1243–1248. [CrossRef]

26. Hama, Y.; Kanazawa, M.; Minakuchi, S.; Uchida, T.; Sasaki, Y. Properties of a color-changeable chewing gum used to evaluate masticatory performance. *J. Prosthodont. Res.* **2014**, *58*, 102–106. [CrossRef]

27. Ramsay, S.E.; Papachristou, E.; Watt, R.G.; Tsakos, G.; Lennon, L.T.; Papacosta, A.O.; Moynihan, P.; Sayer, A.A.; Whincup, P.H.; Wannamethee, S.G. Influence of Poor Oral Health on Physical Frailty: A Population-Based Cohort Study of Older British Men. *J. Am. Geriatr. Soc.* **2018**, *66*, 473–479. [CrossRef]

28. Horibe, Y.; Ueda, T.; Watanabe, Y.; Motokawa, K.; Edahiro, A.; Hirano, H.; Shirobe, M.; Ogami, K.; Kawai, H.; Obuchi, S.; et al. A 2-year longitudinal study of the relationship between masticatory function and progression to frailty or pre-frailty among community-dwelling Japanese aged 65 and older. *J. Oral Rehabil.* **2018**, *45*, 864–870. [CrossRef]

29. Horibe, Y.; Watanabe, Y.; Hirano, H.; Edahiro, A.; Ishizaki, K.; Ueda, T.; Sakurai, K. Relationship between masticatory function and frailty in community-dwelling Japanese elderly. *Aging Clin. Exp. Res.* **2018**, *30*, 1093–1099. [CrossRef]

30. Dent, E.; Lien, C.; Lim, W.S.; Wong, W.C.; Wong, C.H.; Ng, T.P.; Woo, J.; Dong, B.; de la Vega, S.; Hua Poi, P.J.; et al. The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty. *J. Am. Med. Dir. Assoc.* **2017**, *18*, 564–575. [CrossRef]

31. Watanabe, Y.; Yamada, Y.; Yoshida, T.; Yokoyama, K.; Miyake, M.; Yamagata, E.; Yamada, M.; Yoshinaka, Y.; Kimura, M.; Kyoto-Kameoka Study Group. Comprehensive geriatric intervention in community-dwelling older adults: A cluster-randomized controlled trial. *J. Cachexia Sarcopenia Muscle* **2020**, *11*, 26–37. [CrossRef] [PubMed]

32. Watanabe, D.; Yoshida, T.; Watanabe, Y.; Yamada, Y.; Kimura, M. Objectively measured daily step counts and prevalence of frailty in 3616 older adults. *J. Am. Geriatr. Soc.* **2020**. [CrossRef]

33. Watanabe, D.; Yoshida, T.; Nanri, H.; Watanabe, Y.; Date, H.; Itoi, A.; Goto, C.; Goto, C.; Ishikawa-Takata, K.; Sagayama, H.; et al. Association between the prevalence of frailty and doubly labeled water-calibrated energy intake among community-dwelling older adults. *J. Gerontol. A. Biol. Sci. Med. Sci.* **2020**, glaa133. [CrossRef] [PubMed]

34. Watanabe, D.; Yoshida, T.; Watanabe, Y.; Yamada, Y.; Kimura, M.; Kyoto-Kameoka Study, G. A U-Shaped Relationship Between the Prevalence of Frailty and Body Mass Index in Community-Dwelling Japanese Older Adults: The Kyoto-Kameoka Study. *J. Clin. Med.* **2020**, *9*. [CrossRef]

35. Yamada, Y.; Nanri, H.; Watanabe, Y.; Yoshida, T.; Yokoyama, K.; Itoi, A.; Date, H.; Yamaguchi, M.; Miyake, M.; Yamagata, E.; et al. Prevalence of Frailty Assessed by Fried and Kihon Checklist Indexes in a Prospective Cohort Study: Design and Demographics of the Kyoto-Kameoka Longitudinal Study. *J. Am. Med. Dir. Assoc.* **2017**, *18*, e733–e737. [CrossRef]

36. Makizako, H.; Shimada, H.; Doi, T.; Tsutsumimoto, K.; Suzuki, T. Impact of physical frailty on disability in community-dwelling older adults: A prospective cohort study. *BMJ Open* **2015**, *5*, e008462. [CrossRef]

37. Sewo Sampaio, P.Y.; Sampaio, R.A.; Yamada, M.; Ogita, M.; Arai, H. Validation and translation of the Kihon Checklist (frailty index) into Brazilian Portuguese. *Geriatr. Gerontol. Int.* **2014**, *14*, 561–569. [CrossRef]

38. Murakami, M.; Hirano, H.; Watanabe, Y.; Sakai, K.; Kim, H.; Katakura, A. Relationship between chewing ability and sarcopenia in Japanese community-dwelling older adults. *Geriatr. Gerontol. Int.* **2015**, *15*, 1007–1012. [CrossRef]

39. Hama, Y.; Kanazawa, M.; Minakuchi, S.; Uchida, T.; Sasaki, Y. Reliability and validity of a quantitative color scale to evaluate masticatory performance using color-changeable chewing gum. *J. Med. Dent. Sci.* **2014**, *61*, 1–6.

40. van Buuren, S.; Groothuis-Oudshoorn, K. Multivariate Imputation by Chained Equations in R. *J. Stat. Softw* **2011**, *45*, 1–67. [CrossRef]

41. Roohafza, H.; Afshar, H.; Keshteli, A.H.; Shirani, M.J.; Afghari, P.; Vali, A.; Adibi, P. Masticatory ability with depression, anxiety, and stress: Does there exist any association? *Dent. Res. J. (Isfahan)* **2016**, *13*, 211–216. [CrossRef]

42. Rockwood, K.; Rockwood, M.R.; Mitnitski, A. Physiological redundancy in older adults in relation to the change with age in the slope of a frailty index. *J. Am. Geriatr. Soc.* **2010**, *58*, 318–323. [CrossRef] [PubMed]

43. Ensrud, K.E.; Ewing, S.K.; Taylor, B.C.; Fink, H.A.; Cawthon, P.M.; Stone, K.L.; Hillier, T.A.; Cauley, J.A.; Hochberg, M.C.; Rodondi, N.; et al. Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women. *Arch. Intern. Med.* **2008**, *168*, 382–389. [CrossRef] [PubMed]

44. Petersen, P.E.; Kandelman, D.; Arpin, S.; Ogawa, H. Global oral health of older people–call for public health action. *Community Dent. Health* **2010**, *27*, 257–267. [PubMed]

Article

Spousal Concordance of Physical Frailty in Older Korean Couples

Suah Kang [1], Miji Kim [2],* and Chang Won Won [3],*

[1]   Department of Medicine, College of Medicine, Kyung Hee University, Seoul 02447, Korea;
     skang39@khu.ac.kr
[2]   Department of Biomedical Science and Technology, College of Medicine, East-West Medical Research
     Institute, Kyung Hee University, Seoul 02447, Korea
[3]   Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee
     University, Seoul 02447, Korea
*   Correspondence: mijiak@khu.ac.kr (M.K.); chunwon62@naver.com (C.W.W.); Tel.: +82-2-958-2840 (M.K.);
     +82-2-958-8700 (C.W.W.); Fax: +82-2-958-2836 (M.K.); +82-2-958-8699 (C.W.W.)

Abstract: Marital status is an important risk factor for physical frailty. However, there are limited data on spousal concordance of physical frailty among married couples. Here, we evaluate the spousal concordance of frailty as defined by the Fried frailty phenotype and specific phenotype components that contribute to this association. Data on 315 married couples (630 individuals) aged between 70 and 84 years were obtained from the Korean Frailty and Aging Cohort Study (KFACS). Multivariate logistic regressions were used for the analysis. After adjusting for covariates (age, body mass index, education, house ownership, comorbidity, cognition, depressive symptoms, cohabitation with adult children for both partners), a husband's frailty was positively associated with his wife's frailty (odds ratio (OR) 3.34, 95% confidence interval (CI) 1.04–10.73, $p < 0.05$), and a wife's frailty was significantly associated with her husband's frailty (OR 4.62, 95% CI 1.31–16.33, $p < 0.05$), indicating a greater effect of the frailty status of the spouse among women than among men. Among the five components of the Fried frailty phenotype, weight loss, slowness, and exhaustion were the main contributing factors to the spousal association for frailty. In conclusion, having a frail spouse is a strong and independent risk factor for frailty among community-living older adults.

Keywords: frailty; spousal concordance; aging

1. Introduction

The aged population is growing rapidly. By 2050, the proportion of the population over 60 years old will almost double from 12% to 22%, reaching up to 434 million worldwide [1]. Frailty has become an area of interest for those concerned with healthy aging [2,3]. Frailty is a state of functional decline and increased vulnerability, commonly defined by the Fried phenotype model and the frailty index [4–6]. The Fried phenotype model is a physical frailty criterion, and the frailty index is a cumulative health deficits index including physical, psychological, mental, and social functions [4,6]. In community-dwelling adults aged ≥65 years, the estimated prevalence of frailty is around 10%, and the incidence may increase with age [7,8]. Frailty may have a high health care burden since it is associated with increased morbidity and mortality in the elderly [9,10].

Frailty is associated with sociodemographic, physical, biological, lifestyle, and psychological risk factors [11]. A recent study identified marital status as an important risk factor for physical frailty [12]. Most caregivers of frail older adults are their spouses [13–15]. Spousal caregivers experience reduced quality of life because of their restricted participation in daily activities [16]. There are negative impacts on the physical and mental health of spousal caregivers [17]. Furthermore, in a case–control study,

frailty status worsened in one-third of the spousal caregivers of older patients with cognitive and functional impairment [18]. However, limited studies have examined the spousal correlation of frailty among community-living older adults. One study found a positive correlation between an individual's frailty and the spouse's frailty [19]. However, the study failed to control for the major risk factors for frailty, including comorbid conditions, cognitive impairment, and depression. It is unclear to what extent having a frail spouse contributes to one's frailty status after adjusting for these risk factors. In this study, we evaluated the spousal concordance of frailty among older adults and determined the specific frailty phenotype components that contribute to this association.

2. Materials and Methods

2.1. Participants

Data were mainly derived from the Korean Frailty and Aging Cohort Study (KFACS) 2016 and 2017 baseline database. The KFACS is a 2-year, nationwide, multicenter, prospective cohort study to identify risk factors and outcomes of frailty and develop interventions for prevention and management. The KFACS recruited 3014 community-living elderly individuals aged between 70 and 84 years in 2016 and 2017. The participants were recruited from 10 study centers across different regions and different residential locations (urban, suburban, and rural) [20]. Each center recruited participants using quota sampling stratified by age (70–74, 75–79, and 80–84 years with a ratio of 6:5:4) and sex (male and female with same ratio) [20]. Participants were recruited from diverse settings (local senior welfare centers, community health centers, apartments, housing complexes, and outpatient clinics) to minimize selection bias [20]. The inclusion criteria for KFACS participants were as follows: aged 70–84 years, currently living in the community, having no plans to move out in the next 2 years, and having no problems with communication and no prior dementia diagnosis [20]. In this case, "move out" refers to relocating to areas outside the three neighboring towns [20]. Exclusion criteria included individuals with difficulty in giving opinion, those unable to comply with the study requirements, or those deemed inappropriate on the basis of the findings or evaluation by the researcher. The detailed study design has been published previously [20]. Spousal pairs were identified by marital status, cohabitation status, and home address. Subjects were considered spouses if both male and female adults reported being married, currently lived with their spouse, and had the same home address. A total of 333 samples of married couples were confirmed to be eligible for the present study. The final analysis included 315 married couples, after excluding 18 with missing data, for assessing the Fried physical frailty phenotype. The Clinical Research Ethics Committee of the Kyung Hee University Hospital approved the KFACS protocol (institutional review board (IRB) number 2015-12-103). The present study was exempt from the requirement for IRB approval by the Clinical Research Ethics Committee of the Kyung Hee University Medical Center (IRB number: 2020-05-066).

2.2. Frailty Assessment

The primary outcome of this study was the frailty status. Frailty was defined by the Fried frailty phenotype. The Fried frailty phenotype comprises five criteria, namely weight loss, weakness, exhaustion, slowness, and low physical activity [4]. Those satisfying ≥3 components were considered frail. Weight loss was defined as an unintentional weight loss of ≥10 pounds. Weakness was defined as a baseline grip strength in the lower 20%, adjusted for sex and body mass index (BMI) in the KFACS population distribution. Exhaustion was assessed by the responses to two statements from the Center for Epidemiologic Studies Depression Scale: (1)" I felt that everything I did was an effort", and (2) "I could not get going". Slowness was defined as the slowest 20% at baseline on the basis of the 4-m usual gait speed, adjusted for sex and height in the KFACS population distribution. Low physical activity was defined as the lower 20% of sex-specific kcals per week, calculated on the basis of the International Physical Activity Questionnaire in a general Korean population-based survey of older adults [21].

2.3. Covariates

Age, BMI, education, house ownership, comorbidity, cognition, depressive symptoms, and cohabitation with adult children of both husband and wife were used as covariates in this study. Data on demographics, including age, BMI, education, house ownership, and cohabitation with adult children were self-reported. Comorbidity was defined as having ≥2 comorbid conditions. Cognitive impairment was assessed using the Mini-Mental State Examination (MMSE). Depressive symptoms were assessed using the short version of the Geriatric Depression Scale. Nutritional status was determined using the Korean version of the short form of the Mini Nutritional Assessment (MNA-SF).

2.4. Statistical Analysis

All analyses were conducted using SPSS (ver. 25.0; IBM Corp., Armonk, NY, USA). A comparison of characteristics by sex was performed using the chi-squared test for categorical variables and the independent *t*-test for continuous variables. The spousal association of frailty and the five components of the Fried frailty phenotype were analyzed using multivariate logistic regression models and described by odds ratios (ORs) with 95% confidence intervals (CIs). Four models were considered in addition to the unadjusted model: (1) adjusted for age; (2) additionally adjusted for BMI, education, house ownership, comorbidity, and cognition; (3) additionally adjusted for depressive symptoms; and (4) additionally adjusted for cohabitation with adult children of both partners in all analyses. A two-sided $p < 0.05$ was considered statistically significant.

3. Results

The demographic and health characteristics of the study population (630 subjects, or 315 married couples) are listed in Table 1. The mean ages of husbands and wives were 77.6 ± 3.4 and 74.7 ± 3.6 years, respectively. Husbands had a lower mean BMI (23.7 ± 3.0 kg/m^2) and higher education status (77.1%) than wives. Wives were more likely to have house ownership (31.1%). There was no significant difference in the current employment status. Wives had higher prevalence of cognitive impairment (24.1%), comorbidities (61.2%), and depressive symptoms (23.5%) than husbands. In addition, the demographic and health characteristics of the frail and nonfrail groups of study participants are presented in Appendix A.

Table 2 shows the frailty status determined by the Fried frailty phenotype and its five components by sex. Subjects classified as robust or prefrail in the Fried frailty phenotype were considered nonfrail. Frailty was more prevalent among husbands than wives; 35 (11.1%) husbands and 28 (8.9%) wives were classified as frail. The percentages of all five components except exhaustion were higher in husbands.

Tables 3 and 4 summarize the multivariate logistic regression models examining the spousal association of frailty and for the five components of the Fried frailty phenotype. The wife's frailty was significantly associated with the frailty of her husband in all models (OR 3.13–4.76, $p < 0.05$). Similarly, the husband's frailty was positively associated with the frailty of his wife in all models (OR 2.91–4.76, $p < 0.05$) except model 3 (OR 3.19, 95% CI 1.00–10.22, $p = 0.05$). After adjusting for possible covariates, a frail husband had 4.62 odds of having a frail wife, and a frail wife had 3.34 odds of having a frail husband (model 4). While adjusting for other covariates reduced the odds ratio, adjusting for depressive symptoms (model 3) and cohabitation with adult children (model 4) increased the odds ratio.

Among the five components of the Fried frailty phenotype, there was an association between the husband and wife in regard to weight loss, exhaustion, and slowness. Weight loss in one spouse was significantly associated with the increased risk of weight loss in the partner in all models (husband, OR 6.89–8.56, $p < 0.01$; wife, OR 4.91–6.95, $p < 0.05$). After adjusting for covariates, wives with weight loss had 8.34 odds of having a husband with weight loss ($p < 0.01$). A husband with weight loss had 4.91 odds of having a wife with weight loss ($p < 0.01$). Exhaustion in one spouse was also associated with greater risk of exhaustion in the partner in all models (husband, OR 2.00–2.23, $p < 0.05$; wife,

OR 1.94–2.23, *p* < 0.05). Slowness in one spouse was associated with higher odds of slowness in the partner in all models (husband, OR 2.50–2.82, *p* < 0.05; wife, OR 2.52–2.82, *p* < 0.05) except model 2 (husband, OR 1.87, 95% CI 0.95–2.51; wife, OR 1.88, 95% CI 0.95–3.72). There was no significant association between spouses for low activity and muscle weakness.

Table 1. Demographic and health characteristics of study participants.

Variables	Husband (*n* = 315)	Wife (*n* = 315)	*p*-Value
Demographics			
Age, mean (SD), year	77.6 (3.4)	74.7 (3.6)	<0.001
BMI, mean (SD), kg/m^2	23.7 (3.0)	24.7 (2.8)	<0.001
Education, *n* (%)			
Less than 7 years	72 (22.9)	168 (53.3)	<0.001
Residence, *n* * (%)			
Urban	80 (25.6)	80 (25.6)	1.000
Suburban	148 (47.4)	148 (47.4)	
Rural	84 (26.9)	84 (26.9)	
House ownership, *n* (%)	30 (9.5)	98 (31.1)	<0.001
Currently employed, *n* * (%)	81 (25.8)	68 (21.7)	0.223
Living with adult children, *n* * (%)	64 (20.6)	64 (20.6)	
Health Characteristics			
Cognitive Impairment			
MMSE score <24	46 (14.6)	76 (24.1)	0.002
Health Behavior			
Current smoker, *n* (%)	33 (10.5)	0 (0.0)	<0.001
Heavy drinking, *n* (%)	106 (33.7)	10 (3.0)	<0.001
Comorbid Conditions			
Number of comorbid conditions, mean (SD)	1.46 (1.24)	1.99 (1.36)	<0.001
Comorbidity, *n* (%)	141 (42.7)	202 (61.2)	<0.001
Hypertension, *n* (%)	174 (55.2)	174 (55.2)	1.000
Diabetes mellitus, *n* (%)	77 (24.4)	69 (21.9)	0.450
Mental Health			
Depressive symptom (GDS score ≥6), yes, *n* (%)	49 (15.6)	74 (23.5)	0.012
Physical Activity			
Moderate/vigorous activity, none, *n* (%)	107 (34.0)	116 (36.8)	0.453
Social Activity			
Religious meeting, none, *n* * (%)	155 (49.4)	93 (29.6)	<0.001
Social meeting, none, *n* (%)	72 (22.9)	108 (34.3)	0.001
Possible Malnutrition			
MNA score ≤11, *n* * (%)	30 (9.6)	19 (6.1)	0.102
Self-perceived health, poor, *n* (%)	81 (25.7)	119 (37.8)	0.001

Notes: Comorbidity: ≥2 comorbid conditions; BMI = body mass index; GDS = Geriatric Depression Scale; MMSE = Mini-Mental State Examination; MNA = Mini Nutritional Assessment. Chi-squared test for categorical variables and independent *t*-test for continuous variables. *n* * indicates missing data.

Table 2. Proportion of Fried frailty phenotype by sex.

Variable	Husband (*n* = 315)	Wife (*n* = 315)	Both (*n* = 315 Pairs)	*p*-Value
	Total, *n* (%)	Total, *n* (%)	Total, *n* (%)	
Fried Frailty Phenotype				
Frail	35 (11.1)	28 (8.9)	9 (2.9)	0.353
Five Components of Frailty Phenotype				
Weight loss	22 (7.0)	17 (5.4)	5 (1.6)	0.408
Exhaustion	77 (24.4)	133 (42.2)	44 (14.0)	<0.001
Low activity	42 (13.3)	25 (7.9)	6 (1.9)	0.028
Weakness	74 (23.5)	56 (17.8)	17 (5.4)	0.076
Slowness	79 (25.0)	53 (16.8)	23 (7.3)	0.011

Notes: *p*-values were determined using the chi-squared test for categorical variables.

Table 3. Husband's odds of frailty when the wife is frail in 315 married couples.

Frailty of Wife	Frailty of Husband (n = 315)				
	Unadjusted	Model 1	Model 2	Model 3	Model 4
			OR (95% CI)		
Frailty of Wife					
Frail wife	4.76 (1.95–11.58) ***	3.86 (1.50–9.92) **	2.91 (1.04–8.16) *	3.19 (1.00–10.22)	3.34 (1.04–10.73) *
Five Components of Frailty Phenotype among Wives					
Weight loss	6.89 (2.18–21.80) ***	6.95 (2.10–23.02) ***	6.87 (1.71–27.64) **	5.03 (1.14–22.23) *	4.91 (1.10–21.97) *
Exhaustion	2.23 (1.32–3.76) ***	2.18 (1.28–3.70) ***	1.94 (1.10–3.42) *	2.09 (1.09–3.98) *	2.14 (1.11–4.101) *
Low activity	2.23 (0.83–5.95)	1.66 (0.60–4.62)	1.85 (0.59–5.78)	2.00 (0.60–6.63)	2.12 (0.63–7.08)
Weakness	1.54 (0.81–2.93)	1.30 (0.67–2.52)	1.05 (0.51–2.15)	1.04 (0.50–2.18)	1.02 (0.49–2.13)
Slowness	2.82 (1.52–5.23) ***	1.88 (0.95–3.72)	2.55 (1.17–5.59) *	2.58 (1.16–5.70) *	2.75 (1.23–6.14) *

Notes: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$. BMI = body mass index; CI = confidence interval; OR = odds ratio. Model 1 was adjusted for age; model 2 was adjusted for variables in model 1 plus BMI, education, house ownership, comorbidity, and cognition; model 3 was adjusted for variables in model 2 plus depressive symptoms; and model 4 was adjusted for cohabitation with adult children plus model 3.

Table 4. Wife's odds of frailty when the husband is frail in 315 married couples.

Frailty of Husband	Frailty of Wife (n = 315)				
	Unadjusted	Model 1	Model 2	Model 3	Model 4
			OR (95% CI)		
Frailty of Husband					
Frail husband	4.76 (1.95–11.58) ***	3.96 (1.52–10.33) ***	3.13 (1.06–9.27) *	4.10 (1.16–14.56) *	4.62 (1.31–16.33) *
Five Components of Frailty Phenotype among Husbands					
Weight loss	6.89 (2.18–21.80) ***	7.07 (2.13–23.47) ***	8.47 (2.02–35.52) ***	8.56 (1.76–41.65) **	8.34 (1.70–40.85) **
Exhaustion	2.23 (1.32–3.76) ***	2.17 (1.27–3.68) ***	2.00 (1.13–3.57) *	2.11 (1.10–4.05) *	2.17 (1.12–4.22) *
Low activity	2.23 (0.83–5.95)	1.75 (0.63–4.83)	2.02 (0.63–6.48)	2.46 (0.72–8.37)	2.49 (0.72–8.55)
Weakness	1.54 (0.81–2.93)	1.29 (0.67–2.51)	1.04 (0.50–2.15)	1.03 (0.49–2.19)	1.03 (0.49–2.19)
Slowness	2.82 (1.52–5.23) ***	1.87 (0.95–3.69)	2.50 (1.13–5.53) *	2.48 (1.12–5.50) *	2.77 (1.24–6.31) *

Notes: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$. BMI = body mass index; CI = confidence interval; OR = odds ratio. Model 1 was adjusted for age; model 2 was adjusted for variables in model 1 plus BMI, education, house ownership, comorbidity, and cognition; model 3 was adjusted for variables in model 2 plus depressive symptoms; and model 4 was adjusted for cohabitation with adult children plus model 3.

4. Discussion

In this study, we found that older adults with frail spouses had significantly higher odds of being frail. Husbands and wives with a frail partner had 3.34 and 4.62 times higher odds of being frail, respectively, than if their partner was not frail. Thus, women were more affected by spousal frailty status than men. Among the five components of the Fried frailty phenotype, there was a spousal association in regard to weight loss, slowness, and exhaustion. The odds ratio for a wife to experience weight loss if her husband had weight loss was twice the odds ratio for weight loss in a husband if his wife had weight loss. These results suggest the presence of sex differences in our findings.

We found a spousal concordance for frailty among community-living older adults. This finding is consistent with the results from a previous study that reported that frailty in one spouse is related to greater subsequent frailty in the other [19]. It is also consistent with the previously reported concordance of physical, functional, and mental health and health behavior change in married couples [22–25]. Concordant health decline, especially in an elderly couple, is a significant risk factor for difficulties in physical activities, functional disabilities, and depressive symptoms that have an increased caregiver burden [26]. Thus, spousal frailty can be used to detect, prevent, and manage a couple's frailty among community-living older adults.

Our study suggests an independent association between frailty status of marital partners in the older population. The logistic regression models were adjusted for recognized frailty-related factors, including age, education, cognition, comorbidity, and depression [27]. The significant association for frailty within married couples remained after the adjustment for these factors. Additionally, the adjustment for the covariates not only decreased but also increased the size of the odds ratios. The change in the direction of the association may be due to the interplay of positive and negative confounding [28,29]. Further research is needed to examine the relationship between these factors, especially the cohabitation with adult children, as its impact on frailty has not been fully investigated. In previous studies, concordance of mood (depressive symptoms, neuroticism) [30,31], social activity [32], chronic conditions [23,33,34], and cognitive decline [35] between married couples have been observed. The multifactorial nature of spousal association and frailty may explain the varying strength of the spousal association.

We identified that three components of the Fried frailty phenotype, namely, weight loss, slowness, and exhaustion, mainly contribute to the spousal association for frailty. The strength of the spousal association was strongest for weight loss in both husbands and wives. There are various causes of weight loss among the elderly, and they often coexist. Common causes are classified as organic (neoplastic, nonneoplastic, and age-related physiological changes), psychological (depression, dementia, and anxiety disorders), nonmedical (socioeconomic conditions such as poverty), and unknown [36,37]. These conditions can be directly (such as environmental factors) and indirectly (such as depression [31]) shared by married couples. Furthermore, activities related to food preparation are mainly performed by women rather than men, especially among older adults in Korea [38]. The influence of gender role needs is discussed later.

Exhaustion is associated with the psychosocial condition of older adults. Older adults can be affected by the depressive symptoms and poor physical health of their spouses [39]. Those living with a depressed spouse are more likely to experience depressive mood or episodes [40,41], contributing to the increased association for exhaustion among married couples. A recent study suggested an association between slow gait speed and social networks among older adults [42]. Thus, the sharing of a couple's social network may influence the spousal concordance in slowness.

We found that women were more affected by the frailty status and weight loss of their spouses than men. This finding may be due to gender role orientation and socialization [43]. These perspectives are deeply ingrained in the minds of the Korean elderly and are widely reflected in their daily lives. According to the 2017 national survey of living conditions and welfare needs of the Korean elderly, 93.7% of male adults aged >65 years received instrumental support from their spouse compared to only 54% of females aged >65 years [44]. Similarly, men were less likely to provide and more likely to

receive caregiving than women [44]. Poor spousal health, low education, and unemployment decreased the rate of receiving instrumental support and caregiving [44]. Thus, it can be deduced that elderly women do more housework and have a higher caregiving burden than men [45]. Furthermore, female caregivers are more likely to experience physical and psychosocial distress [46–48]. Our findings are in agreement with women's vulnerability to spousal influence and its negative health effects as reported in previous studies on cognitive functioning [35], vision impairment [49], and depressive symptoms [50].

There are limitations to our study. First, due to the cross-sectional study design, it is difficult to understand the causal relationship from our analysis. Further longitudinal studies are needed to evaluate the temporal changes in the frailty status in married couples. Second, as the KFACS was designed to target the elderly population regardless of marital status, the sample size of married couples was relatively small. However, our results suggest a similar prevalence of frailty and concordant frailty within couples as reported in previous studies [19]. In addition, the quality of the marital relationship was not accounted for in our study.

5. Conclusions

In conclusion, having a frail spouse is a strong and independent risk factor for frailty. Among the five components of the Fried frailty phenotype, weight loss, exhaustion, and slowness were associated within married couples. Weight loss had the strongest association. Knowledge of the spousal association for frailty can help to prevent spousal frailty by managing risk factors and developing interventions designed for older married couples. Further prospective and longitudinal investigations will help corroborate our findings.

Appendix A

Table A1. Demographic and health characteristics of frail and nonfrail groups.

Variables	Frail (*n* = 63)	Nonfrail (*n* = 567)	*p*-Value
Demographics			
Sex			
Male	35 (5.6)	280 (44.4)	0.864
Female	28 (4.4)	287 (45.6)	
Age, mean (SD), year	78.2 (3.4)	75.9 (3.7)	<0.001
BMI, mean (SD), kg/m^2	24.0 (3.2)	24.2 (2.9)	0.551
Education, *n* (%)			
Less than 7 years	40 (63.5)	200 (35.3)	<0.001
Residence, *n* * (%)			
Urban	4 (27.7)	4 (6.5)	<0.001
Suburban	32 (51.6)	265 (47.0)	
Rural	26 (41.9)	143 (25.4)	
House ownership, *n* (%)	53 (84.1)	514 (90.7)	<0.001
Currently employed, *n* * (%)	11 (17.5)	138 (24.4)	0.220

Table A1. *Cont.*

Variables	Frail (*n* = 63)	Nonfrail (*n* = 567)	*p*-Value
Living with adult children, *n* * (%)	10 (15.9)	121 (21.4)	0.026
Health Characteristics			
Cognitive Impairment			
MMSE score <24	27 (42.9)	95 (16.8)	<0.001
Health Behavior			
Current smoker, *n* (%)	4 (6.3)	29 (5.1)	0.676
Heavy drinking, *n* (%)	12 (19.0)	104 (18.3)	0.891
Comorbid Conditions			
Number of comorbid conditions, mean (SD)	2.16 (1.36)	1.68 (1.32)	0.006
Comorbidity, *n* (%)	31 (49.2)	202 (35.6)	0.034
Hypertension, *n* (%)	41 (65.1)	307 (54.1)	0.098
Diabetes mellitus, *n* (%)	18 (28.6)	128 (22.6)	0.285
Mental Health			
Depressive symptom (GDS score ≥6), yes, *n* (%)	36 (57.1)	87 (15.3)	<0.001
Physical Activity			
Moderate/vigorous activity, none, *n* (%)	38 (60.3)	185 (32.6)	<0.001
Social Activity			
Religious meeting, none, *n* * (%)	31 (49.2)	217 (38.3)	0.094
Social meeting, none, *n* (%)	19 (30.2)	161 (28.4)	0.769
Possible Malnutrition			
MNA score ≤11, *n* * (%)	14 (22.6)	71.4 (6.2)	<0.001
Self-perceived health, poor, *n* (%)	43 (68.3)	157 (27.7)	<0.001

Notes: Comorbidity: ≥2 comorbid conditions; GDS = Geriatric Depression Scale; MNA = Mini Nutritional Assessment; MMSE = Mini-Mental State Examination. Chi-squared test for categorical variables and independent *t*-test for continuous variables. *n* * indicates missing data.

References

1. World Health Organization: WHO. (2018b, February 5). Ageing and Health. Available online: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health (accessed on 20 April 2020).
2. Friedman, S.M.; Shah, K.; Hall, W.J. Failing to Focus on Healthy Aging: A Frailty of Our Discipline? *J. Am. Geriatr. Soc.* **2015**, *63*, 1459–1462. [CrossRef]
3. Kojima, G.; Liljas, A.; Iliffe, S. Frailty Syndrome: Implications and Challenges for Health Care Policy. *RMHP* **2019**, *12*, 23–30. [CrossRef]
4. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in Older Adults: Evidence for a Phenotype. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M157. [CrossRef] [PubMed]
5. Hoogendijk, E.O.; Afilalo, J.; Ensrud, K.E.; Kowal, P.; Onder, G.; Fried, L.P. Frailty: Implications for Clinical Practice and Public Health. *Lancet* **2019**, *394*, 1365–1375. [CrossRef]
6. Rockwood, K.; Mitnitski, A. Frailty in Relation to the Accumulation of Deficits. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2007**, *62*, 722–727. [CrossRef] [PubMed]
7. Collard, R.M.; Boter, H.; Schoevers, R.A.; Oude Voshaar, R.C. Prevalence of Frailty in Community-Dwelling Older Persons: A Systematic Review. *J. Am. Geriatr. Soc.* **2012**, *60*, 1487–1492. [CrossRef]
8. He, B.; Ma, Y.; Wang, C.; Jiang, M.; Geng, C.; Chang, X.; Ma, B.; Han, L. Prevalence and Risk Factors for Frailty Among Community-Dwelling Older People in China: A Systematic Review and Meta-Analysis. *J. Nutr. Health Aging* **2019**, *23*, 442–450. [CrossRef]
9. Buckinx, F.; Rolland, Y.; Reginster, J.-Y.; Ricour, C.; Petermans, J.; Bruyère, O. Burden of Frailty in the Elderly Population: Perspectives for a Public Health Challenge. *Arch. Public Health* **2015**, *73*, 19. [CrossRef]
10. Klein, B.E.K.; Klein, R.; Knudtson, M.D.; Lee, K.E. Frailty, Morbidity and Survival. *Arch. Gerontol. Geriatr.* **2005**, *41*, 141–149. [CrossRef]
11. Feng, Z.; Lugtenberg, M.; Franse, C.; Fang, X.; Hu, S.; Jin, C.; Raat, H. Risk Factors and Protective Factors Associated with Incident or Increase of Frailty among Community-Dwelling Older Adults: A Systematic Review of Longitudinal Studies. *PLoS ONE* **2017**, *12*, e0178383. [CrossRef]

12. Kojima, G.; Walters, K.; Iliffe, S.; Taniguchi, Y.; Tamiya, N. Marital Status and Risk of Physical Frailty: A Systematic Review and Meta-Analysis. *J. Am. Med. Dir. Assoc.* **2020**, *21*, 322–330. [CrossRef] [PubMed]

13. Aggar, C.; Ronaldson, S.; Cameron, I.D. Reactions to Caregiving during an Intervention Targeting Frailty in Community Living Older People. *BMC Geriatr.* **2012**, *12*, 66. [CrossRef] [PubMed]

14. Mui, A.C. Perceived Health and Functional Status among Spouse Caregivers of Frail Older Persons. *J. Aging Health* **1995**, *7*, 283–300. [CrossRef] [PubMed]

15. Wolff, J.L.; Kasper, J.D. Caregivers of Frail Elders: Updating a National Profile. *Gerontology* **2006**, *46*, 344–356. [CrossRef] [PubMed]

16. Comans, T.A.; Currin, M.L.; Brauer, S.G.; Haines, T.P. Factors Associated with Quality of Life and Caregiver Strain amongst Frail Older Adults Referred to a Community Rehabilitation Service: Implications for Service Delivery. *Disabil. Rehabil.* **2011**, *33*, 1215–1221. [CrossRef]

17. Pinquart, M.; Sörensen, S. Spouses, Adult Children, and Children-in-Law as Caregivers of Older Adults: A Meta-Analytic Comparison. *Psychol. Aging* **2011**, *26*, 1–14. [CrossRef]

18. Potier, F.; Degryse, J.-M.; Bihin, B.; Debacq-Chainiaux, F.; Charlet-Renard, C.; Martens, H.; de Saint-Hubert, M. Health and Frailty among Older Spousal Caregivers: An Observational Cohort Study in Belgium. *BMC Geriatr.* **2018**, *18*, 291. [CrossRef]

19. Monin, J.; Doyle, M.; Levy, B.; Schulz, R.; Fried, T.; Kershaw, T. Spousal Associations between Frailty and Depressive Symptoms: Longitudinal Findings from the Cardiovascular Health Study. *J. Am. Geriatr. Soc.* **2016**, *64*, 824–830. [CrossRef]

20. Won, C.W.; Lee, S.; Kim, J.; Chon, D.; Kim, S.; Kim, C.-O.; Kim, M.K.; Cho, B.; Choi, K.M.; Roh, E.; et al. Korean Frailty and Aging Cohort Study (KFACS): Cohort Profile. *BMJ Open* **2020**, *10*, e035573. [CrossRef]

21. Jeon, S.Y.; Won, C.W.; Choi, H.R.; Kim, B.S.; Kim, S.Y.; Hur, J.H. Physical frailty predicts cognitive decline in elderly people: Prospective findings from the living profiles of older people survey in Korea. *Korean J. Fam. Pract.* **2015**, *5*, 702–707.

22. Hoppmann, C.A.; Gerstorf, D.; Hibbert, A. Spousal Associations between Functional Limitation and Depressive Symptom Trajectories: Longitudinal Findings from the Study of Asset and Health Dynamics among the Oldest Old (AHEAD). *Health Psychol.* **2011**, *30*, 153–162. [CrossRef] [PubMed]

23. Kim, H.; Kang, D.; Choi, K.; Nam, C.; Thomas, G.; Suh, I. Spousal Concordance of Metabolic Syndrome in 3141 Korean Couples: A Nationwide Survey. *Ann. Epidemiol.* **2006**, *16*, 292–298. [CrossRef] [PubMed]

24. Meyler, D.; Stimpson, J.P.; Peek, M.K. Health Concordance within Couples: A Systematic Review. *Soc. Sci. Med.* **2007**, *64*, 2297–2310. [CrossRef]

25. Jackson, S.E.; Steptoe, A.; Wardle, J. The Influence of Partner's Behavior on Health Behavior Change: The English Longitudinal Study of Ageing. *JAMA Intern. Med.* **2015**, *175*, 385. [CrossRef] [PubMed]

26. Lu, W.-H.; Chiou, S.-T.; Chen, L.-K.; Hsiao, F.-Y. Functional and Mental Health Outcomes of the Joint Effects of Spousal Health: The Potential Threats of "Concordant Frailty". *J. Am. Med. Dir. Assoc.* **2016**, *17*, 324–330. [CrossRef]

27. Clegg, A.; Young, J.; Iliffe, S.; Rikkert, M.O.; Rockwood, K. Frailty in Elderly People. *Lancet* **2013**, *381*, 752–762. [CrossRef]

28. Mehio-Sibai, A.; Feinleib, M.; Sibai, T.A.; Armenian, H.K. A Positive or a Negative Confounding Variable? A Simple Teaching Aid for Clinicians and Students. *Ann. Epidemiol.* **2005**, *15*, 421–423. [CrossRef]

29. Lachin, J.M. *Biostatistical Methods: The Assessment of Relative Risks*; John Wiley & Sons: Hoboken, NJ, USA, 2009.

30. Kreitman, N. The Patient's Spouse. *Br. J. Psychiatry* **1964**, *110*, 159–173. [CrossRef]

31. Eagles, J.M.; Walker, L.G.; Blackwood, G.W.; Beattie, J.A.G.; Restall, D.B. The Mental Health of Elderly Couples II. Concordance for Psychiatric Morbidity in Spouses. *Br. J. Psychiatry* **1987**, *150*, 303–308. [CrossRef]

32. Hoppmann, C.A.; Gerstorf, D.; Luszcz, M. Spousal Social Activity Trajectories in the Australian Longitudinal Study of Ageing in the Context of Cognitive, Physical, and Affective Resources. *J. Gerontol. Ser. B* **2008**, *63*, P41–P50. [CrossRef]

33. Hippisley-Cox, J. Married Couples' Risk of Same Disease: Cross Sectional Study. *BMJ* **2002**, *325*, 636. [CrossRef] [PubMed]

34. Stimpson, J.P.; Peek, M.K. Concordance of Chronic Conditions in Older Mexican American Couples. *Prev. Chronic Dis.* **2005**, *2*, 7.

35. Gerstorf, D.; Hoppmann, C.A.; Anstey, K.J.; Luszcz, M.A. Dynamic Links of Cognitive Functioning among Married Couples: Longitudinal Evidence from the Australian Longitudinal Study of Ageing. *Psychol. Aging* **2009**, *24*, 296–309. [CrossRef] [PubMed]

36. Alibhai, S.M.H. An Approach to the Management of Unintentional Weight Loss in Elderly People. *Can. Med. Assoc. J.* **2005**, *172*, 773–780. [CrossRef]

37. McMinn, J.; Steel, C.; Bowman, A. Investigation and Management of Unintentional Weight Loss in Older Adults. *BMJ* **2011**, *342*, d1732. [CrossRef]

38. Kim, C. Having meals together state of couples of after retirement. *Korea J. Popul. Stud.* **2010**, *33*, 123–142.

39. Siegel, M.J.; Bradley, E.H.; Gallo, W.T.; Kasl, S.V. The Effect of Spousal Mental and Physical Health on Husbands' and Wives' Depressive Symptoms, Among Older Adults: Longitudinal Evidence from the Health and Retirement Survey. *J. Aging Health* **2004**, *16*, 398–425. [CrossRef]

40. Benazon, N.R.; Coyne, J.C. Living with a Depressed Spouse. *J. Fam. Psychol.* **2000**, *14*, 71–79. [CrossRef]

41. McLeod, J.D. Spouse Concordance for Depressive Disorders in a Community Sample. *J. Affect. Disord.* **1993**, *27*, 43–52. [CrossRef]

42. Shafie, S.; Shahwan, S.; Abdin, E.; Vaingankar, J.; Picco, L.; Sambasivam, R.; Zhang, Y.; Ng, L.L.; Chong, S.A.; Subramaniam, M. The Correlates of Slow Gait and Its Relation with Social Network among Older Adults in Singapore. *Aging Ment. Health* **2017**, *21*, 1171–1176. [CrossRef]

43. Miller, B. Gender Differences in Spouse Caregiver Strain: Socialization and Role Explanations. *J. Marriage Fam.* **1990**, *52*, 311. [CrossRef]

44. Chung, Kyunghee. Survey of Living Conditions and Welfare Needs of Korean Older Persons (Publication No. 11-1352000-000672-12). Korean Institute for Health and Social Affair. 2017. Available online: https://data.kihasa.re.kr/micro/subject_view.jsp?WT.ac=favor_data&grp_seq=&project_seq=673 (accessed on 21 April 2020).

45. Oh, Y.; Han, E. Review of Studies on Spousal Caregivers of Frail Spouses in South Korea. *Int. Soc. Work* **2019**, *62*, 529–548. [CrossRef]

46. Barusch, A.S.; Spaid, W.M. Gender Differences in Caregiving: Why Do Wives Report Greater Burden? *Gerontology* **1989**, *29*, 667–676. [CrossRef] [PubMed]

47. Chiu, C.-J.; Lin, Y.-C. Spousal Health and Older Adults' Biomarker Change over Six Years: Investigation of Gender Differences. *Arch. Gerontol. Geriatr.* **2019**, *83*, 44–49. [CrossRef]

48. Pinquart, M.; Sorensen, S. Gender Differences in Caregiver Stressors, Social Resources, and Health: An Updated Meta-Analysis. *J. Gerontol. Ser. B Psychol. Sci. Soc. Sci.* **2006**, *61*, P33–P45. [CrossRef]

49. Strawbridge, W.J.; Wallhagen, M.I.; Shema, S.J. Impact of Spouse Vision Impairment on Partner Health and Well-Being: A Longitudinal Analysis of Couples. *J. Gerontol. Ser. B Psychol. Sci. Soc. Sci.* **2007**, *62*, S315–S322. [CrossRef]

50. Hagedoorn, M.; Sanderman, R.; Ranchor, A.V.; Brilman, E.I.; Kempen, G.I.J.M.; Ormel, J. Chronic Disease in Elderly Couples. *J. Psychosom. Res.* **2001**, *51*, 693–696. [CrossRef]

Article

Falls in Community-Dwelling Older Adults with Lower Back or Knee Pain Are Associated with Cognitive and Emotional Factors

Tatsuya Hirase [1], Hyuma Makizako [2,*], Yoshiro Okubo [3], Stephen R. Lord [3], Minoru Okita [1], Yuki Nakai [2], Toshihiro Takenaka [4], Takuro Kubozono [5] and Mitsuru Ohishi [5]

[1]   Department of Physical Therapy Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki 852-8520, Japan; htatsuya@nagasaki-u.ac.jp (T.H.); mokita@nagasaki-u.ac.jp (M.O.)
[2]   Department of Physical Therapy, School of Health Sciences, Faculty of Medicine, Kagoshima University, Kagoshima 890-8544, Japan; nakai@health.nop.kagoshima-u.ac.jp
[3]   Falls, Balance and Injury Research Centre, Neuroscience Research Australia, Sydney, NSW 2031, Australia; y.okubo@neura.edu.au (Y.O.); s.lord@neura.edu.au (S.R.L.)
[4]   Tarumizu Municipal Medical Center, Tarumizu Chuo Hospital, Kagoshima 891-2124, Japan; takenaka@tarumizumh.jp
[5]   Department of Cardiovascular Medicine and Hypertension, Graduate School of Medical and Dental Science, Kagoshima University, Kagoshima 890-8520, Japan; kubozono@m.kufm.kagoshima-u.ac.jp (T.K.); ohishi@m2.kufm.kagoshima-u.ac.jp (M.O.)
*   Correspondence: makizako@health.nop.kagoshima-u.ac.jp; Tel.: +81-99-275-677

Abstract: (1) Background: The present study aimed to examine physical, cognitive and emotional factors affecting falls in community-dwelling older adults with and without pain; (2) Methods: Data from 789 older adults who participated in a community-based health survey were analyzed. Participants completed questionnaires on the presence of pain and previous falls. Muscle weakness (handgrip strength < 26.0 kg for men and < 18.0 kg for women) and low skeletal muscle mass (appendicular skeletal muscle mass index < 7.0 kg/m^2 for men and < 5.7 kg/m^2 for women) were determined. Mild cognitive impairment (MCI) and depressive symptoms were assessed using the National Center for Geriatrics and Gerontology-Functional Assessment Tool and 15-item geriatric depression scale (GDS-15), respectively; (3) Results: In participants with pain, MCI and GDS-15 were associated with previous falls after adjusting for age, sex, education and medication use. In participants without pain, muscle weakness and low skeletal muscle mass were associated with previous falls when adjusting for the above covariates; (4) Conclusions: Falls in participants with pain were associated with cognitive and emotional factors, whereas falls in those without pain were associated with physical factors. Fall prevention interventions for older adults with pain may require tailored strategies to address cognitive and emotional factors.

Keywords: aged; accidental falls; pain; mild cognitive impairment; depressive symptoms

1. Introduction

More than one third of people aged 65 years or older fall at least once per year, with about half doing so recurrently [1]. Between 20% and 30% of those who fall suffer moderate to severe injuries, including fractures and head trauma, which can lead to disability, early admission to nursing homes and even death [2,3].

Pain is also common in community-dwelling older adults, with prevalence rates ranging from 37% to 53% [4,5]. Pain has been identified as a significant risk factor for falls in community-dwelling older adults, and systematic review evidence suggests those with pain have a two-fold increased

risk of falling compared to those without pain [6,7]. Among the general older population, reduced physical function, cognitive impairment and depressive mood have also been identified as risk factors for falls [3,8,9]. However, reasons why older adults with pain are at such increased risk of falling are not well understood, therefore limiting our ability to design an effective fall prevention approach for older adults with pain.

The impact of pain on physical function has been relatively well documented [4,10]. Our systematic review evidence has suggested that pain is associated with poor dynamic, static, multicomponent and reactive balance measurements [11], all of which can contribute to an increased fall risk [1]. Furthermore, pain may also influence the risk of falling, through the psychological pathway. It has been reported that pain is associated with poor cognition and impaired executive function, inattention and depressed mood [12–14]. Since executive function and depression have been identified as risk factors for falls [8,15], the above findings suggest cognitive and emotional factors may also play a role in increasing fall risk in older people with pain. However, further research is required to identify risk factors for falls in this group and whether such risk factors differ from those found in older people without pain.

Therefore, the aim of this cross-sectional study was to determine whether risk factors for falls differ between community-dwelling older adults with and without pain while adjusting for relevant covariates. This information may be useful for facilitating fall prevention strategies for both those with and without pain.

2. Materials and Methods

2.1. Participants

This study utilized cross-sectional data conducted as part of the Tarumizu Study, a longitudinal study that has been conducted jointly by Kagoshima University (Faculty of Medicine), Tarumizu City Office and Tarumizu Chuo Hospital since 2017 [16]. The Tarumizu Study 2018 was conducted between July and December 2018 as a community-based health survey for older adults living in Tarumizu City, a local city of Kagoshima, Japan. A total of 859 adults aged ≥ 65 years participated in the survey. Data for participants with diagnosed dementia (n = 19), stroke (n = 19) and Parkinson's disease (n = 3) were excluded. Outcome data were also missing for an additional 29 participants. Thus, data from 789 participants (mean age 74.8 years, 64.1% women) were analyzed. Informed consent was obtained from all participants before study participation, and the ethics committee of the Faculty of Medicine, Kagoshima University approved the study protocol (ref no. 170351).

2.2. Assessments

Prior to commencing the study, all staff were trained by a study author regarding the assessment protocol to ensure consistency across the staff members.

2.2.1. Pain

Pain was assessed with the question "Do you currently have lower back or knee pain?" These pain sites were chosen as they have a high prevalence in older adults, and because they are the main pain sites that lead to mobility disability in this population [4]. Consistent with previous studies [10,17], participants with either lower back or knee pain were defined as the "pain" group, while participants without lower back or knee pain were defined as the "nonpain" group.

2.2.2. Falls

Falls were assessed with the question "Have you experienced falls within the past 12 months?" Falls were defined as "an unexpected event in which the person comes to rest on the ground, floor or lower level" [18]. Participants who experienced at least one fall in the past 12 months were classified as fallers, and those with no falls in the past 12 months were classified as nonfallers.

2.2.3. Physical Function

Walking speed was measured using a stopwatch on a flat and straight 10 m path at a comfortable walking speed. Two markers were used to indicate the start and end of the 10 m walk path, with a 2 m section to be traversed before passing the start marker, such that participants were walking at a comfortable pace at the first marker. Participants were also instructed to continue walking past the end of the 10-m path for a further two meters to ensure that the walking pace was kept constant throughout the task. Slow walking speed was defined as a walking speed < 1.0 m/s [10].

Muscle strength was assessed by dominant handgrip strength and measured using a Smedley-type handheld dynamometer (GRIP-D; Takei, Niigata, Japan). Muscle weakness was determined based on the Asian Working Group for Sarcopenia (AWGS) criteria for sarcopenia; handgrip strength was < 26.0 kg for men and < 18.0 kg for women [19].

Appendicular skeletal muscle mass was assessed using a multifrequency bioelectrical impedance analyser (BIA) (InBody 430, InBody Japan, Tokyo, Japan). The BIA instrument uses a tetrapolar, eight-point tactile electrode system that separately measures impedance of the arms, trunk and legs at three different frequencies (5, 50 and 250 kHz) for each segment [20]. The surface of the hand electrode was placed in contact with each of the five fingers, while the participant's heels and forefoot were placed on the circular-shaped foot electrode. Participants held out their arms and separated their legs so that they did not contact other body parts during the assessment. Appendicular skeletal muscle mass was derived as the sum of the muscle mass of the four limbs, and the appendicular skeletal muscle mass index (ASMI; kg/m^2) was calculated. Low skeletal muscle mass was determined based on the AWGS criteria for sarcopenia; ASMI < 7.0 kg/m^2 for men and < 5.7 kg/m^2 for women [19].

2.2.4. Cognitive Function and Emotional Status

Cognitive assessments were conducted using the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT) to identify participants with MCI [21]. The NCGG-FAT comprises four domains: memory (immediate and delayed word list memory), visual motor speed (trail-making test-part A (TMT-A)), executive function (trail making test-part B (TMT-B)) and processing speed (symbol digit substitution test (SDST)). The NCGG-FAT has been shown to have high test-retest reliability [21], moderate-to-high criterion validity [21] and predictive validity for dementia [22], in community-dwelling older adults. Participants were given approximately 20 minutes to complete the tests. MCI was defined as a score below 1.5 SD of the age and education-specific means in one or more of the cognitive tests, based on the population sample of community-dwelling older adults [23]. Depressive symptoms was assessed using the 15-item geriatric depression scale (GDS-15) [24].

2.3. Statistical Analysis

Chi-square tests for cross-tabulation tables and student t-tests were used to examine differences in categorical and continuously scored measures, respectively, between the fallers and nonfallers, and the pain and nonpain groups. A multivariable logistic regression analysis with slow walking speed, muscle weakness, low skeletal muscle mass, MCI and GDS-15 as the independent variables and previous falls as the dependent variable were separately conducted in the pain and nonpain groups. Model 1 was unadjusted, and Model 2 was adjusted for relevant covariates: age, sex, education and medication use. All analyses were performed using SPSS 25.0 for Windows (SPSS Inc., Armonk, NY, USA), and significance levels were set at 0.05.

3. Results

3.1. Comparisons of Physical, Cognitive and Emotional Factors Between the Fallers and NonFallers Stratified by the Pain Status

Of the 789 participants, 421 (53.4%) reported pain, while 368 (46.6%) did not. The mean age of participants with and without pain was 75.8 and 73.7 years, respectively. Seventy-six participants in the pain group (18.1%) and 35 participants in the nonpain group (9.5%) were classified as fallers and nonfallers.

The pain group was significantly older than the nonpain group ($p < 0.001$), and the pain group comprised more women than men ($p < 0.001$) (Table 1). Compared with the nonpain group, the pain group took more prescribed medications ($p < 0.001$), had reduced handgrip strength ($p = 0.008$) and slower walking speed ($p < 0.001$) and had a greater proportion of slow walkers ($p < 0.001$). Regarding cognitive function and emotional status, the pain groups performed worse than the nonpain group in the immediate and delayed word list memory and SDST tests ($p = 0.021$, $p = 0.006$ and $p = 0.014$, respectively) and had higher GDS-15 scores ($p < 0.001$).

Table 1. Comparisons of physical, cognitive and emotional factors between the fallers and nonfallers in the pain and nonpain groups.

Characteristics	Pain Group (*n* = 421)			Nonpain Group (*n* = 368)	
	Fallers (*n* = 76)	Nonfallers (*n* = 345)		Fallers (*n* = 35)	Nonfallers (*n* = 333)
Age (years)	77.1 (7.0)	75.5 (6.4)	††	74.1 (5.5)	73.6 (5.9)
Female, n (%)	53 (69.7)	235 (68.1)	††	23 (65.7)	195 (58.6)
Education (years)	11.0 (2.4)	11.0 (2.2)	††	10.9 (2.2)	11.4 (2.3)
Medications (n/day)	4.9 (4.5)	4.5 (4.5)	††	4.3 (7.1)	3.1 (4.6)
Physical function					
Slow walking speed, n (%)	18 (24.0)	60 (17.4)	††	3 (8.6)	25 (7.5)
Walking speed (m/s)	1.15 (0.25) **	1.24 (0.25)	††	1.29 (0.24)	1.33 (0.22)
Muscle weakness, n (%)	23 (30.3)	82 (24.5)		13 (37.1) **	59 (18.2)
Handgrip strength (kg)	23.1 (7.3)	23.5 (8.6)	††	23.0 (7.9)	25.2 (8.1)
Low skeletal muscle mass, n (%)	30 (40.0)	112 (33.7)		20 (57.1) **	120 (36.6)
ASMI (kg/m^2)	6.2 (1.0)	6.3 (1.0)		6.1 (0.9)	6.4 (1.0)
Cognitive function					
MCI, n (%)	34 (44.7) **	95 (27.7)		12 (34.3)	96 (28.9)
Memory					
Immediate word list memory (score)	7.0 (1.6)	7.3 (1.6)	†	7.6 (1.2)	7.5 (1.4)
Delayed word list memory (score)	3.6 (2.0)	4.0 (2.1)	††	4.4 (2.1)	4.3 (2.1)
Visual motor speed					
TMT-A (s)	25.8 (8.7)	24.4 (10.8)		22.9 (6.3)	23.8 (15.0)
Executive function					
TMT-B (s)	70.0 (49.6)	54.7 (46.8)		57.4 (53.1)	51.2 (40.0)
Processing speed					
SDST (score)	36.0 (11.1) *	39.2 (11.3)	†	39.1 (9.4)	40.8 (11.9)
Emotional status					
GDS-15 (points)	3.7 (3.2) **	2.7 (2.5)	††	2.3 (2.6)	2.0 (2.1)

Data are presented as mean (SD) or number (percentage). ** $p < 0.01$, * $p < 0.05$ versus nonfallers, †† $p < 0.01$, † $p < 0.05$ versus nonpain group; ASMI: appendicular skeletal muscle mass index. MCI: mild cognitive impairment. TMT: trail-making test. SDST: symbol digit substitution test. GDS-15: 15-item geriatric depression scale.

In the pain group, the fallers had significantly slower walking speed, lower SDST scores, a higher prevalence of MCI and higher GDS-15 scores than the nonfallers ($p < 0.05$) (Table 1). In the nonpain group, the fallers had a significantly higher prevalence of muscle weakness and lower skeletal muscle mass than the nonfallers (Table 1). No significant differences in the remaining variables were observed between the fallers and nonfallers in either pain group ($p > 0.05$).

3.2. Multivariable Logistic Regression to Determine the Fall Risks Of Physical, Cognitive and Emotional Factors in the Pain and NonPain Groups

In the pain group, MCI and GDS-15 scores were significantly associated with previous falls in both the unadjusted (Model 1) and adjusted models that included relevant covariates (Model 2) (Table 2). No physical function measures were significantly associated with previous falls in either model. In the nonpain group, muscle weakness and low skeletal muscle mass were significantly associated with previous falls in both the unadjusted (Model 1) and the adjusted models that included relevant covariates (Model 2). Slow walking speed, MCI and GDS-15 scores were not significantly associated with previous falls in either model.

Table 2. Multivariable logistic regression analyses of the relationships between falls and physical, cognitive and emotional factors in the pain and nonpain groups.

Independent Variables	Dependent Variables: Previous Falls					
	Pain Group (n = 421)			NonPain Group (n = 368)		
	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Slow walking speed						
Model 1	1.50	0.82–2.72	0.188	1.16	0.33–4.04	0.821
Model 2	1.13	0.69–2.54	0.405	1.15	0.30–4.31	0.841
Muscle weakness						
Model 1	1.34	0.77–2.32	0.298	2.66	1.27–5.59	0.010
Model 2	1.16	0.63–2.12	0.637	2.57	1.12–5.91	0.026
Low skeletal muscle mass						
Model 1	1.31	0.78–2.19	0.305	2.31	1.14–4.68	0.020
Model 2	1.01	0.60–1.85	0.848	2.18	1.03–4.60	0.041
MCI						
Model 1	2.11	1.27–3.52	0.004	1.28	0.61–2.68	0.508
Model 2	2.00	1.08–3.38	0.010	1.24	0.57–2.73	0.591
GDS-15						
Model 1	1.13	1.04–1.24	0.004	1.07	0.92–1.24	0.393
Model 2	1.14	1.04–1.24	0.005	1.04	0.89–1.21	0.620

Model 1: Unadjusted model, Model 2: Adjusted for age, sex, education and number of prescribed medications. OR: odds ratio. CI: confidence interval. MCI: mild cognitive impairment. GDS-15: 15-item geriatric depression scale.

4. Discussion

This study revealed older people with pain were significantly older and had slower gait speed, reduced muscle strength, impaired cognition and more depressive symptoms than those without pain. Further, the subgroup analysis unmasked some important information in that falls in the participants with pain were associated with cognitive and emotional factors, whereas falls in those without pain were associated with physical factors, including muscle weakness and low skeletal muscle mass in multivariable models adjusting for age, sex, education and medication use.

Although slow walking speed was identified as a risk factor for falls in the participants with pain in univariate analysis, this measure was not independently associated with falls in multivariable modelling. In contrast, the logistic regression analysis revealed the presence of MCI (assessed with tests of visual motor speed, memory, executive function and processing speed) and was independently associated with falls. Pain can interfere with attention in older adults [12,25], and insufficient or divided attention when negotiating environment hazards may lead to trips and slips [26,27]. Furthermore, pain is associated with slow processing speed [28], which is identified as a risk factor for falls in older adults [29]. Thus, it is possible that pain requires an attentional demand limiting the attentional resources allocated for avoiding daily life hazards and decision making, resulting in an increased risk of falls. Additionally, we found that depressive symptoms were associated with falls in those with pain. Depressive symptomatology has consistently been reported to increase the risk of falling in older people [8], and several studies have reported people with depression are more likely to develop chronic

pain [14,30]. Further, pain-related fear can lead to avoidance behaviors and hypervigilance to bodily sensations followed by disability, disuse and depression [31], all factors that can exacerbate fall risk.

In the older adults without pain, those who reported falls were weaker and had lower skeletal muscle mass than those who did not report falls, and these two measures were independently associated with falls in the multivariate models. These findings are consistent with many previous studies conducted in older community-dwelling people [9,32], as well as complementary studies that have found that reduced muscle strength is associated with reduced balance control, slow sit-to-stand times and slow gait speed [33,34].

Our findings have implications for clinical practice. First, our findings that the pain group had slower gait speed and reduced muscle strength, compared to the nonpain group, provides insight into why this group is at increased fall risk [6,7]. Targeted exercise interventions could address these risk factors in addition to treatments for pain. Further, our subgroup analysis findings show that falls in participants with pain were associated with cognitive and emotional factors, including MCI and depressive symptoms, whereas falls in those without pain were associated with physical factors, including muscle weakness and low skeletal muscle mass. These findings suggest fall prevention interventions for older adults with and without pain may require special tailoring to address cognitive and emotional risk factors and physical factors for falls, respectively.

We acknowledge certain study limitations. First, our pain assessments were not detailed and additional assessments of pain intensity, duration and interference in activities of daily living may have provided further understanding of pain-related factors affecting falls. However, considering the high prevalence of chronic pain (25–76%) in community-dwelling older adults [35], the majority of our pain group participants would likely fall into this category. Second, the cross-sectional design precludes the prospective delineation of the relationship between falls and physical, cognitive and emotional factors among older adults with and without pain. Thus, our current study cannot confirm the causality between pain and risk of falling. Future research on prospective fall follow-up, and on detailed pain and physical, neuropsychological and functional assessments, is required to confirm the current findings. Furthermore, the retrospective recording of falls may have underestimated their true prevalence, although the overall proportion of fallers (16.4%) is consistent with most previous studies of fall incidence in older people undertaken in Japan.

5. Conclusions

Community-dwelling older people with pain were more likely to have depressive symptoms and impaired gait, strength and cognition than their peers without pain. Further, falls in those with pain were associated with cognitive and emotional factors whereas falls in those without pain were associated with physical factors (i.e., weakness and low skeletal muscle mass). Thus, fall-prevention interventions for older adults with pain may require tailoring to address cognitive and emotional risk factors for falls. Future research with prospective fall follow-up and detailed pain and physical, neuropsychological and functional assessments are required to confirm the current findings.

References

1. Tinetti, M.E.; Speechley, M.; Ginter, S.F. Risk factors for falls among elderly persons living in the community. *N. Engl. J. Med.* **1988**, *319*, 1701–1707. [CrossRef] [PubMed]
2. Stevens, J.A.; Corso, P.S.; Finkelstein, E.A.; Miller, T.R. The costs of fatal and non-fatal falls among older adults. *Inj. Prev. J. Int. Soc. Child Adolesc. Inj. Prev.* **2006**, *12*, 290–295. [CrossRef]
3. Ambrose, A.F.; Paul, G.; Hausdorff, J.M. Risk factors for falls among older adults: A review of the literature. *Maturitas* **2013**, *75*, 51–61. [CrossRef] [PubMed]
4. Patel, K.V.; Guralnik, J.M.; Dansie, E.J.; Turk, D.C. Prevalence and impact of pain among older adults in the United States: Findings from the 2011 National Health and Aging Trends Study. *Pain* **2013**, *154*, 2649–2657. [CrossRef] [PubMed]
5. Shah, R.C.; Buchman, A.S.; Boyle, P.A.; Leurgans, S.E.; Wilson, R.S.; Andersson, G.B.; Bennett, D.A. Musculoskeletal pain is associated with incident mobility disability in community-dwelling elders. *J. Gerontol. Ser. ABiol. Sci. Med Sci.* **2011**, *66*, 82–88. [CrossRef] [PubMed]
6. Stubbs, B.; Binnekade, T.; Eggermont, L.; Sepehry, A.A.; Patchay, S.; Schofield, P. Pain and the risk for falls in community-dwelling older adults: Systematic review and meta-analysis. *Arch. Phys. Med. Rehabil.* **2014**, *95*, 175–187.e179. [CrossRef] [PubMed]
7. Stubbs, B.; Schofield, P.; Binnekade, T.; Patchay, S.; Sepehry, A.; Eggermont, L. Pain is associated with recurrent falls in community-dwelling older adults: Evidence from a systematic review and meta-analysis. *Pain Med.* **2014**, *15*, 1115–1128. [CrossRef]
8. Kvelde, T.; McVeigh, C.; Toson, B.; Greenaway, M.; Lord, S.R.; Delbaere, K.; Close, J.C. Depressive symptomatology as a risk factor for falls in older people: Systematic review and meta-analysis. *J. Am. Geriatr. Soc.* **2013**, *61*, 694–706. [CrossRef]
9. Yeung, S.S.Y.; Reijnierse, E.M.; Pham, V.K.; Trappenburg, M.C.; Lim, W.K.; Meskers, C.G.M.; Maier, A.B. Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis. *J. Cachexia Sarcopenia Muscle* **2019**, *10*, 485–500. [CrossRef]
10. Nakai, Y.; Makizako, H.; Kiyama, R.; Tomioka, K.; Taniguchi, Y.; Kubozono, T.; Takenaka, T.; Ohishi, M. Association between Chronic Pain and Physical Frailty in Community-Dwelling Older Adults. *Int. J. Environ. Res. Public Health* **2019**, *16*, 1330. [CrossRef]
11. Hirase, T.; Okubo, Y.; Sturnieks, D.L.; Lord, S.R. Pain Is Associated with Poor Balance in Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. *J. Am. Med Dir. Assoc.* **2020**, *21*, 597–603.e598. [CrossRef]
12. Van der Leeuw, G.; Eggermont, L.H.; Shi, L.; Milberg, W.P.; Gross, A.L.; Hausdorff, J.M.; Bean, J.F.; Leveille, S.G. Pain and Cognitive Function Among Older Adults Living in the Community. *J. Gerontol. Ser. ABiol. Sci. Med. Sci.* **2016**, *71*, 398–405. [CrossRef] [PubMed]
13. Murata, S.; Nakakubo, S.; Isa, T.; Tsuboi, Y.; Torizawa, K.; Fukuta, A.; Okumura, M.; Matsuda, N.; Ono, R. Effect of Pain Severity on Executive Function Decline in Community-Dwelling Older Adults. *Gerontol. Geriatr. Med.* **2018**, *4*, 2333721418811490. [CrossRef] [PubMed]
14. Si, H.; Wang, C.; Jin, Y.; Tian, X.; Qiao, X.; Liu, N.; Dong, L. Prevalence, Factors, and Health Impacts of Chronic Pain Among Community-Dwelling Older Adults in China. *Pain Manag. Nurs. Off. J. Am. Soc. Pain Manag. Nurses* **2019**, *20*, 365–372. [CrossRef] [PubMed]
15. Kearney, F.C.; Harwood, R.H.; Gladman, J.R.; Lincoln, N.; Masud, T. The relationship between executive function and falls and gait abnormalities in older adults: A systematic review. *Dement. Geriatr. Cogn. Disord.* **2013**, *36*, 20–35. [CrossRef]
16. Makizako, H.; Kubozono, T.; Kiyama, R.; Takenaka, T.; Kuwahata, S.; Tabira, T.; Kanoya, T.; Horinouchi, K.; Shimada, H.; Ohishi, M. Associations of social frailty with loss of muscle mass and muscle weakness among community-dwelling older adults. *Geriatr. Gerontol. Int.* **2019**, *19*, 76–80. [CrossRef]
17. Makino, K.; Lee, S.; Lee, S.; Bae, S.; Jung, S.; Shinkai, Y.; Shimada, H. Daily Physical Activity and Functional Disability Incidence in Community-Dwelling Older Adults with Chronic Pain: A Prospective Cohort Study. *Pain Med.* **2018**. [CrossRef]
18. Lamb, S.E.; Jorstad-Stein, E.C.; Hauer, K.; Becker, C. Development of a common outcome data set for fall injury prevention trials: The Prevention of Falls Network Europe consensus. *J. Am. Geriatr. Soc.* **2005**, *53*, 1618–1622. [CrossRef]

19. Chen, L.K.; Liu, L.K.; Woo, J.; Assantachai, P.; Auyeung, T.W.; Bahyah, K.S.; Chou, M.Y.; Chen, L.Y.; Hsu, P.S.; Krairit, O.; et al. Sarcopenia in Asia: Consensus report of the Asian Working Group for Sarcopenia. *J. Am. Med. Dir. Assoc.* **2014**, *15*, 95–101. [CrossRef]

20. Seino, S.; Shinkai, S.; Iijima, K.; Obuchi, S.; Fujiwara, Y.; Yoshida, H.; Kawai, H.; Nishi, M.; Murayama, H.; Taniguchi, Y.; et al. Reference Values and Age Differences in Body Composition of Community-Dwelling Older Japanese Men and Women: A Pooled Analysis of Four Cohort Studies. *PLoS ONE* **2015**, *10*, e0131975. [CrossRef]

21. Makizako, H.; Shimada, H.; Park, H.; Doi, T.; Yoshida, D.; Uemura, K.; Tsutsumimoto, K.; Suzuki, T. Evaluation of multidimensional neurocognitive function using a tablet personal computer: Test-retest reliability and validity in community-dwelling older adults. *Geriatr. Gerontol. Int.* **2013**, *13*, 860–866. [CrossRef] [PubMed]

22. Shimada, H.; Makizako, H.; Park, H.; Doi, T.; Lee, S. Validity of the National Center for Geriatrics and Gerontology-Functional Assessment Tool and Mini-Mental State Examination for detecting the incidence of dementia in older Japanese adults. *Geriatr. Gerontol. Int.* **2017**, *17*, 2383–2388. [CrossRef] [PubMed]

23. Shimada, H.; Makizako, H.; Doi, T.; Yoshida, D.; Tsutsumimoto, K.; Anan, Y.; Uemura, K.; Ito, T.; Lee, S.; Park, H.; et al. Combined prevalence of frailty and mild cognitive impairment in a population of elderly Japanese people. *J. Am. Med Dir. Assoc.* **2013**, *14*, 518–524. [CrossRef] [PubMed]

24. Yesavage, J.A. Geriatric Depression Scale. *Psychopharmacol. Bull.* **1988**, *24*, 709–711.

25. Eccleston, C.; Crombez, G. Pain demands attention: A cognitive-affective model of the interruptive function of pain. *Psychol. Bull.* **1999**, *125*, 356–366. [CrossRef]

26. Berg, W.P.; Alessio, H.M.; Mills, E.M.; Tong, C. Circumstances and consequences of falls in independent community-dwelling older adults. *Age Ageing* **1997**, *26*, 261–268. [CrossRef]

27. Talbot, L.A.; Musiol, R.J.; Witham, E.K.; Metter, E.J. Falls in young, middle-aged and older community dwelling adults: Perceived cause, environmental factors and injury. *BMC Public Health* **2005**, *5*, 86. [CrossRef]

28. Murata, S.; Sawa, R.; Nakatsu, N.; Saito, T.; Sugimoto, T.; Nakamura, R.; Misu, S.; Ueda, Y.; Ono, R. Association between chronic musculoskeletal pain and executive function in community-dwelling older adults. *Eur. J. Pain* **2017**, *21*, 1717–1722. [CrossRef]

29. Davis, J.C.; Best, J.R.; Khan, K.M.; Dian, L.; Lord, S.; Delbaere, K.; Hsu, C.L.; Cheung, W.; Chan, W.; Liu-Ambrose, T. Slow Processing Speed Predicts Falls in Older Adults with a Falls History: 1-Year Prospective Cohort Study. *J. Am. Geriatr. Soc.* **2017**, *65*, 916–923. [CrossRef]

30. Bair, M.J.; Robinson, R.L.; Katon, W.; Kroenke, K. Depression and pain comorbidity: A literature review. *Arch. Intern. Med.* **2003**, *163*, 2433–2445. [CrossRef]

31. Vlaeyen, J.W.; Linton, S.J. Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. *Pain* **2000**, *85*, 317–332. [CrossRef]

32. Nevitt, M.C.; Cummings, S.R.; Kidd, S.; Black, D. Risk factors for recurrent nonsyncopal falls. A prospective study. *JAMA* **1989**, *261*, 2663–2668. [CrossRef] [PubMed]

33. Bijlsma, A.Y.; Pasma, J.H.; Lambers, D.; Stijntjes, M.; Blauw, G.J.; Meskers, C.G.; Maier, A.B. Muscle strength rather than muscle mass is associated with standing balance in elderly outpatients. *J. Am. Med Dir. Assoc.* **2013**, *14*, 493–498. [CrossRef]

34. Lord, S.R.; Murray, S.M.; Chapman, K.; Munro, B.; Tiedemann, A. Sit-to-stand performance depends on sensation, speed, balance, and psychological status in addition to strength in older people. *J. Gerontol. Ser. ABiol. Sci. Med Sci.* **2002**, *57*, M539–M543. [CrossRef] [PubMed]

35. Abdulla, A.; Adams, N.; Bone, M.; Elliott, A.M.; Gaffin, J.; Jones, D.; Knaggs, R.; Martin, D.; Sampson, L.; Schofield, P. Guidance on the management of pain in older people. *Age Ageing* **2013**, *42* (Suppl. 1), i1–i57. [CrossRef]

Article

Frailty Status Typologies in Spanish Older Population: Associations with Successful Aging

José M. Tomás [1,2], Trinidad Sentandreu-Mañó [2,3,*] and Irene Fernández [1,2]

[1] Department of Methodology for the Behavioural Sciences, University of Valencia, 46010 Valencia, Spain;
Jose.M.Tomas@uv.es (J.M.T.); Irene.Fernandez@uv.es (I.F.)

[2] Advanced Research Methods Applied to Quality of Life Promotion (ARMAQoL), University of Valencia,
46010 Valencia, Spain

[3] Department of Physiotherapy, University of Valencia, 46010 Valencia, Spain

[*] Correspondence: trinidad.sentandreu@uv.es; Tel.: +34-963-864-007

Abstract: Background: Defining frailty typologies would contribute to guiding specific care interventions. These typologies could additionally be related to different health outcomes. This study aims at identifying subgroups of frail older adults based on the physical frailty phenotype and examining the relationships of these frailty profiles with quality of life and perceived health. Methods: This study relies on data from the SHARE project, namely a representative sample of 1765 Spanish-dwelling older adults identified as frail or pre-frail. Analysis included general descriptive statistics, exploratory latent class analysis (LCA) to determine the number of frailty subgroups, and LCA with covariates to examine differential relationships with markers of successful aging. Results: Statistical criteria and interpretability of the classes suggested that the LCA model with four classes should be retained. Class 1 was identified as the "frail people" group, Class 2 "activity problems" group, Class 3 "fatigued" group, and those belonging to Class 4 "lack of strength" group. Final LCA with covariates showed lower levels of quality of life and perceived health of the "frail" as compared to other frailty subgroups. Conclusion: This study revealed four different patterns of frailty attributes and further offered evidence on individuals' differential status of health regarding distinct frailty conditions.

Keywords: older adults; frailty profiles; latent class analysis; quality of life; perceived health

1. Introduction

The aging of society constitutes an important challenge for health care systems due to the increase in the life expectancy [1]. The current generation of older adults expects to age well, and to maintain their general well-being and, ultimately, enhance the quality of later life [2].

A fundamental issue in elderly care is targeting those older people at risk and in need of care interventions [3]. An age-related condition is frailty, which is a syndrome probably due to multiple causes and characterized by diminished strength, endurance, and physiological function that promotes dependency and ultimately death [4]. Different operational definitions of frailty have been proposed, but the most commonly used is the frailty phenotype by Fried et al. [5]. Although there is no consensus, this definition has been used as a gold-standard in many studies [6]. Criteria describing Fried's phenotype include: unintentional weight loss, exhaustion, weakness, slowness and reduced physical activity. In this regard, other studies have used modified versions [7–9] or other physical frailty criteria [10] in order to define this syndrome.

Further specification of frailty by defining profiles of frail older people contributes to the ongoing debate on the conceptualization of frailty and could improve interventions [3]. Evidence suggests that frail individuals are not a clinically homogeneous group [11], but to date, the heterogeneity in the

frail population has not been fully acknowledged in care interventions [3]. Identification of different profiles within the frailty people may be of great help in clinical settings, in order to better manage frail people [12].

Some studies have looked at profiles or clusters of frailty. Some of them have used cluster analytical techniques, while others have used latent class analytic techniques. All these studies have had different scopes, for example using samples from the general population [13–15], only a part of the general population such as women [16], or patients of a hospital [17]. Additionally, the studies on frailty profiles have used a variety of indicators to get the profiles. Some of these studies only used Fried's criteria [13–16,18], while others included psychosocial indicators of frailty and/or related problems [3,11,17,19].

Few studies have looked for classes or clusters only employing the physical dimensions of frailty. Among them, Bandeen-Roche et al. [16] studied older women (65 years or older) in the general population and used latent class analysis (LCA) to get classes from the five physical conditions of the frailty syndrome. Their results point out two classes, frail and robust older women. Frail women had a higher risk of disability, institutionalization, or death. Chen et al. [13] also studied a sample of community-dwelling older adults, men and women, and performed LCA analyses on the five physical indicators of frailty, and again found two classes, frail and robust. Then, they used logistic regression to relate the two classes with other variables and found frailty associated with age, poorer health, more depression and anxiety, less social activity, not consuming alcohol and higher rates of cognitive impairment. Lohman et al. [15] also employed LCA on the five indicators of frailty in a sample of 51 years or older Americans, and found the same two classes (frail and robust) and frailty condition was associated to a number of negative health outcomes. Nevertheless, they also estimated LCA including persistent pain and they argued that the classes from this LCA model better related to health outcomes. However, Liu et al. [14] employed LCA to find frailty classes in a sample of community-dwelling Taiwanese adults aged 50 or older, and contrary to the aforementioned evidence, they found four classes: robust, mobility group, low activity and non-mobility group.

With regard to the outcomes frailty may be linked to, quality of life (QoL) is a salient one in old age. The concept of QoL includes dimensions such as the feeling of well-being and the health-related quality of life (HRQoL), which are strong indicators of successful aging [20]. Different studies have shown a negative association between physical frailty and quality of life [21–26] or perceived health [9,21,23,27–31], but there is no evidence whatsoever on how quality of life may be differently related to different frailty profiles. However, relating frailty profiles to quality of life and healthy aging markers allows for a patient-centered approach rather than an approach centered in the syndrome.

Therefore, the aim of the present study was: firstly, to identify subgroups or profiles of frailty in older adults based on the physical conditions that define the frailty status; and secondly, to estimate the relationships of these profiles with quality of life and perceived health indicators. The novelty of this research is analyzing only pre-frail and frail subjects in order to avoid the simple clustering into two groups of frail and non-frail. That is, the aim of this research is to distinguish classes within the people that are already frail or at least have pre-frail conditions.

2. Materials and Methods

2.1. Sample and Procedure

This study was carried out using data from the Survey of Health, Aging and Retirement in Europe (SHARE) Wave 6 [32,33]. SHARE is a longitudinal study focused on the study of European populations aged 50 and older. Data were gathered using probability-based sampling, whose further details can be found in Malter and Börsch-Supan [34].

From the 6th Wave of SHARE data, we selected the pre-frail and frail Spanish-dwelling participants that were 60 years old and older, yielding a total of 1765 individuals.

2.2. Instruments and Measures

Frailty was measured as previously operationalized in SHARE [7,8]. This frailty approach is based on the five criteria established by Fried et al. [5] and has been tested and validated by different authors [8,35,36]. The specific five attributes used in this study were:

- Unintentional weight loss was operationalized using the question "What has your appetite been like". It scored positive when the participants reported "a diminution in desire for food". In the case of an uninterpretable response to the question, the participant was asked whether they had been eating more or less than usual. Answering "less" was also considered a positive indicator of unintentional weight loss.
- Fatigue, resulting from a positive response to the question, "In the last month, have you had too little energy to do things you wanted to do?"
- Slowness was defined as a positive answer to any of the following two mobility questions strongly associated with low speed: "Because of a health problem, do you have difficulty walking 100 m?' or "Because of a health problem, do you have difficulty climbing one flight of stairs without resting?". Both questions referred to difficulties lasting more than three months.
- Weakness was assessed by handgrip strength measurements (twice for each hand) using a dynamometer. The maximum grip strength measure was analyzed according to the cut-off points stratified by gender and body max index, as proposed by Fried et al. [5].
- Physical activity was measured using the question "How often do you engage in activities that require a moderate level of energy such as gardening, cleaning the car, or going for a walk?" The criterion was fulfilled for participants answering either "one to three times a month" or "hardly ever or never."

One point was allocated for each fulfilled criterion. Participants with zero points were classified as robust, those with one or two points were classified as pre-frail, and those with three to five points were classified as frail [5]. Robust older adults were excluded from the study.

Quality of life was measured using the abridged version of the Control, Autonomy, Self-realization, Pleasure scale (CASP-19) [37] designed for SHARE purposes [38]. Items were answered in a 4-point Likert scale ranging from 1 (never) to 4 (often). A total score was obtained by summing all item scores. The final score ranged from 12 to 48, with the highest values indicating better quality of life.

Perceived health was measured by means of an item of general perceived health included within the SF-36 [39], namely "Would you say your health is . . . ?". A 5-point Likert scale was used, ranging from 1 (poor) to 5 (excellent).

2.3. Ethical Clearance

The Ethical Approval for gathering of the data used in this study was obtained by the SHARE project and it can be publicly consulted at: http://www.share-project.org/fileadmin/pdf_documentation/MPG_Ethics_Council_SHARE_overall_approval_29.05.2020__en_.pdf. More information at: http://www.share-project.org/.

2.4. Statistical Analyses

Descriptive statistics for all variables under study were calculated in SPSS 26. Mplus 8 [40] was used for latent mixture modeling. All models were estimated with robust (full information) maximum likelihood estimation (MLR). The mixture model used was LCA. In LCA, subgroup membership is not observed and must be inferred from the data [41]. LCA was used in an exploratory way, and the number of classes retained was based on several statistical criteria. Firstly, we used information criteria such as the Bayesian information criterion (BIC), sample size-adjusted BIC (ABIC), and Akaike information criterion (AIC), with smaller values indicating better fit. Secondly, entropy, a statistic that assesses accuracy and can range from 0 to 1 (perfect accuracy), was considered. Statistical

model comparison likelihood ratio tests and bootstrapping procedures were also used—pecifically, the Lo-Mendell-Rubin test (LMR) [42] and the Bootstrap likelihood ratio test (BLRT) [43]. These tests compare the improvement between neighboring class models with a statistically significant result interpreted as fit improvement due to the extra class. Beyond these criteria, interpretability of the results was also considered [44]. The recent developments in LCA consider relating the indicators to the latent classes and also relating the classes extracted to a set of external variables [45]. Once the number of latent classes was determined, groups of participants based on these classes were compared based on several markers of successful aging. This new LCA with covariates was also tested. In this LCA with covariates, quality of life and perceived health were treated as continuous.

3. Results

3.1. Descriptive Statistics

Among the 1765 participants, 1044 participants out of the total sample were female (59.2%) and the remaining 721 were male (40.8%). Their mean age was 75.22 years old (SD = 8.86). Overall, 1285 (72.8%) were pre-fail and 480 (27.2%) were frail, classified according to the Fried frailty phenotype [5]. Descriptive statistics of the categorical variables involved in the study are shown in Table 1. Prefrail and frail groups were compared by age and gender. There was a significant mean difference in age (t (1763) = −7.17, $p < 0.001$), with frail people being older (Mean = 77.66, SD = 8.5) than pre-frail people (Mean = 74.31, SD = 8.82). Regarding gender, there was also a significant association with frailty condition ($\chi^2(1) = 14.57$, $p < 0.001$). Among the women, 30.6% were frail, while only 22.3% of the men were.

Table 1. Descriptive statistics of the categorical variables involved in the study.

Variable	Mean ± SD or n (%)
Gender	
Female	1044 (59.2%)
Male	721 (40.8)
Frailty condition	
Pre-frail	1285 (72.8%)
Frail	480 (27.2%)
Age	75.22 (8.86)
Appetite (Loss)	321 (20.5)
Fatigue (Yes)	1002 (63.9)
Slowness (Yes)	731 (41.4)
Strength (Lack)	767 (57.1)
Activity (Inactive)	728 (41.2)
Perceived Health	
Poor	451 (25.6)
Fair	672 (38.1)
Good	508 (28.8)
Very good	114 (6.5)
Excellent	20 (1.1)
Quality of Life	33.40 ± 6.32

Notes: SD = Standard Deviation; n = number of observations.

3.2. Frailty Classes

LCAs from one to four classes were estimated, because with only five frailty indicators more than four classes do not reduce complexity. The model with one class was used as a baseline model against which to compare the models with extra classes. Table 2 shows all statistical criteria considered to decide the number of classes retained. The model with four classes had the lowest information criteria, and had statistically significant LMR and BLRT tests. However, the best entropy data were obtained with three classes. Therefore, the criteria are slightly contradictory, and attending to results

by Nylund et al. [46], we have given priority to the results of the BRLT test and BIC because they work better for this type of model. We also found four classes being more interpretable than three.

Table 2. Models' fit for 1 to 4 classes.

#Classes	AIC	BIC	ABIC	Entropy	LMR Test	*p*	BLR Test	*p*
1	10,271.1	10,298.5	10,282.6	NA	NA	NA	NA	NA
2	9993.4	10,053.7	10,018.7	0.717	283.3	<0.001	289.6	<0.001
3	9828.1	9921.2	9867.2	0.787	173.4	<0.001	177.3	<0.001
4	9737.3	9863.2	9790.2	0.680	100.5	<0.001	102.8	<0.001

Notes: AIC = Akaike information criterion; BIC = Bayesian information criterion; ABIC = adjusted BIC; LMR = Lo-Mendell-Rubin test; BLRT = bootstrapped log-likelihood ratio test; NA = not applicable.

3.3. Relations with the Latent Classes

Once the number of classes to retain has been decided, we proceed to estimate an LCA with four classes and four covariates, age, gender as control variables, and health status and quality of life as markers of quality of life. Model fit statistics for this model were even better than those of the LCA with four classes and no covariates. Model fit was: AIC = 7998.5, BIC = 8184.1, ABIC = 8072.8, with entropy = 0.755. Class 1 included 526 (35.51%) participants, with class 2 including 207 or 13.98% of the cases, class 3 had 364 (24.58%) cases, and the rest (384, 25.92%) of the participants were included in class 4.

Table 3 offers the conditional probabilities of each class for every indicator of frailty. These conditional probabilities allow for interpreting the sub-groups or classes. Class 1 has relatively high probabilities in all frailty indicators, and thus this group represents "frail people". Class 2 is characterized for high probabilities in slowness and activity, this group represents people with "activity problems". Class 3 has very high probability of being fatigued and very low probabilities in the rest of indicators, and therefore are old adults that are "fatigued". Finally, class 4 is characterized by being high in the weakness indicator (lack of strength) and therefore will be labeled "lack of strength".

Table 3. Conditional probabilities of the manifestations in each class.

Indicators	Class 1. Frail n = 526	Class 2. Mobility Problems n = 207	Class 3. Fatigued n = 364	Class 4. Lack of Strength n = 384
1. Appetite	0.377	0.172	0.117	0.072
2. Fatigue	0.826	0.259	1.00	0.245
3. Slowness	0.697	0.374	0.120	0.076
4. Strength	0.779	0.000	0.160	1.00
5. Activity	0.595	0.598	0.062	0.132

A graphical representation of the conditional probabilities is offered in Figure 1.

In this LCA model with covariates, the key point is the effects of the covariates on the classes. Class 1 (frail people) is taken as the reference group, and therefore all effects in a class are compared to frail people. The effects in terms of coefficients and odds-ratios are presented in Table 4. All effects of age, gender, quality of life and perceived health were statistically significant.

Regarding the effects of covariates in the comparison between class 2 (mobility problems) and class 1 (frail), the sign of the coefficients indicates that an increase in age make a person more likely to be frail than having only mobility problems, and the same is true for being male. However, increases in quality of life and perceived health increase the probability of being in the group of mobility group rather than in the frailty group. When odds ratios are considered, the probability of being in the frailty group and not in the mobility problems group is 1.14-fold increased per year of age, while it is increased 1.62-fold if you are a man. On the contrary, the odds of being in the mobility group (vs. frail) increases 5.88-fold with each point increase in perceived health.
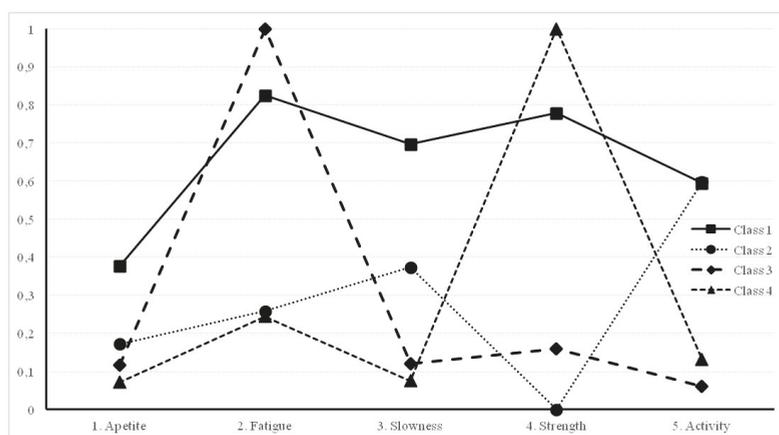
Figure 1. Conditional probabilities of symptoms depending on the class.

Table 4. Effects, standard errors, odds-ratio, confidence intervals and significance tests for all covariates in the model with class 1 as the reference group.

Covariate	Class 2 vs. Class 1						
	Effect	**SE**	*p*	**Odd-Ratio**	**SE**	*95% CI*	*p*
Age	−0.133	0.02	<0.01	0.875	0.02	0.835–0.914	<0.01
Gender (0 = female, 1 = male)	−0.489	0.03	0.11	0.614	0.18	0.254–0.974	0.04
Quality of Life	0.023	0.03	<0.01	1.225	0.04	1.145–1.305	<0.01
Perceived Health	1.772	0.31	<0.01	5.882	1.81	2.262–9.502	<0.01

Covariate	Class 3 vs. Class 1						
	Effect	**SE**	*p*	**Odd-Ratio**	**SE**	*95% CI*	*p*
Age	−0.18	0.02	<0.01	0.804	0.01	0.784–0.824	<0.01
Gender (0 = female, 1 = male)	−0.53	0.28	0.06	0.585	0.16	0.265–0.905	0.01
Quality of Life	0.169	0.03	<0.01	1.184	0.04	1.104–1.264	<0.01
Perceived Health	1.676	0.25	<0.01	5.347	1.37	2.607–8.807	<0.01

Covariate	Class 4 vs. Class 1						
	Effect	**SE**	*p*	**Odd-Ratio**	**SE**	*95% CI*	*p*
Age	−0.084	0.02	<0.01	0.919	0.02	0.879–0.959	<0.01
Gender (0 = female, 1 = male)	−1.099	0.28	<0.01	0.333	0.09	0.153–0.513	<0.01
Quality of Life	0.169	0.03	<0.01	1.265	0.04	1.185–1.345	<0.01
Perceived Health	1.679	0.26	<0.01	7.011	1.86	3.290–10.73	<0.01

When class 3 (fatigued) is compared to class 1 (frail), it follows the same pattern of relationship. That is, being older and male makes a person more likely to be in the frail group, while a better quality of life and health increase the likelihood of being in the fatigued group (vs. frail). In terms of odd-ratios, being a year older increases the odds of being frail (vs. fatigued) 1.24-fold. Being male increases the odds of being frail (vs. fatigued) 1.70-fold. Regarding quality of life and health, we estimated that the odds of being in the fatigued group (vs. frail) increases 1.18-fold with a change of one point in quality of life and 5.34-fold per one unit change in perceived health.

Finally, class 4 (lack of strength) is compared with class 1 (frail), and again the pattern of relationships remains the same. The odds of being frail (vs. lack of strength) increases 1.08-fold with each added year of life, and 3.03-fold for being male. On the other hand, the odds of being in the group of lack of strength (vs. frail) increases 1.26 with each unit increase in quality of life, and 7.011 with each unit increase in perceived.

In sum, the analyses of the effects reflect that age and being male are associated with the probabilities of being frail vs. the other "less severe" groups of frailty symptoms. On the contrary, a better perceived health and quality of life are expected in classes 2 (mobility problems), 3 (fatigued), and 4 (lack of strength) compared to the frail group.

4. Discussion

The present study reports four different classes of frailty. All individuals involved in the study were already displaying pre-frail or frail conditions, implying that the four subtypes of frailty are all substantive. The "Frail" class (35.51% of the sample) is composed of those individuals with high probabilities of displaying all five indicators of physical frailty. The "Activity problems" class (13.98%) comprises older adults who most likely present slowness and physical inactivity. The "fatigued" class (24.58%) is made up of individuals whose only expected symptom is fatigue, and who do not have problems regarding any other indicators of physical frailty. Finally, "lack of strength" class (25.92%) is similar to the "fatigued" class in that it includes individuals whose only probable ailment is a relevant lack of strength, but who are expected to perform well in any other indicator.

One of the goals of the study was to disentangle frailty subtypes only among those individuals whose frail or pre-frail physical conditions were already evident. Previous studies on general population samples found a two-class solution of frail vs. non-frail individuals [13–16]. An exception was the study by Liu et al. [14], in which up to four subtypes of frailty were found. In the four-class model retained by the authors, more than half of the sample was identified as non-frail, and the rest were assigned to three different groups: mobility-type frailty, with a higher prevalence of slowness and weakness; non-mobility-type frailty, with higher exhaustion and weight loss; and the low physical activity group. To some point, the mobility-type frailty was similar to the "activity problems" class found in our study, while non-mobility-type frailty is more similar to the "fatigued" class. However, in the study by Liu et al. [14], weight loss and fatigue were not salient symptoms for any of the four classes, nor was there a frail class. Although the physical indicators may be associated through interrelated pathways, different underlying mechanisms may determine these subtypes. Wasting or chronic inflammatory processes may contribute to the non-mobility group, and, on the other hand, the mobility group could be largely due to neurodegeneration [14]. Existing bibliography refers to the existence of different trigger conditions that could activate the frailty process [47,48]. Initially, such conditions could be associated with the physical manifestations of frailty that characterize different frailty profiles obtained in this study: "fatigued", "activity problems" and "lack of strength". Studies show that alterations of the neuroendocrine system, micronutrients deficiency, or other factors related to energy and nutritional imbalance could be key point in this activation of frailty [47]. These alterations could be related to fatigue, among other manifestations. The literature has also referred to a lack of activity as a precursor of frailty and how sedentary lifestyle can be decisive in this process [47,49]. On the other hand, Fried et al. [5] presented a construct based on energy imbalance and sarcopenia to activate the cycle of frailty, whose first manifestation could be weakness [48].

A second goal of this study was relating frailty profiles to successful aging-related outcomes. Indicators of successful aging employed in the study were quality of life and perceived health. We compared all classes against the "frail" class, in order to determine whether the effects of frailty on quality of life and perceived health varied between those with high probabilities of displaying all physical indicators of frailty and those whose frailty conditions were not as widespread. The results show statistically significant better quality of life and perceived health in "activity problems", "fatigued" and "lack of strength" classes compared to the "frail" class. These results are in line with previous literature pointing to a negative association between quality of life and physical frailty, and between perceived health and physical frailty [9,21–28,30,31]. Some of the studies classified the general population and obtained two groups that then related to outcomes such as health and wellbeing indicators, which makes it difficult to compare their results with ours because our groups only include pre-frail and frail people [13,15,16]. However, their overall results show that frailty is negatively

associated with health and wellbeing measures, which is in line with our results in the sense that the frail group with the presence of most indicators of a frail condition had worse health and worse quality of life (wellbeing). Additionally, our results offer a first glimpse of the idiosyncratic relationships between markers of successful aging and frailty profiles. Thus, the "activity problems", "fatigued" and "lack of strength" frailty typologies had higher probabilities (with odd ratios of 1.22, 1.18 and 1.26, respectively) of displaying better quality of life than the "frail" frailty status typology. On its part, perceived health followed similar patterns of relationship, but the odd ratios were higher in the "lack of strength" typology (odd-ratio 7.01), where a higher score of perceived health is more likely when compared to the "frail" typology, followed by the "mobility problems" typology (5.88) and "fatigued" typology (5.34). This result points out that as the number of frailty symptoms accumulates, the negative impact on quality of life and perceived health is stronger. In other words, the presence of more frailty symptoms in a person notoriously undermines self-reported health and quality of life.

Age and gender were also included as covariates in LCA models to provide a better description of the profiles. A large volume of the literature has demonstrated that frailty is associated with age, when comparing frail versus non-frail groups [5,9,13]. Additionally, the evidence generated in this study shows that increased age increases the odds of being in the "frail" class, described as the most severe one (or at least with higher probabilities in all criteria). Regarding gender differences, several studies have consistently shown a higher prevalence of frailty in women [50]. In line with the literature data, we observed that the proportion of frail women was significantly higher than the proportion of frail men according to the modified version of Fried's phenotype. Additionally, when the frailty status typologies were considered, this study shows that being male is associated with the probability of being in the frail subtype. This class has high probabilities in the five frailty attributes and therefore could be considered the most severe class compared to the other groups of manifestations. These findings could be masked when using an overall frailty label and could give some explanation to another gender-related condition in the existing bibliography, the higher mortality among men resulting from frailty [18,51,52]. Sex-specific pathways to frailty could also explain specific gender-related profiles [19].

Among studies examining different frailty profiles or clusters, the ones using the physical operationalization of frailty employed samples of the general population in Japan [13], Taiwan [14] and the United States [15], or a sample of the general female population in the United States [16]. As all these studies took place in North America or Asia, there is a lack of knowledge in reference to frailty subtypes or classes in other populations. The present study offered evidence of frailty profiles in a representative sample of Spanish-dwelling older adults, giving a first glimpse of frailty subtypes in Europe. Moreover, in three out of four of these previous studies, the same two frailty classes were found, representing the robust and frail groups of individuals [13,15,16]. By excluding non-frail individuals, this study revealed four different patterns of frailty attributes, which sets the basis for differential treatment in order to lessen the detrimental effects of frailty in quality of life and perceived health.

Despite the contributions made by this study, there are some limitations too. For example, despite examining differences in quality of life and perceived health among classes, there is still no evidence on how these frailty classes may differently predict markers of successful aging, or vice-versa. Previous longitudinal evidence points to a bidirectional relationship between frailty and quality of life [24] and a causal relationship between frailty and reduced health-related quality of life [28]. The cross-sectional design of our study does not allow conclusions of directional relationships between frailty classes and markers of good aging. Moreover, in this study, frailty was operationalized by its physical indicators. However, other operationalizations of frailty, or a combination of them, were also employed in the literature. Even though physical frailty has been used as the gold-standard for frailty measurement [6], these other frailty measurements are also possible and might lead to different results.

5. Conclusions

All in all, this study contributes to the pre-existing literature on frailty classes by studying substantive frailty typologies. To the best of our knowledge, this is the first time a representative sample of Spanish-dwelling older adult population has been used, meaning that inferences about population can be drawn and hence "frail", "activity problems", "fatigued" and "lack of strength" classes perfectly mirror frailty heterogeneity in Spanish dwelling older adults. This research also examined differences in quality of life and perceived health among "activity problems", "fatigued" and "lack of strength" classes against the "frail" class. However, future research should focus on interclass comparisons among all classes using these and other age-relevant variables, in order to gather information regarding the specific characteristics of every frailty class, which could foster patient-centered intervention development.

Author Contributions: Conceptualization, J.M.T., T.S.-M. and I.F.; methodology, J.M.T., formal analysis, J.M.T. and I.F.; data curation, J.M.T. and I.F.; writing—original draft preparation, J.M.T., T.S.-M. and I.F.; writing—review and editing, J.M.T., T.S.-M. and I.F.; project administration, J.M.T.; funding acquisition, J.MT. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Machón, M.; Mateo-Abad, M.; Vrotsou, K.; Zupiria, X.; Güell, C.; Rico, L.; Vergara, I. Dietary patterns and their relationship with frailty in functionally independent older adults. *Nutrients* **2018**, *10*, 406. [CrossRef] [PubMed]

2. Bowling, A.; Iliffe, S. Psychological approach to successful ageing predicts future quality of life in older adults. *Health Qual. Life Outcomes* **2011**, *9*, 13. [CrossRef] [PubMed]

3. Looman, W.M.; Fabbricotti, I.N.; Blom, J.W.; Jansen, A.P.D.; Lutomski, J.E.; Metzelthin, S.F.; Huijsman, R.; TOPICS-MDS Research Consortium. The frail older person does not exist: Development of frailty profiles with latent class analysis. *BMC Geriatr.* **2018**, *18*, 84. [CrossRef] [PubMed]

4. Morley, J.E.; Vellas, B.; van Kan, G.A.; Anker, S.D.; Bauer, J.M.; Bernabei, R.; Cesari, M.; Chumlea, W.C.; Doehner, W.; Evans, J.; et al. Frailty consensus: A call to action. *J. Am. Med. Dir. Assoc.* **2013**, *14*, 392–397. [CrossRef]

5. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M156. [CrossRef]

6. Clegg, A.; Rogers, L.; Young, J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: A systematic review. *Age Ageing* **2015**, *44*, 148–152. [CrossRef]

7. Santos-Eggimann, B.; Cuénoud, P.; Spagnoli, J.; Junod, J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J. Gerontol. A Biol. Sci. Med. Sci.* **2009**, *64*, 675–681. [CrossRef]

8. Romero-Ortuno, R.; Walsh, C.D.; Lawlor, B.A.; Kenny, R.A. A frailty instrument for primary care: Findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). *BMC Geriatr.* **2010**, *10*, 57. [CrossRef]

9. Jürschik, P.; Nunin, C.; Botigué, T.; Escobar, M.A.; Lavedán, A.; Viladrosa, M. Prevalence of frailty and factors associated with frailty in the elderly population of Lleida, Spain: The FRALLE survey. *Arch. Gerontol. Geriatr.* **2012**, *55*, 625–631. [CrossRef]

10. Ensrud, K.E.; Ewing, S.K.; Taylor, B.C.; Fink, H.A.; Cawthon, P.M.; Stone, K.L.; Hillier, T.A.; Cauley, J.A.; Hochberg, M.C.; Rodondi, N.; et al. Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women. *Arch. Intern. Med.* **2008**, *168*, 382–389. [CrossRef]

11. Nguyen, Q.D.; Wu, C.; Odden, M.C.; Kim, D.H. Multimorbidity Patterns, Frailty, and Survival in Community-Dwelling Older Adults. *J. Gerontol. A Biol. Sci. Med. Sci.* **2019**, *74*, 1265–1270. [CrossRef] [PubMed]

12. Marcucci, M.; Franchi, C.; Nobili, A.; Mannucci, P.M.; Ardoino, I.; REPOSI Investigators. Defining aging phenotypes and related outcomes: Clues to recognize frailty in hospitalized older patients. *J. Gerontol. A Biol. Sci. Med. Sci.* **2017**, *72*, 395–402. [CrossRef] [PubMed]

13. Chen, S.; Honda, T.; Chen, T.; Narazaki, K.; Haeuchi, Y.; Supartini, A.; Kumagai, S. Screening for frailty phenotype with objectively-measured physical activity in a west Japanese suburban community: Evidence from the Sasaguri Genkimon Study. *BMC Geriatr.* **2015**, *15*, 36. [CrossRef] [PubMed]

14. Liu, L.K.; Guo, C.Y.; Lee, W.J.; Chen, L.Y.; Hwang, A.C.; Lin, M.H.; Peng, L.N.; Chen, L.K.; Liang, K.Y. Subtypes of physical frailty: Latent class analysis and associations with clinical characteristics and outcomes. *Sci. Rep.* **2017**, *7*, 46417. [CrossRef]

15. Lohman, M.C.; Whiteman, K.L.; Greenberg, R.L.; Bruce, M.L. Incorporating persistent pain in phenotypic frailty measurement and prediction of adverse health outcomes. *J. Gerontol. A Biol. Sci. Med. Sci.* **2017**, *72*, 216–222. [CrossRef]

16. Bandeen-Roche, K.; Xue, Q.L.; Ferrucci, L.; Walston, J.; Guralnik, J.M.; Chaves, P.; Zeger, S.L.; Fried, L.P. Phenotype of frailty: Characterization in the women's health and aging studies. *J. Gerontol. A Biol. Sci. Med. Sci.* **2006**, *61*, 262–266. [CrossRef]

17. Sadiq, F.; Kronzer, V.L.; Wildes, T.S.; McKinnon, S.L.; Sharma, A.; Helsten, D.L.; Scheier, L.M.; Avidan, M.S.; Ben Abdallah, A. Frailty Phenotypes and Relations with surgical outcomes: A latent class analysis. *Anesth. Analg.* **2018**, *127*, 1017–1027. [CrossRef]

18. Romero-Ortuno, R.; Soraghan, C. A Frailty Instrument for primary care for those aged 75 years or more: Findings from the Survey of Health, Ageing and Retirement in Europe, a longitudinal population based cohort study (SHARE-FI75+). *BMJ Open* **2014**, *4*, e006645. [CrossRef]

19. Segaux, L.; Oubaya, N.; Broussier, A.; Baude, M.; Canouï-Poitrine, F.; Naga, H.; Laurent, M.; Leissing-Desprez, C.; Audureau, E.; Ferrat, E.; et al. Identification of five frailty profiles in community-dwelling individuals aged 50–75: A latent class analysis of the SUCCEED survey data. *Maturitas* **2019**, *127*, 1–11. [CrossRef]

20. Ingrand, I.; Paccalin, M.; Liuu, E.; Gil, R.; Ingrand, P. Positive perception of aging is a key predictor of quality-of-life in aging people. *PLoS ONE* **2018**, *13*, e0204044. [CrossRef]

21. Sentandreu-Mañó, T.; Badenes-Ribera, L.; Fernández, I.; Oliver, A.; Burks, D.J.; Tomás, J.M. Frailty in the old age as a direct marker of quality of life and health: Gender differences. *Soc. Indic. Res.* **2019**. [CrossRef]

22. Chang, S.F.; Wen, G.M. Association of frail index and quality of life among community-dwelling older adults. *J. Clin. Nurs.* **2016**, *25*, 2305–2316. [CrossRef] [PubMed]

23. Pinto, J.M.; Fontaine, A.M.; Neri, A.L. The influence of physical and mental health on life satisfaction is mediated by self-rated health: A study with Brazilian elderly. *Arch. Gerontol. Geriatr.* **2016**, *65*, 104–110. [CrossRef] [PubMed]

24. Gale, C.R.; Cooper, C.; Deary, I.J.; Aihie Sayer, A. Psychological well-being and incident frailty in men and women: The English Longitudinal Study of Ageing. *Psychol. Med.* **2014**, *44*, 697–706. [CrossRef]

25. Mulasso, A.; Roppolo, M.; Rabaglietti, E. The role of individual characteristics and physical frailty on health related quality of life (HRQOL): A cross sectional study of Italian community-dwelling older adults. *Arch. Gerontol. Geriatr.* **2014**, *59*, 542–548. [CrossRef] [PubMed]

26. Bilotta, C.; Bowling, A.; Casè, A.; Nicolini, P.; Mauri, S.; Castelli, M.; Vergani, C. Dimensions and correlates of quality of life according to frailty status: A cross-sectional study on community-dwelling older adults referred to an outpatient geriatric service in Italy. *Health Qual. Life Outcomes* **2010**, *8*, 56. [CrossRef]

27. Lenardt, M.H.; Carneiro, N.H.; Binotto, M.A.; Willig, M.H.; Lourenço, T.M.; Albino, J. Frailty and quality of life in elderly primary health care users. *Rev. Bras. Enferm* **2016**, *69*, 478–483. [CrossRef]

28. Ferrer, A.; Formiga, F.; Cunillera, O.; Megido, M.J.; Corbella, X.; Almeda, J. Predicting factors of health-related quality of life in octogenarians: A 3-year follow-up longitudinal study. *Qual. Life Res.* **2015**, *24*, 2701–2711. [CrossRef]

29. Chang, Y.W.; Chen, W.L.; Lin, F.G.; Fang, W.H.; Yen, M.Y.; Hsieh, C.C.; Kao, T.W. Frailty and its impact on health-related quality of life: A cross-sectional study on elder community-dwelling preventive health service users. *PLoS ONE* **2012**, *7*, e38079. [CrossRef]

30. Lin, C.C.; Li, C.I.; Chang, C.K.; Liu, C.S.; Lin, C.H.; Meng, N.H.; Lee, Y.D.; Chen, F.N.; Li, T.C. Reduced health-related quality of life in elders with frailty: A cross-sectional study of community-dwelling elders in Taiwan. *PLoS ONE* **2011**, *6*, e21841. [CrossRef]

31. Masel, M.C.; Graham, J.E.; Reistetter, T.A.; Markides, K.S.; Ottenbacher, K.J. Frailty and health related quality of life in older Mexican Americans. *Health Qual. Life Outcomes* **2009**, *7*, 70. [CrossRef] [PubMed]

32. Börsch-Supan, A. Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 6. Release version: 6.1.1 SHARE-ERIC. Data Set. 2018. Available online: http://www.share-project.org/home0.html (accessed on 16 September 2020).

33. Börsch-Supan, A.; Brandt, M.; Hunkler, C.; Kneip, T.; Korbmacher, J.; Malter, F.; Schaan, B.; Stuck, S.; Zuber, S.; SHARE Central Coordination Team. Data Resource Profile: The Survey of Health, Ageing and Retirement in Europe (SHARE). *Int. J. Epidemiol.* **2013**, *42*, 992–1001. [CrossRef] [PubMed]

34. Malter, F.; Börsch-Supan, A. *SHARE Wave 6: Panel innovations and collecting Dried Blood Spots*; MEA, Max Planck Institute for Social Law and Social Policy: Munich, Germany, 2017.

35. Romero-Ortuno, R. The Frailty Instrument of the Survey of Health, Ageing and Retirement in Europe (SHARE-FI) predicts mortality beyond age, comorbidities, disability, self-rated health, education and depression. *Eur. Geriatr. Med.* **2011**, *2*, 323–326. [CrossRef]

36. Macklai, N.S.; Spagnoli, J.; Junod, J.; Santos-Eggimann, B. Prospective association of the SHARE-operationalized frailty phenotype with adverse health outcomes: Evidence from 60+ community-dwelling Europeans living in 11 countries. *BMC Geriatr.* **2013**, *13*, 3. [CrossRef] [PubMed]

37. Hyde, M.; Wiggins, R.D.; Higgs, P.; Blane, D.B. A measure of quality of life in early old age: The theory, development and properties of a needs satisfaction model (CASP-19). *Aging Ment. Health* **2003**, *7*, 186–194. [CrossRef]

38. Von dem Knesebeck, O.; Hyde, M.; Higgs, P.; Kupfer, A.; Siegrist, J. Quality of life and wellbeing. In *Health, Ageing and Retirement in Europe—First Results from the Survey of Health, Ageing and Retirement in Europe*; Börsch-Supan, A., Brugiavini, A., Jürges, H., Mackenbach, J., Siegrist, J., Weber, G., Eds.; Mannheim Research Institute for the Economics of Aging (MEA): Mannheim, Germany, 2005; pp. 199–203.

39. Ware, J.E., Jr.; Gandek, B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *J. Clin. Epidemiol.* **1998**, *51*, 903–912. [CrossRef]

40. Muthén, L.K.; Muthén, B.O. *Mplus User's Guide*, 7th ed.; Muthén & Muthén: Los Angeles, CA, USA, 2012.

41. Muthén, B. Latent variable hybrids: Overview of old and new models. In *Advances in Latent Variable Mixture Models*; Hancock, G.R., Samuelsen, K.M., Eds.; Information Age Publishing, Inc.: Charlotte, NC, USA, 2008; pp. 1–24.

42. Lo, Y.; Mendell, N.; Rubin, D. Testing the number of components in a normal mixture. *Biometrika* **2001**, *88*, 767–778. [CrossRef]

43. McLachlan, G.; Peel, D. *Finite Mixture Models*; Wiley: New York, NY, USA, 2000.

44. Lukočienė, O.; Varriale, R.; Vermunt, J.K. The simultaneous decision(s) about the number of lower- and higher-level classes in multilevel latent class analysis. *Sociol. Methodol.* **2010**, *40*, 247–283. [CrossRef]

45. Janssen, J.H.M.; van Laar, S.; de Rooij, M.J.; Kuha, J.; Bakk, Z. The Detection and modeling of direct effects in latent class analysis. *Struct. Equ. Model.* **2018**, *26*, 280–290. [CrossRef]

46. Nylund, K.L.; Asparouhov, T.; Muthén, B.O. Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Struct. Equ. Model.* **2007**, *14*, 535–569. [CrossRef]

47. García-García, F.J.; Larrión Zugasti, J.L.; Rodríguez Mañas, L. Frailty: A phenotype under review. *Gac. Sanit.* **2011**, *25*, 51–58. [CrossRef] [PubMed]

48. Xue, Q.L. The frailty syndrome: Definition and natural history. *Clin. Geriatr. Med.* **2011**, *27*, 1–15. [CrossRef] [PubMed]

49. Satake, S.; Arai, H. Chapter 1 Frailty: Definition, diagnosis, epidemiology. *Geriatr. Gerontol. Int.* **2020**, *20*, 7–13. [CrossRef] [PubMed]

50. Collard, R.M.; Boter, H.; Schoevers, R.A. Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: A systematic review. *J. Am. Geriatr. Soc.* **2012**, *60*, 1487–1492. [CrossRef] [PubMed]
51. Romero-Ortuno, R.; Fouweather, T.; Jagger, C. Cross-national disparities in sex differences in life expectancy with and without frailty. *Age Ageing* **2014**, *43*, 222–228. [CrossRef] [PubMed]
52. Hubbard, R.E.; Rockwood, K. Frailty in older women. *Maturitas* **2011**, *69*, 203–207. [CrossRef] [PubMed]

Evaluation of Psychophysical Factors in Individuals with Frailty Syndrome Following a 3-Month Controlled Physical Activity Program

Wioletta Dziubek [1], Weronika Pawlaczyk [2,*], Małgorzata Stefańska [1], Joanna Waligóra [3], Maria Bujnowska-Fedak [3] and Joanna Kowalska [1]

[1] Department of Physiotherapy, University School of Physical Education, 51-612 Wroclaw, Poland;
     wioletta.dziubek@awf.wroc.pl (W.D.); malgorzata.stefanska@awf.wroc.pl (M.S.);
     joanna.kowalska@awf.wroc.pl (J.K.)
[2] Lower Silesia Oncology Center, 53-413 Wroclaw, Poland
[3] Department of Family Medicine, Wroclaw Medical University, 51-141 Wroclaw, Poland;
     joanna.waligora@student.umed.wroc.pl (J.W.); maria.bujnowska-fedak@umed.wroc.pl (M.B.-F.)
*   Correspondence: weronika.pawlaczyk13@gmail.com

Abstract: Background: The aim of the study was to compare the emotional state and strength-velocity parameters of patients with frailty and pre-frailty syndrome undertaking a 12-week training programme. Methods: The study was completed by 36 individuals, including 17 with frailty syndrome (FS) and 19 with pre-frailty syndrome (PFS). The age of the subjects ranged from 63 to 89 years, with a mean 69.2 years ($\pm$5.0). The Beck Depression Inventory (BDI), Spielberg's State-Trait Anxiety Inventory (STAI), and Satisfaction with Life Scale (SWLS) were used. The strength of knee muscles was evaluated. The above tests were conducted at two time points: before the training sessions (T1); and after 12 weeks of regular training sessions (T2). Results: After completion of the training programme, statistically significant differences in BDI were observed between the PFS and FS groups (especially in somatic symptoms). Following the training, BDI values in the PFS group were significantly lower (fewer depressive symptoms) than in the FS group. The parameter values describing strength capacities of the lower limbs, both at T1 and T2, proved to be higher in the PFS group. Conclusions: In individuals with pre-frailty and frailty syndrome, the 3-month physical training programme improved the strength parameters of lower limb muscles. An improvement in mood and reduction in depressive symptoms were only observed in the group of subjects with pre-frailty syndrome. Rehabilitation programmes for people with frailty syndrome should include psychotherapeutic activities in addition to physical training in order to improve the psychophysical condition of patients.

Keywords: frailty syndrome; physiotherapy; exercise; mood; BDI; STAI; SWLS; muscle strength

1. Introduction

Advancing age is associated with decreased fitness and physical performance, a deterioration in psychophysical condition, decreased strength and muscle mass (sarcopenia) and impaired balance and neuromuscular coordination. Additionally, elderly people with a sedentary lifestyle suffer from bone weakness and increased susceptibility to injuries and fractures.

Frailty syndrome, otherwise known as weakness or fragility syndrome, is defined as a clinically recognised state of increased sensitivity of the body to endo- and exogenous stress factors due to reduced physiological reserves, resulting from a reduced capacity of various physiological systems [1].

The aetiology of frailty syndrome is not entirely understood. An international group of experts has defined frailty as a clinical state in which there is an increase in an individual's vulnerability for

developing increased dependency and/or mortality when exposed to a stressor [2]. Many interconnected negative stress factors are known to contribute to its development, causing a decrease in systemic reserves at the molecular, cellular and physiological levels, and exacerbating pre-existing pathologies [3].

Elderly people who have been diagnosed with frailty syndrome due to depleting functional organ reserves experience accelerated aging processes [3]. Deterioration of the body's ability to react to stress, disruptions to homeostasis and impairment in regeneration function lead to a more severe disease course, which increases their susceptibility to adverse events such as falls, disability, hospitalisation and death [4]. Additionally, in people over 60 years of age with frailty syndrome, changes to the skeletal muscles such as a reductions in muscle mass and muscle contraction strength, nerve atrophy and slowing of the contractility of muscle fibres are very common. These changes are associated with sarcopenia, a reduction in muscle mass, and, consequently, a reduction in muscle strength. This is associated with a loss of motor units present in muscle fibres. This phenomenon occurs to a similar extent in both genders, with the most significant changes occurring in the lower limbs. Hormonal changes are also thought to have a destructive influence, with decreased hormone concentrations leading to reductions in muscle mass, strength and muscle function. In addition, a lack of physical activity is known to increase the risk of sarcopenia [5].

Changes in the musculoskeletal system may contribute to a loss of physical fitness, impaired balance and falls, leading to a loss of independence and difficulty performing simple and complex activities.

The most frequently used criteria to identify frailty syndrome were proposed by Fried et al. (2001) [6]. These criteria include five indicators: weight loss of more than 5 kg per year, reduced hand grip strength measured on a dynamometer, exhaustion assessed by the CES-D depression scale, reduced gait speed and reduced physical activity measured by the modified Minnesota Leisure Time Activity Questionnaire. The patient must meet three or more criteria for frailty syndrome (FS) to be recognised. If one to two criteria are met, a condition referred to as pre-frailty syndrome (PFS) is declared, which precedes the diagnosis of frailty syndrome [6].

A lack of physical activity is known to accelerate the aging process of the body and may lead to physical disability. Undertaking physical activity has a positive impact not only on physical fitness, but also on mental health, contributing to an improvement in mood and reduced levels of depression and anxiety [7].

The latest scientific reports on frailty syndrome suggest that it can be prevented and treated with regular physical activity [8,9]. According to Mazurek et al. (2018), health training activities positively influence each of the diagnostic criteria that are typical of frailty syndrome, such as weight loss, exercise intolerance, slowing down of gait, weakening of muscle strength and a subjective feeling of weakness and fatigue [10].

Very few scientific reports on this topic have focused on exploring such forms of training that would benefit patients with frailty syndrome at various stages of the disease, as well as to promote effective and scientifically proven physical activity among the elderly as a generally accepted intervention to prevent frailty syndrome [2,11].

Study Aim

The aim of the study was to compare the emotional state and strength-velocity parameters of patients with frailty and pre-frailty syndrome undertaking a 12-week training programme. Specifically, we wanted to assess the emotional state of subjects with frailty and pre-frailty syndrome and determine whether a 12-week training programme improves their mood, and to investigate whether there is a relationship between the emotional state and strength-velocity parameters in the two groups of patients.

2. Material and Methods

2.1. Study Group

Studies were conducted at the Scientific Research Laboratory of the Department of Physiotherapy at the University of Physical Education in Wroclaw. Each participant was informed about the purpose and method of the study and about the possibility of withdrawing from the study at any stage. Participants provided informed consent to take part in the study. The study was approved by the Bioethics Committee of the University School of Physical Education in Wroclaw, Poland (reference no. 15/2020) and conducted in accordance with the Declaration of Helsinki.

Individuals with frailty and pre-frailty syndrome who met the following inclusion criteria qualified for the study: at least three out of five symptoms of frailty syndrome or one to two symptoms in the case of pre-frailty (according to Fried frailty index) confirmed by a doctor, no contraindications to the tests and trials, no participation in another rehabilitation programme, absence of dementia (MMSE > 24), and consent to participate in tests and trainings. Exclusion criteria were also adopted: contraindications to exercise tests and physical training, dysfunctions that make it impossible to perform tests and participate in trainings, less than 70% of training attendance.

The study was completed by 36 individuals, including 17 with frailty syndrome and 19 with pre-frailty syndrome. The age of the subjects ranged from 63 to 89 years, mean 72.1 years (±6.4).

Patients from both groups took part in regular training sessions (Figure 1).
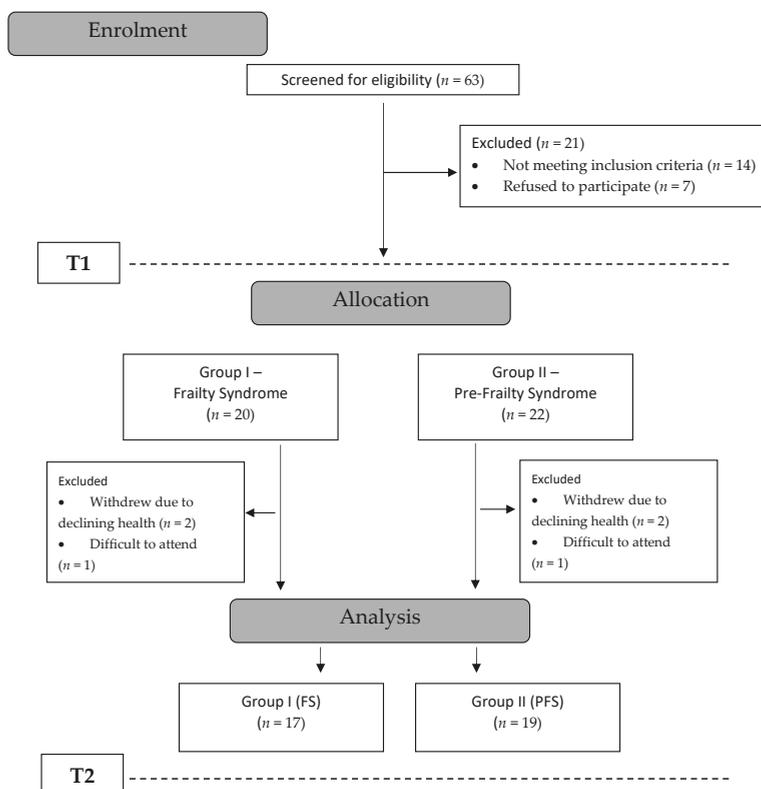
Figure 1. Design and flow of participants throughout the study.

2.2. Measurement Tools

The Beck Depression Inventory (BDI), Spielberg's State-Trait Anxiety Inventory (STAI), and Satisfaction with Life Scale (SWLS) were used.

The BDI contains 21 items that relate to most significant symptoms of depression. The Polish version of the BDI is a translation of the original tool with very good psychometric properties similar to the original (Cronbach's α was 0.95 for clinical trial and 0.93 for control group). The first 13 questions focus on cognitive-affective aspects and the remaining questions relate to somatic symptoms that accompany mood disorders. Scores of 0–11 points indicate no depressive disorders, while higher total scores indicate more severe depressive symptoms according to the applicable standards [12,13].

The SWLS measures an individual's subjective sense of satisfaction with life. The higher the score, the more satisfied with life the respondent is. This study used raw results of the Polish standards, where scores of 5–17 indicate low satisfaction, 18–23 indicate average satisfaction and 24–35 represent high satisfaction with life. The psychometric properties of the Polish version are satisfactory and similar to the original [14,15].

The STAI was used to assess the level of anxiety as a state and as a trait. The subscale of anxiety as a state (X-1) is used to study the current mood of the respondent, while the trait anxiety subscale (X-2) illustrates how the assessed person usually feels. Measurement does not include somatic manifestations of anxiety. The criterion for dividing patients into subgroups of low and high levels of anxiety for the STAI (X-1) is a score of 44, and for STAI (X-2) it is a score of 46. The overall result for each of the two parts of the questionnaire ranges from 20 points, indicating mild anxiety, to 80 points, indicating very severe anxiety. The psychometric properties of the Polish version are similar to the original [16,17].

2.3. Examination of Force–Velocity Parameters

The right and left flexor and extensor muscles of the knee joint were evaluated. The following parameters were analysed: peak torque (Nm), total work (J), and average power (W). The measurements were made using a Multi Joint 4 dynamometer (Biodex, Shirley, NY, USA).

The subject performed flexion and extension tests in isokinetic conditions. Before the measurement, the attachment, seat and dynamometer were adjusted so that extension of the axis of rotation of particular joint was achieved. With appropriate stabilisation, the measurement began with the maximum flexion of the knee, performed fast and with the greatest possible strength. For angular velocity $\omega = 60°/s$, five repetitions were performed [18].

The above tests were conducted at two time points: before the training sessions (T1); and after 12 weeks of regular training sessions (T2).

2.4. Training Sessions

The respondents exercised regularly twice a week for 60 min for 12 weeks. The exercises were carried out in the gymnasium of the Faculty of Physiotherapy of the University of Physical Education in Wroclaw. A single session consisted of a warm-up (10 min) and the main physical workout (about 40 min), followed by stretching, breathing and relaxation exercises (10 min). During the session, the subjects performed general fitness exercises, improving coordination and balance, as well as resistance exercises using Thera-Band with an individually adjusted load. Other sporting equipment was also used, including mats, gym rods and balls.

2.5. Statistical Analysis

The study group was characterised using descriptive statistics, including mean, standard deviation, median, minimum and maximum values, and numbers, confidence interval and percentages were used in the case of qualitative variables. The Shapiro–Wilk test was used to check for normal distribution of the data. Non-parametric tests were used for BDI, SWLS and STAI data (Wilcoxon test to compare two dependent groups and Mann–Whitney U test to compare two independent groups) and parametric

tests for force–velocity parameters (Student's *t*-test to compare two dependent groups and to compare two independent groups). Cohen's d coefficient, pairs rank biserial correlation coefficient as well as Glass rank-biserial correlation coefficient were calculated to assess the magnitude of the effect of the observed relationships [19–22]. The calculations were carried out using STATISTICA 13.1. (StatSoft Polska, Kraków, Poland).

2.6. Results

The comparative analysis of both groups showed that the group of patients with PFS was significantly younger than those with FS (Table 1).

Table 1. Characteristics of the groups.

	PFS Group n = 19			FS Group n = 17			Test T		Cohen's d
	Mean	Median	SD	Mean	Median	SD	t	p	
Age (Years)	69.16	67.00	5.01	75.35	73.00	6.40	−3.25	0.0026 *	1.12
Height (cm)	153.97	162.00	37.68	149.91	160.00	39.05	0.32	0.7528	0.11
Body mass (kg)	77.05	76.00	11.99	70.35	70.00	14.16	1.54	0.1336	0.53
BMI (kg/m^2)	29.39	29.00	3.68	27.98	27.34	5.30	0.94	0.3543	0.32

PFS—pre-frailty syndrome group, FS—frailty syndrome group, * Differences were considered statistically significant at $p < 0.05$.

Before the commencement of training sessions (T1), depressive symptoms (BDI ≥ 12) were recorded in 16 respondents (44%), most of whom were in the PFS group (10 subjects, 53%). After 12 weeks of training (T2), 14 people (39%) still had depressive symptoms. However, at this time point, the number of people with depressive symptoms increased to 10 in the FS group (59%) (Table 2).

Table 2. Percentage distribution of Beck Depression Inventory (BDI) results in the study groups.

Group	BDI Results	T1		T2		Chi^2 p-Value
		n	%	n	%	
PFS	No depression BDI < 12	9	47	15	79	0.0328 *
	Depression BDI ≥ 12	10	53	4	21	
FS	No depression BDI < 12	11	65	7	41	0.6275
	Depression BDI ≥ 12	6	35	10	59	

PFS—pre-frailty syndrome group, FS—frailty syndrome group, BDI—Beck Depression Inventory. * Differences were considered statistically significant at $p < 0.05$.

In the PFS group, a statistically significant decrease in the values describing depressive symptoms (BDI) was observed. The levels of both state anxiety (STAI X-1) and trait anxiety (STAI X-2) were also significantly decreased in this group. Similar trends were not observed in the group with frailty syndrome. Moreover, the level of life satisfaction (SWLS) did not change in either group. The observed relationships were confirmed by a low effect size ($r_c ≤ 0.4$) with no statistical significance and a medium to high effect in the case of statistically significant changes ($r_c ≥ 0.55$) (Table 3).

Table 3. Comparison of initial (T1) and final (T2) results in both groups (PFS and FS).

Group		T1			T2			T1 vs. T2		
		Median	Min	Max	Median	Min	Max	Wilcoxon Test		r_c
								Z	p	
PFS	SWLS	22.00	9.00	30.00	23.00	10.00	30.00	0.00	0.5228	0.15
	BDI (1–13)	5.00	0.00	13.00	3.00	0.00	12.00	2.77	0.0058 *	0.77
	BDI (14–21)	4.00	0.00	11.00	3.00	0.00	10.00	2.41	0.0413 *	0.55
	BDI all	12.00	0.00	20.00	5.00	0.00	21.00	2.07	0.0031 *	0.76
	STAI X-1	44.00	26.00	73.00	40.00	26.00	75.00	1.84	0.0079 *	0.61
	STAI X-2	44.00	25.00	74.00	41.00	23.00	53.00	2.07	0.0070 *	0.70
FS	SWLS	24.00	20.00	30.00	24.00	13.00	28.00	0.49	0.1075	0.39
	BDI 1–13	2.00	0.00	16.00	5.00	0.00	12.00	0.00	0.2934	0.27
	BDI 14–21	5.00	1.00	12.00	8.00	0.00	13.00	1.46	0.0976	0.40
	BDI all	7.00	1.00	21.00	14.00	1.00	22.00	1.34	0.2093	0.34
	STAI X-1	37.00	26.00	55.00	40.00	23.00	56.00	−0.25	0.4229	0.20
	STAI X-2	38.00	25.00	61.00	40.00	25.00	56.00	1.94	0.1488	0.35

PFS—pre-frailty syndrome group, FS—frailty syndrome group, SWLS-Satisfaction with Life Scale; BDI-Beck Depression Inventory; STAI-Spielberg's State-Trait Anxiety Inventory; r_c—pairs rank biserial correlation coefficient; * Differences were considered statistically significant at *p* < 0.05.

The peak torque (PT [Nm]), total work (TW [J]), and average power (aP [W]) were evaluated twice (T1 and T2) during flexion and extension of the knee joint under isokinetic conditions with 60°/s load. The results for these parameters observed after the completion of the training programme in both study groups were higher than the baseline values (Table 4).

Prior to the training programme, no significant differences in the level of depression and anxiety symptoms were observed between the groups. After completion of the training programme, statistically significant differences in BDI were observed between the PFS and FS groups (especially in somatic symptoms). Following the training, BDI values in the PFS group were significantly lower (fewer depressive symptoms) than in the FS group (Tables 3 and 5).

The parameter values describing strength capacities of the lower limbs, both at T1 and T2, proved to be higher in the PFS group (Tables 4 and 5). In the case of statistically significant differences between values obtained in the first and second study, the effect size was greater than 0.2 in both studied groups in most cases (Table 5). For statistically significant differences observed between the groups in both study 1 and 2, the effect size was greater than 0.72 (Table 5).

Table 4. Strength characteristics of the knee joint flexor and extensor muscles at a load of 60°/s, recorded before (T1) and after (T2) the 12-week training programme in both study groups (PFS and FS).

Group		T1			T2			T1 vs. T2		
		Mean	CI	SD	Mean	CI	SD	Student's t-Test		Cohen's d
								t	p	
	PT E 60 R (Nm)	97.25	83.56–110.94	27.5	106.19	89.13–123.25	35.4	−0.97	0.3446	0.29
	PT E 60 L (Nm)	92.81	77.80–107.82	31.1	98.28	83.83–112.74	30.0	−2.20	0.0413 *	0.18
	PT F 60 R (Nm)	42.97	35.47–50.47	15.1	50.97	42.40–59.55	17.8	−3.13	0.0062 *	0.50
	PT F 60 L (Nm)	45.52	37.91–53.12	15.8	50.86	42.35–59.37	17.7	−3.19	0.0051 *	0.33
	TW E 60 R (J)	440.89	379.77–502.02	122.9	513.22	436.71–589.72	158.7	−2.39	0.0284 *	0.52
	TW E 60 L (J)	423.96	375.20–472.71	98.0	467.03	394.30–539.76	150.9	−0.92	0.3685	0.35
PFS	TW F 60 R (J)	222.12	184.32–259.91	78.4	258.24	213.58–302.90	92.7	−2.99	0.0078 *	0.43
	TW F 60 L (J)	237.64	195.78–279.50	86.8	260.99	216.14–305.84	93.0	−2.56	0.0196 *	0.27
	aP E 60 R (W)	61.04	51.89–70.20	18.4	64.02	54.00–74.04	20.8	−0.26	0.7993	0.16
	aP E 60 L (W)	58.44	49.24–67.63	19.1	61.52	51.10–71.93	21.6	−1.11	0.2800	0.16
	aP F 60 R (W)	27.63	22.14–33.13	11.0	31.04	25.17–36.91	12.2	−1.58	0.1337	0.30
	aP F 60 L (W)	29.40	23.58–35.22	12.1	31.25	25.28–37.23	12.4	−1.13	0.2728	0.16
	PT E 60 R (Nm)	69.35	53.56–85.13	30.7	77.68	61.53–93.82	31.4	−2.91	0.0103 *	0.28
	PT E 60 L (Nm)	68.65	52.86–84.44	30.7	75.31	57.09–93.53	35.4	−2.97	0.0090 *	0.21
	PT F 60 R (Nm)	33.36	25.52–41.20	15.2	39.35	30.28–48.41	17.6	−3.01	0.0083 *	0.37
	PT F 60 L (Nm)	30.86	22.70–39.02	15.9	36.75	28.11–45.39	16.8	−4.98	0.0001 *	0.37
	TW E 60 R (J)	369.06	269.86–468.25	192.9	395.15	308.36–481.94	168.8	−0.98	0.3410	0.15
	TW E 60 L (J)	346.18	259.83–432.53	167.9	373.01	280.36–465.66	180.2	−1.83	0.0861	0.16
FS	TW F 60 R (J)	168.82	118.11–219.52	98.6	185.09	126.74–243.44	113.5	−0.88	0.3923	0.16
	TW F 60 L (J)	154.66	103.93–205.40	98.7	176.48	129.61–223.35	91.2	−2.40	0.0287 *	0.24
	aP E 60 R (W)	42.33	32.18–52.48	19.7	46.41	36.35–56.47	19.6	−2.25	0.0387 *	0.21
	aP E 60 L (W)	41.10	31.10–51.10	19.4	45.49	34.24–56.75	21.9	−3.04	0.0077 *	0.22
	aP F 60 R (W)	18.83	13.55–24.11	10.3	25.48	19.51–31.44	11.6	−2.56	0.0211 *	0.63
	aP F 60 L (W)	16.83	11.41–22.24	10.5	20.80	15.36–26.24	10.6	−4.47	0.0004 *	0.39

PFS—pre-frailty syndrome group; FS—frailty syndrome group; PT—peak torque; TW—total work; aP—average power; E—knee extensors; F—knee flexors; R—right side; L—left side. * Differences were considered statistically significant at $p < 0.05$; CI—confidence interval ±95%.

Table 5. Statistically significant differences in the parameters between the FS group and PFS group in the initial (T1) and final (T2) tests.

Parameters	PFS vs. FS	T1		T2		PFS vs. FS	T1	T2
		U/t	p	U/t	p			
SWLS		111.00	0.1131	160.00	0.9747		−0.31	−0.01
BDI (1–13)		126.50	0.2743	104.50	0.0734		0.22	−0.35
BDI (14–21)	Mann–Whitney	148.00	0.6804	91.00	0.0265 *		−0.08	−0.44
BDI all	U test	156.50	0.8866	95.00	0.0365 *	r_{rb}	0.03	−0.41
STAI X-1		104.00	0.0709	138.50	0.4759		0.36	−0.14
STAI X-2		103.50	0.0685	143.00	0.5684		0.36	−0.11
PT E 60 R		2.83	0.0078*	2.54	0.0157 *		0.78	0.87
PT E 60 L		2.34	0.0254 *	2.11	0.0426 *		1.10	0.72
PT F 60 R		1.88	0.0696	1.97	0.0576		0.81	0.68
PT F 60 L		2.77	0.0089 *	2.45	0.0196 *		1.75	0.84
TW E 60 R		1.32	0.1954	2.16	0.0377 *		0.37	0.74
TW E 60 L	Student's *t*-test	1.69	0.1014	1.70	0.0976	Cohen's d	0.99	0.59
TW F 60 R		1.80	0.0801	2.13	0.0407 *		0.76	0.73
TW F 60 L		2.68	0.0112 *	2.75	0.0096 *		1.38	0.94
aP E 60 R		2.90	0.0065 *	2.61	0.0134 *		0.85	0.90
aP E 60 L		2.70	0.0108 *	2.21	0.0341*		0.88	0.76
aP F 60 R		2.44	0.0203 *	1.40	0.1708		0.97	0.48
aP F 60 L		3.31	0.0022 *	2.70	0.0106		2.83	0.93

PFS—pre-frailty syndrome group; FS—frailty syndrome group; SWLS-Satisfaction with Life Scale; BDI-Beck Depression Inventory; STAI-Spielberg's State-Trait Anxiety Inventory; PT-peak torque; TW-total work; aP-average power; E-knee extensors; F-knee flexors; R-right side; L-left side; rrb—Glass rank-biserial correlation coefficient; * Differences were considered statistically significant at *p* < 0.05.

3. Discussion

Individuals with frailty syndrome are more susceptible to stress and exhibit a poorer psychophysical condition compared to their peers. It has been found that too little physical activity activates the so-called "cycle of weakness", which further deteriorates fitness that is already hindered by the ageing process [10].

For the elderly, maintaining an active lifestyle and continuing daily activities are particularly important. A planned and systematic physical activity routine positively influences not only the individual's physical health, but also their cognitive-emotional state. Many published studies have confirmed these findings [10,23–26]. According to Chris et al. (2017), physical activity shapes a personality, which can also indirectly influence the individual's emotional state [27].

The training performed in this study had a clear impact on the emotional state of patients. In the group of patients with a pre-frailty syndrome, a significant improvement in mood and reduced anxiety were observed. This was in contrast to the group of patients with frailty syndrome, in whom a deterioration in mood and increase in anxiety symptoms were observed following the training, but this difference did not reach statistical significance. It is worth mentioning that, in the pre-frailty syndrome group, the number of depressive disorders was significantly decreased. What is striking, however, was that the number of cases of depressive disorders was increased in the frailty syndrome group. This may be due to the severity of the disease and its late diagnosis. It is important to note that the frailty syndrome diagnosis has not been standardised. For instance, Sutorius et al. (2016) present discrepancies resulting from the use of different research scales [28]. Many factors influence the development of frailty syndrome. As a result, there are a wide variety of disease presentations. At present, the five criteria that describe frailty syndromes are the most important [29]. The sooner the patient is diagnosed with frailty syndrome, in this case at an early stage, the greater the probability of successful prophylaxis and treatment. Nevertheless, the obtained results indicate that, at the frailty syndrome diagnosis stage, physical training alone, even best adapted to the individual, is insufficient. Consistent with the comprehensive nature of rehabilitation, patients with frailty syndrome should be

offered additional forms of support, especially emotional support, so that their condition does not deteriorate. This is even more important considering that our other results show an improvement in lower limb strength in these individuals. These additional forms (e.g., group psychotherapy) are very effective in elderly patients with various chronic diseases [30].

The improvement in the emotional state of the group of patients with pre-frailty syndrome is encouraging and suggests that preventive measures are most effective at this stage of the illness. Therefore, it is worth encouraging patients to start physical activity as early as possible and to perform standard screening tests for depressive disorders. The sooner a patient is diagnosed with the syndrome, in this case at the earlier stage of pre-frailty syndrome, the more effective the prophylaxis and treatment measures.

The difference in emotional status results may also be related to age. The group of patients with pre-frailty syndrome was significantly younger than the group with frailty syndrome. However, many studies have indicated that even the oldest patients still benefit from rehabilitation [25,31].

Changes in the level of anxiety of patients in the studied groups were analogous to mood changes. This is not surprising as anxiety is one of the basic symptoms of depression. This relationship is multidirectional because increased levels of anxiety may intensify the symptoms of depression. The relationship between these characteristics was confirmed by Jaeschke et al. (2010) who described the coexistence of anxiety disorders and depression [32].

Every training programme is considered to be a good way to increase physical fitness among the elderly. People with frailty syndrome experience the so-called "cycle of frailty", associated with reduced energy expenditure due to insufficient activity. One of the elements that is known to improve the functioning of the elderly and reduce the risk of falls is maintaining an appropriate level of muscle strength, especially in the lower limbs. Studies indicate that resistance training increases muscle strength, walking speed and reduces pain [10,33]. Resistance training using a Thera-band and fitness balls was used in the present research. In our study, systematic physical activity significantly improved the strength of the lower limbs.

High intensity resistance training can be effective in the fight against muscle weakness and decreased fitness in elderly patients. Furthermore, it has been shown that nutritional supplementation without physical activity does not have a significant effect on muscle strength. Beaudart et al. (2017) investigated whether aerobic activity improves VO2 max and muscle strength in the elderly [34]. The procedure consisted of resistance exercises and nine months of gait training, which was found to improve the subjects' exercise capacity by 14%. It has been demonstrated that multicomponent training, which is one that includes different types of exercises combined with psychological support and patient education, can result in elimination of frailty syndrome by 14.7% relative to a control group [35]. Our training programme included various forms of workouts, including resistance training with the use of equipment, together with aerobic training and stretching exercises. This resulted in improved strength parameters of the lower limbs. In a randomised study where resistance, stretching, neuromuscular control and aerobic exercise were carried out for 24 weeks at 65 min per day, the frailty syndrome elimination was found in 31.4% of elderly people, with no changes in the control group [36]. In our study, training was performed only twice a week, which may not have been sufficient for all results to be statistically significant.

The processes associated with aging include reduced neuromuscular control, reduced muscle strength and cardiovascular diseases; therefore, it is worth trying to prevent these outcomes using endurance and strength training. The research carried out by Cadore et al. (2014) examined the influence of the aforementioned training types on physical fitness of people with frailty syndrome and a control group [37]. Strength training resulted in improvements in muscle strength, speed and ability to recruit motor units. In the second test, endurance training was conducted simultaneously with strength training. It turned out that this combination had a very positive effect on the functionality of the elderly, but it also resulted in a smaller increase in muscle strength compared to strength training alone. Comparing the group of older people to the control group, it was concluded that, when used

to improve strength and muscle mass, strength training impacts both groups to the same extent [37]. In our study, the peak torque, total work and average power increased in both groups following the exercise programme.

Other studies revealed that, in elderly women, even short-term strength training (about six weeks) increased the strength of the extensor muscles of knee joint, which also improved their functioning [38]. In our study, exercises were also conducted under the supervision of a specialist, which ensured greater safety and control of the whole training programme.

Research by Tracy et al. (1999) concerned the influence of strength training on the condition of lower limb muscles [39]. An increase in the strength of the dominant limb was observed in both women and men, although it was greater in men. The increase in isometric strength was $13 \pm 6\%$ in men and $7 \pm 3\%$ in women, but this difference was not statistically significant. Regarding isokinetic strength, significant changes in peak torque of the knee extensors were achieved, but only in the male group. Additionally, the volume of the thigh quadriceps muscle of the trained limb was measured, and a 12% increase was recorded. In our study, we also investigated peak torque in addition to the total work and average power of muscles acting on the knee joint. As a result of the training sessions, these parameters increased in both groups. In terms of percentage, greater differences were observed in subjects with frailty syndrome for most of the parameters. This may be due to the greater muscle weakness observed in this group, evidenced by significantly lower values of strength parameters recorded during the initial study in comparison to the pre-frailty group. The workload for subjects with increased sarcopenia was relatively higher, which resulted in a greater increase in strength capacity of the examined muscles. Higher relative training load of the group of subjects with frailty syndrome may also explain the lack of improvement in mood, or even a slight increase in anxiety and depression.

A study by Batista et al. (2014) examined how the strength of the lower extremities affects independence among elderly outpatients in relation to gender, age and the frailty syndrome criteria [40]. It was noted that men over 80 years of age who met one or two frailty criteria and had greater lower limb strength showed better independence compared to women who were slightly younger but with three or more syndrome criteria. It was also found that men and the elderly with greater strength in the lower extremities had better results with regard to their independence.

Each and every physical activity has a positive impact on the body, evidenced by the improvement in strength parameters observed in both groups investigated in this study. Individuals with diagnosed frailty or pre-frailty syndrome can, with the help of appropriate training, prevent the development of symptoms. This is also important as we observed a simultaneous improvement in the emotional state of patients with a diagnosis of pre-frailty syndrome. On the other hand, deterioration of the emotional state and increased number of cases of depressive disorders were observed among patients with frailty syndrome following training, suggesting that other forms of support and emotional state therapy should be introduced at the same time.

4. Limitations

Screening tests were used to assess mood and anxiety in subjects, which is not equivalent to a medical diagnosis and requires more extensive diagnostic tests. The study should be continued with bigger sample size and with the control group of patients. The functional status of patients with frailty syndrome made it necessary for them to be brought to the training sessions by informal caregivers, which could be a stressful factor for the respondents. Further research should consider organising free transportation of patients to the training sessions.

5. Conclusions

1. In individuals with pre-frailty and frailty syndrome, the 3-month physical training programme improved the strength parameters of lower limb muscles.
2. An improvement in mood and reduction in depressive symptoms was only observed in the group of subjects with pre-frailty syndrome.

3. Rehabilitation programmes for people with frailty syndrome should include psychotherapeutic activities in addition to physical training in order to improve the psychophysical condition of patients.

Abbreviations

PFS	pre-frailty syndrome group
FS	frailty syndrome group
SWLS	satisfaction with life scale
BDI	Beck depression inventory
STAI	Spielberg's state-trait anxiety inventory
PT	peak torque
TW	total work
aP	average power
E	knee extensors
F	knee flexors
R	right side
L	left side
T1	initial results
T2	final results

References

1. Leng, S.X.; Chen, X.; Mao, G. Frailty syndrome: An overview. *Clin. Interv. Aging* **2014**, *9*, 433–441. [CrossRef] [PubMed]
2. Billot, M.; Calvani, R.; Urtamo, A.; Sánchez-Sánchez, J.L.; Ciccolari-Micaldi, C.; Chang, M.; Roller-Wirnsberger, R.; Wirnsberger, G.; Sinclair, A.; Vaquero-Pinto, M.N.; et al. Preserving Mobility in Older Adults with Physical Frailty and Sarcopenia: Opportunities, Challenges, and Recommendations for Physical Activity Interventions. *Clin. Interv. Aging* **2020**, *15*, 1675–1690. [CrossRef] [PubMed]
3. Kojima, G.; Liljas, A.E.; Iliffe, S. Frailty syndrome: Implications and challenges for health care policy. *RMHP* **2019**, *2*, 23–30. [CrossRef] [PubMed]
4. Terroso, M.; Rosa, N.; Marques, A.; Simoes, R. Physical consequences of falls in the elderly: A literature review from 1995 to 2010. *Eur. Rev. Aging Phys. Act.* **2013**, *11*, 51–59. [CrossRef]
5. Tieland, M.; Trouwborst, I.; Clark, B.C. Skeletal muscle performance and ageing. *J. Cachexia Sarcopenia Muscle* **2017**, *9*, 3–19. [CrossRef] [PubMed]
6. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in Older Adults: Evidence for a Phenotype. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M157. [CrossRef] [PubMed]
7. Sharma, A.; Madaan, V.; Petty, F.D. Exercise for Mental Health. *Prim. Care Companion J. Clin. Psychiatry* **2006**, *8*, 106. [CrossRef]
8. Bilotta, C.; Bergamaschini, L.; Nicolini, P.; Casè, A.; Pina, G.; Rossi, S.V.; Vergani, C. Frailty syndrome diagnosed according to the Study of Osteoporotic Fractures criteria and mortality in older outpatients suffering from Alzheimer's disease: A one-year prospective cohort study. *Aging Ment. Health* **2011**, *16*, 273–280. [CrossRef]

9. Dressendorfer, R.; Palmer, E. Frailty Syndrome: Physical Therapy. Clinahl Information System EBSCO, 2016. Available online: https://www.ebscohost.com/promoMaterials/January_2017_-_Fraily_Syndrome.pdf (accessed on 30 December 2016).
10. Mazurek, J.; Kowalska, J.; Rymaszewska, J. Physical exercise as prevention and therapy for frailty syndrome. *Przegląd Lekarski* **2018**, *75*, 91–93.
11. Gallè, F.; Di Onofrio, V.; Spica, V.R.; Mastronuzzi, R.; Krauss, P.R.; Belfiore, P.; Liguori, G.; Buono, P. Improving physical fitness and health status perception in community-dwelling older adults through a structured program for physical activity promotion in the city of Naples, Italy: A randomized controlled trial. *Geriatr. Gerontol. Int.* **2016**, *17*, 1421–1428. [CrossRef]
12. Zawadzki, B.; Popiel, A.; Pragłowska, E. Charakterystyka psychometryczna polskiej adaptacji Kwestionariusza Depresji BDI-II Aarona Becka. *Psychol.-Etiol.-Genet.* **2009**, *19*, 71–95.
13. Beck, A.T.; Steer, R.A.; Ball, R.; Ranieri, W.F. Comparison of Beck Depression Inventories-IA and-II in Psychiatric Outpatients. *J. Pers. Assess.* **1996**, *67*, 588–597. [CrossRef] [PubMed]
14. Diener, E.; Emmons, R.A.; Larsen, R.J.; Griffin, S. The Satisfaction with Life Scale. *J. Pers. Assess.* **1985**, *49*, 71–75. [CrossRef]
15. Juczyński, Z. *Narzędzia Pomiaru w Promocji i Psychologii Zdrowia (Measurement Tools in Health Promotion and Psychology)*, 2nd ed.; Laboratory of Psychological Tests of the Polish: Warsaw, Poland, 2009.
16. Skapinakis, P. The Spielberger State-Trait Anxiety Inventory. In *Encyclopedia of Quality of Life and Well-Being Research*; Michalos, A.C., Ed.; Springer: Berlin/Heidelberg, Germany, 2014; pp. 6261–6264. [CrossRef]
17. Sosnowski, T.; Wrześniewski, K.; Jaworska, A.; Fecenec, D. *STAI—Inwentarz Stanu i Cechy Lęku STAI. Polska Adaptacja STAI*; Pracownia Testów Psychologicznych: Warsaw, Poland, 2011.
18. Davies, G. *Compendium of Isokinetics in Clinical Usage and Rehabilitation Techniques*, 4th ed.; S&S Publishers: Onalaska, WI, USA, 1992.
19. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences*, 2nd ed.; Lawrence Erlbaum: Hillsdale, NJ, USA, 1988.
20. Willson, V.L. Critical Values of the Rank-Biserial Correlation Coefficient. *Educ. Psychol. Meas.* **1976**, *36*, 297–300. [CrossRef]
21. Fritz, C.O.; Morris, P.E.; Richler, J.J. Effect size estimates: Current use, calculations, and interpretation. *J. Exp. Psychol. Gen.* **2012**, *141*, 2–18. [CrossRef] [PubMed]
22. Field, A. *Discovering Statistics Using SPSS*, 2nd ed.; Sage Publications: London, UK, 2005.
23. Peluso, M.A.M.; De Andrade, L.H.S.G. Physical activity and mental health: The association between exercise and mood. *Clinics* **2005**, *60*, 61–70. [CrossRef] [PubMed]
24. Grasdalsmoen, M.; Eriksen, H.R.; Lønning, K.J.; Sivertsen, B. Physical exercise, mental health problems, and suicide attempts in university students. *BMC Psychiatry* **2020**, *20*, 175. [CrossRef]
25. Dziubek, W.; Kowalska, J.; Kusztal, M.; Rogowski, Ł.; Gołębiowski, T.; Nikifur, M.; Szczepańska-Gieracha, J.; Zembroń-Łacny, A.; Klinger, M.; Woźniewski, M. The Level of Anxiety and Depression in Dialysis Patients Undertaking Regular Physical Exercise Training—A Preliminary Study. *Kidney Blood Press. Res.* **2016**, *41*, 86–98. [CrossRef]
26. Mikkelsen, K.; Stojanovska, L.; Polenakovic, M.; Bosevski, M.; Apostolopoulos, V. Exercise and mental health. *Maturitas* **2017**, *106*, 48–56. [CrossRef]
27. Guure, C.B.; Ibrahim, N.A.; Adam, M.B.; Said, S.M. Impact of Physical Activity on Cognitive Decline, Dementia, and Its Subtypes: Meta-Analysis of Prospective Studies. *BioMed Res. Int.* **2017**, *2017*. [CrossRef]
28. Sutorius, F.L.; Hoogendijk, E.O.; Prins, B.A.H.; Van Hout, H.P.J. Comparison of 10 single and stepped methods to identify frail older persons in primary care: Diagnostic and prognostic accuracy. *BMC Fam. Pract.* **2016**, *17*, 1–12. [CrossRef]
29. Faller, J.W.; Pereira, D.D.N.; De Souza, S.; Nampo, F.K.; Orlandi, F.D.S.; Matumoto, S. Instruments for the detection of frailty syndrome in older adults: A systematic review. *PLoS ONE* **2019**, *14*, e0216166. [CrossRef] [PubMed]
30. Szczepańska-Gieracha, J.; Kowalska, J.; Pawik, M.; Rymaszewska, J. Evaluation of a short-term group psychotherapy used as part of the rehabilitation process in nursing home patients. *Disabil. Rehabil.* **2013**, *36*, 1027–1032. [CrossRef]
31. Kowalska, J.; Mazurek, J.; Kubasik, N.; Rymaszewska, J. Effectiveness of physiotherapy in elderly patients with dementia: A prospective, comparative analysis. *Disabil. Rehabil.* **2017**, *41*, 815–819. [CrossRef]

32. Jaeschke, R.; Siwek, M.; Grabski, B.; Dudek, D. Współwystępowanie zaburzeń depresyjnych i lękowych. *Psychiatria* **2010**, *7*, 189–197.

33. Zembroń-Łacny, A.; Dziubek, W.; Rogowski, Ł.; Skorupka, E.; Dąbrowska, G. Sarcopenia: Monitoring, molecular mechanisms, and physical intervention. *Physiol. Res.* **2014**, *63*, 683–691.

34. Beaudart, C.; Dawson, A.; Shaw, S.C.; Harvey, N.C.; Kanis, J.A.; Binkley, N.; Reginster, J.Y.; Chapurlat, R.; Chan, D.C.; IOF-ESCEO Sarcopenia Working Group; et al. Nutrition and physical activity in the prevention and treatment of sarcopenia: Systematic review. *Osteoporos. Int.* **2017**, *28*, 1817–1833. [CrossRef]

35. Cameron, I.D.; Fairhall, N.; Langron, C.; Lockwood, K.; Monaghan, N.; Aggar, C.; Sherrington, C.; Lord, S.R.; Kurrle, S.E. A multifactorial interdisciplinary intervention reduces frailty in older people: Randomized trial. *BMC Med.* **2013**, *11*, 65. [CrossRef]

36. Tarazona-Santabalbina, F.J.; Gómez-Cabrera, M.C.; Pérez-Ros, P.; Martínez-Arnau, F.M.; Cabo, H.; Tsaparas, K.; Salvador-Pascual, A.; Rodriguez-Mañas, L.; Viña, J. A Multicomponent Exercise Intervention that Reverses Frailty and Improves Cognition, Emotion, and Social Networking in the Community-Dwelling Frail Elderly: A Randomized Clinical Trial. *J. Am. Med. Dir. Assoc.* **2016**, *17*, 426–433. [CrossRef]

37. Cadore, E.L.; Pinto, R.S.; Bottaro, M.; Izquierdo, M. Strength and Endurance Training Prescription in Healthy and Frail Elderly. *Aging Dis.* **2014**, *5*, 183. [CrossRef] [PubMed]

38. Pinto, R.S.; Correa, C.S.; Radaelli, R.; Cadore, E.L.; Brown, L.E.; Bottaro, M. Short-term strength training improves muscle quality and functional capacity of elderly women. *Age* **2013**, *36*, 365–372. [CrossRef] [PubMed]

39. Tracy, B.L.; Ivey, F.M.; Hurlbut, D.; Martel, G.F.; Lemmer, J.T.; Siegel, E.L.; Metter, E.J.; Fozard, J.L.; Fleg, J.L.; Hurley, B.F. Muscle quality. II. Effects of strength training in 65- to 75-yr-old men and women. *J. Appl. Physiol.* **1999**, *86*, 195–201. [CrossRef] [PubMed]

40. Batista, F.S.; Gomes, G.A.D.O.; D'Elboux, M.J.; Cintra, F.A.; Neri, A.L.; Guariento, M.E.; Souza, M.D.L.R.D. Relationship between lower-limb muscle strength and functional independence among elderly people according to frailty criteria: A cross-sectional study. *Sao Paulo Med. J.* **2014**, *132*, 282–289. [CrossRef] [PubMed]

Article

Prevalence of Physical Frailty and Its Multidimensional Risk Factors in Korean Community-Dwelling Older Adults: Findings from Korean Frailty and Aging Cohort Study

Heeeun Jung [1], Miji Kim [2,*], Yunhwan Lee [3] and Chang Won Won [4,*]

[1] Department of Biomedical Science and Technology, Graduate School, Kyung Hee University, Seoul 02447, Korea; heeeun.jung@khu.ac.kr
[2] Department of Biomedical Science and Technology, College of Medicine, East-West Medical Research Institute, Kyung Hee University, Seoul 02447, Korea
[3] Department of Preventive Medicine and Public Health, Ajou University School of Medicine, Suwon 16499, Korea; yhlee@ajou.ac.kr
[4] Elderly Frailty Research Center, Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul 02447, Korea
* Correspondence: mijiak@khu.ac.kr (M.K.); chunwon62@naver.com (C.W.W.); Tel.: +82-2-958-2840 (M.K.); +82-2-958-8700 (C.W.W.); Fax: +82-2-958-2836 (M.K.); +82-2-958-8699 (C.W.W.)

Abstract: Frailty is defined as a state of increased vulnerability to stressors, and it predicts disability and mortality in the older population. This study aimed to investigate the standardized prevalence and multidimensional risk factors associated with frailty among Korean community-dwelling older adults. We analyzed the baseline data of 2907 adults aged 70–84 years (mean age 75.8 ± 3.9 years, 57.8% women) in the Korean Frailty and Aging Cohort Study. The Fried frailty phenotype was used to define frailty. Analyzed data included sociodemographic, physical, physical function, biological, lifestyle, health condition, medical condition, psychological, and social domains. Data were standardized using the national standard population composition ratio based on the Korean Population and Housing Census. The standardized prevalence of frailty and prefrailty was 7.9% (95% confidence interval (CI) 6.8–8.9%) and 47.0% (95% CI, 45.1–48.8%), respectively. The following 14 risk factors were significantly associated with frailty: at risk of malnutrition, sarcopenia, severe mobility limitation, poor social capital, rural dwellers, depressive symptoms, poor self-perceived health, polypharmacy, elevated high-sensitivity C-reactive protein, elevated glycosylated hemoglobin, low 25-hydroxy vitamin D level, longer Timed Up and Go, and low Short Physical Performance Battery score ($p < 0.05$). Physiconutritional, psychological, sociodemographic, and medical factors are strongly associated with frailty.

1. Introduction

Frailty is characterized by a significant decline in the functional reserve capacity of multiple organ systems with an increased vulnerability to stressors, leading to a higher risk of adverse health outcomes such as falls, disability, hospitalization, and mortality in older adults [1,2]. The wide range in prevalence among the studies is due to the different definitions of frailty. In a systematic review, the prevalence of frailty in community-dwelling older adults aged ≥65 years was found to vary from 4.0% to 59.1% [3]. The Fried Frailty Phenotype (FFP) and the Frailty Index (FI) represent commonly known as operational definitions of frailty in older adults [3,4]. The physical phenotypic approach, the FFP

was defined as the presence of three or more of five physical characteristics: weakness, slowness, weight loss, exhaustion, and low physical activity [1]. Moreover, the FFP was originally constructed from an epidemiological study and has drawn the highest degree of attention of researchers. It has predicted adverse clinical outcomes like mortality. Conversely, many clinical studies have adopted the FI for frailty assessment. The FI, is a comprehensive geriatric assessment composed of a long checklist of clinical conditions and diseases that constitutes the deficit accumulation approach. The FI was composed of psychological, mental, and social as well as physical functions and was expressed as a ratio [4]. In recent studies, FFP has been the most widely used definition of frailty in recent studies [5].

There is a rapid increase in the number of older adults aged ≥65 years globally [6]. According to Statistics Korea, the prevalence of older adults aged ≥65 years in Korea was 14.3% in 2018 and is expected to double by 2028 [7]. Recently, the Korean Longitudinal Study on Health and Aging Study performed in hospital-based populations residing in the city of Seongnam in Korea reported that the prevalence of frailty and prefrailty was 13.2% and 59.4%, respectively [8]. The aging study of the Pyeongchang Rural Area in older adults of Pyeongchang reported the prevalence of frailty and prefrailty as 17.4% and 52.6%, respectively [9]. They identified instrumental activities of daily living (IADL) and activities of daily living (ADL) disability, depression symptoms, dysmobility, malnutrition, incontinence, and medical aid as risk factors for frailty. However, these studies were restricted to a selected residential area in Korea and do not represent community-dwelling older adults.

Frailty is a dynamic reversible state, and identification of the risk factors of frailty will enable prevention and management. Previous studies have identified risk factors for physical frailty, focusing on sociodemographic factors such as age, gender, marital status, education level, and physical factors such as body composition and physical function [10–12]. However, more recent studies have identified a wider range of risk and protective factors, including biological, lifestyle, and psychological factors [13]. As risk factors of physical frailty have been identified in multiple domains, it is necessary to comprehensively identify the influential risk factors to prioritize targets.

This study aimed to investigate the age-, sex-, and residence-adjusted prevalence and characteristics of physical frailty in the Korean Frailty and Aging Cohort Study (KFACS). We also identified risk factors with a significant association with physical frailty using multidimensional domains in Korean community-dwelling older adults.

2. Materials and Methods

2.1. Study Population

The KFACS is a nationwide, longitudinal study, with the baseline survey conducted in 2016–2017 [14]. The KFACS recruited participants using quota sampling methods stratified by sex (male and female in a ratio of 1:1) and age (70–74, 75–79, and 80–84 years in a ratio of 6:5:4, respectively). The participants were recruited from among community-dwelling residents in urban and rural areas in 10 study centers covering different residential locations (urban, suburban, and rural): three from the Seoul Metropolitan Area, two from Gyeonggi Province, and one from each of Gangwon Province, Chungcheongbuk Province, Jeolla-nam Province, Gyeongsang-nam Province, and Jeju Island in South Korea. Of the 3014 participants who were enrolled at 10 centers at baseline, 2907 participants completed the assessment of 5 components of FFP and were selected for the final analysis, after excluding 109 with missing frailty assessment components. The KFACS protocol was approved by the Clinical Research Ethics Committee of Kyung Hee University Hospital (IRB number: 2015-12-103). All participants were given prior explanations and signed consent forms. This study had an IRB approval from the Clinical Research Ethics Committee of Kyung Hee University Hospital (IRB number: 2020-06-062).

2.2. Frailty Assessment

Physical frailty was defined using FFP based on weight loss, weakness, slowness, exhaustion, and low physical activity with modified cutoff points [1,14]. Weight loss was defined as a "yes" response

to the question "In the last year, have you unintentionally lost more than 4.5 kg?". Handgrip strength was measured twice for both hands using a hand dynamometer (Takei TKK 5401; Takei Scientific Instruments, Tokyo, Japan). Weakness was defined as a handgrip strength in the lower 20%, adjusted for sex and body mass index (BMI) quartiles based on the KFACS baseline survey. The 4 m usual gait speed was measured using an automatic timer (Gaitspeedometer; Dyphi, Daejeon, Korea), with acceleration and deceleration phases of 1.5 m. Slowness was defined as the lowest 20% of gait speed on the basis of the 4 m usual gait speed stratified by sex and height based on the KFACS population distribution. Exhaustion was defined as a "yes" response to either of "I felt that everything I did was an effort" and "I could not get going" on 3 or more days per week from the Center for Epidemiological Studies-Depression scale. Energy expenditure estimates (kcal/week) for physical activity levels were calculated using the International Physical Activity Questionnaire. Low physical activity was defined as the lowest 20% of sex-specific total energy consumed in a population-based Korean survey of older adults from among the general population (Table S1). Physical frailty scores ranged from 0 to 5. Participants with scores ≥3, 1–2, and 0 were classified as frail, prefrail, and robust, respectively.

2.3. Measurements

We obtained information on sociodemographic (age, sex, education level, living status, marital status, residential area, social security benefits, and occupation), lifestyle (smoking status, alcohol consumption, and sleep habits), self-perceived health status, history of falls and hospitalization in the past year, current use of prescription medications, oral health, and self-reported history of medical conditions based on Charlson's classification [15].

Underweight was defined as a body mass index (BMI) $<18.5 \text{ kg/m}^2$. Appendicular skeletal muscle (ASM) was measured using dual-energy X-ray absorptiometry (DXA) (Lunar, GE Healthcare, Madison, WI, USA and Hologic DXA, Hologic Inc., Bedford MA, USA) or bioelectrical impedance analysis (InBody 72, InBody Co., Ltd., Seoul, Korea, and X-SCAN PLUS II, Jawon Medical Inc., Seoul, Korea). A low ASM mass was defined as the lowest 20% of the KFACS participants. Sarcopenia was defined according to the consensus report of the Asian Working Group for sarcopenia based on low muscle strength, low muscle mass, and/or low physical performance [16]. Low calf circumference was defined as <32 cm [17]. High waist circumference was defined as ≥102 cm for men and ≥88 cm for women [18].

Severe mobility limitation was defined if the patient found it "very difficult" or "impossible" to either walk about 400 m or climb 10 steps without resting [19]. ADL disability was defined as answering at least one dependency in 7 domains (bathing, continence, dressing, eating, transfer, and washing face and hands). Disability of IADL was defined as answering two or more dependencies in 10 domains (food preparation, household chores, going out for a short distance, grooming, handling finances, laundry, taking personal medication, shopping, using public transportation, and using the telephone) [20]. The Timed Up and Go (TUG) test measured the participants standing up from an armchair of standard height, walking 3 m at their own comfortable and safe gait pace, turn at a marker, return to the chair, and sit down. The TUG time was defined as the time from standing up to sitting down [21]. The Short Physical Performance Battery (SPPB) consists of three standing balance measures (tandem, semitandem, and side-by-side stands), five repeated chair rise tests, and usual gait speed. Each test is scored from 0 to 4 scores, with a total of 12 scores [22]. Nutritional status was assessed using the Korean version of the Mini-Nutritional Assessment Short Form (MNA-SF) [23]. The risk of malnutrition was defined as an MNA-SF score of ≤11 [24].

Comorbidity was defined as ≥2 of the following chronic diseases: hypertension, diabetes, myocardial infarction, peripheral vascular disease, angina, cerebrovascular disease, congestive heart failure, dyslipidemia, rheumatoid arthritis, osteoarthritis, osteoporosis, asthma, or chronic obstructive pulmonary disease [15]. Polypharmacy was defined as taking ≥5 medications [25]. Hearing impairment was defined as the minimum pure-tone average value of >40 dB [26]. Visual impairment was defined as a maximum visual acuity of <0.3 [27]. Blood samples were tested at 8 am after fasting for 8 h.

A participant was determined to be depressed if she/he had a score of ≥6 on the Korean version of the Short Form Geriatric Depression Scale (SGDS-K) [28]. Global cognitive dysfunction was diagnosed if the Korean version of the Mini-Mental State Examination (MMSE-KC) score was <24 [29]. Cognitive impairment was defined as a score of 1.5 standard deviations below the score of the age, sex, and education-matched controls on the cognitive function tests: processing speed (trail making test A), executive function (Frontal Assessment Battery), verbal episodic memory (word list recall test), and working memory (digit span backward) [30]. Quality of life was determined using the EuroQol 5-dimension scale (EQ-5D) [31], EuroQol Visual Analog Scale (EQ-VAS) [32], and 12-items Short Form Health Survey (SF-12) [33]. The SF-12 was used to measure physical and mental health summary [34].

Poor social capital was defined as a lack of participation in social gatherings. Social support was assessed using the Enhancing Recovery in Coronary Artery Disease Social Support Instrument [35,36]. The social network was assessed using the Practitioner Assessment of Network Type Instrument [37]. Interaction with family, friends, and neighbors was dichotomized as high (every day, 2–3/week, or ≥1/week) and low (≤1/month).

2.4. Statistical Analysis

We developed age-, sex-, and residence-standardized prevalence. The KFACS population is of nation-wide community-dwelling older adults, but quota sampling stratified by age and sex can limit the generalization of the prevalence rate. To ensure generalization, we performed poststratification adjustment using general population distribution data from the Korean Population and Housing Census conducted by Statistics Korea in 2017. We computed the poststratification adjustments by calibrating the distribution of age (3 groups: 70–74, 75–79, and 80–84 years), sex (2 groups: male and female), and residence (2 groups: urban and rural) in the general population. We calculated mean with standard errors (SE) for continuous variables and frequencies with percentage and 95% confidence intervals (CIs) for categorical variables to investigate the prevalence and characteristics of frailty. We used analysis of variance tests for continuous variables and the chi-square test for categorical variables.

In the unweighted sample, we performed multiple forward stepwise logistic regression analyses to identify the most influential risk factors for frailty. First, we identified the risk factors in each of the 9 domains (sociodemographic, physical, physical function, lifestyle, biological, health condition, medical condition, psychological, and social domain). Then, we identified the risk factors with the strongest association with frailty using the variables selected in the 9 domains. Statistical analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical significance was determined using a two-sided *p*-value of <0.05.

3. Results

3.1. Sociodemographic Characteristics of the Study Population

The sociodemographic characteristics of the unstandardized and standardized samples are shown in Table 1. The mean age was 75.8 years, and the majority of the participants were aged 70–74 years in both the unweighted (39.7%) and weighted (41.8%) sample populations. There was a significant difference in the regional proportions between men and women in the unweighted sample (*p* = 0.035), but not in the weighted sample (*p* = 0.72).

3.2. Prevalence of Frailty

In the standardized sample, the prevalence of frailty and prefrailty was 7.9% (95% CI 6.8–8.9%) and 45.2% (95% CI 45.1–48.8%), respectively. Among the individual frailty components, the prevalence was highest for exhaustion (32.5%), followed by slowness (20.1%) and weakness (19.7%). There was a higher prevalence of exhaustion (40.8% vs. 21.0%) and weakness (21.0% vs. 18.0%) among women compared to men, respectively. However, there was no significant difference in low physical activity,

slowness, and unintentional weight loss between women and men. Overall, 54.8% of the participants had ≥1 frailty component (Table 2). The prevalence of frailty increased significantly in the 80–84 years compared to 70–74 years (16.1% vs. 2.7%) (Figure 1). The prevalence of frailty was significantly higher in women than in men in the unstandardized (8.5% and 7.1%) and standardized samples (9.2% and 6.0%) (Table 2 and Table S2). The prevalence of frailty was significantly higher in rural than in cities in the unstandardized (12.0% and 6.2%) and standardized samples (12.7% and 6.0%) (data not shown).
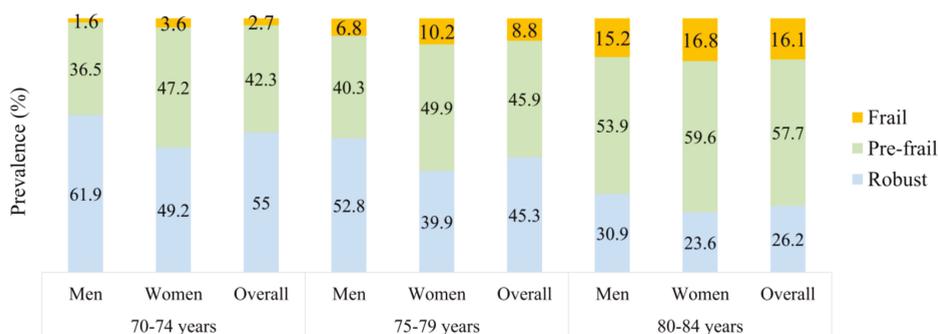
Figure 1. Prevalence of frailty with age groups (standardized sample).

3.3. Characteristics of the Study Population across Frailty Status

The characteristics of frailty status in the standardized sample are presented in Table 3. There were significant differences in the sociodemographic ($p < 0.05$), physical ($p < 0.05$), physical function ($p < 0.001$), health condition ($p < 0.05$), and psychological ($p < 0.001$) domains between the three groups. Biological domains, except serum creatinine, cortisol, vitamin B12, thyroid-stimulating hormone (TSH), and low-density lipoprotein (LDL) cholesterol levels were significantly different among the three groups (all, $p < 0.05$). The prevalence of hypertension, diabetes, incontinence, cardiovascular disease, osteoarthritis, osteoporosis, rheumatoid arthritis, digestive system ulceration, and depressive disorder were significantly higher in the frail group ($p < 0.05$). There was a significant difference in lifestyle domain except current smoking ($p = 0.238$) across frailty status. Social domain, except for low interaction with neighbors ($p = 0.294$) and social activities ($p = 0.491$) were also significantly different across frailty status.

3.4. Risk Factors Associated with Physical Frailty

Table 4 shows the significant influential risk factors in a multivariate forward logistic regression analysis. Risk factors for frailty were at risk of malnutrition (odds ratio (OR) 2.51; 95% confidence interval (CI) 1.57–4.03), sarcopenia (OR 2.39, 95% CI 1.61–3.56), severe mobility limitation (OR 2.13, 95% CI 1.45–3.15), poor social capital (OR 1.99, 95% CI 1.13–3.56), rural residence (OR 1.89, 95% CI 1.13–3.18), depressive symptoms (OR 1.89, 95% CI 1.29–2.76), poor self–perceived health (OR 1.65, 95% CI 1.12–2.44), polypharmacy (OR 1.61, 95% CI 1.13–2.30), elevated high-sensitivity C-reactive protein (hs-CRP) (OR 1.29, 95% CI 1.07–1.55), elevated glycated hemoglobin (HbA1c) (OR 1.28, 95% CI 1.04–1.56), longer TUG time (OR 1.27, 95% CI 1.17–1.37), and increasing age (OR 1.08, 95% CI 1.03–1.14). High 25-hydroxy vitamin D (OR 0.98, 95% CI 0.96–1.00) and high SPPB scores (OR 0.87, 95% CI 0.76–0.98) were preventable factors. Based on these results, the frequency and percentage of risk factors among frail individuals (n = 214) are shown in Figure 2. For analyses, the significant influential risk factors of frailty presented in Table 4 were classified as physiconutritional, psychological, sociodemographic, and medical domains. About a third (27.1%) of the frail participants had all four risk domains. Overlapping physiconutritional, psychological, and medical risk domains were found in 46.6% of the participants. The prevalence of risk domains in frail participants was as

follows: physiconutritional (90.7%), medical (82.2%), psychological (78.0%), and sociodemographic (44.9%) (all, $p < 0.001$) (Figure S1).
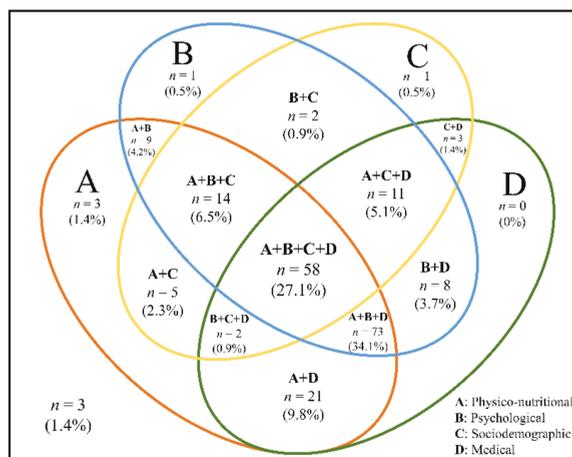
Figure 2. Venn diagram displaying the extent of overlap of risk domains in the frail group (unstandardized sample). A total of 214 adults aged 70–84 years were frail. The physiconutritional domain was defined as having ≥1 risk of malnutrition, sarcopenia, severe mobility limitation, longer Timed Up and Go (>12 s), and low Short Physical Performance Battery (≤9 scores). The psychological domain was defined as having ≥1 depressive symptom and poor self-perceived health. The sociodemographic domain was defined as having ≥1 of rural residence and poor social capital. The medical domain was defined as having ≥1 of polypharmacy, elevated hs-CRP (≥3 mg/L), elevated HbA1c (≥6.5%), and low 25-hydroxyvitamin D (≤20 ng/mL).

Table 1. Sociodemographic characteristics of the unstandardized and standardized study samples.

Variable	Unstandardized Sample, n (%)				Standardized Sample (%)			
	Overall n = 2907	Men n = 1383 (47.6%)	Women n = 1524 (52.4%)	p-Value	Overall	Men (42.2%)	Women (57.8%)	p-Value
Age (years)								
70–74	1154 (39.7)	505 (36.5)	649 (42.6)		41.8	45.4	39.2	
75–79	1080 (37.2)	529 (38.3)	551 (36.2)	**<0.001**	36.1	35.8	36.3	**<0.001**
80–84	673 (23.2)	349 (25.2)	324 (21.3)		22.1	18.8	24.5	
Low education level (<7 years)	1265 (43.5)	361 (26.1)	904 (31.1)	**<0.001**	45.5	25.5	60.5	**<0.001**
Live alone	659 (22.7)	120 (8.7)	539 (35.4)	**<0.001**	24.3	8.2	36.2	**<0.001**
Marital status (without partner)	948 (32.6)	145 (10.5)	803 (52.7)	**<0.001**	35.2	9.9	53.7	**<0.001**
Residence								
Urban	822 (28.4)	387 (28.1)	435 (28.7)		28.4	29.1	27.9	
Suburban	1250 (43.2)	569 (41.4)	681 (45.0)	**0.035**	43.6	43.5	43.6	0.720
Rural	819 (28.3)	420 (30.5)	399 (26.3)		28.0	27.3	28.4	
Social security recipient	204 (7.0)	86 (6.2)	118 (7.8)	0.058	7.2	6.3	7.9	0.055
Current worker	758 (26.1)	425 (30.8)	333 (21.9)	**<0.001**	25.8	31.1	21.9	**<0.001**

p < 0.05 indicated in bold.

Table 2. Prevalence of frailty status and component (standardized sample).

Variable	Overall		Men (42.2%)		Women (57.8%)		*p*-Value
	%	(95% CI)	%	(95% CI)	%	(95% CI)	
Frailty status							
Robust	45.2	(43.3–47.0)	52.8	(50.1–55.5)	39.6	(37.1–42.0)	
Prefrail	47.0	(45.1–48.8)	41.1	(38.5–43.8)	51.3	(48.7–53.8)	**<0.001**
Frail	7.9	(6.8–8.9)	6.0	(4.9–7.2)	9.2	(7.7–10.7)	
Frailty component							
Exhaustion	32.5	(30.7–34.2)	21.1	(18.9–23.2)	40.8	(38.3–43.3)	**<0.001**
Low physical activity	10.2	(8.7–11.8)	10.7	(9.1–12.3)	10.5	(9.4–11.6)	0.695
Slowness	20.1	(18.6–21.6)	18.8	(16.8–20.8)	21.1	(19.0–23.2)	0.131
Weakness	19.7	(18.3–21.2)	18.0	(16.0–20.0)	21.0	(18.9–23.1)	**0.042**
Unintentional weight loss	4.9	(4.1–5.7)	5.2	(4.0–6.3)	4.6	(3.5–5.7)	0.527
Frailty score							
0	45.2	(43.3–47.0)	52.8	(50.1–55.5)	39.6	(37.1–42.0)	
1	32.1	(30.3–33.8)	28.8	(26.3–31.2)	34.5	(32.1–36.9)	
2	15.0	(13.6–16.3)	12.4	(10.7–14.1)	16.8	(14.9–18.7)	**<0.001**
3	5.8	(4.9–6.7)	4.5	(3.4–5.5)	6.8	(5.5–8.1)	
4	1.9	(1.4–2.4)	1.5	(1.0–2.1)	2.2	(1.4–2.9)	
5	0.1	(0.0–0.3)	0.1	(0.0–0.2)	0.2	(0.0–0.4)	

CI, confidence interval. *p* < 0.05 indicated in bold.

Table 3. Characteristics of the standardized study sample according to frailty status.

Variable	Overall		Robust (45.2%)		Prefrail (47.0%)		Frail (7.9%)		*p*-Value
Sociodemographic									
Age (years)	75.8	± 0.07	74.9	± 0.09	76.3	± 0.10	78.5	± 0.23	<0.001
70–74	41.8		51.0		37.7		14.5		
75–79	36.1		36.2		35.2		40.4		<0.001
80–84	22.1		12.8		27.1		45.2		
Female sex	57.8		50.6		63.1		67.5		<0.001
Low education level (<7 years)	45.5		33.7		52.5		71.8		<0.001
Live alone	24.3		19.4		27.5		33.6		<0.001
Marital status (without partner)	35.3		29.3		39.2		46.2		<0.001
Residence									
Urban	28.4		34.2		25.5		13.2		
Suburban	43.6		43.9		43.6		41.7		<0.001
Rural	28.0		21.9		30.9		45.2		
Social security recipient	7.2		5.8		8.0		11.1		0.017
Current worker	25.8		26.2		26.6		17.9		0.010
Physical									
Underweight (BMI < 18.5 kg/m^2)	1.6		1.1		1.7		4.0		0.030
Low appendicular skeletal muscle (lower 20%)	22.3		16.3		25.9		35.6		<0.001
Low calf circumference (<32 cm)	27.6		19.5		31.9		48.1		<0.001
High waist circumference (M ≥ 102 cm; F ≥ 88 cm)	51.4		48.1		54.1		53.6		0.007
Sarcopenia (AWGS-defined)	10.1		1.1		14.6		34.5		<0.001
ADL disability (>1 point)	2.2		0.8		2.1		10.2		<0.001
IADL disability (>2 points)	6.3		3.9		6.8		17.3		<0.001
Falls in the past year	20.6		16.0		22.3		36.6		<0.001

Table 3. *Cont.*

Variable	Overall		Robust (45.2%)		Prefrail (47.0%)		Frail (7.9%)		p-Value
Physical function									
Severe mobility limitation	10.1		1.1		14.6		34.5		<0.001
Timed Up and Go (seconds)	10.5	± 0.05	9.4	± 0.04	10.8	± 0.1	14.9	± 0.3	<0.001
Short Physical Performance Battery (score)	10.8	± 0.03	11.4	± 0.02	10.6	± 0.04	8.6	± 0.15	<0.001
Gait speed (m/s)	1.10	± 0.00	1.22	± 0.01	1.04	± 0.00	0.76	± 0.01	<0.001
Grip strength (kg)	25.7	± 0.1	28.7	± 0.2	24.0	± 0.2	18.9	± 0.4	<0.001
Biological									
Albumin (g/dL)	4.4	± 0.00	4.4	± 0.01	4.3	± 0.01	4.3	± 0.02	<0.001
Serum creatinine (mg/dL)	0.84	± 0.01	0.83	± 0.01	0.84	± 0.01	0.87	± 0.02	0.271
HbA1c (%)	6.0	± 0.02	6.0	± 0.02	6.0	± 0.02	6.2	± 0.08	<0.001
WBC (X1000/uL)	5.9	± 0.03	5.7	± 0.04	6.0	± 0.05	6.2	± 0.12	<0.001
RBC (Mil/uL)	4.4	± 0.01	4.4	± 0.01	4.3	± 0.01	4.2	± 0.03	<0.001
Cortisol (ug/dL) at 8 a.m.	10.1	± 0.08	10.2	± 0.10	10.1	± 0.11	10.2	± 0.30	0.740
hs-CRP (mg/L)	1.34	± 0.04	1.29	± 0.05	1.31	± 0.05	1.85	± 0.19	<0.001
Vitamin B12 (pg/mL)	610.1	± 5.34	614.8	± 7.77	608.3	± 7.77	593.4	± 22.02	0.551
TSH (uIU/mL)	2.8	± 0.10	2.9	± 0.20	2.6	± 0.07	2.7	± 0.22	0.306
Insulin (uU/mL)	8.0	± 0.18	7.3	± 0.20	8.3	± 0.21	9.9	± 1.41	<0.001
Triglyceride (mg/dL)	122.6	± 1.15	120.3	± 1.69	122.5	± 1.60	137.1	± 5.15	0.001
Total cholesterol (mg/dL)	174.6	± 0.68	176.5	± 1.01	173.1	± 1.01	172.5	± 2.26	0.037
HDL-cholesterol (mg/dL)	52.5	± 0.26	53.4	± 0.39	52.0	± 0.38	50.5	± 0.93	0.003
LDL-cholesterol (mg/dL)	108.2	± 0.63	109.7	± 0.95	107.1	± 0.92	106.0	± 2.10	0.069
25-hydroxy vitamin D (mg/mL)	23.2	± 0.19	23.6	± 0.28	23.2	± 0.27	21.0	± 0.56	0.001
eGFR (mL/min/1.73 m^2) [a]	77.5	± 0.27	78.9	± 0.35	76.9	± 0.41	73.3	± 1.14	<0.001

Table 3. *Cont.*

Variable	Overall		Robust (45.2%)		Prefrail (47.0%)		Frail (7.9%)		*p*-Value
Lifestyle									
Current smoker	5.2		4.7		5.3		7.7		0.238
Alcohol intake (≥2–3 time/week)	16.3		19.1		14.1		13.4		**0.001**
Sleep latency (>1 h)	4.3		3.1		4.9		7.0		**0.019**
Long night-time sleep (>8 h)	5.9		4.8		6.5		9.2		**<0.001**
Dairy products (not every day)	60.9		56.3		62.8		74.0		**<0.001**
Legumes and eggs intake (<2 times/week)	19.7		13.8		22.8		33.5		**<0.001**
Meat, fish, and poultry intake (not every day)	80.8		78.0		83.2		82.0		**0.045**
Risk of malnutrition (MNA score ≤11)	8.0		3.7		10.0		20.0		**<0.001**
Health condition									
Number of drugs	4.4	± 0.06	3.9	± 0.08	4.7	± 0.09	5.7	± 0.23	**<0.001**
Comorbidity (≥2 diseases)	55.6		48.3		61.3		63.2		**<0.001**
Polypharmacy (≥5 medications)	32.2		24.4		36.0		55.0		**<0.001**
Hospitalization in the past year	12.9		8.6		15.8		20.5		**<0.001**
Hearing impairment	15.3		13.9		15.7		21.2		**0.033**
Visual impairment	2.6		1.4		3.4		4.4		**0.002**
Low chewing ability	46.7		39.1		48.8		64.0		**<0.001**
Low pronouncing ability	25.0		18.9		27.4		45.5		**<0.001**

Table 3. *Cont.*

Variable	Overall	Robust (45.2%)	Prefrail (47.0%)	Frail (7.9%)	*p*-Value
Medical condition					
Hypertension	58.4	54.0	61.4	66.2	**<0.001**
Diabetes	21.9	18.3	23.9	31.3	**<0.001**
Urinary incontinence	4.1	2.2	5.0	10.4	**<0.001**
Cardiovascular disease [b]	13.3	11.2	14.4	18.6	**0.004**
Dyslipidemia	33.6	34.2	33.7	29.1	0.326
Osteoarthritis	26.7	20.1	31.6	34.8	**<0.001**
Osteoporosis	17.5	13.2	20.6	23.4	**<0.001**
Rheumatoid arthritis	2.2	1.0	3.0	4.2	**<0.001**
Digestive system ulceration	6.3	4.9	7.5	7.2	**0.019**
Chronic obstructive pulmonary disease	0.9	0.9	0.8	1.3	0.703
Allergic rhinitis	4.1	4.8	3.6	3.3	0.241
Bronchitis	1.5	1.0	1.9	2.1	0.137
Asthma	3.6	3.1	3.7	5.2	0.369
Thyroid disease	4.7	4.9	4.5	4.4	0.889
Kidney disease	1.5	1.0	1.8	2.8	0.087
Prostate disease	14.7	16.8	13.0	12.6	**0.011**
Depressive disorder	3.0	1.9	2.8	10.7	**<0.001**

Table 3. *Cont.*

Variable	Overall		Robust (45.2%)		Prefrail (47.0%)		Frail (7.9%)		p-Value
Psychological									
EQ-5D index	0.88	± 0.00	0.92	± 0.00	0.86	± 0.00	0.73	± 0.01	**<0.001**
EQ-VAS	74.2	± 0.33	79.6	± 0.40	71.3	± 0.49	60.1	± 1.49	**<0.001**
SF-12		±		±		±		±	
Physical health	43.3	± 0.21	48.1	± 0.23	40.9	± 0.30	30.7	± 0.72	**<0.001**
Mental health	52.7	± 0.20	55.6	± 0.22	51.3	± 0.32	44.7	± 0.87	**<0.001**
Poor self-perceived health	31.0		17.2		37.9		68.9		**<0.001**
Depressive symptoms (GDS score ≥ 6)	22.7		9.4		29.8		57.0		**<0.001**
Cognitive dysfunction (MMSE score < 24)	22.3		12.4		27.3		49.6		**<0.001**
Cognitive impairment	24.4		17.9		27.7		41.7		**<0.001**
Social									
Social support	5.5	± 0.02	5.5	± 0.03	5.4	± 0.04	5.3	± 0.10	**0.026**
Poor social capital	6.4		5.2		6.3		13.7		**0.002**
Social network									
Low interaction with family	39.5		37.1		40.6		46.4		**0.019**
Low interaction with friends	23.1		17.1		25.8		41.9		**<0.001**
Low interaction with neighbor	28.7		30.2		27.6		26.9		0.294
Religious activities (none)	41.7		41.5		40.6		49.8		**0.044**
Social activities (none)	21.6		20.6		22.3		23.3		0.491

Values are presented as mean ± standard error or percentage. [a] eGFR, estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation; M, male; F; female. [b] Cardiovascular diseases were included myocardial infarction, congestive heart failure, angina, peripheral vascular disease, and cerebrovascular disease. ADL, activities of daily living; IADL, instrumental activities of daily living; HbA1c, glycosylated hemoglobin; WBC, white blood cell; RBC, red blood cell; hs-CRP high-sensitivity C-reactive protein; TSH, thyroid-stimulating hormone; HDL-cholesterol, high-density lipoprotein; LDL-cholesterol, low-density lipoprotein; eGFR, estimated glomerular filtration rate; MNA, Mini-Nutritional Assessment; EQ-5D, EuroQol-5 dimension; EQ-vas, EuroQol Visual Analogue Scale; SF-12, 12 item short form health survey; GDS, Global Deterioration Scale; MMSE, Mini-Mental State Exam. *p* < 0.05 indicated in bold.

Table 4. Risk factors associated with physical frailty in the final forward logistic regression models (unstandardized sample).

Variable	B	S.E.	p-Value	OR	95% CI	
					Lower	Upper
At risk of malnutrition [a]	0.922	0.240	<0.001	2.51	1.57	4.03
Sarcopenia [b]	0.872	0.202	<0.001	2.39	1.61	3.56
Severe mobility limitation [c]	0.758	0.199	<0.001	2.13	1.45	3.15
Poor social capital [d]	0.687	0.287	0.017	1.99	1.13	3.49
Residence						
Urban	Ref.					
Suburban	0.571	0.259	0.027	1.77	1.07	2.94
Rural	0.673	0.265	0.016	1.89	1.13	3.18
Depressive [e]	0.634	0.194	0.001	1.89	1.29	2.76
Poor self-perceived health	0.502	0.199	0.012	1.65	1.12	2.44
Polypharmacy [f]	0.478	0.181	0.008	1.61	1.13	2.30
hs-CRP, mg/L	0.252	0.095	0.008	1.29	1.07	1.55
HbA1c, %	0.243	0.103	0.018	1.28	1.04	1.56
Timed Up and Go, seconds	0.236	0.039	<0.001	1.27	1.17	1.37
Age, years	0.081	0.025	0.001	1.08	1.03	1.14
25-hydroxyvitamin D, ng/mL	−0.023	0.010	0.024	0.98	0.96	1.00
Short Physical Performance Battery	−0.144	0.064	0.025	0.87	0.76	0.98

Independent forward stepwise logistic regression analysis with adjustment for multiple comparisons. Controlled age, education level, residence, current worker, low calf circumference, sarcopenia, severe mobility limitation, ADL disability, IADL disability, fall in the past year, Timed Up and Go, Short Physical Performance Battery, albumin, serum creatinine, hemoglobin A1c, HbA1c, red blood cell, free thyroxine, triglyceride, 25-hydroxyvitamin D, estimated glomerular filtration rate, risk of malnutrition, polypharmacy, hospitalization in the past year, low pronouncing ability, diabetes, urinary incontinence, osteoarthritis, rheumatoid arthritis, EuroQol-5 dimensions, depressive symptoms, cognitive impairment, social support, poor social capital, low interaction with friends, and social activities. [a] At risk of malnutrition: Mini-Nutritional Assessment Short Form score of ≤11. [b] Sarcopenia: defined according to the consensus report of the Asian Working Group for sarcopenia. [c] Severe mobility limitation: "very difficult" or "impossible" to either walk about 400 m or climb 10 steps without resting. [d] Poor social capital: any lack of participation in social gatherings. [e] Depressive: a score of ≥6 on the Korean version of the Short Form Geriatric Depression Scale (SGDS-K). [f] Polypharmacy: taking ≥5 medications. hs-CRP, high-sensitivity C-reactive protein; HbA1c, glycosylated hemoglobin; *B*, regression coefficient; S.E., standard error; OR, odds ratio; CI, confidence interval.

4. Discussion

Our study was designed to estimate the standardized prevalence of physical frailty using the national standard population composition ratio and to explore comprehensive risk factors for physical frailty among older adults in Korea. Our study showed that the age-, sex-, and residence-standardized prevalence of physical frailty among older adults aged 70–84 years in Korea is 7.9%, increases with age, and is higher among women and those living in rural areas. Furthermore, our study indicates that physiconutritional, medical, psychological, and sociodemographic risk domains were most relevant to physical frailty.

Our study used the FFP to define physical frailty that has been used in many countries and found to predict adverse health outcomes among the older population. In a systematic review, the prevalence of frailty using the FFP varied from 4.0% to 17.0% in community-dwelling older adults aged ≥65 years [3]. The prevalence of physical frailty among Korean community-dwelling adults is comparatively lower than the pooled prevalence of 9.9% (95% CI 9.6–10.2%) in 15 studies [3]. Several studies have estimated the prevalence of frailty using the population structure ratio. Recent epidemiological studies report that the weighted prevalence of frailty using the FFP in community-dwelling older adults varies from 5.2% to 15.2% in Asian countries [11,38,39]. The weighted prevalence of frailty among older adults aged ≥60 years in Singapore was 5.7% (95% CI 4.6–7.1%) and increased significantly with age, with no difference among men and women [11]. In a longitudinal cohort study of a nationally representative sample of community-dwelling adults from 28 provinces in China, the weighted prevalence of frailty was 7.0% and was higher among women than among men (8.0% vs. 5.9%) [39]. This study also observed geographic heterogeneity and urban–rural differences in the prevalence of frailty. In Sri Lankan rural areas, the weighted prevalence of frailty was 15.2% in community-dwelling adults aged ≥60 years, which was higher than that in high- and upper-middle-income countries [38]. The differences in prevalence across countries could be due to the modified components used to define frailty in different studies. The wide variation in the prevalence of frailty has been attributed to the characteristics of a population such as environment, ethnicity, and social culture.

The KFACS recruited participants using quota sampling stratified by age and sex in 10 study centers. To avoid biased results caused by the disproportionate sampling design, adjustment was performed by adjusting for age, sex, and residential areas using the Korean Population and Housing Census conducted by Statistics Korea in 2017. Our study recruited men and women in a 1:1 ratio, with 47.6% men and 52.4% women. However, the proportion of women increased to 57.8% in the standardized sample. These results were consistent with those of previous studies in which the proportion of women increased after age- and sex adjustment [38]. Furthermore, the regional distribution of the overall sample is similar in unstandardized and standardized samples. However, the distribution of residence between men and women was significantly different in the unstandardized sample, but not in the standardized sample. Since the participants were recruited without considering the sex ratio of the residential areas, there may be differences in the residential distribution by sex between unstandardized and standardized samples. The prevalence of physical frailty in the overall samples, in urban and rural areas, was similar regardless of standardization. However, age-, sex-, and residence-adjusted prevalence of frailty was estimated to be lower in men and higher in women than in the unstandardized sample. Similarly, the prevalence of frailty differed after weighting in the community-dwelling aged ≥55 years in Beijing, China [40]. The overall weighted and unweighted prevalence of frailty was estimated to be 9.1% and 12.3%, respectively. Additionally, the prevalence of frailty according to sex and residential area was estimated to be lower after sex and age adjustment.

In this nationwide community-dwelling population of Korean older adults, we found that 7.9% of Korean adults aged 70–84 years were frail. A similar prevalence (7.8%) was reported in Korean community-dwelling older adults aged 65 years and older using the data from the Living Profiles of Older People Survey based on home visits in 2008 [41]. In contrast, the prevalence in our study was lower than that reported in a previous Korean hospital-based study [8]. This could be because our study population (70–84 years) was younger than that in the previous study population involving

oldest–old (≥85 years). Moreover, the KFACS participants were ambulatory community-dwelling older adults who may be less frail compared to hospital-based participants. Our study showed that the standardized prevalence of frailty in rural areas was 12.7%, which was lower than that in the Pyeongchang rural area in Korea (12.7% vs. 17.4%). However, the prevalence of prefrailty was similar (52.0% vs. 52.6%) [9]. Both studies recruited ambulatory community-dwelling older adults. The prevalence of frailty may differ depending on the area of residence.

Physical frailty requires a comprehensive range of prevention and management [42], and it is important to identify risk factors for physical frailty in multidimensional domains. We have explored risk factors in a comprehensive range of multidimensional domains. Our study shows that physiconutritional, psychological, sociodemographic, and medical domains are the strongest risk factors for frailty among the 9 domains in older adults. In the physical frail population, participants with all domains (27.1%) were more common than those with none (1.4%) or one (0–1.4%) of the four domains. Our results show that participants have overlapping risk factors and need to manage modifiable risk factors using a multidimensional approach. In the physical domain, we found a correlation between sarcopenia and physical frailty. By definition, sarcopenia includes a low physical function, which means that sarcopenia is an essential component of physical frailty [42]. Previous studies have shown that physical frailty is associated with sarcopenia, and both conditions tend to overlap [43,44]. Therefore, sarcopenia should be considered in the management of physical frailty, as suggested in recent international clinical practice guidelines [42]. In addition, our study identified a significant correlation between physical frailty and physical function domains, including severe mobility limitation, longer TUG times, and lower SPPB scores. We have identified the correlation between physical function and frailty in cross-section, and physical function has been used as a simple tool for physical frailty. In a systematic review, the TUG test was found to have a high sensitivity for identifying physical frailty [45]. SPPB scores might also be used as a screening tool to detect physical frailty and correlate with physical frailty in community-dwelling older adults [46]. These physical functions cannot be used as a single test to diagnose physical frailty, but can help assess physical frailty. Our finding of a strong correlation between physical frailty and polypharmacy is consistent with previous studies [47]. In French older adults aged ≥70 years, polypharmacy with 5–9 drugs (OR 1.77, 95% CI 1.20–2.61) and excessive polypharmacy with 10 drugs or more (OR 4.47, 95% CI 2.37–8.42) were associated with physical frailty. Frail people usually have a number of chronic conditions [1] and may be at risk of polypharmacy. Therefore, physical frailty can be managed by reducing polypharmacy through medication management. Our results show that malnutrition has the strongest association with frailty. This association has also been reported in recent cross-sectional studies [48]. Malnutrition is an important pathogenic factor of frailty [49]. International clinical practice guidelines recommend a broad nutritional assessment as part of an appropriate approach to frailty [42,50,51]. In addition, we report a relationship between a low concentration of 25-hydroxyvitamin D and frailty. Because vitamin D deficiency in older adults increases the risk of adverse outcomes such as osteoporosis and low muscle strength, vitamin D might be associated with frailty [52]. We observed a strong correlation between frailty and biological factors. Previous studies have reported a relationship between inflammatory markers and frailty [53–55], which is consistent with our results. Additionally, HbA1c, an indicator of diabetes diagnosis, was associated with frailty in our study. Several studies have shown that older adults with diabetes are more likely to be frail than those without diabetes [56,57]. In the psychological domain, physical frailty has been correlated with depressive symptoms. In a systematic review, people with depression were at increased odds of having physical frailty (OR 4.07, 95% CI 1.93–8.55), while frail people were also at increased odds of having depression (OR = 2.64; 95% CI: 1.59–4.37) [58]. As the symptoms of physical frailty and depression are common among older adults and correlated, appropriate interventions are needed. In the social domain, we demonstrated that social capital is related to frailty. Poor social participation can lead to social isolation and loneliness as well as frailty among older adults [59]. In a recent systematic review, there were correlations between physical frailty and social environments including social networks, social support, social participation, subjective neighborhood experience,

and sociodemographic neighborhood characteristics. Among them, neighborhood dimensions and social participation had more consistent results. Thus, the social environment should be considered in the management of physical frailty. Our findings of a strong correlation between frailty and age and residence are consistent with previous studies [11,60]. Systematic reviews have shown that physical frailty is a common age-related syndrome, and most studies have been associated with increasing age and physical frailty [61]. Therefore, we should be able to intervene and manage modifiable risk factors.

Our study has several limitations. Due to the cross-sectional design, a causal relationship between risk factors and frailty cannot be determined. The characteristics of the oldest-old (≥85 years) population were unexplored in this study. Despite these limitations, we standardized the study population by sex, age, and residence based on the Korean Population and Housing Census conducted by Statistics Korea in 2017. Furthermore, we examined a comprehensive range of risk factors for frailty status in a homogeneous population. We determined the strongest risk factors associated with frailty.

5. Conclusions

The standardized prevalence of physical frailty increases with age and is higher among women and in rural areas. Furthermore, our study showed that multiple domains, such as physiconutritional, psychological, sociodemographic, and medical domains, are strongly associated with physical frailty. Management of modifiable risk factors might help in multidimensional prevention and intervention to reduce physical frailty among the older population in Korea.

Supplementary Materials: The following are available online at http://www.mdpi.com/1660-4601/17/21/7883/s1, Figure S1: The proportion of risk domains across the frailty status (unstandardized sample), Table S1: Criteria used to physical frailty, and Table S2: Prevalence of frailty status and component (unstandardized sample).

References

1. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M157. [CrossRef] [PubMed]
2. Vermeiren, S.; Vella-Azzopardi, R.; Beckwee, D.; Habbig, A.-K.; Scafoglieri, A.; Jansen, B.; Bautmans, I.; Verté, D.; Beyer, I.; Petrovic, M. Frailty and the prediction of negative health outcomes: A meta-analysis. *J. Am. Med. Dir. Assoc.* **2016**, *17*, 1163.e1–1163.e17. [CrossRef] [PubMed]
3. Collard, R.M.; Boter, H.; Schoevers, R.A.; Oude Voshaar, R.C. Prevalence of frailty in community-dwelling older persons: A systematic review. *J. Am. Geriatr. Soc.* **2012**, *60*, 1487–1492. [CrossRef] [PubMed]
4. Cesari, M.; Gambassi, G.; Abellan van Kan, G.; Vellas, B. The frailty phenotype and the frailty index: Different instruments for different purposes. *Age Ageing* **2014**, *43*, 10–12. [CrossRef] [PubMed]
5. Yaksic, E.; Lecky, V.; Sharnprapai, S.; Tungkhar, T.; Cho, K.; Driver, J.A.; Orkaby, A.R. Defining frailty in research abstracts: A systematic review and recommendations for standardization. *J. Frailty Aging* **2019**, *8*, 67–71. [CrossRef] [PubMed]
6. Cesari, M.; Prince, M.; Thiyagarajan, J.A.; De Carvalho, I.A.; Bernabei, R.; Chan, P.; Gutierrez-Robledo, L.M.; Michel, J.-P.; Morley, J.E.; Ong, P. Frailty: An emerging public health priority. *J. Am. Med. Dir. Assoc.* **2016**, *17*, 188–192. [CrossRef]

7.   Statistics Korea. Population Projections for Korea (2017–2067). Available online: http://kostat.go.kr (accessed on 28 March 2019).

8.   Jung, H.-W.; Kim, S.-W.; Ahn, S.; Lim, J.-Y.; Han, J.-W.; Kim, T.-H.; Kim, K.-W.; Kim, K.-I.; Kim, C.-H. Prevalence and outcomes of frailty in Korean elderly population: Comparisons of a multidimensional frailty index with two phenotype models. *PLoS ONE* **2014**, *9*, e87958. [CrossRef]

9.   Jung, H.-W.; Jang, I.-Y.; Lee, Y.S.; Lee, C.K.; Cho, E.-I.; Kang, W.Y.; Chae, J.H.; Lee, E.J.; Kim, D.H. Prevalence of frailty and aging-related health conditions in older Koreans in rural communities: A cross-sectional analysis of the aging study of Pyeongchang rural area. *J. Korean Med. Sci.* **2016**, *31*, 345–352. [CrossRef]

10. Poli, S.; Cella, A.; Puntoni, M.; Musacchio, C.; Pomata, M.; Torriglia, D.; Vello, N.; Molinari, B.; Pandolfini, V.; Torrigiani, C. Frailty is associated with socioeconomic and lifestyle factors in community-dwelling older subjects. *Aging Clin. Exp. Res.* **2017**, *29*, 721–728. [CrossRef]

11. Vaingankar, J.A.; Chong, S.A.; Abdin, E.; Picco, L.; Chua, B.Y.; Shafie, S.; Ong, H.L.; Chang, S.; Seow, E.; Heng, D. Prevalence of frailty and its association with sociodemographic and clinical characteristics, and resource utilization in a population of Singaporean older adults. *Geriatr. Gerontol. Int.* **2017**, *17*, 1444–1454. [CrossRef]

12. Wong, C.H.; Weiss, D.; Sourial, N.; Karunananthan, S.; Quail, J.M.; Wolfson, C.; Bergman, H. Frailty and its association with disability and comorbidity in a community-dwelling sample of seniors in Montreal: A cross-sectional study. *Aging Clin. Exp. Res.* **2010**, *22*, 54–62. [CrossRef]

13. Feng, Z.; Lugtenberg, M.; Franse, C.; Fang, X.; Hu, S.; Jin, C.; Raat, H. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: A systematic review of longitudinal studies. *PLoS ONE* **2017**, *12*, e0178383. [CrossRef] [PubMed]

14. Won, C.W.; Lee, S.; Kim, J.; Chon, D.; Kim, S.; Kim, C.-O.; Kim, M.K.; Cho, B.; Choi, K.M.; Roh, E. Korean frailty and aging cohort study (KFACS): Cohort profile. *BMJ Open* **2020**, *10*, e035573. [CrossRef] [PubMed]

15. Charlson, M.E.; Pompei, P.; Ales, K.L.; MacKenzie, C.R. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J. Chronic. Dis.* **1987**, *40*, 373–383. [CrossRef]

16. Chen, L.-K.; Liu, L.-K.; Woo, J.; Assantachai, P.; Auyeung, T.-W.; Bahyah, K.S.; Chou, M.-Y.; Chen, L.-Y.; Hsu, P.-S.; Krairit, O. Sarcopenia in Asia: Consensus report of the Asian Working Group for Sarcopenia. *J. Am. Med. Dir. Assoc.* **2014**, *15*, 95–101. [CrossRef]

17. Kim, S.; Kim, M.; Lee, Y.; Kim, B.; Yoon, T.Y.; Won, C.W. Calf circumference as a simple screening marker for diagnosing sarcopenia in older Korean adults: The Korean frailty and aging cohort study (KFACS). *J. Korean Med. Sci.* **2018**, *33*. [CrossRef]

18. Lean, M.; Han, T.; Morrison, C. Waist circumference as a measure for indicating need for weight management. *BMJ* **1995**, *311*, 158–161. [CrossRef] [PubMed]

19. Cesari, M.; Demougeot, L.; Boccalon, H.; Guyonnet, S.; Van Kan, G.A.; Vellas, B.; Andrieu, S. A self-reported screening tool for detecting community-dwelling older persons with frailty syndrome in the absence of mobility disability: The FiND questionnaire. *PLoS ONE* **2014**, *9*, e101745. [CrossRef]

20. Won, C.W.; Yang, K.Y.; Rho, Y.G.; Kim, S.Y.; Lee, E.J.; Yoon, J.L.; Cho, K.H.; Shin, H.C.; Cho, B.R.; Oh, J.R. The development of Korean activities of daily living (K-ADL) and Korean instrumental activities of daily living (K-IADL) scale. *J. Korean Geriatr. Soc.* **2002**, *6*. [CrossRef]

21. Podsiadlo, D.; Richardson, S. The timed "Up & Go": A test of basic functional mobility for frail elderly persons. *J. Am. Geriatr. Soc.* **1991**, *39*, 142–148. [CrossRef]

22. Guralnik, J.M.; Simonsick, E.M.; Ferrucci, L.; Glynn, R.J.; Berkman, L.F.; Blazer, D.G.; Scherr, P.A.; Wallace, R.B. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *J. Gerontol.* **1994**, *49*, M85–M94. [CrossRef] [PubMed]

23. Kaiser, M.J.; Bauer, J.M.; Ramsch, C.; Uter, W.; Guigoz, Y.; Cederholm, T.; Thomas, D.R.; Anthony, P.; Charlton, K.E.; Maggio, M. Validation of the Mini Nutritional Assessment Short-Form (MNA®-SF): A practical tool for identification of nutritional status. *J. Nutr. Health Aging* **2009**, *13*, 782. [CrossRef] [PubMed]

24. Kim, J.; Lee, Y.; Won, C.; Lee, K.; Chon, D. Nutritional status and frailty in community-dwelling older Korean adults: The Korean Frailty and Aging Cohort Study. *J. Nutr.* **2018**, *22*, 774–778. [CrossRef] [PubMed]

25. Gnjidic, D.; Hilmer, S.N.; Blyth, F.M.; Naganathan, V.; Waite, L.; Seibel, M.J.; McLachlan, A.J.; Cumming, R.G.; Handelsman, D.J.; Le Couteur, D.G. Polypharmacy cutoff and outcomes: Five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J. Clin. Epidemiol.* **2012**, *65*, 989–995. [CrossRef]

26. Yoo, M.; Kim, S.; Kim, B.; Yoo, J.; Lee, S.; Jang, H.; Cho, B.; Son, S.; Lee, J.; Park, Y. Moderate hearing loss is related with social frailty in a community-dwelling older adults: The Korean frailty and aging cohort study (KFACS). *Arch. Gerontol. Geriatr.* **2019**, *83*, 126–130. [CrossRef]

27. Maberley, D.; Hollands, H.; Chuo, J.; Tam, G.; Konkal, J.; Roesch, M.; Veselinovic, A.; Witzigmann, M.; Bassett, K. The prevalence of low vision and blindness in Canada. *Eye* **2006**, *20*, 341–346. [CrossRef]

28. Bae, J.N.; Cho, M.J. Development of the Korean version of the Geriatric Depression Scale and its short form among elderly psychiatric patients. *J. Psychoson. Res.* **2004**, *57*, 297–305. [CrossRef]

29. Lee, D.Y.; Lee, K.U.; Lee, J.H.; Kim, K.W.; Jhoo, J.H.; Kim, S.Y.; Yoon, J.C.; Woo, S.I.; Ha, J.; Woo, J.I. A normative study of the CERAD neuropsychological assessment battery in the Korean elderly. *J. Int. Neuropsychol. Soc.* **2004**, *10*, 72–81. [CrossRef]

30. Won, C.W.; Lee, Y.; Kim, S.; Yoo, J.; Kim, M.; Ng, T.-P.; Kim, H.; Son, S.J. Modified criteria for diagnosing "cognitive frailty". *Psychiatry Investig.* **2018**, *15*, 839. [CrossRef]

31. Jo, M.-W.; Yun, S.-C.; Lee, S.-I. Estimating quality weights for EQ-5D health states with the time trade-off method in South Korea. *Value Health* **2008**, *11*, 1186–1189. [CrossRef]

32. Kim, S.; Won, C.W.; Kim, B.; Yoo, J.; Byun, S.; Jang, H.C.; Cho, B.; Son, S.; Lee, J.; Park, Y. EuroQol Visual Analogue Scale (EQ-VAS) as a Predicting Tool for Frailty in Older Korean Adults: The Korean Frailty and Aging Cohort Study (KFACS). *J. Nutr.* **2018**, *22*, 1275–1280. [CrossRef] [PubMed]

33. Kim, S.H.; Jo, M.W.; Ahn, J.; Ock, M.; Shin, S.; Park, J. Assessment of psychometric properties of the Korean SF-12 v2 in the general population. *BMC Public Health* **2014**, *14*, 1086. [CrossRef]

34. Brazier, J.E.; Roberts, J. The estimation of a preference-based measure of health from the SF-12. *Med. Care* **2004**, 851–859. [CrossRef]

35. Mitchell, P.H.; Powell, L.; Blumenthal, J.; Norten, J.; Ironson, G.; Pitula, C.R.; Froelicher, E.S.; Czajkowski, S.; Youngblood, M.; Huber, M. A short social support measure for patients recovering from myocardial infarction: The ENRICHD Social Support Inventory. *J. Cardiopulm. Rehabil. Prev.* **2003**, *23*, 398–403. [CrossRef] [PubMed]

36. Shin, N.; Kang, Y. The relationships among health locus of control and resilience, social support and health promoting behavior in patients with newly diagnosed coronary artery diseases. *Korean J. Adult Nurs.* **2015**, *27*, 294–303. [CrossRef]

37. Wenger, G.C.; Tucker, I. Using network variation in practice: Identification of support network type. *Health Soc. Care Community* **2002**, *10*, 28–35. [CrossRef] [PubMed]

38. Siriwardhana, D.D.; Weerasinghe, M.C.; Rait, G.; Falcaro, M.; Scholes, S.; Walters, K.R. Prevalence of frailty in rural community-dwelling older adults in Kegalle district of Sri Lanka: A population-based cross-sectional study. *BMJ Open* **2019**, *9*. [CrossRef]

39. Wu, C.; Smit, E.; Xue, Q.-L.; Odden, M.C. Prevalence and correlates of frailty among community-dwelling Chinese older adults: The China Health and Retirement Longitudinal Study. *J. Gerontol. A Biol. Sci. Med. Sci.* **2018**, *73*, 102–108. [CrossRef]

40. Zheng, Z.; Guan, S.; Ding, H.; Wang, Z.; Zhang, J.; Zhao, J.; Ma, J.; Chan, P. Prevalence and incidence of frailty in community-dwelling older people: Beijing Longitudinal Study of Aging II. *J. Am. Geriatr. Soc.* **2016**, *64*, 1281–1286. [CrossRef]

41. Lee, Y.; Kim, J.; Han, E.S.; Ryu, M.; Cho, Y.; Chae, S. Frailty and body mass index as predictors of 3-year mortality in older adults living in the community. *Gerontology* **2014**, *60*, 475–482. [CrossRef]

42. Dent, E.; Lien, C.; Lim, W.S.; Wong, W.C.; Wong, C.H.; Ng, T.P.; Woo, J.; Dong, B.; de la Vega, S.; Poi, P.J.H. The Asia-Pacific clinical practice guidelines for the management of frailty. *J. Am. Med. Dir. Assoc.* **2017**, *18*, 564–575. [CrossRef]

43. Cruz-Jentoft, A.J.; Kiesswetter, E.; Drey, M.; Sieber, C.C. Nutrition, frailty, and sarcopenia. *Aging Clin. Exp. Res.* **2017**, *29*, 43–48. [CrossRef] [PubMed]

44. Samper-Ternent, R.; Reyes-Ortiz, C.; Ottenbacher, K.J.; Cano, C.A. Frailty and sarcopenia in Bogotá: Results from the SABE Bogotá Study. *Aging Clin. Exp. Res.* **2017**, *29*, 265–272. [CrossRef] [PubMed]

45. Clegg, A.; Rogers, L.; Young, J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: A systematic review. *Age Ageing* **2014**, *44*, 148–152. [CrossRef] [PubMed]

46. Da Câmara, S.M.A.; Alvarado, B.E.; Guralnik, J.M.; Guerra, R.O.; Maciel, Á.C.C. Using the Short Physical Performance Battery to screen for frailty in young-old adults with distinct socioeconomic conditions. *Geriatr. Gerontol. Int.* **2013**, *13*, 421–428. [CrossRef] [PubMed]

47. Herr, M.; Robine, J.M.; Pinot, J.; Arvieu, J.J.; Ankri, J. Polypharmacy and frailty: Prevalence, relationship, and impact on mortality in a French sample of 2350 old people. *Pharmacoepidemiol. Drug Saf.* **2015**, *24*, 637–646. [CrossRef]

48. Pérez-Ros, P.; Vila-Candel, R.; López-Hernández, L.; Martínez-Arnau, F.M. Nutritional Status and Risk Factors for Frailty in Community-Dwelling Older People: A Cross-Sectional Study. *Nutrients* **2020**, *12*, 1041. [CrossRef]

49. Walston, J.; Hadley, E.C.; Ferrucci, L.; Guralnik, J.M.; Newman, A.B.; Studenski, S.A.; Ershler, W.B.; Harris, T.; Fried, L.P. Research agenda for frailty in older adults: Toward a better understanding of physiology and etiology: Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. *J. Am. Geriatr. Soc.* **2006**, *54*, 991–1001. [CrossRef]

50. Dent, E.; Kowal, P.; Hoogendijk, E.O. Frailty measurement in research and clinical practice: A review. *Eur. J. Intern. Med.* **2016**, *31*, 3–10. [CrossRef]

51. Turner, G.; Clegg, A. Best practice guidelines for the management of frailty: A British Geriatrics Society, Age UK and Royal College of General Practitioners report. *Age Ageing* **2014**, *43*, 744–747. [CrossRef]

52. Holick, M.F. Vitamin D deficiency. *N. Engl. J. Med.* **2007**, *357*, 266–281. [CrossRef] [PubMed]

53. Hubbard, R.E.; O'Mahony, M.S.; Savva, G.M.; Calver, B.L.; Woodhouse, K.W. Inflammation and frailty measures in older people. *J. Cell Mol. Med.* **2009**, *13*, 3103–3109. [CrossRef]

54. Leng, S.; Chaves, P.; Koenig, K.; Walston, J. Serum interleukin-6 and hemoglobin as physiological correlates in the geriatric syndrome of frailty: A pilot study. *J. Am. Geriatr. Soc.* **2002**, *50*, 1268–1271. [CrossRef] [PubMed]

55. Soysal, P.; Stubbs, B.; Lucato, P.; Luchini, C.; Solmi, M.; Peluso, R.; Sergi, G.; Isik, A.T.; Manzato, E.; Maggi, S. Inflammation and frailty in the elderly: A systematic review and meta-analysis. *Ageing Res. Rev.* **2016**, *31*, 1–8. [CrossRef] [PubMed]

56. Hubbard, R.; Andrew, M.; Fallah, N.; Rockwood, K. Comparison of the prognostic importance of diagnosed diabetes, co-morbidity and frailty in older people. *Diabet. Med.* **2010**, *27*, 603–606. [CrossRef] [PubMed]

57. Ottenbacher, K.J.; Graham, J.E.; Al Snih, S.; Raji, M.; Samper-Ternent, R.; Ostir, G.V.; Markides, K.S. Mexican Americans and frailty: Findings from the Hispanic established populations epidemiologic studies of the elderly. *Am. J. Public Health Nations Health* **2009**, *99*, 673–679. [CrossRef] [PubMed]

58. Soysal, P.; Veronese, N.; Thompson, T.; Kahl, K.G.; Fernandes, B.S.; Prina, A.M.; Solmi, M.; Schofield, P.; Koyanagi, A.; Tseng, P.-T. Relationship between depression and frailty in older adults: A systematic review and meta-analysis. *Ageing Res. Rev.* **2017**, *36*, 78–87. [CrossRef]

59. Gale, C.R.; Westbury, L.; Cooper, C. Social isolation and loneliness as risk factors for the progression of frailty: The English Longitudinal Study of Ageing. *Age Ageing* **2018**, *47*, 392–397. [CrossRef]

60. Ma, L.; Tang, Z.; Zhang, L.; Sun, F.; Li, Y.; Chan, P. Prevalence of frailty and associated factors in the community-dwelling population of China. *J. Am. Geriatr. Soc.* **2018**, *66*, 559–564. [CrossRef]

61. Mello, A.d.C.; Engstrom, E.M.; Alves, L.C. Health-related and socio-demographic factors associated with frailty in the elderly: A systematic literature review. *Cad. Saude Publica* **2014**, *30*, 1143–1168. [CrossRef]

Article

Determinants of Multidimensional and Physical Frailty and Their Individual Components: Interactions between Frailty Deficits

Magdalena Sacha [1,*], Jerzy Sacha [2,3,*] and Katarzyna Wieczorowska-Tobis [1]

1   Department of Palliative Medicine, Poznan University of Medical Sciences, 61-701 Poznan, Poland;
    tobis@ump.edu.pl
2   Faculty of Physical Education and Physiotherapy, Opole University of Technology, 45-758 Opole, Poland
3   Department of Cardiology, University Hospital, University of Opole, 45-401 Opole, Poland
*   Correspondence: magda0074@op.pl (M.S.); sacha@op.pl (J.S.); Tel.: +48-77-452-06-60 (J.S.)

Abstract: *Purpose:* To identify the interrelations among determinants of multidimensional frailty, physical frailty, and their individual components. *Methods:* A group of 1024 community-dwelling people older than 65 years completed questionnaires regarding: multidimensional frailty (Tilburg Frailty Indicator, TFI) and physical frailty (FRAIL scale), and common frailty risk factors. *Results:* Multidimensional frailty was recognized in 559 subjects (54.6%) and determined by 13 factors ($R^2 = 0.21$ in logistic regression). After incorporating TFI components to the models, the majority of previous risk factors became non-essential, and the frailty deficits mainly determined each other with R^2 ranging between 0.07–0.67. Physical frailty and non-robust status (i.e., either physical frailty or pre-frailty) were recognized in 64 (6.3%) and 542 (52.9%) participants, and were determined by 5 factors ($R^2 = 0.33$) and 11 factors ($R^2 = 0.34$), respectively. Associations between the frailty deficits were detected within and between different dimensions (i.e., physical, psychological and social); the physical domain was mainly related to the psychological one which in turn was additionally associated with the social one. *Conclusion:* Frailty is the accumulation of deficits and is determined by factors other than the determinants of the individual deficits. The associations between deficits coming from various dimensions of human functioning presumably amplify their effects and accelerate frailty development.

Keywords: frailty; non-robust; FRAIL scale; Tilburg Frailty Indicator; determinants

1. Introduction

Frailty is a pre-clinical condition that is associated with a decline in physiological reserves among the elderly people and it predisposes them to various adverse outcomes including functional deterioration, disability and death [1–3]. Frailty is usually considered as a set of physical impairments, such as sarcopenia, weight loss, poor mobility and fatigue; but in fact, frailty is an accumulation of deficits in different dimensions of human functioning, i.e., physical, psychological and social ones; and for its diagnosis, a certain number of such deficits must be identified [3–5]. Many risk factors for frailty development have been determined; yet, frailty as an accumulation of impairments combines conditions which certainly constitute risk factors for each other and their interplay most likely amplify their effects. Moreover, since frailty is a multidimensional entity, the interaction between impairments in various dimensions presumably accelerates the overall functional degradation associated with aging [6,7].

To recognize physical and multidimensional frailty, respective diagnostic tools must be employed which should allow a quick detection of frailty symptoms and an early identification of subjects at risk.

In terms of physical frailty, a questionnaire named the FRAIL scale appears to be a simple and sensitive measure for selecting people with physical impairments [8,9]; but in terms of multidimensional frailty, the Tilburg Frailty Indicator (TFI) is gaining popularity as an effective questionnaire for an early diagnosis of deficits in multiple dimensions [5]. Combination of unidimensional (i.e., physical) and multidimensional frailty diagnostic tools may yield more information about the character of functional disturbances associated with age than either of these tools employed exclusively. Indeed, it has been recently shown that a simultaneous employment of TFI and the FRAIL scale, may identify subgroups of the elderly people that present different functional profiles—i.e., those presenting predominantly social and psychological frailty or those with mainly physical deficits [7]. Such subgroups potentially require different management and, therefore, the approach to frail people should be individualized according to their functional state. However, for the individualized frailty prevention and treatment, determinants of frailty itself along with determinants of the individual frailty deficits should be recognized in order to design the appropriate strategy in a given deficits' constellation. Moreover, particular attention should be paid to the interactions between frailty components originating from various domains, e.g., physical and psychological frailty deficits probably constitute a vicious cycle in which one feeds the development of the other [1,7]. An early recognition of subjects at risk is paramount to employing an effective preventative strategy against frailty; and, therefore, frailty screening and seeking its determinants should be focused on a general (not institutionalized) elderly population [7].

In this study, a large group of community-dwelling elderly people was investigated for the presence of frailty, its risk factors and the relationships between various deficits associated with aging. The primary goal of the study was to identify independent determinants of multidimensional and physical frailty, as well as, each of the frailty components in two diagnostic frailty tools, i.e., TFI (dedicated to multidimensional frailty) and the FRAIL scale (devoted to physical frailty) [5,8,9]. The secondary goal was to investigate the association and interaction between deficits in different frailty dimensions.

2. Materials and Methods

2.1. Participants

Community-dwelling people at the age of 65 years or older living in Opole District (southwest Poland) took part in this cross-sectional study. The participants were recruited during healthy lifestyle promotion meetings arranged by local community-based senior organizations between December 2017 and December 2018—in total, there were 30 meetings during this period, and they gathered around 50 participants on average. These meetings were devoted to all elderly people living in a region (not only to the organizations' members) and they were advertised by suitable posters. There were no specific exclusion criteria except the age below 65 years and a lack of consent to take part in the study—due to these reasons, about one third of the meetings' attendees were not eligible for this research. Since the study was conducted among people coming to the meetings, all participants were moving around by themselves and they were not dependent on other people, and therefore represented an active part of the elderly population. The subjects completed by themselves questionnaires concerning multidimensional and physical frailty, as well as risk factors related to frailty (selected on the basis of previous research on frailty) [5,8–10]. The questionnaires were anonymous and included a short description of the study rationale. The research protocol was approved by the Ethics Committee at the Poznan University of Medical Sciences and all participants gave their informed consent. More details on the activities of community-based senior organizations in Poland may be found elsewhere [11].

2.2. Frailty Instruments

Multidimensional frailty has been investigated by using part B of the TFI which consists of 15 frailty deficits arranged according to three different domains. The physical domain (0–8 points) contains eight items: poor physical health, unintentional weight loss, difficulty in walking, difficulty in maintaining balance, poor hearing, poor vision, lack of strength in hands, and physical tiredness.

The psychological domain (0–4 points) consists of four components: problems with memory, feeling down, feeling nervous or anxious, and inability to cope with problems. The social domain (0–3 points) comprises three elements: living alone, missing other people, and lack of support from other people. The TFI total score may range from 0 to 15; by definition, frailty is recognized if the TFI score is at least 5 [5]. Part A of TFI contains risk factors leading to frailty which have been selected in the previous research on frailty, and this includes age, gender, education level, economic status, lifestyle, marital status, experiences with different unfavorable events in the recent period, and satisfaction with living conditions [5,10,12,13].

Physical frailty has been ascertained with the FRAIL scale which contains 5 components: physical tiredness/fatigue, inability to walk up one flight of stairs, inability to walk 200 m, unexplained body mass loss, and a number of chronic diseases [8,9]. Unexplained body mass loss is scored 1 if respondents communicate their weight loss of 6 kg or more during the last six months, or 3 kg or more during the last month. The presence of 5 or more chronic illnesses yields score 1, otherwise it is scored 0. FRAIL scale scores range from 0–5 and may reflect frail (3–5), prefrail (1–2), and robust (0) status [8,9].

The participants were also asked about a place of living (village or city), former occupation (physical or intellectual one) and if they are members of community-based senior organizations.

2.3. Statistical Analysis

The continuous variables were presented as mean ± standard deviation (SD). Categorical variables were presented as numeric values and percentages. Relationship between two variables was investigated with Pearson correlation. Independent determinants for different types of frailty and their components were identified with logistic regression through multiple testing—for each model, a determination coefficient was calculated which expressed the proportion of variance in the dependent variable explained by independent variables. Variables with $p > 0.1$ in adjusted analyses were not retained in the final model. To validate the models and exclude bias, a bootstrapping technique with 2000 samples was employed. In addition, the analyses (employing logistic regression) were performed to investigate the interaction between TFI components in determining another TFI component or FRAIL scale component. The associations between different frailty dimensions and their determinants were explored with multiple linear regression analysis—their interaction was checked with a calculation of centered product terms. Each model was validated in the bootstrapping analysis. The threshold probability of $p < 0.05$ was taken as the level of statistical significance. All analyses were performed using NCSS 12 Statistical Software (2018), NCSS, LLC, Kaysville, Utah, USA, and the Statistical Package for Social Sciences (SPSS, v. 22.0, IBM SPSS xStatistics, IBM Corporation, Chicago, IL, USA).

3. Results

3.1. Frailty Prevalence

Of the approximately 1500 attendees of the meetings arranged by senior organizations, 1024 community-dwelling individuals over the age of 65 years (72.6 ± 6.3 years; range 65–93 years; 270 males) took part in this cross-sectional study. The baseline participants' characteristics are presented in Table 1. The multidimensional frailty was diagnosed in 559 subjects (54.6%), whereas physical frailty, pre-frailty and non-robust status (i.e., either physical frailty or pre-frailty) were recognized in 64 (6.3%), 478 (46.7%) and 542 (52.9%) participants, respectively.

Table 1. Study group characteristics.

Characteristic	Overall Group
Age (years)	72.6 ± 6.3
Male sex	270 (26.4)
Primary school education level	258 (25.2)
High school education level	464 (45.3)
University education level	302 (29.5)
Low economic status	152 (14.8)
Moderate economic status	835 (81.5)
High economic status	37 (3.6)
Unhealthy lifestyle	54 (5.3)
Partially healthy lifestyle	532 (52.0)
Healthy lifestyle	438 (42.8)
Participation in a senior organization	460 (44.9)
Living in a city	746 (72.9)
Living in a relationship	529 (51.7)
Former intellectual occupation	646 (63.1)
Death of a loved person in the recent time	389 (38.0)
Serious illness in the recent time	229 (22.4)
Serious illness of a loved person in the recent time	245 (23.9)
End of an important relationship in the recent time	70 (6.8)
Traffic accident in the recent time	59 (5.8)
Criminal event in the recent time	23 (2.2)
Satisfaction with living conditions	903 (88.2)
Number of chronic diseases *	1.9 ± 1.6
Inability to walk up one flight of stairs *	87 (8.5)
Inability to walk 200 m *	101 (9.9)
Physical Domain of Tilburg Frailty Indicator (TFI)	
1. Poor physical health	331 (32.3)
2. Unexplained body mass loss *	133 (13.0)
3. Difficulty in walking	371 (36.2)
4. Difficulty in maintaining balance	261 (25.5)
5. Poor hearing	358 (35.0)
6. Poor vision	414 (40.4)
7. Lack of strength in hands	283 (27.6)
8. Physical tiredness/fatigue *	465 (45.4)
Psychological Domain of TFI	
9. Problems with memory	138 (13.5)
10. Feeling down	671 (65.5)
11. Feeling nervous or anxious	675 (65.9)
12. Inability to cope with problems	188 (18.4)
Social Domain of TFI	
13. Living alone	384 (37.5)
14. Missing other people	682 (66.6)
15. Lack of support from other people	185 (18.1)

Table 1. *Cont.*

Characteristic	Overall Group
Sum of physical deficits (components: 1–8)	2.6 ± 2.1
Sum of psychological deficits (components: 9–12)	1.6 ± 1.1
Sum of social deficits (components: 13–15)	1.2 ± 0.9
Total score of TFI (all components)	5.4 ± 3.1
Multidimensional frailty according to TFI	559 (54.6)
Total score for physical frailty according to FRAIL scale	0.8 ± 0.9
Physical frailty according to the FRAIL scale	64 (6.3)
Physical pre-frailty according to the FRAIL scale	478 (46.7)
Non-robust status according to the FRAIL scale	542 (52.9)

Notes: Values are mean ± SD or n (%). * Denotes components of the FRAIL scale.

3.2. Frailty Determinants

Numerous risk factors were independently associated with different types of frailty (Table 2), i.e., the multidimensional frailty was determined by 13 variables that explained 21% of the variance; whereas physical frailty and non-robust status were associated with 5 variables (explaining 33% of the variance) and 11 variables (explaining 34% of the variance), respectively. Age significantly increased the risk of multidimensional frailty akin to serious illness, the end of an important relationship, chronic diseases, and an inability to walk up one flight of stairs. However, male sex, a high school or university education level, a healthy lifestyle, participation in senior groups, living in a city or in a relationship as well as satisfaction with living conditions, they all reduced the likelihood of multidimensional frailty.

The risk of physical frailty was elevated by poor physical health, difficulty in walking or maintaining balance, and a lack of strength in hands. Of note, missing other people decreased the risk of being physically frail. The non-robust status was determined by more factors, i.e.,: serious illness, poor physical health, difficulty in walking or maintaining balance, poor vision, a lack of strength in hands, and feeling down increased the risk of being non-robust; whereas, a partially healthy or healthy lifestyle, participation in senior organizations, and serious illness of a loved person in the recent time independently diminished the risk.

The logistic regression analysis was performed to identify independent factors associated with each individual component of TFI and the FRAIL scale—the results are exhibited in Table 3. After incorporating TFI components to the models, majority of the previous risk factors of multidimensional frailty (Table 2) became non-essential, moreover, the TFI components appeared to be significantly related to each other. The regression models in Table 3 explain 7% to 67% (on average, 38%) of the variance of TFI deficits. In the validation bootstrapping analysis, all models in Tables 2 and 3 appeared to be valid, and in general, only few variables (i.e., 5 out of 196) presented discordant significance compared to the primary models (Table 3). On average, each TFI element was independently associated with 4.9 different TFI elements and 3 other risk factors (Table 3). Specifically, physical tiredness, and living alone were related to 7 other TFI components; whereas, a lack of strength in hands, feeling down, and feeling nervous or anxious were associated with 6 different TFI items; difficulty in maintaining balance, poor vision, problems with memory, an inability to cope with problems, missing other people, and a lack of support from other people were related to 5 various TFI components—other components were associated with no more than 4 TFI items.

Regarding the FRAIL scale, after incorporating their components to the models, the variance of the particular scale components could be explained in 7% to 51% (on average, 33%), and they (in majority) revealed the association with one of the other FRAIL scale components (Table 3). In addition, some of them were related to feeling down and missing other people (Table 3), and there was a significant interaction between poor vision and feeling down in determining the non-robust status (Table 2).

Table 2. Independent risk factors of multidimensional and physical frailty as well as non-robust status.

Independent Variables	Multidimensional Frailty $R^2 = 0.21, p < 0.00001$		Physical Frailty $R^2 = 0.33, p < 0.00001$		Non-Robust Status $R^2 = 0.34, p < 0.00001$	
	B (SE)	*p*-Value	**B (SE)**	*p*-Value	**B (SE)**	*p*-Value
Age	**0.07 (0.01)**	**<0.00001**				
Male sex	**−0.38 (0.17)**	**<0.05**				
High school education level	**−0.69 (0.2)**	**<0.001**			−0.42 (0.21)	0.051
University education level	**−0.66 (0.22)**	**<0.01**			−0.41 (0.23)	0.08
Moderate economic status						
High economic status						
Partially healthy lifestyle	−0.68 (0.37)	0.07			**−1.43 (0.48)**	**<0.01**
Healthy lifestyle	**−1.05 (0.38)**	**<0.01**			**−1.64 (0.48)**	**<0.001**
Participation in a senior organization	**−0.38 (0.15)**	**<0.05**			**−0.45 (0.16)**	**<0.01**
Living in a city	**−0.47 (0.18)**	**<0.01**			−0.34 (0.19)	0.07
Living in a relationship	**−0.45 (0.16)**	**<0.01**				
Former intellectual occupation						
Death of a loved person in the recent time					0.31 (0.16)	0.06
Serious illness in the recent time	**0.69 (19)**	**<0.001**			**0.48 (0.2)**	**<0.05**
Serious illness of a loved person in the recent time	0.3 (0.17)	0.08			**−0.39 (0.19)**	**<0.05**
End of an important relationship in the recent time	**0.87 (0.33)**	**<0.01**				
Traffic accident in the recent time	0.61 (0.33)	0.06				
Criminal event in the recent time						
Satisfaction with living conditions	**−2.12 (0.37)**	**<0.00001**				
Number of chronic diseases *	**0.12 (0.05)**	**<0.05**	–	–		
Inability to walk up one flight of stairs *	**0.96 (0.34)**	**<0.01**	–	–	–	–
Inability to walk 200 m *			–	–	–	–

* Physical Domain of Tilburg Frailty Indicator (TFI)

136

Table 2. *Cont.*

Independent Variables	Multidimensional Frailty R² = 0.21, p < 0.00001		Physical Frailty R² = 0.33, p < 0.00001		Non-Robust Status R² = 0.34, p < 0.00001	
	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
1. Poor physical health	–	–	2.08 (0.44)	<0.00001	1.18 (0.2)	<0.00001
2. Unexplained body mass loss *	–	–	–	–	–	–
3. Difficulty in walking	–	–	0.97 (0.42)	<0.05	0.85 (0.18)	<0.00001
4. Difficulty in maintaining balance	–	–	1.48 (0.36)	<0.0001	0.65 (0.22)	<0.01
5. Poor hearing	–	–				
6. Poor vision	–	–			0.53 (0.17) a	<0.01
7. Lack of strength in hands	–	–	0.75 (0.32)	<0.05	1.13 (0.21)	<0.00001
8. Physical tiredness/fatigue *	–	–	–	–	–	–
Psychological Domain of TFI						
9. Problems with memory	–	–				
10. Feeling down	–	–			0.53 (0.17) a	<0.01
11. Feeling nervous or anxious	–	–				
12. Inability to cope with problems	–	–			–0.44 (0.24)	0.07
Social Domain of TFI						
13. Living alone	–	–				
14. Missing other people	–	–	–0.72 (0.31)	<0.05		
15. Lack of support from other people	–	–				

Notes: * Denotes components of the FRAIL scale. Same letters (i.e., a) next to the coefficients correspond to the variables which significantly interact with p-values less than 0.05. Statistically significant coefficients and p-values are marked in bold. The validation bootstrapping analysis confirmed the statistical significance of the models and their variables.

Table 3. Independent determinants for each component of TFI and the FRAIL scale.

Independent Variables	1. Poor Physical Health R² = 0.49, p < 0.00001		2. Unexplained Body Mass Loss * R² = 0.07, p < 0.00001		3. Difficulty in Walking R² = 0.4, p < 0.00001		4. Difficulty in Maintaining Balance R² = 0.33, p < 0.00001		5. Poor Hearing R² = 0.23, p < 0.00001		6. Poor Vision R² = 0.48, p < 0.00001	
	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
Age			0.03 (0.01)	<0.05	0.06 (0.01)	<0.00001	0.04 (0.01)	<0.05	0.05 (0.01)	<0.0001	0.05 (0.01)	<0.0001
Male sex									0.47 (0.16)	<0.01		
High school education level											−0.55 (0.18)	<0.01
University education level											−0.49 (0.19)	<0.05
Moderate economic status												
High economic status												
Partially healthy lifestyle												
Healthy lifestyle												
Participation in a senior group									−0.56 (0.15)	<0.001		
Living in a city												
Living in a relationship							−0.63 (0.18)	<0.001	−0.29 (0.15)	0.054 ‡		
Former intellectual occupation												
Death of a loved person in the recent time												
Serious illness in the recent time												
Serious illness of a loved person in the recent time												
End of an important relationship in the recent time												
Traffic accident in the recent time	−1.11 (0.39)	<0.01			0.66 (0.33)	<0.05 ‡						
Criminal event in the recent time	1.95 (0.56)	<0.001										
Satisfaction with living conditions	−1.38 (0.27)	<0.00001	−0.91 (0.24)	<0.001								
Number of chronic diseases *	0.25 (0.05)	<0.00001										
Inability to walk up one flight of stairs *	0.99 (0.31)	<0.01	0.55 (0.28)	0.053 ‡								
Inability to walk 200 m *					1.08 (0.31)	<0.001	0.94 (0.27)	<0.001				
Physical Domain of Tilburg Frailty Indicator (TFI)												
1. Poor physical health	—	—			1.01 (0.18)	<0.00001	0.58 (0.19)	<0.01				
2. Unexplained body mass loss *	—	—	—	—								
3. Difficulty in walking	1.02 (0.18)	<0.00001			—	—	1.18 (0.19) a	<0.00001			0.29 (0.16)	0.06 a
4. Difficulty in maintaining balance	0.58 (0.2)	<0.01			1.12 (0.19)	<0.00001	—	—				

138

Table 3. *Cont.*

Independent Variables	1. Poor Physical Health R² = 0.49, p < 0.00001		2. Unexplained Body Mass Loss * R² = 0.07, p < 0.00001		3. Difficulty in Walking R² = 0.4, p < 0.00001		4. Difficulty in Maintaining Balance R² = 0.33, p < 0.00001		5. Poor Hearing R² = 0.23, p < 0.00001		6. Poor Vision R² = 0.48, p < 0.00001	
	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
5. Poor hearing									–	–	0.84 (0.15)	<0.00001
6. Poor vision									0.91 (0.14)	<0.00001	–	–
7. Lack of strength in hands					0.6 (0.19)	<0.01	0.67 (0.19)	<0.001			0.46 (0.17)	<0.01
8. Physical tiredness/fatigue *	1.25 (0.18)	<0.00001	0.66 (0.21)	<0.01	0.92 (0.17)	<0.00001	0.6 (0.2) [b]	<0.01			0.63 (0.16)	<0.0001
Psychological Domain of TFI												
9. Problems with memory							1.19 (0.23) [ab]	<0.00001	0.77 (0.21)	<0.001	0.68 (0.22)	<0.01 [a]
10. Feeling down												
11. Feeling nervous or anxious											0.4 (0.15)	<0.01
12. Inability to cope with problems	0.92 (0.22)	<0.0001										
Social Domain of TFI												
13. Living alone			−0.35 (0.21)	0.09	−0.3 (0.17)	0.08						
14. Missing other people												
15. Lack of support from other people	0.39 (0.21)	0.07										

Table 3. *Cont.*

Part II

Independent Variables	7. Lack of Strength in Hands $R^2 = 0.45$, $p < 0.00001$		8. Physical Tiredness * $R^2 = 0.51$, $p < 0.00001$		9. Problems with Memory $R^2 = 0.23$, $p < 0.00001$		10. Feeling Down $R^2 = 0.57$, $p < 0.00001$		11. Feeling Nervous or Anxious $R^2 = 0.44$, $p < 0.00001$		12. Inability to Cope with Problems $R^2 = 0.27$, $p < 0.00001$	
	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value
Age	−0.7 (0.2)	<0.001			0.05 (0.02)	<0.01						
Male sex											−0.44 (0.22)	<0.05 †
High school education level												
University education level												
Moderate economic status			0.52 (0.24)	<0.05	−0.61 (0.25)	<0.05						
High economic status			0.97 (0.47)	<0.05	−1.39 (0.69)	<0.05						
Partially healthy lifestyle			−1.25 (0.42)	<0.01								
Healthy lifestyle			−1.41 (0.43)	<0.001								
Participation in a senior group												
Living in a city			−0.71 (0.18)	<0.0001								
Living in a relationship							0.35 (0.21)	0.095	−0.39 (0.21)	0.069		
Former intellectual occupation									0.54 (0.16)	<0.001		
Death of a loved person in the recent time									−0.34 (0.16)	<0.05		
Serious illness in the recent time					0.46 (0.23)	<0.05					0.56 (0.2)	<0.01
Serious illness of a loved person in the recent time												
End of an important relationship in the recent time												
Traffic accident in the recent time	0.97 (0.32)	<0.01										
Criminal event in the recent time												
Satisfaction with living conditions							−1.06 (0.36)	<0.01			−1.01 (0.24)	<0.0001
Number of chronic diseases *												
Inability to walk up one flight of stairs *											0.6 (0.29)	<0.05
Inability to walk 200 m *												
Physical Domain of Tilburg Frailty Indicator (TFI)												
1. Poor physical health			1.13 (0.18)	<0.0001							0.82 (0.2)	<0.0001
2. Unexplained body mass loss *			0.53 (0.25)	<0.05								

Table 3. *Cont.*

Part II

Independent Variables	7. Lack of Strength in Hands R² = 0.45, p < 0.00001		8. Physical Tiredness * R² = 0.51, p < 0.00001		9. Problems with Memory R² = 0.23, p < 0.00001		10. Feeling Down R² = 0.57, p < 0.00001		11. Feeling Nervous or Anxious R² = 0.44, p < 0.00001		12. Inability to Cope with Problems R² = 0.27, p < 0.00001	
	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
3. Difficulty in walking	0.73 (0.18)	<0.0001	0.92 (0.18)	<0.00001								
4. Difficulty in maintaining balance	0.73 (0.19) [a]	<0.001	0.58 (0.2)	<0.01	1.19 (0.22)	<0.00001						
5. Poor hearing					0.74 (0.22)	<0.001						
6. Poor vision	0.53 (0.17)	<0.01	0.7 (0.16)	<0.0001	0.67 (0.22)	<0.01						
7. Lack of strength in hands	–	–	1.21 (0.19)	<0.00001			0.57 (0.21) [a]	<0.01	0.5 (0.19)	<0.01		
8. Physical tiredness/fatigue *	1.26 (0.19)	<0.00001	–	–			0.64 (0.17)	<0.001				
Psychological Domain of TFI												
9. Problems with memory					–	–					0.8 (0.23)	<0.001
10. Feeling down	0.61 (0.21) [ab]	<0.01	0.56 (0.17)	<0.001			–	–	1.53 (0.16) [a]	<0.00001	0.78 (0.27)	<0.01
11. Feeling nervous or anxious	0.34 (0.2) [b]	0.097					1.48 (0.16) [ab]	<0.00001	–	–	0.8 (0.25)	<0.01
12. Inability to cope with problems	0.44 (0.21)	<0.05			0.83 (0.23) [a]	<0.001	0.93 (0.26)	<0.001	0.77 (0.24)	<0.01	–	–
Social Domain of TFI												
13. Living alone					−0.47 (0.22) [a]	<0.05	0.65 (0.22) [b]	<0.01	−0.63 (0.22)	<0.01		
14. Missing other people							0.63 (0.16)	<0.0001	0.75 (0.16) [a]	<0.00001	0.47 (0.23)	<0.05
15. Lack of support from other people									0.75 (0.23)	<0.01		

141

Table 3. *Cont.*

	Part III											
Independent Variables	13. Living Alone R² = 0.64, *p* < 0.00001		14. Missing Other People R² = 0.41, *p* < 0.00001		15. Lack of Support from Other People R² = 0.12, *p* < 0.00001		Inability to Walk Up One Flight of Stairs * R² = 0.44, *p* < 0.00001		Inability to Walk 200 m * R² = 0.46, *p* < 0.00001		More than Four Illnesses * R² = 0.15, *p* < 0.00001	
	B (SE)	*p*-value	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value	B (SE)	*p*-Value
Age					−0.06 (0.2)	<0.001					0.05 (0.15)	0.001
Male sex							−0.64 (0.37)	0.09				
High school education level			−0.37 (0.2)	0.054					−0.56 (0.33)	0.08	0.57 (0.25)	<0.05
University education level			−0.47 (0.21)	<0.05					−1.95 (0.47)	<0.0001	0.74 (0.28)	<0.01
Moderate economic status					−0.67 (0.23)	<0.01						
High economic status												
Partially healthy lifestyle												
Healthy lifestyle			−0.35 (0.14)	<0.05								
Participation in a senior group	0.68 (0.21)	<0.01	0.27 (0.15)	0.07					−1.01 (0.36)	<0.01	−0.38 (0.21)	0.08
Living in a city	−3.93 (0.24)	<0.00001	−0.55 (0.18)	<0.01			−0.61 (0.33)	0.06	0.91 (0.34)	<0.01		
Living in a relationship												
Former intellectual occupation												
Death of a loved person in the recent time	0.45 (0.19)	<0.05					0.82 (0.32)	<0.05			1.16 (0.21)	<0.0001
Serious illness in the recent time												
Serious illness of a loved person in the recent time							−1.1 (0.42)	<0.01				
End of an important relationship in the recent time	0.66 (0.37)	0.07							0.94 (0.46)	<0.05 †		
Traffic accident in the recent time											0.82 (0.34)	<0.05
Criminal event in the recent time												
Satisfaction with living conditions					−0.47 (0.26)	0.07 ‡			−1.21 (0.35)	<0.001		
Number of chronic diseases *							0.25 (0.08)	<0.01				
Inability to walk up one flight of stairs *			−0.66 (0.26)	<0.05			–	–	3.66 (0.34)	<0.0001	–	–
Inability to walk 200 m *							3.7 (0.32)	<0.0001	–	–		
Physical Domain of Tilburg Frailty Indicator (TFI)												
1. Poor physical health					0.49 (0.2)	<0.05	1.26 (0.32)	<0.0001			0.77 (0.21)	<0.001
2. Unexplained body mass loss *	−0.62 (0.29)	<0.05										

Table 3. *Cont.*

Part III

Independent Variables	13. Living Alone R² = 0.64, p < 0.00001		14. Missing Other People R² = 0.41, p < 0.00001		15. Lack of Support from Other People R² = 0.12, p < 0.00001		Inability to Walk Up One Flight of Stairs * R² = 0.44, p < 0.00001		Inability to Walk 200 m * R² = 0.46, p < 0.00001		More than Four Illnesses * R² = 0.15, p < 0.00001	
	B (SE)	p-value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
3. Difficulty in walking									1.42 (0.32)	<0.0001		
4. Difficulty in maintaining balance												
5. Poor hearing	−0.44 (0.2)	<0.05			0.42 (0.18)	<0.05						
6. Poor vision												
7. Lack of strength in hands												
8. Physical tiredness/fatigue *											0.47 (0.22)	<0.05
Psychological Domain of TFI												
9. Problems with memory	−0.74 (0.28)	<0.01										
10. Feeling down	0.59 (0.22)	<0.01	0.62 (0.16) ᵃ	<0.0001								
11. Feeling nervous or anxious	−0.58 (0.22)	<0.01	0.7 (0.16) ᵃ	<0.0001	0.71 (0.22)	<0.01					−0.44 (0.21)	<0.05
12. Inability to cope with problems			0.45 (0.22) ᵇ	<0.05	0.41 (0.22)	0.06						
Social Domain of TFI												
13. Living alone	–	–	0.72 (0.16)	<0.00001	0.7 (0.18)	<0.001						
14. Missing other people	0.86 (0.22)	<0.0001	–	–	0.5 (0.22)	<0.05	−0.78 (0.32)	<0.05				
15. Lack of support from other people	0.78 (0.25)	<0.01	0.49 (0.22) ᵇ	<0.05	–	–			−0.63 (0.38)	0.098		

Notes: * Denotes components of the FRAIL scale. † Denotes variables that did not reach significance in the primary model. ‡ Denotes variables that reached significance in the validation bootstrapping analysis. Same letters (i.e., ᵃ, ᵇ) next to the coefficients correspond to the variables which significantly interact with *p*-values less than 0.05. Since the number of subjects with more than five illnesses was low, the dataset had quasi-complete separation, therefore "more than four illnesses" criterion was used in the regression analysis. Statistically significant coefficients and *p*-values are marked in bold.

3.3. Relationships between Frailty Dimensions

The associations between the TFI elements were detected not only within a given dimension (i.e., physical dimension, item 1–8; psychological dimension, item 9–12; and social dimension, item 13–15), but also between different dimensions. The scores for each dimension (i.e., the sums of corresponding deficits) significantly correlated with each other, i.e., the physical domain correlated with psychological and social ones (r = 0.43 and r = 0.15, respectively, *p* < 0.0001 for both), and the psychological domain correlated with social one (r = 0.27, *p* < 0.0001). However, in the multiple regression analysis, the physical domain was determined by the psychological domain only; the psychological domain was independently associated with both the physical and social ones; but the social domain was exclusively determined by the psychological one (Table 4). In the interaction analysis, there was no statistically significant buffering effect between the domains (Table 4). Table 5 presents determinants for each of the TFI domains pointing out which of the variables are independently associated with a given domain. The data in Tables 4 and 5 reflect the associations among frailty deficits coming from different dimensions of human functioning, and in addition some interactions between individual deficits can be found (Table 5). Moreover, in Table 3, significant interactions are seen between physical and psychological TFI components, within some psychological TFI components, and between psychological and social ones.

Table 4. The association between different frailty domains according to TFI and their interactions in the multiple regression analysis.

Independent Variables	TFI Physical Domain $R^2 = 0.19$, $p < 0.00001$		*p*-Value for Interaction
	B (SE)	*p*-Value	
TFI psychological domain	**0.82 (0.06)**	**<0.001**	0.06
TFI social domain	0.08 (0.07)	0.26	
	TFI Psychological Domain $R^2 = 0.22$, $p < 0.00001$		
TFI physical domain	**0.2 (0.01)**	**<0.001**	0.082
TFI social domain	**0.25 (0.03)**	**<0.001**	
	TFI Social Domain $R^2 = 0.07$, $p < 0.00001$		
TFI physical domain	0.02 (0.01)	0.15	0.43
TFI psychological domain	**0.2 (0.03)**	**<0.001**	

Notes: Statistically significant coefficients and *p*-values are marked in bold. The validation bootstrapping analysis confirmed the statistical significance of the models and their variables.

Table 5. Independent determinants for each TFI domain.

Independent Variables	TFI Physical Domain R² = 0.45, p < 0.00001		TFI Psychological Domain R² = 0.28, p < 0.00001		TFI Social Domain R² = 0.31, p < 0.00001	
	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
Age	0.07 (0.01)	<0.00001				
Male sex	−0.27 (0.12)	<0.05				
University/high school/primary education level						
High/moderate/low economic status					−0.14 (0.06)	<0.05
Healthy/partially healthy/unhealthy lifestyle	−0.35 (0.09)	<0.001			−0.1 (0.4)	<0.05
Participation in a senior group	−0.63 (0.11)	<0.00001				
Living in a city	−0.29 (0.12)	<0.05				
Living in a relationship					−0.74 (0.05)	<0.00001
Former intellectual occupation	−0.38 (0.15)	<0.05				
Death of a loved person in the recent time			−0.16 (0.07)	<0.05	0.13 (0.5)	<0.05
Serious illness in the recent time	0.29 (0.13)	<0.05	0.3 (0.08)	<0.001	−0.1 (0.06)	<0.05
Serious illness of a loved person in the recent time					0.28 (0.1)	<0.01
End of an important relationship in the recent time						
Traffic accident in the recent time	0.46 (0.22)	<0.05				
Criminal event in the recent time						
Satisfaction with living conditions	−0.69 (0.18)	<0.0001	−0.48 (0.1)	<0.00001		
Number of chronic diseases *	0.14 (0.03)	<0.0001				
Inability to walk up one flight of stairs *	0.73 (0.23)	<0.01				
Inability to walk 200 m *	0.77 (0.22)	<0.001				
Physical Domain of Tilburg Frailty Indicator (TFI)						
1. Poor physical health	–	–	0.23 (0.08)	<0.01		
2. Unexplained body mass loss *	–	–	0.2 (0.09)	<0.05		
3. Difficulty in walking	–	–				
4. Difficulty in maintaining balance	–	–	0.18 (0.08)	<0.05		

Table 5. *Cont.*

Independent Variables	TFI Physical Domain $R^2 = 0.45, p < 0.00001$		TFI Psychological Domain $R^2 = 0.28, p < 0.00001$		TFI Social Domain $R^2 = 0.31, p < 0.00001$	
	B (SE)	**p-Value**	**B (SE)**	**p-Value**	**B (SE)**	**p-Value**
5. Poor hearing	–	–				
6. Poor vision	–	–	0.25 (0.07)	<0.001		
7. Lack of strength in hands	–	–	0.29 (0.08)	<0.001		
8. Physical tiredness/fatigue *	–	–	0.15 (0.07)	<0.05		
Psychological Domain of TFI						
9. Problems with memory	0.88 (0.16) ab	<0.00001	–	–		
10. Feeling down	0.52 (0.12) ac	<0.0001	–	–	0.25 (0.06)	<0.0001
11. Feeling nervous or anxious			–	–	0.18 (0.05)	<0.01
12. Inability to cope with problems	0.53 (0.14)	<0.001	–	–	0.17 (0.07)	<0.05
Social Domain of TFI						
13. Living alone					–	–
14. Missing other people			0.44 (0.06)	<0.00001	–	–
15. Lack of support from other people	0.4 (0.14) bc	<0.01	0.29 (0.08)	<0.001	–	–

Notes: * Denotes components of the FRAIL scale. Same letters (i.e., ᵃ, ᵇ, ᶜ) next to the coefficients correspond to the variables which significantly interact with *p*-values less than 0.05. Of note, the interaction was inverse between 'problems with memory' and 'lack of support from other people'; other interactions were direct. Statistically significant coefficients and *p*-values are marked in bold. The validation bootstrapping analysis confirmed the statistical significance of the models and their variables.

4. Discussion

Multidimensional frailty has been recognized in 54.6% of the study population, whereas, physical frailty and pre-frailty have been diagnosed in 6.3% and 46.7%, respectively. This corresponds to the data coming from other populations and shows that the prevalence of these conditions is similar in different regions and cultures [14–16].

Numerous elements have been identified as independent risk factors for both multidimensional and physical frailty as well as non-robust status (i.e., either physical frailty or pre-frailty) [6,10,17,18]; however, for prevention or therapeutic intervention, such analyses may be incomplete since the individual frailty components could not be considered in these models and the associations between different frailty dimensions could not be discerned. In fact, frailty is an accumulation of deficits and as such is determined by factors other than factors determining its particular components. Therefore, for the purpose of intervention, determinants of the individual deficits should be considered along with determinants of their accumulation; moreover, the relationships between various dimensions of human functioning (i.e., physical, psychological and social) must be taken into account.

In line with TFI, the association among frailty deficits is especially valid between physical and psychological domains, i.e., most of the physical deficits were independently associated with psychological ones, and the correlation between these domains was quite high (i.e., r = 0.43). In a sample of more than 35,000 community-dwelling Dutch people older than 65 years, the correlation was very similar, i.e., equal to 0.45 [17]. Moreover, in the multivariate analysis, the physical domain of TFI was determined by only the psychological one, and there was no buffering effect of the social domain. Conversely, the psychological domain was impacted by the physical one, and in addition by the social one. There were also some interactions between physical and psychological TFI components in determining various frailty deficits. These observations indicate that physical frailty is associated with psychological frailty with a possible bidirectional causal relationship [1,19,20]. Indeed, there is a number of data showing that a poor cognitive performance predicts physical decline, but also, physical frailty may determine cognitive frailty which in turn may lead to dementia [21–24]. However, a precise mechanism how physical frailty or pre-frailty can cause a cognitive decline is not fully clarified [25–27].

Regarding the social domain in TFI, it had no independent effect on the TFI physical domain in the multivariate analysis. However, missing other people (i.e., a social component of TFI) significantly but inversely determined an inability to walk up one flight of stairs (i.e., a physical component of the FRAIL scale); moreover, it was also inversely associated with the prevalence of physical frailty. Hence, a lack of other people may probably impose some activities that in turn may result in higher physical tolerance. On the other hand, the association between social and psychological dimensions in TFI was significant and mutual in the regression models, and all psychological TFI deficits were determined by some social ones. Of note, living alone was inversely associated with problems with memory, and feeling nervous or anxious. This presumably stems from the fact that lonely people have to utilize their memory for daily needs, and they are not exposed to psychological tensions with home dwellers. There were also certain interactions between social and psychological TFI components in regard to some other frailty deficits.

The aforementioned inverse relationships between frailty components suggest that some deficits may prevent other ones. Indeed, circumstances and external stimuluses may provoke kinds of activity among the elderly subjects provided that the intensity of such factors does not cross the limits of their capabilities [11,28]. The necessity to address daily needs and different types of issues may access some energy layers in the elderly individuals and enable them to preserve good functioning and independence. Such mechanisms constitute fundamentals for the concept of aging in place, the ideology promoted worldwide by the World Health Organization (WHO) [29]. However, basic conditions for aging in place are some levels of competence and control over one's environment [30–32]. Therefore, to ensure the wellbeing of elderly people in their place, a holistic approach is needed where the identification of factors predisposing them to and preventing them from different forms of frailty is paramount. In this context, a simultaneous employment of both unidimensional (i.e., physical) and

multidimensional frailty diagnostic tools may more precisely characterize the deficits' structure than any of these tools employed exclusively [7]. By uncovering the individual's lacks and needs, one may more effectively assist in supporting his/her functional independence in aging in place.

From the practical point of view, the most crucial frailty risk factors are those which pose a chance of being modified by the appropriate management. Many of the common risk factors are not modifiable (e.g., age, sex, education level); yet, the majority of multidimensional and physical frailty components may be the subject of intervention; moreover, most of their determinants are in fact other frailty deficits suitable for modification. Among the physical TFI and FRAIL scale deficits, the majority reflect muscle weakness and sarcopenia which can be prevented and treated with the suitable training programs associated with proper nutritional interventions [33,34]. Problems with vision and hearing should be managed with appropriate glasses and hearing devices [35–37]; this is critical because, in our data, these sensory deficits are associated with the development of deficits in other frailty dimensions; in particular, they determine the memory problems. In fact, the physical impairments are mutually associated with the psychological ones, and the most influential ingredient of this relationship is 'feeling down'. Indeed, depression is a common element in aging processes, and thus, it must be early recognized and properly treated in order to improve people's mood and their motivation for an active life [38–40]. In this context, our study suggests that social deficits may intensify psychological problems, due to their mutual association. Loneliness and lack of support from other people are the principal reasons for low quality of life in elderly people, and they contribute to functional deterioration and mortality [18,41–44]. Therefore, proper social programs involving families and local communities should be arranged in order to alleviate loneliness associated with aging.

The awareness of the interplay among deficits is paramount in designing individualized management in the elderly people. Ideally, a profile of functional abnormalities in a given subject should be first recognized, and then, after considering the deficits' relationships, an individualized interventional strategy could be appropriately designed. The findings of the present study are in line with the recent study where simultaneous employment of TFI and the FRAIL scale enabled us to identify subgroups of elderly people presenting different functional profiles, i.e., those presenting predominantly social and psychological frailty and those with mainly physical deficits [7]. Such different subgroups probably require different management and, therefore, the approach to frail subjects should be individualized according to the functional state. However, the feasibility, practicability and clinical efficiency of such a strategy must be first prospectively tested in subjects with different degrees of functional deterioration, before it will be recommended for a wide application.

The present study has some limitations that need to be acknowledged. The observational and cross-sectional nature of this research does not allow cause–effect interpretations of the associations between frailty deficits and various risk factors. Despite the internal validation with the bootstrapping technique, the study results should be externally validated in other seniors' groups. The use of self-reported questionnaires distributed among the elderly people attending healthy lifestyle promotion meetings may impose some selection bias. The variance of some deficits could only be explained in a small portion (e.g., a lack of support from other people), which means that factors other than those considered in this study determine these deficits and, therefore, it requires further investigation. Both TFI and the FRAIL scale have been validated in different populations and clinical circumstances, however, their value in picturing different functional profiles of elderly people and designing the individualized interventional strategies have never been tested. The strength of this study is the observation that the individual frailty deficits determine each other, and the impairments in the physical domain are mainly affected by psychological deficits which in turn are additionally impacted by social deficits. This may shed more light for mechanisms accelerating frailty development and help to design a more comprehensive approach to frailty [6,7,11,17,18].

5. Conclusions

Multidimensional frailty and non-robust physical status (i.e., either physical frailty or prefrailty) are common in community-dwelling elderly people, and numerous demographic and clinical variables are associated with these conditions. However, frailty as an accumulation of deficits is determined by factors other than factors determining its individual deficits, and the interplay between these deficits presumably amplify their effects and may accelerate frailty development. In particular, a bidirectional association exists between physical and psychological frailty dimensions; the latter is additionally impacted by deficits in the social domain. Therefore, for preventative and therapeutic purposes, determinants of each individual deficit should be considered along with determinants of their accumulation; and the associations between various dimensions of human functioning should also be taken into account. By unravelling a functional profile in a given elderly subject, an individualized management may be designed, however, the feasibility and clinical efficacy of such an approach need to be tested in suitable prospective studies.

Author Contributions: Conceptualization, M.S.; methodology, M.S., J.S. and K.W.-T.; investigation, M.S.; resources, M.S. and J.S.; data curation, M.S.; writing—original draft preparation, M.S. and J.S.; supervision, K.W.-T.; funding acquisition, M.S. and J.S. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Gill, T.M.; Williams, C.S.; Richardson, E.D.; Tinetti, M.E. Impairments in Physical Performance and Cognitive Status as Predisposing Factors for Functional Dependence Among Nondisabled Older Persons. *J. Gerontol. Ser. A Boil. Sci. Med. Sci.* **1996**, *51*, M283–M288. [CrossRef]
2. Fried, L.P.; Tangen, C.M.; Walston, J.D.; Newman, A.B.; Hirsch, C.; Gottdiener, J.S.; E Seeman, T.; Tracy, R.P.; Kop, W.J.; Burke, G.L.; et al. Frailty in Older Adults: Evidence for a Phenotype. *J. Gerontol. Ser. A Boil. Sci. Med. Sci.* **2001**, *56*, M146–M157. [CrossRef] [PubMed]
3. Walston, J.; Hadley, E.C.; Ferrucci, L.; Guralnik, J.M.; Newman, A.B.; Studenski, S.; Ershler, W.B.; Harris, T.; Fried, L.P. Research Agenda for Frailty in Older Adults: Toward a Better Understanding of Physiology and Etiology: Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. *J. Am. Geriatr. Soc.* **2006**, *54*, 991–1001. [CrossRef] [PubMed]
4. Van Kan, G.A.; Rolland, Y.; Houles, M.; Gillette-Guyonnet, S.; Soto, M.; Vellas, B. The Assessment of Frailty in Older Adults. *Clin. Geriatr. Med.* **2010**, *26*, 275–286. [CrossRef] [PubMed]
5. Gobbens, R.J.J.; Van Assen, M.A.L.M.; Luijkx, K.G.; Wijnen-Sponselee, M.T.; Schols, J.M.G.A. The Tilburg Frailty Indicator: Psychometric Properties. *J. Am. Med. Dir. Assoc.* **2010**, *11*, 344–355. [CrossRef] [PubMed]
6. Sacha, J.; Sacha, M.; Soboń, J.; Borysiuk, Z.; Feusette, P. Is It Time to Begin a Public Campaign Concerning Frailty and Pre-frailty? A Review Article. *Front. Physiol.* **2017**, *8*, 484. [CrossRef]
7. Sacha, M.; Sacha, J.; Wieczorowska-Tobis, K. Simultaneous Employment of the FRAIL Scale and the Tilburg Frailty Indicator May Identify Elderly People Who Require Different Interventional Strategies. *Clin. Interv. Aging* **2020**, *15*, 683–690. [CrossRef]
8. Van Kan, G.A.; Rolland, Y.M.; Morley, J.E.; Vellas, B. Frailty: Toward a Clinical Definition. *J. Am. Med. Dir. Assoc.* **2008**, *9*, 71–72. [CrossRef]
9. Morley, J.E.; Malmstrom, T.K.; Miller, D.K. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J. Nutr. Health Aging* **2012**, *16*, 601–608. [CrossRef]
10. Gobbens, R.J.J.; Luijkx, K.G.; Wijnen-Sponselee, M.T.; Schols, J.M.G.A. Towards an integral conceptual model of frailty. *J. Nutr. Health Aging* **2010**, *14*, 175–181. [CrossRef]
11. Sacha, M.; Sacha, J.; Wieczorowska-Tobis, K. Multidimensional and Physical Frailty in Elderly People: Participation in Senior Organizations Does Not Prevent Social Frailty and Most Prevalent Psychological Deficits. *Front. Public Health* **2020**, *8*, 276. [CrossRef] [PubMed]

12. Uchmanowicz, I.; Jankowska-Polanska, B.; Loboz-Rudnicka, M.; Manulik, S.; Loboz-Grudzien, K.; Gobbens, R.J. Cross-cultural adaptation and reliability testing of the Tilburg Frailty Indicator for optimizing care of Polish patients with frailty syndrome. *Clin. Interv. Aging* **2014**, *9*, 997–1001. [CrossRef] [PubMed]

13. Uchmanowicz, I.; Jankowska-Polańska, B.; Uchmanowicz, B.; Kowalczuk, K.; Gobbens, R.J.J. Validity and Reliability of the Polish Version of the Tilburg Frailty Indicator (TFI). *J. Frailty Aging* **2016**, *5*, 27–32. [PubMed]

14. Theou, O.; Brothers, T.D.; Mitnitski, A.; Rockwood, K. Operationalization of Frailty Using Eight Commonly Used Scales and Comparison of Their Ability to Predict All-Cause Mortality. *J. Am. Geriatr. Soc.* **2013**, *61*, 1537–1551. [CrossRef] [PubMed]

15. Mulasso, A.; Roppolo, M.; Gobbens, R.J.; O Mosso, C.; Rabaglietti, E. A comparison between uni- and multidimensional frailty measures: Prevalence, functional status, and relationships with disability. *Clin. Interv. Aging* **2015**, *10*, 1669–1678. [CrossRef]

16. González, E.D.D.L.; Hermosillo, H.G.; Beltran, J.A.M.; Chavez, J.H.M.; Corona, R.P.; Garza, D.P.S.; Quintanilla, K.A.R. Validation of the FRAIL scale in Mexican elderly: Results from the Mexican Health and Aging Study. *Aging Clin. Exp. Res.* **2015**, *28*, 901–908. [CrossRef]

17. Gobbens, R.J.J.; Schols, J.M.; Van Assen, M.A. Exploring the efficiency of the Tilburg Frailty Indicator: A review. *Clin. Interv. Aging* **2017**, *12*, 1739–1752. [CrossRef]

18. Gobbens, R.J.; Van Assen, M.A. Associations between multidimensional frailty and quality of life among Dutch older people. *Arch. Gerontol. Geriatr.* **2017**, *73*, 69–76. [CrossRef]

19. Buchner, D.M.; Wagner, E.H. Preventing Frail Health. *Clin. Geriatr. Med.* **1992**, *8*, 1–18. [CrossRef]

20. Strawbridge, W.J.; Shema, S.J.; Balfour, J.L.; Higby, H.R.; Kaplan, G.A. Antecedents of Frailty Over Three Decades in an Older Cohort. *J. Gerontol. Ser. B* **1998**, *53*, S9–S16. [CrossRef]

21. Solfrizzi, V.; Scafato, E.; Lozupone, M.; Seripa, D.; Giannini, M.; Sardone, R.; Bonfiglio, C.; Abbrescia, D.I.; Galluzzo, L.; Gandin, C.; et al. Additive Role of a Potentially Reversible Cognitive Frailty Model and Inflammatory State on the Risk of Disability: The Italian Longitudinal Study on Aging. *Am. J. Geriatr. Psychiatry* **2017**, *25*, 1236–1248. [CrossRef] [PubMed]

22. Montero-Odasso, M.M.; Barnes, B.; Speechley, M.; Hunter, S.W.M.; Doherty, T.J.; Duque, G.; Gopaul, K.; Sposato, L.A.; Casas-Herrero, A.; Borrie, M.J.; et al. Disentangling Cognitive-Frailty: Results From the Gait and Brain Study. *J. Gerontol. Ser. A Boil. Sci. Med. Sci.* **2016**, *71*, 1476–1482. [CrossRef] [PubMed]

23. Feng, L.; Nyunt, M.S.; Gao, Q.; Feng, L.; Lee, T.-S.; Tsoi, T.; Chong, M.S.; Lim, W.S.; Collinson, S.; Yap, P.; et al. Physical Frailty, Cognitive Impairment, and the Risk of Neurocognitive Disorder in the Singapore Longitudinal Ageing Studies. *J. Gerontol. Ser. A Boil. Sci. Med. Sci.* **2017**, *72*, 369–375. [CrossRef] [PubMed]

24. Solfrizzi, V.; Scafato, E.; Seripa, D.; Lozupone, M.; Imbimbo, B.P.; D'Amato, A.; Tortelli, R.; Schilardi, A.; Galluzzo, L.; Gandin, C.; et al. Reversible Cognitive Frailty, Dementia, and All-Cause Mortality. The Italian Longitudinal Study on Aging. *J. Am. Med. Dir. Assoc.* **2017**, *18*, 89.e1–89.e8. [CrossRef] [PubMed]

25. Kelaiditi, E.; Cesari, M.; Canevelli, M.; Van Kan, G.A.; Ousset, P.-J.; Gillette-Guyonnet, S.; Ritz, P.; Duveau, F.; Soto, M.E.; Provencher, V.; et al. Cognitive frailty: Rational and definition from an (I.A.N.A./I.A.G.G.) International Consensus Group. *J. Nutr. Health Aging* **2013**, *17*, 726–734. [CrossRef]

26. Panza, F.; Seripa, D.; Solfrizzi, V.; Tortelli, R.; Greco, A.; Pilotto, A.; Logroscino, G. Targeting Cognitive Frailty: Clinical and Neurobiological Roadmap for a Single Complex Phenotype. *J. Alzheimer's Dis.* **2015**, *47*, 793–813. [CrossRef]

27. Ruan, Q.; Yu, Z.; Chen, M.; Bao, Z.; Li, J.; He, W. Cognitive frailty, a novel target for the prevention of elderly dependency. *Ageing Res. Rev.* **2015**, *20*, 1–10. [CrossRef]

28. Alimujiang, A.; Wiensch, A.; Boss, J.; Fleischer, N.L.; Mondul, A.M.; McLean, K.; Mukherjee, B.; Pearce, C.L. Association Between Life Purpose and Mortality Among US Adults Older Than 50 Years. *JAMA Netw. Open* **2019**, *2*, e194270. [CrossRef]

29. World health organisation (WHO). *World Report on Ageing and Health*; WHO: Geneva, Switzerland, 2015.

30. Cutchin, M. The process of mediated aging-in-place: A theoretically and empirically based model. *Soc. Sci. Med.* **2003**, *57*, 1077–1090. [CrossRef]

31. Marek, K.D.; Stetzer, F.; Adams, S.J.; Popejoy, L.L.; Rantz, M. Aging in Place Versus Nursing Home Care: Comparison of Costs to Medicare and Medicaid. *Res. Gerontol. Nurs.* **2012**, *5*, 123–129. [CrossRef]

32. Bacsu, J.; Jeffery, B.; Abonyi, S.; Johnson, S.; Novik, N.; Martz, D.; Oosman, S. Healthy Aging in Place: Perceptions of Rural Older Adults. *Educ. Gerontol.* **2014**, *40*, 327–337. [CrossRef]

33. E Bauman, A.; Merom, D.; Bull, F.C.; Buchner, D.M.; Singh, M.A.F. Updating the Evidence for Physical Activity: Summative Reviews of the Epidemiological Evidence, Prevalence, and Interventions to Promote "Active Aging". *Gerontologist* **2016**, *56* (Suppl. 2), S268–S280. [CrossRef] [PubMed]

34. Dent, E.; Lien, C.; Lim, W.S.; Wong, W.C.; Wong, C.H.; Shiong, L.W.; Woo, J.; Dong, B.; De La Vega, S.; Poi, P.J.H.; et al. The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty. *J. Am. Med. Dir. Assoc.* **2017**, *18*, 564–575. [CrossRef] [PubMed]

35. Kamil, R.J.; Betz, J.; Powers, B.B.; Pratt, S.; Kritchevsky, S.; Ayonayon, H.N.; Harris, T.B.; Helzner, E.; Deal, J.A.; Martin, K.; et al. Association of Hearing Impairment With Incident Frailty and Falls in Older Adults. *J. Aging Health* **2016**, *28*, 644–660. [CrossRef]

36. Liljas, A.E.M.; A Carvalho, L.; Papachristou, E.; De Oliveira, C.; Wannamethee, S.G.; E Ramsay, S.; Walters, K. Self-Reported Hearing Impairment and Incident Frailty in English Community-Dwelling Older Adults: A 4-Year Follow-Up Study. *J. Am. Geriatr. Soc.* **2017**, *65*, 958–965. [CrossRef]

37. Liljas, A.E.M.; A Carvalho, L.; Papachristou, E.; De Oliveira, C.; Wannamethee, S.G.; E Ramsay, S.; Walters, K.R. Self-reported vision impairment and incident prefrailty and frailty in English community-dwelling older adults: Findings from a 4-year follow-up study. *J. Epidemiol. Community Health* **2017**, *71*, 1053–1058. [CrossRef]

38. Alexopoulos, G.S. Depression in the elderly. *Lancet* **2005**, *365*, 1961–1970. [CrossRef]

39. Chu, W.; Chang, S.-F.; Ho, H.; Lin, H. The Relationship between Depression and Frailty in Community-Dwelling Older People: A Systematic Review and Meta-Analysis of 84,351 Older Adults. *J. Nurs. Sch.* **2019**, *51*, 547–559. [CrossRef]

40. Krause, M.; Gutsmiedl, K.; Bighelli, I.; Schneider-Thoma, J.; Chaimani, A.; Leucht, S. Efficacy and tolerability of pharmacological and non-pharmacological interventions in older patients with major depressive disorder: A systematic review, pairwise and network meta-analysis. *Eur. Neuropsychopharmacol.* **2019**, *29*, 1003–1022. [CrossRef]

41. Gabriel, Z.; Bowling, A. Quality of life from the perspectives of older people. *Ageing Soc.* **2004**, *24*, 675–691. [CrossRef]

42. Puts, M.T.E.; Shekary, N.; Widdershoven, G.; Heldens, J.; Lips, P.; Deeg, D.J.H. What does quality of life mean to older frail and non-frail community-dwelling adults in the Netherlands? *Qual. Life Res.* **2006**, *16*, 263–277. [CrossRef] [PubMed]

43. Luo, Y.; Hawkley, L.C.; Waite, L.J.; Cacioppo, J.T. Loneliness, health, and mortality in old age: A national longitudinal study. *Soc. Sci. Med.* **2012**, *74*, 907–914. [CrossRef] [PubMed]

44. Perissinotto, C.M.; Cenzer, I.S.; Covinsky, K.E. Loneliness in Older Persons. *Arch. Intern. Med.* **2012**, *172*, 1078–1083. [CrossRef] [PubMed]

Article

Correlation between Sleep Quality and Frailty Status among Middle-Aged and Older Taiwanese People: A Community-Based, Cross-Sectional Study

An-Chen Shih [1], Lee-Hwa Chen [2], Chin-Chueh Tsai [2] and Jau-Yuan Chen [1,3,*]

[1]   Department of Family Medicine, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan 333, Taiwan;
      cooker791022@gmail.com
[2]   Department of Athletic Training and Health, National Taiwan Sport University, Taoyuan 333, Taiwan;
      lhchen@ntsu.edu.tw (L.-H.C.); cctsai@ntsu.edu.tw (C.-C.T.)
[3]   Department of Medicine, College of Medicine, Chang Gung University, Taoyuan 333, Taiwan
*   Correspondence: welins@cgmh.org.tw; Tel.: +886-975362672

Abstract: Poor sleep quality and frailty are common problems among aged people. However, the association between sleep quality and frailty in middle-aged and older people is seldom discussed in Asia, especially in Taiwan. This study investigated this association hopefully to provide pertinent knowledge for the prevention of frailty. We conducted a cross-sectional study and enrolled 828 subjects, 237 male and 591 female, aged 50–85 years old, from a community in Northern Taiwan. Poor sleep quality was defined as the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) > 5. Prefrailty and frailty were defined as fulfillment of one or two and three, respectively, of five phenotypic criteria: exhaustion, weakness, slowness, weight loss, and low physical activity. Our univariate analysis showed that the incidence of prefrailty/frailty in the group of poor sleep quality was higher than that in the group of CPSQI ≤ 5 ($p < 0.001$). Further multiple logistic regression analysis revealed that poor sleep quality was an independent factor for prefrailty and frailty status (odds ratio = 1.95, 95% confidence interval = 1.38–2.77), after adjustment for confounding factors. We concluded that poor sleep quality is independently associated with prefrailty and frailty status in our study population.

Keywords: frailty; community-based; sleep quality; middle-aged and older adults

1. Introduction

Population aging, which describes a rise in life expectancy and a fall in birth rates, constitutes a major problem worldwide, particularly in Taiwan. According to data from the National Development Council, Taiwan became an aging society in 1993; then, it became an aged society in 2018, and it is projected to become a superaged society in 2025 [1]. Taiwan's population is aging at an alarming rate, with only eight years to advance from the "aged society" stage to the "super-aged society" stage, which is much faster than the 11 years for Japan, 14 years for the U.S., 29 years for France, and 51 years for the UK [2]. People aged 65 years and older in Taiwan were estimated to represent 16% of the overall population in 2020. The costs resulting from the high proportion of elderly people in Taiwan's population are considered a heavy burden on the national health insurance system [3]. Thus, population aging is a major social challenge.

Poor sleep, a common health problem, has a high incidence among elderly people [4,5]. Even in healthy people, destruction of the sleep cycle may lead to a greater response to stress, an increase in painful musculoskeletal sensitivity, and a decrease the quality of life. It may cause multi-comorbidities including cardiovascular and metabolic diseases in the long term [6]. Poor sleep quality is associated

with the risk of hypertension and adverse cardio-metabolic effects [7]. Furthermore, sleep disorders such as obstructive sleep apnea were reported to be a major risk factor for psychiatric, cardiovascular, metabolic, or hormonal co-morbidity and mortality [7]. Sleep problems are associated with a range of adverse health outcomes [8], such as depression, anxiety, chronic pain, cardiovascular diseases (CVDs), metabolic diseases, cognitive impairment, physical disability, and even mortality [7,9]. These problems result in an economic burden exceeding $40 million annually in Taiwan [10].

Frailty is defined as an aging-related syndrome of physiological decline, which is characterized by marked vulnerability to adverse health outcomes including loss of function, loss of physiologic reserve, and increased vulnerability to disease and death [11]. Frailty is prevalent in elderly people and increases the risk of falls, disability, hospitalization, and mortality. Studies in Taiwan showed the prevalence of frailty and prefrailty were 6.8% and 40.5%, respectively [12]. Research reported that the prevalence estimates are 31.3–45.8% for prefrailty and 10.4–37.0% for frailty among community-dwelling elderly people [13]. In comparison, the prevalence of frailty in Taiwan was relatively lower, but the prevalence of prefrailty was above the average. The incidence of frailty and prefrailty was estimated to be 43.4 and 150.6 new cases per 1000 person-years worldwide, respectively [14]. The incidence of frailty was significantly higher in prefrail individuals than robust individuals [14]. Frailty among elderly people is identified through the presence of sarcopenia, reduced activity, poor appetite, osteoporosis, easy fatigability, frequent falls, and poor general health. Many medical conditions can cause fatigue, including cardiopulmonary, endocrinological or metabolic, hematologic or neoplastic, and psychological diseases as well as other reversible problems. Sleep disturbance is a problem that causes fatigue [15].

Although the association between frailty and poor sleep quality has been reported [16,17], two important issues may be raised. Firstly, the population of previous studies enrolled people mainly over 65 years old with some over 60 years old. The middle-aged population was seldom discussed about the relationship between sleep quality and frailty/prefrailty status. Recent large-scale studies have advocated that efforts to identify, manage, and prevent frailty should include middle-aged individuals, particularly those with multimorbidity [18]. Secondly, as mentioned above, there is a relatively higher prevalence rate of prefrailty in Taiwan, and the incidence of frailty was significantly higher in prefrail people. Thus, prevention from becoming frail or attaining prefrailty status is an important issue in Taiwan. This issue also deserves attention, given the fact that sleep problems are commonly found in middle-aged and older Taiwanese. Thus, the main aim of this study was to investigate the association between sleep quality and the risk of frailty among community-dwelling middle-aged and older adults Taiwanese people. Our findings hopefully may provide valuable information for the prevention of frailty by improving sleep problems in this population.

2. Materials and Methods

2.1. Study Design and Participants

This research was a community-based and cross-sectional study, which was programmed between April and October 2017. Initially, 1308 people were recruited. The inclusion criteria were (1) age from 50 to 85 years and (2) residence in the same district for more than half a year. The exclusion criteria were (1) failure to complete body composition analysis; (2) inability to communicate adequately to complete an interview; (3) functional dependency such as inability to walk 6 m; (4) recent diagnosis of CVDs in 2 weeks; and (5) current residence in long-term care facilities. Thus, a total of 828 participants, 237 male and 591 female, were enrolled for analysis, as shown in Figure 1. The data were validated by the Institutional Review Board, and consent was obtained from all participants before enrollment.

```
┌─────────────────────────────────────────────────────────┐
│   Community screening in Guishan district, Taoyuan city   │
└─────────────────────────────────────────────────────────┘
                            │
                            ▼
┌─────────────────────────────────────────────────────────┐
│ Sampling design (27 cluster-randomized of 32 villages)   │
│   •    Aged from 50–85 years old                          │
│   •    Residents lived in the community for half one year │
│ and above                                                 │
└─────────────────────────────────────────────────────────┘
```

Excluded:
- Unable to contact
- Empty house
- Functional dependent
- Current residents in long-term care facilities

Available and ambulatory subjects ($n = 1308$)

Excluded: ($n = 458$)
- Decline to participate ($n = 440$)
- Recent CVD ($n = 8$)
- Unable to communicate to complete an interview($n = 10$)

Interviewed ambulatory subjects ($n = 850$)

Excluded: ($n = 22$)
- Unable to complete all physical performance examinations ($n = 8$)
- Incomplete body composition ($n = 14$)

Subjects for final analysis ($n = 828$, including 237 male and 591 female)

Figure 1. Study participant selection.

2.2. Data Collection

Data collection encompassed systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), waist circumference, body composition, gait speed, hand grip strength, exercise habit, marital status, education, past history, and frailty status. Blood pressure was checked after rest in a chair. BMI was calculated as the weight (in kg) divided by the height squared (in m^2). Waist circumference was measured midway between the lowest ribs and the iliac crest, as recommended by the World Health Organization and International Diabetes Federation [19]. Body composition was checked with a TANITA body composition analyzer BC-418 to establish appendicular skeletal muscle mass (ASM) and appendicular skeletal mass index (ASMI). ASM was defined as the sum of the muscle

mass of the four limbs, and ASMI was calculated as ASM/height^2 (m^2), as per the European Working Group for Sarcopenia guidelines [20]. We measured time to walk 6 m three times and calculated the average gait speed. Grip strength in both hands was measured twice with the Takei T.K.K.5401 GRIP-D handgrip dynamometer (Takei Scientific Instruments Co., Ltd., Tokyo, Japan), and we collected the best measurement. Personal information was assessed with a questionnaire administered face-to-face by a trained research assistant. Questionnaires established exercise habit, marital status, education level, and underlying diseases. Marital status featured two groups for respondents who were currently single (divorced, separated, widowed, or never married) and respondents who were currently in a couple. The participants were divided into four groups according to education level: Group 1 (uneducated), Group 2 (graduated from primary school), Group 3 (graduated from secondary school), and Group 4 (graduated from college). The underlying diseases considered were diabetes mellitus (DM), hypertension (HTN), hyperlipidemia, and CVD.

2.3. Assessment of Sleep Quality

Sleep quality was measured with the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI). The questions of CPSQI related to habitual sleep habits during the preceding month only. The CPSQI is a reliable and valid assessment tool for use in community-based studies on poor sleep quality [21]. The cutoff point of the CPSQI was 5, which yielded high sensitivity for primary insomniacs versus controls [21]. Thus, in our study, a CPSQI score > 5 indicated poor sleep quality.

2.4. Definition of Frailty

To fulfill the diagnostic criteria for frailty, three of the following five components had to be satisfied: low grip strength, low energy, slow walking speed, low physical activity level, or unintentional weight loss [22]. Moreover, the definition of prefrailty satisfied one or two of five phenotypic criteria. We used two questions from the Center for Epidemiologic Studies Scale to measure low energy [23]. For the statements, "I felt that everything I did was an effort" or "I could not get going", self-reported questionnaire answers were "occasionally" or answers indicating higher frequency. Low grip strength indicated measured grip strength of <26 kg in men or <18 kg in women. The definition of slowed walking speed was an average walking speed over six meters of <0.8 m/s. Low physical activity indicated weekly energy expenditure of less than 383 kcal for men and 270 kcal for women based on the Community Health Activities Model Program for Seniors Physical Activity Questionnaire [24]. Unintentional weight loss indicated body weight loss of >3 kg or >5% of the preceding year's body weight.

2.5. Statistical Analysis

The quantitative variables used were the mean standard deviation (SD) for continuous variables and number (%) for categorical variables. Continuous variables with non-normal distributions were shown as median (interquartile range) and were calculated p values by Mann–Whitney U test. The independent two-sample t test and the chi-square test were used to calculate p values for continuous variables and categorical variables, respectively. Multiple logistic regression models were applied to explore the relationship between sleep quality and frailty. All statistical analyses were conducted with IBM Statistical Product and Service Solutions Statistics for Windows (version 19.0; IBM Corp., Armonk, NY, USA). Statistical significance was considered to be a p value of <0.05, which was corrected by false discovery rate (FDR).

3. Results

The results from 828 participants aged 50–85 years (28.62% male) were enrolled in this study. According to general characteristics, the study population was divided into two groups, one with CPSQI scores > 5 and one with scores ≤ 5, as shown in Table 1. Of the 828 participants, 440 (53.14%) with CPSQI scores > 5 had poor sleep quality. The proportions of participants with prefrailty or frailty

status in the group with CPSQI scores ≤ 5 and the group with CPSQI scores > 5 were 21.13% and 35.00% ($p < 0.001$), respectively, suggesting that prefrailty or frailty status was more prevalent in the group with CPSQI scores > 5 than in the group with CPSQI scores ≤ 5. Moreover, SBP, ASMI, gait speed, and hand grip strength were significantly lower in the group with CPSQI scores > 5. Female, people with a low education level, and participants with HTN or hyperlipidemia had the higher proportion in the group with CPSQI scores >5. However, no significant difference was noted between two groups in age, BMI, waist circumference, exercise habit, marital status, or underlying DM or CVDs.

Table 1. General characteristics of the study population according to Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) score.

| Variables | CPSQI | | | |
	Total (*n* = 828)	CPSQI ≤ 5 (*n* = 388)	CPSQI > 5 (*n* = 440)	*p* Value
Age (year) ¶	64.00 (59.00, 70.00)	64.00 (59.00, 69.00)	65.00 (60.00, 71.00)	0.21
SBP (mmHg) ¶	127.00 (116.00, 138.00)	128.00 (118.00, 139.00)	125.50 (115.00, 136.75)	0.047 *
BMI (kg/m²) ¶	24.20 (22.00, 26.60)	24.35 (22.10, 26.70)	24.20 (21.93, 26.60)	0.75
WC (cm)	85.08 ± 10.07	85.56 ± 9.82	84.67 ± 10.28	0.20
ASMI (kg/m²) ¶	7.07 (6.55, 8.05)	7.21 (6.58, 8.25)	6.97 (6.52, 7.89)	0.02 *
Gait speed (m/s) ¶	1.43 (1.30, 1.58)	1.46 (1.29, 1.61)	1.41 (1.26, 1.56)	0.02 *
Hand grip strength (kg) ¶	25.60 (21.70, 31.68)	26.50 (21.80, 33.85)	24.80 (21.43, 29.70)	0.002 §
Men, *n* (%)	237 (28.62%)	126 (32.47%)	111 (25.23%)	0.02 *
Exercise habit, *n* (%)	602 (72.71%)	282 (72.68%)	320 (72.73%)	0.99
Marital status (single), *n* (%)	171 (20.65%)	70 (18.04%)	101 (22.95%)	0.08
Education level				0.03 *
No, *n* (%)	65 (7.85%)	27 (6.96%)	38 (8.64%)	
Primary, *n* (%)	314 (37.92%)	132 (34.02%)	182 (41.36%)	
Secondary, *n* (%)	366 (44.20%)	181 (46.65%)	185 (42.05%)	
College, *n* (%)	83 (10.02%)	48 (12.37%)	35 (7.95%)	
DM, *n* (%)	119 (14.37%)	51 (13.14%)	68 (15.45%)	0.34
HTN, *n* (%)	265 (32.00%)	107 (27.58%)	158 (35.91%)	0.01 *
Hyperlipidemia, *n* (%)	111 (13.41%)	41 (10.57%)	70 (15.91%)	0.02 *
CVD, *n* (%)	63 (7.61%)	22 (5.67%)	41 (9.32%)	0.05
Frailty status				<0.001 §
Non-frailty, *n* (%)	592 (71.50%)	306 (78.87%)	286 (65.00%)	
Pre-frailty/frailty, *n* (%)	236 (28.50%)	82 (21.13%)	154 (35.00%)	

Notes: Clinical characteristics are expressed as mean ± SD values for continuous variables and *n* (%) for categorical variables. ¶ Continuous variables with non-normal distributions are shown as median (interquartile range). *p* values were derived from the independent two-sample *t* test and Mann–Whitney U test for continuous variables and the chi-square test for categorical variables. * *p* value < 0.05; § *p* value < (0.05/16). Abbreviations: SBP, systolic blood pressure; BMI, body mass index; WC, waist circumference; ASMI, appendicular skeletal muscle index; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease.

According to their general characteristics, members of the study population were categorized into a nonfrailty group and prefrailty/frailty group, as shown in Table 2. Of the 828 individuals, 236 (28.5%) had prefrailty or frailty status. The proportions of participants with poor sleep quality (CPSQI score > 5) increased with the severity of frailty (nonfrailty: prefrailty/frailty, 48.31%: 65.25%, $p < 0.001$), suggesting that the prefrailty/frailty group had a higher prevalence of poor sleep quality than the nonfrailty group did. In addition, participants of the prefrailty and frailty group were older. Participants with DM or CVD had the higher proportion in the prefrailty and frailty group. Gait speed and hand grip strength were lower in the prefrailty and frailty group. People of the prefrailty and frailty group had less exercise habits and lower education levels. The higher proportion of being single was seen in the prefrailty and frailty group. No significant difference was found for SBP, BMI, waist circumference, ASMI, sex, or underlying HTN or hyperlipidemia.

The results of multiple logistic regression analysis are shown in Table 3. Model 1 was adjusted for age; Model 2 was adjusted for age and sex; and Model 3 was adjusted for factors in Model 2 plus ASMI, BMI, hand grip strength, exercise habit, and gait speed. After the aforementioned confounding factors

were adjusted for, poor sleep quality (CPSQI score > 5) continued to be independently associated with prefrailty or frailty status (odds ratio (OR) = 1.95, 95% confidence interval (CI) = 1.38–2.77).

Table 2. General characteristics of the study population according to frailty status.

Variables	Frailty			*p* Value
	Total	**Non-Frailty**	**Prefrailty/Frailty**	
	(*n* = 828)	**(*n* = 592)**	**(*n* = 236)**	
Age (year) [¶]	64.00 (59.00, 70.00)	64.00 (59.00, 69.00)	66.00 (60.00, 73.00)	<0.001 [§]
SBP (mmHg) [¶]	127.00 (116.00, 138.00)	127.00 (116.00, 138.00)	125.00 (116.25, 137.75)	0.56
BMI (kg/m^2) [¶]	24.20 (22.00, 26.60)	24.20 (22.10, 26.60)	24.30 (21.80, 26.68)	0.98
WC (cm)	85.08 ± 10.07	84.72 ± 9.65	86.00 ± 11.01	0.10
ASMI (kg/m^2) [¶]	7.07 (6.55, 8.05)	7.06 (6.55, 8.06)	7.14 (6.56, 8.06)	0.38
Gait speed (m/s) [¶]	1.43 (1.30, 1.58)	1.46 (1.31, 1.61)	1.34 (1.16, 1.54)	<0.001 [§]
Hand grip strength (kg) [¶]	25.60 (21.70, 31.68)	26.50 (23.00, 32.80)	23.00 (17.60, 29.20)	<0.001 [§]
Men, *n* (%)	237 (28.62%)	166 (28.04%)	71 (30.08%)	0.56
Exercise habit, *n* (%)	602 (72.71%)	450 (76.01%)	152 (64.41%)	0.001 [§]
Marital status (single), *n* (%)	171 (20.65%)	109 (18.41%)	62 (26.27%)	0.01 [*]
Education level				0.001 [§]
No, *n* (%)	65 (7.85%)	35 (5.91%)	30 (12.71%)	
Primary, *n* (%)	314 (37.92%)	215 (36.32%)	99 (41.95%)	
Secondary, *n* (%)	366 (44.20%)	276 (46.62%)	90 (38.14%)	
College, *n* (%)	83 (10.02%)	66 (11.15%)	17 (7.20%)	
DM, *n* (%)	119 (14.37%)	74 (12.50%)	45 (19.07%)	0.02 [*]
HTN, *n* (%)	265 (32.00%)	181 (30.57%)	84 (35.59%)	0.16
Hyperlipidemia, *n* (%)	111 (13.41%)	87 (14.70%)	24 (10.17%)	0.08
CVD, *n* (%)	63 (7.61%)	38 (6.42%)	25 (10.59%)	0.04 [*]
Sleep quality				<0.001 [§]
CPSQI ≦ 5, *n* (%)	388 (46.86%)	306 (51.69%)	82 (34.75%)	
CPSQI > 5, *n* (%)	440 (53.14%)	286 (48.31%)	154 (65.25%)	

Notes: Clinical characteristics are expressed as mean ± SD values for continuous variables and as *n* (%) for categorical variables. [¶] Continuous variables with non-normal distributions are shown as median (interquartile range). *p* values were derived from the independent two-sample *t* test and Mann–Whitney U test for continuous variables and from the chi-square test for categorical variables. [*] *p* value < 0.05; [§] *p* value < (0.05/16). Abbreviations: SBP, systolic blood pressure; BMI, body mass index; WC, waist circumference; ASMI, appendicular skeletal muscle index; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease.

Table 3. Association between sleep quality and frailty status by multiple logistic regression analysis.

Variables	Model 1			Model 2			Model 3		
	OR	95% CI	*p* Value	OR	95% CI	*p* Value	OR	95% CI	*p* Value
CPSQI ≦ 5	1	-	-	1	-	-	1	-	-
CPSQI > 5	2.00	(1.46–2.75)	<0.001	2.01	(1.46–2.76)	<0.001	1.95	(1.38–2.77)	<0.001

Notes: Model 1: Multiple logistic regression adjusted for age. Model 2: Multiple logistic regression adjusted for age and sex. Model 3: Multiple logistic regression adjusted for factors in Model 2 plus ASMI, BMI, hand grip strength, exercise habit, and gait speed. Abbreviations: CI: confidence interval; OR: odds ratio.

4. Discussion

The aim of our study was to investigate the association between sleep quality and the risk of frailty. We collected the real-world data of the community in Taiwan. According to the result, poor sleep quality is independently associated with prefrailty and frailty status among middle-aged and older population members in Taiwan. This report is the first in Taiwan to use a cross-sectional study for assessing the relationship between sleep quality and prefrailty or frailty status specifically among middle-aged and older population members.

In our study, participants with lower ASMI, lower gait speed, lower hand grip strength, female, lower education level, and underlying diseases of HTN and dyslipidemia had higher proportion in the group with CPSQI scores > 5. According to previous studies, people with sarcopenia diagnosed by low ASMI, slow gait speed, and low hand grip strength had poor self-reported sleep quality [25]. Sleep complaints were relatively more prevalent in women compared to men. Poor sleep quality was

reported among women with various stages of the menopause transition and post-menopause [26]. Furthermore, education level was related to insomnia, and more years of education were associated with better sleep quality [27]. Moreover, increasing the numbers of co-morbidities was associated with poor sleep quality [28]. People with poor sleep quality had increased odds of prevalent HTN and were associated with metabolic syndrome [7,29,30]. Interestingly, in our study, lower SBP was found in the group with CPSQI scores > 5. It might be supposed that participants with HTN are under medication control. Thus, the data of SBP we collected was relatively lower than the group with CPSQI scores ≤ 5. On the other hand, participants with older age, lower gait speed, lower hand grip strength, less of an exercise habit, being single, lower education level, and underlying diseases of DM and CVD had the higher proportion in the prefrailty and frailty group. As we know, older people, slow gait speed, and low hand grip strength were risk factors of frailty. Increasing physical activity or regular exercise habit were suggested to prevent for frailty. With increasing age, there is a decline in physical activity associated with decreases in exercise tolerance [31]. Thus, less of an exercise habit might be the risk of frailty. One systematic review and meta-analysis showed that unmarried individuals had a twice as high frailty risk compared to married individuals. Social factors such as living alone or social isolation were associated with frailty. The widows, the widowers, the divorced, and the separated had higher odds of frailty risks than those who never married. Those who lost their partners might experience lots of stress and might lose social support. In addition, it might decrease positive behaviors such as exercise habits [32]. People with a lower education level might have less of a concept of regular exercise and have not enough financial resources or time to do it. Thus, it might increase the risk of frailty. Previous studies showed that muscle strength and quality would decrease in people with DM due to insulin resistance and chronic inflammation. The dysregulation of levels of various hormones and nutrition was described in people with insulin resistance [33]. These would be the risks of frailty. People with CVD would decrease the physical activities, and that is why it would be associated with frailty [34]. Although the relationship between sleep quality and frailty had been discussed, in our study, not only the elderly but also middle-aged population was enrolled; this strength is in good agreement with the notion that middle-aged individuals should be included for the study of identification and prevention of frailty [18]. In addition, our community-based and real-world data widely involved participants with various health statuses. Thus, our data are different from those collected in hospitals, which might have selective bias because non-symptomatic people would not be included.

In our study, poor sleep quality is independently associated with prefrailty and frailty in the community population. In previous research, sleep disorders elevated the risk of CVDs, metabolic diseases, neurogenic diseases, and psychological diseases [7,35]. This is one possible mechanism through which multi-comorbidities related to sleep problems cause poor health status, which would increase the risk of being frail. In addition, sleep disturbance influenced inflammatory regulation and sleep loss, short sleep duration, and complaints of sleep disturbance were associated with increases in inflammation [36]. Moreover, sleep disturbance has demonstrated some connection with frailty in elderly people. One systematic review of six cross-sectional studies revealed an association between sleep disturbance and frailty among elderly people [15]. One systemic review and meta-analysis showed abnormal sleep duration to be associated with an increased risk of frailty among elderly individuals [16]. Other research showed that oxidative stress and inflammation were potential drivers of frailty [37]. Although the pathogenesis between sleep disturbance and frailty is unclear, one possibility, according to the research, is that inflammatory pathways are influenced by the sleep–wake disturbance, which affects the development of frailty.

Frailty causes poor prognosis in elderly people. Three of the five Fried frailty index indicators (slow gait speed, low physical activity, and unintentional weight loss) were independently associated with chronic disability, long-term nursing home stays, and death [38]. In particular, slow gait speed was found to be a predictor of chronic disability (hazard ratio (HR) = 2.97, 95% CI = 2.32–3.80), long-term nursing home care (HR = 3.86, 95% CI = 2.23–6.67) and injurious falls (HR = 2.19,

95% CI = 1.33–3.60) [38]. Furthermore, prefrailty status fulfilling only one or two criteria of frailty also increased the risk of frailty [11]. One study showed some factors including high psychological distress, living alone, having health worries, and poor sleep quality; stair climbing, appetite, hydration; continence, and total food intake might be the predictive capacities for prefrailty to frailty [39]. With increasing age, there is also a decline in physical activity associated with decreases in exercise tolerance, which would lead to an increasing risk of frailty [31]. Thus, early prevention of prefrailty and frailty status is a concern for everyone, particularly elderly people.

Frailty is defined as an age-related syndrome [11]. Aging is a major risk factor for frailty. Women have an increased risk of sleep disturbance across their lifespans compared with men [40]. During times of hormonal changes in women, sleep regulation and arousals are affected, particularly in the menopausal transition and in early postmenopause [40,41]. The average age of menopause in Taiwan is 50–54 years [42]. Participants at the age of menopausal transition and early postmenopause were both enrolled in our study. Therefore, we had to remove these confounding factors before discussing the relationship between poor sleep quality and frailty status. After adjusting for variables with known or suspected impacts on prefrailty and frailty status, poor sleep quality continued to be significantly associated with prefrailty and frailty status in our study. In addition to traditional risk factors for frailty, according to one population-based cohort study, social and behavioral factors including education and marital status were associated with frailty [43]. Notably, this study showed that associations were present among those with an education level lower than high school (OR = 1.57, 95% CI = 1.12–2.22) and among those living with families (versus with spouses; OR = 1.76, 95% CI = 1.05–2.94) [43]. Similar results were observed in our study.

Our study is the first cross-sectional study to investigate the relationship between sleep quality and frailty status in middle-aged and older Taiwanese people. However, some limitations apply. First, the study is cross-sectional and therefore, it is unable to describe the causal relationship between sleep quality and prefrailty or frailty status. Second, because the data collection was community-based, the participants came only from Northern Taiwan, increasing the uncertainty of the ecological validity of the findings and the possibility of healthy volunteer bias. Thus, the results of our study should not be extrapolated to other regions in Taiwan. A potential healthy volunteer bias might have lowered the prevalence of prefrailty and frailty status and decreased our capabilities to control for confounding. Third, approximately 70% of the participants were female, and this would have caused the prevalence of poor sleep quality to be overestimated, because sleep disturbance is more prevalent for women than men [44]. Fourth, prefrailty and frailty status were not discussed separately in our study, and it might be our further vision that we could investigate in the future. Fifth, the information of participants with menopause was insufficient in our study. This could be the further vision for us to investigate in the future. Finally, frailty risk might be increased not only by the aforementioned diseases but also by diseases such as neurologic disorders. More participants with multiple chronic conditions should be enrolled in further studies.

5. Conclusions

Our study suggests that poor sleep quality is independently associated with prefrailty and frailty status among middle-aged and older adults in Taiwan. Therefore, sleep quality should be further assessed for frailty status among middle-aged and older adults, but the effects of sleep quality on frailty incidence require further validation in longitudinal studies.

References

1. National Development Council. Available online: https://pop-proj.ndc.gov.tw/upload/download/Population%20Projections%20for%20the%20Republic%20of%20China%20(Taiwan)-2020~{}2070.pdf (accessed on 13 December 2020).

2. National Development Council. Available online: https://pop-proj.ndc.gov.tw/international.aspx?uid=69&pid=60 (accessed on 13 December 2020).

3. Hu, H.M. Facing an Aging Society: Taiwan's Universities in crisis. *Gerontol. Geriatr. Educ.* **2020**, *41*, 233–241. [CrossRef]

4. Chen, H.-C.; Su, T.-P.; Chou, P. A Nine-Year Follow-up Study of Sleep Patterns and Mortality in Community-Dwelling Older Adults in Taiwan. *Sleep* **2013**, *36*, 1187–1198. [CrossRef]

5. Tian, Y.; Li, L. Epidemiological study of sleep disorder in the elderly. *Zhonghua Liu Xing Bing Xue Za Zhi.* **2017**, *38*, 988.

6. Magnavita, N.; Garbarino, S. Sleep, health and wellness at work: A scoping review. *Int. J. Environ. Res. Public Health* **2017**, *14*, 1347. [CrossRef]

7. Garbarino, S.; Lanteri, P.; Durando, P.; Magnavita, N.; Sannita, W.G. Co-morbidity, mortality, quality of life and the healthcare/welfare/social costs of disordered sleep: A rapid review. *Int. J. Environ. Res. Public Health* **2016**, *13*, 831. [CrossRef]

8. Jike, M.; Itani, O.; Watanabe, N.; Buysse, D.J.; Kaneita, Y. Long sleep duration and health outcomes: A systematic review, meta-analysis and meta-regression. *Sleep Med. Rev.* **2018**, *39*, 25–36. [CrossRef]

9. Gulia, K.K.; Kumar, V.M. Sleep disorders in the elderly: A growing challenge. *Psychogeriatrics* **2018**, *18*, 155–165. [CrossRef]

10. Tai, S.-Y.; Wang, W.-F.; Yang, Y.-H. Current status of sleep quality in Taiwan: A nationwide walk-in survey. *Ann. Gen. Psychiatry* **2015**, *14*, 36. [CrossRef]

11. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M157. [CrossRef]

12. Hwang, A.-C.; Liu, L.-K.; Lee, W.-J.; Chen, L.-Y.; Peng, L.-N.; Lin, M.-H.; Chen, L.-K. Association of frailty and cardiometabolic risk among community-dwelling middle-aged and older people: Results from the I-Lan longitudinal aging study. *Rejuvenation Res.* **2015**, *18*, 564–572. [CrossRef]

13. Hewitt, J.; Long, S.; Carter, B.; Bach, S.; McCarthy, K.; Clegg, A. The prevalence of frailty and its association with clinical outcomes in general surgery: A systematic review and meta-analysis. *Age Ageing* **2018**, *47*, 793–800. [CrossRef]

14. Ofori-Asenso, R.; Chin, K.L.; Mazidi, M.; Zomer, E.; Ilomaki, J.; Zullo, A.R.; Gasevic, D.; Ademi, Z.; Korhonen, M.J.; LoGiudice, D. Global incidence of frailty and prefrailty among community-dwelling older adults: A systematic review and meta-analysis. *JAMA Netw. Open* **2019**, *2*, e198398. [CrossRef]

15. Wai, J.L.-T.; Yu, D.S.-F. The relationship between sleep–wake disturbances and frailty among older adults: A systematic review. *J. Adv. Nurs.* **2020**, *76*, 96–108. [CrossRef]

16. Pourmotabbed, A.; Boozari, B.; Babaei, A.; Asbaghi, O.; Campbell, M.S.; Mohammadi, H.; Hadi, A.; Moradi, S. Sleep and frailty risk: A systematic review and meta-analysis. *Sleep Breath.* **2020**, *24*, 1187–1197. [CrossRef]

17. Ensrud, K.E.; Blackwell, T.L.; Redline, S.; Ancoli-Israel, S.; Paudel, M.L.; Cawthon, P.M.; Dam, T.T.L.; Barrett-Connor, E.; Leung, P.C.; Stone, K.L. Sleep disturbances and frailty status in older community-dwelling men. *J. Am. Geriatr. Soc.* **2009**, *57*, 2085–2093. [CrossRef]

18. Hanlon, P.; Nicholl, B.I.; Jani, B.D.; Lee, D.; McQueenie, R.; Mair, F.S. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: A prospective analysis of 493 737 UK Biobank participants. *Lancet Public Health* **2018**, *3*, e323–e332. [CrossRef]

19. Ma, W.Y.; Yang, C.Y.; Shih, S.R.; Hsieh, H.J.; Hung, C.S.; Chiu, F.C.; Lin, M.S.; Liu, P.H.; Hua, C.H.; Hsein, Y.C.; et al. Measurement of Waist Circumference: Midabdominal or iliac crest? *Diabetes Care* **2013**, *36*, 1660–1666. [CrossRef]

20. Han, Y.; Wu, Z.; Chen, Y.; Kan, Y.; Geng, M.; Xu, N.; Qian, H.; Wang, H.F.; Niu, M. Factors associated with appendicular skeletal muscle mass among male Chinese patients with stable chronic obstructive pulmonary disease: A hospital-based cross-sectional study. *Med. Baltim.* **2019**, *98*, e17361. [CrossRef]

21. Tsai, P.S.; Wang, S.Y.; Wang, M.Y.; Su, C.T.; Yang, T.T.; Huang, C.J.; Fang, S.C. Psychometric evaluation of the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) in primary insomnia and control subjects. *Qual. Life Res.* **2005**, *14*, 1943–1952. [CrossRef]

22. Xue, Q.-L. The frailty syndrome: Definition and natural history. *Clin. Geriatr. Med.* **2011**, *27*, 1–15. [CrossRef]

23. Carleton, R.N.; Thibodeau, M.A.; Teale, M.J.N.; Welch, P.G.; Abrams, M.P.; Robinson, T.; Asmundson, G.J.G. The center for epidemiologic studies depression scale: A review with a theoretical and empirical examination of item content and factor structure. *PLoS ONE* **2013**, *8*, e58067. [CrossRef]

24. Stewart, A.L.; Mills, K.M.; King, A.C.; Haskell, W.L.; Gillis, D.; Ritter, P.L. CHAMPS physical activity questionnaire for older adults: Outcomes for interventions. *Med. Sci. Sports Exerc.* **2001**, *33*, 1126–1141. [CrossRef]

25. Liu, X.; Hou, L.; Xia, X.; Liu, Y.; Zuo, Z.; Zhang, Y.; Zhao, W.; Hao, Q.; Yue, J.; Dong, B. Prevalence of sarcopenia in multi ethnics adults and the association with cognitive impairment: Findings from West-China health and aging trend study. *BMC Geriatr.* **2020**, *20*, 1–10. [CrossRef]

26. Otte, J.L.; Rand, K.L.; Landis, C.A.; Paudel, M.L.; Newton, K.M.; Woods, N.; Carpenter, J.S. Confirmatory factor analysis of the Pittsburgh Sleep Quality Index in women with hot flashes. *Menopause* **2015**, *22*, 1190. [CrossRef]

27. Lichstein, K.L.; Taylor, D.J.; McCrae, C.S.; Petrov, M. Insomnia: Epidemiology and risk factors. In *Principles and Practice of Sleep Medicine: Fifth Edition*; Elsevier Inc.: Amsterdam, The Netherlands, 2010; pp. 827–837.

28. Hayashino, Y.; Yamazaki, S.; Takegami, M.; Nakayama, T.; Sokejima, S.; Fukuhara, S. Association between number of comorbid conditions, depression, and sleep quality using the Pittsburgh Sleep Quality Index: Results from a population-based survey. *Sleep Med.* **2010**, *11*, 366–371. [CrossRef]

29. Zhang, H.; Li, Y.; Zhao, X.; Mao, Z.; Abdulai, T.; Liu, X.; Tu, R.; Wang, Y.; Qian, X.; Jiang, J. The association between PSQI score and hypertension in a Chinese rural population: The Henan Rural Cohort Study. *Sleep Med.* **2019**, *58*, 27–34. [CrossRef]

30. Okubo, N.; Matsuzaka, M.; Takahashi, I.; Sawada, K.; Sato, S.; Akimoto, N.; Umeda, T.; Nakaji, S. Relationship between self-reported sleep quality and metabolic syndrome in general population. *BMC Public Health* **2014**, *14*, 562. [CrossRef]

31. Liu, C.K.; Fielding, R.A. Exercise as an intervention for frailty. *Clin. Geriatr. Med.* **2011**, *27*, 101–110. [CrossRef]

32. Kojima, G.; Walters, K.; Iliffe, S.; Taniguchi, Y.; Tamiya, N. Marital status and risk of physical frailty: A systematic review and meta-analysis. *J. Am. Med. Dir. Assoc.* **2020**, *21*, 322–330. [CrossRef]

33. Cobo, A.; Vázquez, L.A.; Reviriego, J.; Rodríguez-Mañas, L. Impact of frailty in older patients with diabetes mellitus: An overview. *Endocrinol. Y Nutr. Engl. Ed.* **2016**, *63*, 291–303. [CrossRef]

34. Stewart, R. Cardiovascular disease and frailty: What are the mechanistic links? *Clin. Chem.* **2019**, *65*, 80–86. [CrossRef]

35. Kalmbach, D.A.; Pillai, V.; Arnedt, J.T.; Drake, C.L. DSM-5 Insomnia and Short Sleep: Comorbidity Landscape and Racial Disparities. *Sleep* **2016**, *39*, 2101–2111. [CrossRef]

36. Irwin, M.R. Why sleep is important for health: A psychoneuroimmunology perspective. *Annu. Rev. Psychol.* **2015**, *66*, 143–172. [CrossRef]

37. Álvarez-Satta, M.; Berna-Erro, A.; Carrasco-Garcia, E.; Alberro, A.; Saenz-Antoñanzas, A.; Vergara, I.; Otaegui, D.; Matheu, A. Relevance of oxidative stress and inflammation in frailty based on human studies and mouse models. *Aging Albany Ny* **2020**, *12*, 9982. [CrossRef]

38. Rothman, M.D.; Leo-Summers, L.; Gill, T.M. Prognostic significance of potential frailty criteria. *J. Am. Geriatr Soc.* **2008**, *56*, 2211–2216. [CrossRef]

39. Gordon, S.; Baker, N.; Kidd, M.; Maeder, A.; Grimmer, K. Pre-frailty factors in community-dwelling 40–75 year olds: Opportunities for successful ageing. *BMC Geriatr.* **2020**, *20*, 1–13. [CrossRef]

40. Pengo, M.F.; Won, C.H.; Bourjeily, G. Sleep in Women Across the Life Span. *Chest* **2018**, *154*, 196–206. [CrossRef]

41. Woods, N.F.; Mitchell, E.S. Sleep symptoms during the menopausal transition and early postmenopause: Observations from the Seattle Midlife Women's Health Study. *Sleep* **2010**, *33*, 539–549. [CrossRef]

42. Shen, T.-Y.; Strong, C.; Yu, T. Age at menopause and mortality in Taiwan: A cohort analysis. *Maturitas* **2020**, *136*, 42–48. [CrossRef]

43. Chamberlain, A.M.; St Sauver, J.L.; Jacobson, D.J.; Manemann, S.M.; Fan, C.; Roger, V.L.; Yawn, B.P.; Finney Rutten, L.J. Social and behavioural factors associated with frailty trajectories in a population-based cohort of older adults. *BMJ Open* **2016**, *6*, e011410. [CrossRef]
44. Minarik, P.A. Sleep disturbance in midlife women. *J. Obs. Gynecol. Neonatal. Nurs.* **2009**, *38*, 333–343. [CrossRef]

Article

Validation and Screening Capacity of the European Portuguese Version of the SUNFRAIL Tool for Community-Dwelling Older Adults

Ana Filipa Cardoso [1,*], Elzbieta Bobrowicz-Campos [2], Luísa Teixeira-Santos [3], Daniela Cardoso [1], Filipa Couto [4] and João Apóstolo [1]

1   Health Sciences Research Unit, Nursing, Nursing School of Coimbra, Portugal Centre for Evidence-Based Practice, A Joanna Briggs Institute Centre of Excellence, 3004-011 Coimbra, Portugal; dcardoso@esenfc.pt (D.C.); apostolo@esenfc.pt (J.A.)
2   Centre of 20th Century Interdisciplinary Studies, Faculty of Psychology and Educational Sciences, University of Coimbra, 3000-115 Coimbra, Portugal; elzbieta.campos@gmail.com
3   Health Sciences Research Unit, Nursing, Nursing School of Coimbra, 3004-011 Coimbra, Portugal; luisasants@esenfc.pt
4   Alfena Hospital—Trofa Health Group, Health Sciences Research Unit, Nursing, Nursing School of Coimbra, 3000-232 Coimbra, Portugal; filipadccouto@gmail.com
*   Correspondence: fcardoso@esenfc.pt; Tel.: +351-239-487-217

Abstract: Early detection of frailty may prevent or delay adverse health outcomes in community-dwelling older adults. In Portugal, there are currently no valid multidimensional frailty screening tools. SUNFRAIL is a user-friendly multidimensional tool for frailty screening that can be used in primary care. Aims: (i) to determine the validity and reliability of the European Portuguese version of the SUNFRAIL tool for use in community-dwelling older adults; (ii) to assess the screening capacity of this version of SUNFRAIL using Fried's phenotypic model criteria for frailty as a reference test. Methods: Cross-sectional pilot study in a convenience sample of 128 community-dwelling older adults. Objective and subjective data were collected. Internal consistency, concurrent validity, sensitivity, and specificity (ROC curve analysis) were examined. Results: Internal consistency was low. Significant moderate to strong correlations were found between different domains and the total score. The differences between robust, pre-frail, and frail older adults were significant. SUNFRAIL was also correlated with multimorbidity. Sensitivity and specificity were satisfactory. Conclusions: The European Portuguese version of the SUNFRAIL tool is a promising frailty screening tool for community-dwelling older adults to be routinely used in clinical practice. However, more consistent results on its validity and reliability are needed to be used nationwide.

Keywords: SUNFRAIL; psychometric properties; screening tool; frailty; older adults

1. Introduction

The current COVID-19 pandemic has created new challenges for active and healthy aging [1]. Community-dwelling older adults are now more vulnerable and exposed to negative outcomes, and they have been forced to change their active and healthy aging habits. Recent studies [2–4] have shown that the measures applied to contain the coronavirus spread resulted in a relevant decrease in older adults' physical activity, which negatively impacted their subjective well-being.

Geriatric care clinical settings also face a marked increase in demands for effective treatment of age-related clinical conditions, striving to provide personalized and timely comprehensive care. These demands are challenging even in normal times due to the high rates of multimorbidity in advanced age [5–7], which have become much more pronounced over the past year because the health systems' resources had to be carefully distributed

in line with pandemic-related priorities. Therefore, there is an urgent need to implement mechanisms that facilitate the shift from a disease-oriented to a preventive approach to ensure that people live independently and with quality of life for as long as possible and, consequently, contribute to health systems' sustainability. One of the requirements for this shift is the use of tools for early diagnosis and treatment of age-related conditions, especially frailty.

As a common age-related condition, frailty is characterized by an increased vulnerability to adverse health outcomes that affect several domains of human functioning (physical, psychological, and social) [8], resulting from the decline in multiple physiological systems [9]. Due to its malleable nature, the condition of frailty can be reversed to a healthy state if the intervention focuses on the symptoms, adapting the treatment procedures to their clinical relevance and impact on functioning [10]. However, most of the available frailty screening tools do not address all domains of functioning, compromising frailty assessment and management. Early identification of frailty is essential for developing timely and tailored interventions based on evidence-informed clinical decision-making, but it requires easy-to-use instruments [11].

The multidimensional SUNFRAIL tool has a bio-psycho-social approach to address the gaps mentioned above [12]. It is a quick and easy-to-use tool, which facilitates its regular use in clinical practice. This nine-question tool assesses the presence of difficulties or problems in biological (items 1–5), psychological (items 6 and 7), and social domains (items 8 and 9). However, a recent study proposed a different categorization of this tool's items [13]. SUNFRAIL items are scored 1 for "yes" and 0 for "no", except for items 4 and 8, which are scored inversely. Higher scores suggest more frailty [12]. The SUNFRAIL tool proved to be a valid instrument for screening frailty in community-dwelling older adults [8]. Given these characteristics, the authors of this study proceeded with forward-backward translation and cross-cultural adaptation of the SUNFRAIL tool for European Portuguese, as recommended by international guidelines [14]. The detailed results of this process are published elsewhere [15].

The present study aimed (i) to determine whether this European Portuguese version of the SUNFRAIL tool is a valid and reliable instrument to be used in community-dwelling older adults, and (ii) to assess the screening ability of this SUNFRAIL version using Fried's phenotypic model criteria for frailty as a reference test.

2. Materials and Methods

2.1. Participants

This cross-sectional study was conducted in a convenience sample of 128 community-dwelling older adults recruited by family nurses in cultural and sports associations, municipal services, and health and day centers in Portugal's central region. The exclusion criteria were the presence of moderate to severe cognitive decline and unstable clinical condition. Data were collected from November 2018 to September 2019.

2.2. Instruments and Procedures

Sociodemographic and clinical characteristics: All eligible participants were asked to provide information on their sociodemographic characteristics (age, gender, marital status, and education level), anthropometric characteristics (weight and height), chronic conditions (neoplasms, blood and immune system disorders, endocrine and metabolic diseases, central nervous system diseases, special senses disorders, cardiovascular diseases, respiratory diseases, digestive diseases, skin diseases, musculoskeletal and connective tissue disorders, genitourinary disorders, hyperthyroidism, hypothyroidism, hypertension, restless legs syndrome, narcolepsy, obstructive sleep apnea, mental and behavioral disorders, or anxiety), and medication intake (anxiolytics, antihypertensives, beta-blockers, hypnotics, corticosteroids, anti-inflammatory drugs, melatonin receptor agonists, thyroid hormones, muscle relaxants, antipyretics, or melatonin). They were also asked to perform tasks to identify symptoms of physical frailty and assess their cognitive status.

Measures of frailty: All participants were screened for frailty based on Fried's frailty phenotype criteria [16] and completed the European Portuguese version of the SUN-FRAIL [15]. Fried's frailty phenotype model includes five components assessed based on objective or subjective report measures [16]. In this study, both methods were used, as recommended by the authors of the Portuguese version of the test [17]. More specifically, physical activity was assessed using a short version of the International Physical Activity Questionnaire [18], developed for older adults (www.ipaq.ki.se). Inactivity and irregular activity were classified as symptoms of frailty. Gait speed was assessed through the 4.6-m walk test, and the best time of the two trials was used for the final score. Symptoms were classified based on cutoff scores of ≥ 7 and ≥ 6 s for men and women, respectively.

Weakness was assessed through the handgrip strength test using a dynamometer. The best result of the three trials was used for the final score. Symptoms were classified based on the participants' gender and body mass index (BMI). The following cutoff scores were used for women: ≤ 17, ≤ 17.3, ≤ 18, and ≤ 21 for BMI ≤ 23, 23.1–26, 26.1–29, and >29, respectively. In men, the cutoff scores ≤ 29, ≤ 30, and ≤ 32 were used for BMI ≤ 24, 24.1–28, and >28, respectively.

Two questions ("I felt that everything I did was an effort" and "I could not get going") from the Center for Epidemiological Studies-Depression (CES-D) questionnaire [19] were used to assess fatigue. The symptom was classified as present when both statements were evaluated by negative concordance. Weight loss was assessed by subjective report, taking into account the 6-month period prior to assessment. The loss of 4 kg or more was considered an indicator of symptom presence. Frailty status was confirmed by the presence of three to five symptoms and pre-frailty status by the presence of one or two symptoms. In the absence of symptoms, older adults were classified as robust.

Measure of cognitive functioning: Cognitive functioning was assessed using the 6-Item Cognitive Impairment Test (6-CIT) [20]. The 6-CIT is a cognitive screening test composed of six simple questions that assess orientation in time and space, attention and working memory, and verbal memory. The classification of the 6-CIT results as indicative of the presence of changes in cognitive functioning took into account the years of formal education completed by the participants, as proposed by authors of the Portuguese version of the test [21].

2.3. Ethical-Legal Considerations

Permission was obtained from the authors of the original version to use the tool and the institutions to conduct the study. The study was approved by the ethics committee of the Health Sciences Research Unit: Nursing, Nursing School of Coimbra, Portugal (decision number P510/06-2018, 510/06-2018). All ethical and legal principles were met. Participation was voluntary, and all participants signed an informed consent form.

2.4. Statistical Analyses

Data were analyzed using IBM SPSS Statistics software (version 24, IBM Corp., Armonk, NY, USA). Statistical significance was set at 0.05. Chi-square (χ^2) tests, Cramer's V (V) coefficient, Kruskal–Wallis test, Partial eta-squared measure (η^2_p), and two-way ANOVA statistics were used. The H-statistic was calculated by summing the squared ranks of a given factor and dividing them by the total mean square for those ranks [22]. Effect size was calculated using η^2_p. The Kuder–Richardson Formula 20 (KR-20) was used to assess internal consistency. Spearman's correlations between SUNFRAIL domain scores and total scores were calculated. Concurrent validity was determined based on Spearman's correlations between SUNFRAIL total score and the number of chronic conditions and medication intake. The Receiver Operating Characteristic (ROC) curve was plotted to compare the sensitivity and specificity of different cutoff point(s) for frailty screening. The SUNFRAIL score was used as a test variable and the absence/presence of the Fried frailty criteria as a state variable. The Youden index was calculated to select the optimal cutoff

point. The area under the curve (AUC) with 95% confidence interval and other summary measures of test accuracy were also reported.

3. Results

3.1. Sociodemographic and Clinical Characteristics

The participants were mostly female (n = 98), with a mean age of 71.09 ± 7.85 years and a mean education level of 8.08 ± 4.17 years (Table 1). According to Fried's diagnostic criteria for frailty, of the 128 older adults, 23 were frail, 53 were pre-frail, and 52 were robust. Table 2 shows that reduced strength was the most common symptom among frail and pre-frail participants. A large percentage of frail older adults showed reduced speed, activity, and fatigue; however, only one frail person reported unintentional weight loss. Interestingly, BMI in this group was quite high, reaching a mean value of 29.62 (±6.44). For pre-frail participants, reduced activity and reduced speed were the second and third most common symptoms. Fatigue was reported by 8% of pre-frail older adults, and none of them confirmed unintentional weight loss (Table 2). In this group, BMI reached a mean value of 26.96 (±4.02), which was similar to the mean value found in the group of robust older adults (26.59 ± 3.93). Multimorbidity (presence of two or more chronic conditions) was reported in 90% of participants. Frail participants had, on average, more chronic conditions than robust or pre-frail participants (Table 1). Eighty-four percent of participants reported taking medication, and more than half of the sample (53%) reported being polymedicated (two or more drugs) (Table 1).

Table 1. Demographic, clinical, and neuropsychological characteristics of the sample.

	Robust Older Adults (n = 54)	Pre-Frail Older Adults (n = 56)	Frail Older Adults (n = 24)		
	%	%	%	χ^2	Cramer's *V*
Gender: Female/Male	72/28	80/20	75/25	1.021	0.600
Marital Status: single/married/widowed/divorced	4/69/13.5 /13.5	4/54.5/36 /5.5	4/46/37.5 /12.5	9.628	0.141
6-CIT: without cognitive decline/with mild cognitive decline	81.5/18.5	79/21	42/58	14.853	0.001
	Mean (SD)	Mean (SD)	Mean (SD)	Kruskal-Wallis (p)	Pairwise comparisons
Age	70.83 (4.50)	72.15 (5.36)	72.39 (3.86)	0.321	——
Education level	8.76 (3.99)	7.84 (4.14)	7.25 (4.20)	0.299	——
Medication intake	1.5 (1.28)	1.91 (1.37)	2.63 (1.31)	0.003	R < F *
Comorbidities	3.81 (1.84)	3.84 (2.09)	4.88 (1.87)	0.078	——

F: frail older adults; R: robust older adults; * p < 0.01; η^2_p = 0.089.

Table 2. SUNFRAIL score and diagnostic criteria for frailty based on Fried's Phenotype Model.

|		Robust Older Adults (*n* = 54)	Non-Robust Older Adults		
			Total (*n* = 80)	Pre-Frail Older Adults (*n* = 56)	Frail Older Adults (*n* = 24)
SUNFRAIL Total score	Mean ± SD (range)	1.83 ± 1.37 (0–6)	2.84 ± 1.81 (0–7)	2.36 ± 1.63 (0–7)	3.96 ± 1.73 (0–7)
SUNFRAIL -Biological	Mean ± SD (range)	1.07 ± 0.91 (0–4)	1.56 ± 1.21 (0–4)	1.18 ± 1.05 (0–4)	2.46 ± 1.10 (0–4)
SUNFRAIL -Psychological	Mean ± SD (range)	0.57 ± 0.69 (0–2)	0.94 ± 0.68 (0–2)	0.88 ± 0.69 (0–2)	1.08 ± 0.65 (0–2)
SUNFRAIL -Social	Mean ± SD (range)	0.19 ± 0.48 (0–2)	0.34 ± 0.50 (0–2)	0.30 ± 0.50 (0–2)	0.42 ± 0.50 (0–1)
Fried's Phenotype Model criteria	Mean ± SD (range)	0.00 ± 0.00 (0.00–0.00)	1.89 ± 1.06 (1–4)	1.27 ± 0.45 (1–2)	3.33 ± 0.48 (3–4)
Weight loss	% of persons with symptom	——	1.32%	0.00%	4.35%
Fatigue	% of persons with symptom	——	27.63%	7.55%	73.91%
Reduced activity	% of persons with symptom	——	51.32%	39.62%	78.26%
Reduced speed	% of persons with symptom	——	40.79%	20.75%	86.96%
Reduced hangrip strength	% of persons with symptom	——	75.00%	66.04%	95.65%

3.2. Internal Consistency of the SUNFRAIL Tool

Internal consistency was low (0.522). The correlations between the SUNFRAIL total score and the three domain scores were statistically significant ($p < 0.001$). The correlation between the total score and the biological domain score was strong (rho = 0.84), and both the correlations between the total score and the psychological domain score (rho = 0.65) and the total score and the social domain score (rho = 0.55) were moderate. The correlations between the SUNFRAIL domains were significant but weak. The highest correlation was found between the biological and the social domain scores (rho = 0.29; $p = 0.001$), and the lowest between the psychological and the social domain scores (rho = 0.22; $p = 0.011$). The rho coefficient for the biological and the psychological domain scores was 0.25 ($p = 0.004$) (Table 2).

3.3. SUNFRAIL Score in Robust and Non-Robust Older Adults

The analysis of the SUNFRAIL total score using the Kruskal–Wallis test revealed statistically significant differences between groups (H(2) = 21.708; $p < 0.001$). The multiple comparisons of mean ranks showed that robust participants scored significantly lower on the SUNFRAIL tool than pre-frail ($p = 0.048$) and frail ($p < 0.001$) participants. Significant differences were also found between the scores obtained by frail and pre-frail older adults ($p = 0.001$). The effect size was medium ($\eta^2_p = 0.171$). Significant between-group differences were found in the biological (H(2) = 22.385; $p < 0.001$; $\eta^2_p = 0.176$) and the psychological (H(2) = 10.743; $p = 0.005$; $\eta^2_p = 0.085$) domains of the SUNFRAIL tool, but not in the social domain (H(2) = 4.860; $p = 0.088$).

Moreover, the multiple comparisons of mean ranks showed significant differences between robust and frail older adults in both biological ($p < 0.001$) and psychological ($p = 0.008$) domains. Significant differences between robust and pre-frail participants were found in the psychological domain ($p = 0.038$) but not in the biological domain. Significant

differences between pre-frail and frail older adults were only found in the biological domain (*p* < 0.001) (Figure 1).
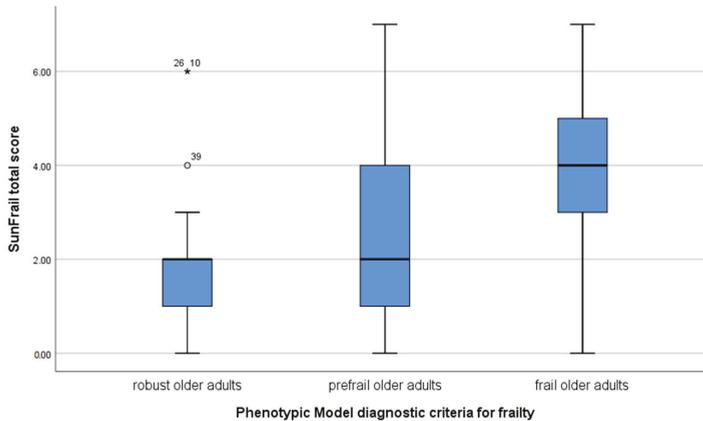
Note. Bold lines indicate mean scores. Hollow circle indicates a mild outlier. Asterisk indicates an extreme outlier. Boxes represent 95% confidence intervals.

Figure 1. SUNFRAIL score for participants classified as robust, pre-frail, and frail based on Fried's Phenotype Model.

### 3.4. SUNFRAIL Tool and 6-CIT

Seventy-three percent of participants showed no significant cognitive changes. Older adults with and without cognitive decline were not equally distributed in the robust, pre-frail, and frail groups (χ^2 = 12.932; *p* = 0.002; Vc = 0.3) (Table 1). A non-parametric two-way ANOVA was used to analyze the effect of cognitive status on SUNFRAIL scores. The correlation between frailty status (robust, pre-frail, and frail) and cognitive status (without cognitive decline and with mild cognitive decline) was statistically significant (H(2) = 22.138, *p* < 0.001, η^2_p = 0.174), explaining 17.4% of total variance. In terms of main effect, the cognitive status did not contribute to the distribution of the SUNFRAIL score (H(1) = 0.431, *p* = 0.51, η^2_p = 0.004). Frailty status proved to have a significant effect on the distribution of the SUNFRAIL score (H(1) = 18.095, *p* < 0.001, η^2_p = 0.147), explaining 14.7% of total variance.

3.5. Concurrent Validity of the SUNFRAIL Tool

Frail participants had, on average, more chronic conditions than robust or pre-frail participants, but these differences (Kruskal–Wallis test) were not significant (*p* > 0.05). The number of chronic conditions correlated significantly but moderately with the total score of the SUNFRAIL tool (rho = 0.44; *p* = 0.01).

3.6. Sensitivity and Specificity of the SUNFRAIL Tool

Figure 2 shows the ROC curve for the SUNFRAIL score, using Fried's frailty criteria (absence of symptoms vs. presence of symptoms) as the gold standard.
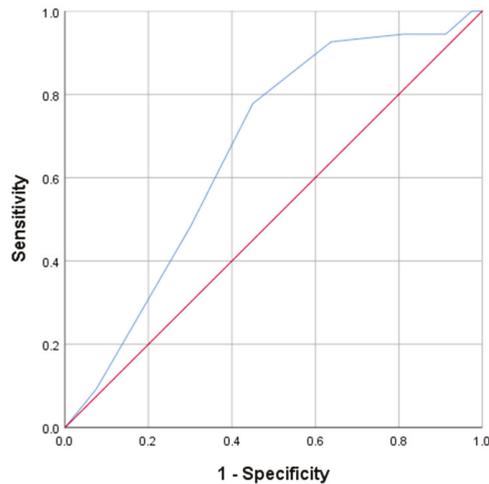
Figure 2. Receiver Operating Characteristic (ROC) curve for the SUNFRAIL tool, using diagnostic criteria for frailty from the Fried phenotype model as a gold standard.

The AUC was 0.671 (95% CI = 0.58–0.77; $p < 0.01$). The cutoff point >2 had the best sensitivity and specificity (Table 3). Predictive values and likelihood ratios for this cutoff point are shown in Table 4.

Table 3. Sensitivity, specificity, and Youden Index of the SUNFRAIL tool.

Cutoff Point	Sensitivity	Specificity	Youden Index
>0	9.26%	92.50%	0.02
>1	48.15%	70.00%	0.18
>2	**77.78%**	**55.00%**	**0.33**
>3	92.59%	36.25%	0.29
>4	94.44%	18.75%	0.13
>5	94.44%	8.75%	0.03
>6	100.00%	2.50%	0.02
>8	100.00%	0.00%	0.00

Note. In bold: cutoff points, sensitivity, and specificity for the maximal Youden Index.

Table 4. Screening properties of the SUNFRAIL tool for cutoff >2.

Sensitivity	Specificity	AUC	PPV	NPV	LR+	LR-
0.78	0.55	0.666 *	0.79	0.54	2.48	0.58
(0.64–0.88)	(0.43–0.66)	(0.57–0.76)	(0.68–0.86)	(0.47–0.61)	(1.45–4.23)	(0.44–0.77)

Note. AUC: area under the curve; LR-: negative likelihood ratio; LR+: positive likelihood ratio; NPV: negative predictive value; PPV: positive predictive value. Numbers in parentheses show a 95% confidence interval. * $p < 0.01$.

4. Discussion

The low internal consistency of the Portuguese European version of the SUNFRAIL tool may have been due to the reduced number of items representing three different domains of individual functioning. On the other hand, significant moderate (psychological and social) to strong (biological) correlations were found between domain scores and total score, proving that the instrument may collect relevant data for defining the follow-up care plan. The correlations between different SUNFRAIL domains showed more satisfactory results than those found in the study conducted in the Netherlands [13]. In the latter study,

no significant correlations were found between the physical and the social domains in the SUNFRAIL tool; the internal consistency value was also not reported.

The results on reliability require further discussion on the SUNFRAIL structure. Although it is an easy-to-use instrument covering three different domains, it may be necessary to increase the number of items in the psychological and social domains. Concerning the social domain, it is important to address older adults' perceived satisfaction with the available social support rather than only questioning if such support exists or not.

The findings on internal consistency also suggest the need for reviewing item content and scoring options. During the construct validity process, lay, research, and clinical practice communities raised questions about the difficulty in understanding some items. Based on their feedback, these items were reformulated [15]. Still, some of them may be ambiguous for the Portuguese context, probably undermining the tool's consistency. In our opinion, items 2, 4, and 9 are more sensitive to cultural issues and items 1 and 7 are more sensitive to the meaning attributed to them. Therefore, we recommend further research on older adults' understanding of the items and how their answers can be influenced by social desirability. As for item scoring, the dichotomous (yes/no) response option makes it easier to use. However, multiple-choice questions may enable a more reliable screening. The training of health and social care professionals in the SUNFRAIL administration may also be helpful. The instrument could also include a detailed description of each item to check if the meaning attributed by the interviewees to these items is the same as that intended by the tool authors. It could also provide guidance on the care-pathways to be suggested or activated in response to the symptoms and information on the available resources, as suggested by other studies [8].

As some SUNFRAIL items seem to be culturally sensitive, the proposed approach may benefit older people by raising their awareness about health changes, which, despite being warning signs, are often assumed as "normal", preventing the search for timely help. The fact that there is an over expression of obesity over weight loss deserved our attention. Several studies [23,24] show that weight loss but also obesity can be a frailty indicator. This aspect may be dependent on the cultural context and deserves further reflection. Although the SUNFRAIL tool can still be improved, we believe it may allow in-depth data collection. One of the strengths of the European Portuguese version [15] is its ability to discriminate between robust, pre-frail, and frail older adults. These results are in line with another study [13]. The differences between groups were predominantly higher in the biological domain and lower in the other domains, which may reinforce the idea that the biological domain is overrated in comparison with the psychological and the social domains, which is also similar to the results found by Gobbens et al. (2012) [7].

The total explained variance of the SUNFRAIL was higher for the interaction between frailty status and cognitive status than when the cognitive status or the frailty status were analyzed per se, which, in our opinion, may reinforce the multidimensionality of frailty [13]. As regards concurrent validity, the SUNFRAIL was significantly correlated with multimorbidity. Previous studies [5–7] also suggested a high prevalence of multiple chronic diseases in frail older adults. Other authors [25] also argue that a mean number of chronic diseases is a relevant determinant of frailty, with overlap rates of frailty and multimorbidity reaching 25%. We are able to determine two-thirds for the cutoff point, with score 2 indicating a robust health status and score 3 or more indicating pre-frailty or frailty, which is consistent with a previous study [13]. The sensitivity and specificity values for a pilot study are satisfactory, but more studies are needed. For being a self-assessment questionnaire, some domains can be underestimated. Carers or other significant people should be included for a more comprehensive assessment.

Strengths and Limitation of the Study

This study's major strength is that it determined the validity and reliability of this European Portuguese version of the SUNFRAIL tool. This cross-cultural adaptation process followed rigorous quality procedures, resulting in the first version of an instrument for

frailty screening suitable for community-dwelling older people and can be easily used in primary health care settings. A most important limitation of this study is the sample size, especially the reduced number of participants with frailty. The latter is due to the fact that most study participants were involved in physical and social activities in the community, which makes them less frail. This fact may have conditioned the instrument's results on sensitivity and specificity. As so, future research should focus both on older adults who maintain physical and cognitive activity and on older adults who are no longer active. Future research should also examine the SUNFRAIL performance in groups of older adults who are socially involved with those who are socially isolated, to obtain more accurate data on the social and psychological domains of the tool. The analysis of SUNFRAIL that considers the distribution of participants into different age groups is additionally recommended. This analysis would enable to verify whether the cutoff score suggested in the present study also applies to the oldest older adults. Finally, other studies should be conducted to reinforce the validity (construct validity against other frailty tests validated for the Portuguese population, concurrent and predictive validity) and reliability (temporal stability) of the European Portuguese version of the SUNFRAIL tool, as well as to explore its association with adverse health outcomes.

5. Conclusions

The European Portuguese version of the SUNFRAIL tool is a promising frailty screening tool for clinical practice. It is an easy-to-use and friendly instrument. More consistent results on validity and reliability are needed for its use in clinical practice nationwide.

References

1. Boreskie, K.F.; Hay, J.L.; Duhamel, T.A. Preventing Frailty Progression during the COVID-19 Pandemic. *J. Frailty Aging* **2020**, *9*, 130–131. [CrossRef] [PubMed]
2. Lesser, I.A.; Nienhuis, C.P. The Impact of COVID-19 on Physical Activity Behavior and Well-Being of Canadians. *Int. J. Environ. Res. Public Health* **2020**, *17*, 3899. [CrossRef] [PubMed]
3. Giustino, V.; Parroco, A.M.; Gennaro, A.; Musumeci, G.; Palma, A.; Battaglia, G. Physical activity levels and related energy expenditure during COVID-19 quarantine among the sicilian active population: A cross-sectional online survey study. *Sustainability* **2020**, *12*, 4356. [CrossRef]

4. Suzuki, Y.; Maeda, N.; Hirado, D.; Shirakawa, T.; Urabe, Y. Physical activity changes and its risk factors among community-dwelling japanese older adults during the COVID-19 epidemic: Associations with subjective well-being and health-related quality of life. *Int. J. Environ. Res. Public Health* **2020**, *17*, 6591. [CrossRef] [PubMed]
5. Jürschik, P.; Nunin, C.; Botigué, T.; Escobar, M.A.; Lavedán, A.; Viladrosa, M. Prevalence of frailty and factors associated with frailty in the elderly population of Lleida, Spain: The FRALLE survey. *Arch. Gerontol. Geriatr.* **2012**, *55*, 625–631. [CrossRef] [PubMed]
6. Bonaga, B.; Sánchez-Jurado, P.M.; Martínez-Reig, M.; Ariza, G.; Rodríguez-Mañas, L.; Gnjidic, D.; Salvador, T.; Abizanda, P. Frailty, Polypharmacy, and Health Outcomes in Older Adults: The Frailty and Dependence in Albacete Study. *J. Am. Med. Dir. Assoc.* **2018**, *19*, 46–52. [CrossRef]
7. Ding, Y.Y.; Kuha, J.; Murphy, M. Multidimensional predictors of physical frailty in older people: Identifying how and for whom they exert their effects. *Biogerontology* **2017**, *18*, 237–252. [CrossRef]
8. Gobbens, R.J.; van Assen, M.A.; Luijkx, K.G.; Schols, J.M. Testing an integral conceptual model of frailty. *J. Adv. Nurs.* **2012**, *68*, 2047–2060. [CrossRef]
9. Clegg, A.; Young, J.; Iliffe, S.; Rikkert, M.O.; Rockwood, K. Frailty in Older People. *Lancet* **2014**, *381*, 752–762. [CrossRef]
10. Gwyther, H.; Bobrowicz-Campos, E.; Luis Alves Apóstolo, J.; Marcucci, M.; Cano, A.; Holland, C. A realist review to understand the efficacy and outcomes of interventions designed to minimise, reverse or prevent the progression of frailty. *Health Psychol. Rev.* **2018**, *12*, 382–404. [CrossRef]
11. Apóstolo, J.; Cooke, R; Bobrowicz-Campos, E.; Santana, S.; MArcucci, M.; Cano, A.; Vollenbroek-Hutten, M.; Germini, F.; Holland, C. Predicting risk and outcomes for frail older adults: An umbrella review of frailty screening tools. *JBI Database Syst. Rev. Implement. Rep.* **2017**, *15*, 1154–1208. [CrossRef] [PubMed]
12. Cesari, M.; Maggio, M.; Palummeri, E.; Poli, S.; Barbolini, M.; Moda, G. *Sunfrail Tools for the Identification of Frailty and Multimorbidity*; European Union: Emilia-Romagna, Italy, 2018; Volume 10, p. 46, Call identifier: H2020-HP-PJ-2014.
13. Gobbens, R.; Maggio, M.; Longobucco, Y.; Barbolini, M. The validity of the sunfrail tool: A cross-sectional study among dutch community-dwelling older people. *J. Frailty Aging* **2020**, *9*, 219–225. [CrossRef] [PubMed]
14. Beaton, D.; Bombardier, C.; Guillemin, F.; Ferraz, M.B. Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine* **2000**, *15*, 3186–3191. [CrossRef] [PubMed]
15. Cardoso, A.F.; Bobrowicz-Campos, E.; Couto, F.; Cardoso, D.; Barata, A.; Apóstolo, J. Feasibility, appropriateness and meaningfulness analysis of the Sunfrail Tool to the European Portuguese population during cross-cultural adaptation process. *Int. J. Evid. Based. Healthc.* **2019**, *17*, S26–S28. [CrossRef] [PubMed]
16. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in Older Adults: Evidence for a Phenotype. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M157. [CrossRef]
17. Furtado, G.; Loureiro, M.; Ferreira, J.; Teixeira, A.; Patrício, M. Predicting frail syndrome using adverse geriatric health outcomes: Comparison of different statistical classifiers. In Proceedings of the IEEE 5th Portuguese Meeting on Bioengineering (ENBENG), Coimbra, Portugal, 16–18 February 2017. [CrossRef]
18. Ainsworth, B.E.; Macera, C.A.; Jones, D.A.; Reis, J.P.; Addy, C.L.; Bowles, H.R.; Kohl, H.W. Comparison of the 2001 BRFSS and the IPAQ physical activity questionnaires. *Med. Sci. Sports Exerc.* **2006**, *38*, 1584–1592. [CrossRef]
19. Gonçalves, B.; Fagulha, T. The Portuguese version of the center of epidemiologic studies depression scale (CES-D). *Eur. J. Psychol. Assess.* **2004**, *20*, 339–348. [CrossRef]
20. Brooke, P.; Bullock, R. Validation of a 6 Item Cognitive Impairment Test with a view to primary care usage. *Int. J. Geriatr. Psychiatry* **1999**, *14*, 936–940. [CrossRef]
21. Apóstolo, J.; Paiva, D.; Silva, R.; Santos, E.; Schultz, T. Adaptation and validation into Portuguese language of the six-item cognitive impairment test (6CIT). *Aging Ment. Health* **2018**, *22*, 1184–1189. [CrossRef]
22. Marôco, J. *Análise Estatística com o SPSS Statistics*, 5th ed.; ReportNumber: Pero Pinheiro, Portugal, 2011; 990p.
23. Crow, R.S.; Lohman, M.C.; Titus, A.J.; Cook, S.B.; Bruce, M.L.; Mackenzie, T.A.; Bartels, S.J.; Batsis, J.A. Association of Obesity and Frailty in Older Adults: NHANES 1999–2004. *J. Nutr. Health Aging* **2019**, *23*, 138–144. [CrossRef]
24. Afonso, C.; Sousa-Santos, A.R.; Santos, A.; Borges, N.; Padrão, P.; Moreira, P.; Amaral, T.F. Frailty status is related to general and abdominal obesity in older adults. *Nutr. Res.* **2021**, *85*, 21–30. [CrossRef] [PubMed]
25. Le Cossec, C.; Perrine, A.L.; Beltzer, N.; Fuhrman, C.; Carcaillon-Bentata, L. Pre-frailty, frailty, and multimorbidity: Prevalences and associated characteristics from two French national surveys. *J. Nutr. Health Aging* **2016**, *20*, 860–869. [CrossRef] [PubMed]

Article

Frailty as a Moderator of the Relationship between Social Isolation and Health Outcomes in Community-Dwelling Older Adults

Fereshteh Mehrabi [1,2,*] and François Béland [1,2,3]

1 School of Public Health (ESPUM), Université de Montréal, 7071 Parc Ave, Montréal, QC H3N 1X9, Canada; francois.beland@umontreal.ca
2 Centre de Recherche en Santé Publique (CReSP), Université de Montréal et CIUSSS du Centre-Sud-de-l'Île-de-Montréal, 7071 Parc Ave, Montréal, QC H3N 1X9, Canada
3 Lady Davis Institute for Medical Research, Jewish General Hospital, 3755, Chemin de la Côte-Ste-Catherine, Montréal, QC H3T 1E2, Canada
* Correspondence: fereshteh.mehrabi@umontreal.ca

Abstract: This research investigated the effects of social isolation on frailty and health outcomes and tested whether these associations varied across different levels of frailty. We performed a multivariate analysis of the first wave of Frailty: A longitudinal study of its expressions (FRéLE) among 1643 Canadian older adults aged 65 years and over. We assessed social isolation using social participation, social networks, and support from various social ties, namely, friends, children, extended family, and partner. Frailty was associated with disability, comorbidity, depression, and cognitive decline. Less social participation was associated with limitations in instrumental activities of daily living (IADLs), depression, and cognitive decline. The absence of friends was associated with depression and cognitive impairment. Less social support from children and partner was related to comorbidity, depression, and cognitive decline. Overall, social isolation is linked to mental health rather than physical health. The associations of having no siblings, receiving less support from friends, and participating less in social activities with ADL limitations, depression, and cognitive decline were higher among frail than prefrail and robust older adults. This study corroborates the pivotal role of social connectedness, particularly the quality of relationships, on the mental health of older adults. Public health policies on social relationships are paramount to ameliorate the health status of frail older adults.

Keywords: frailty; social isolation; social networks; social support; social participation; aging

1. Introduction

The effect of social isolation on health among older people has recently garnered increasing attention from the media and policymakers alike, recognizing it as an emerging public health priority [1,2]. Worldwide, roughly 50% of older people are at risk of social isolation, and about one-third of those aged 60 years and over experience loneliness in later life [3]. In Canada, one in five older adults feels socially isolated [4]. Social isolation is a known risk factor for a wide array of adverse health outcomes among older people, including disability [5], cognitive decline [6,7], depression [8], and mortality [9]. Holt-Lunstad and colleagues [10] posited that the influence of social isolation on health is comparable with that of well-established risk factors, including smoking and obesity.

In recognition of the importance of older adults' social relationships, Berkman and Krishna [11] have developed a comprehensive conceptual model of how social networks impact health, linking social networks, social participation, and social support to health outcomes. Social networks pertain to social interactions and frequency of contact with social ties (i.e., friends, children, extended family, and partner). Emotional social support refers

to the amount of love and caring provided by confident or intimate ties [11]. According to this underpinning theoretical perspective, we use a broad definition of social isolation that encompasses structural and functional aspects. The structural aspect includes social networks and social participation. The functional aspect refers to the quality of relationships or emotional social support. The impact of social isolation on health among older adults may be influenced by other factors associated with increasing age, such as frailty.

Frailty reflects the state of increased vulnerability, deriving from cumulative declines in several physiological systems [12,13]. In a landmark study, Fried and colleagues [13] proposed the "Frailty Phenotype Approach," in which frailty leads to adverse health outcomes, including disability, comorbidity, falls, depression, cognitive impairment, and premature death [12,13]. Prior research has portrayed the link between frequent social contacts and higher social support with a lower level of frailty among older adults [2,14,15]. Researchers have suggested that frequent contact with friends [16–18] and neighbors [18] is more protective against frailty than contact with children. The results of a recent scoping review [2] have highlighted the link between social isolation and frailty; however, discrepancies in research results appeared when examining the effect of social isolation on adverse health outcomes. These discrepancies have led us to the assumption that frailty might moderate the association between social isolation and health outcomes, and therefore, impact this relationship differently based on the frailty status, determining which older adults are most vulnerable to poor health outcomes. Two recent studies [19,20] have investigated the combined effect of social isolation and frailty on health outcomes. The results have shown that frail and isolated older adults have a higher level of falls and mortality compared to older adults without one of these conditions or those with neither of these conditions. Nevertheless, it remains unclear whether or not frailty worsens the effect of social isolation on health. To date, a paucity of research has incorporated three dimensions of social isolation, including social participation, social networks, and social support across different types of social network ties, and little is known about the moderating role of frailty on the pathway from social isolation to health [2]. Hence, the present paper aims to investigate the effects of social isolation on frailty and adverse health outcomes and to explore how this relationship varies according to different levels of frailty. Based on the Berkman theoretical model and prior studies, this research study focuses on the following relationships:

1. Social participation, social networks, and social support across different types of social ties are associated with frailty and adverse health outcomes.
2. Frailty partially moderates the effects of social isolation on poor health outcomes.

From which, we derive the two following hypotheses:

H1. Older adults who have more contact with social ties, receive more social support, and participate more in social activities will be less frail and in better health.

H2. Frail and socially isolated older adults—with fewer social contacts, less social support, and lower participation in social activities—will experience higher levels of disability, cognitive decline, comorbidity, and depression than non-frail isolated older adults. This difference will be reduced among prefrail older adults and will not occur among robust older adults.

2. Materials and Methods

2.1. Data Source and Study Population

For this cross-sectional study, we employed data from the first wave of the FRéLE study (Fragilité, une étude longitudinale de ses expressions/Frailty: A longitudinal study of its expressions), a population-based study of 1643 community-dwelling men and women aged 65 years and over. Participants were recruited from a random sample of the Québec Medicare database in 2010, including a subset of three regions in the province of Québec, Canada, as follows: a metropolitan area (Montréal), a mid-sized city (Sherbrooke), and a small town (Victoriaville). The study population was stratified by gender, age groups, and

study regions. Further details regarding the study sample and data collection procedures have been described in detail elsewhere [21,22]. Ethical approval for the FRéLE study was provided by the Research Ethics Committee of the Jewish General Hospital (12 January 2010). The Research Ethics Committee of the Integrated Health and Social Services University Network for West-Central Montréal (#CODIM-MBM-17-146-10 October 2020) and the Health Research Ethics Board of the Université de Montréal (#17-162-CERES-D-19-08-2020) approved the research protocol of the present study.

2.2. Measures

2.2.1. Independent Variables

Social isolation: Based upon the Berkman theoretical model [11], we measured social isolation through participation in social activities, social networks, and receiving social support from different types of social ties, including friends, children, extended family, and an intimate partner/spouse.

- Social participation was measured by 12 items, including membership in community organizations, participating in religious activities, being a volunteer, playing music, painting, visiting family members or friends, attending a community center, going to restaurants, libraries, shopping malls, cultural and sportive centers, and events [23]. Participants indicated their response on a five-point Likert scale, ranging from 1 (almost every day) to 5 (never). Scores were summed, with greater scores indicating lower social participation. The Cronbach's alpha for this scale was 0.69.
- Social networks were assessed based on the longitudinal International Mobility in Aging Study's (IMIAS) social network scale, which is a validated scale among older populations [24]. We measured social networks using the following four items: (a) the numbers of friends, living children, and extended family (i.e., grandchildren and siblings); (b) the numbers of those social ties that they see at least once a month; (c) that they have a close relationship with; and d) that they speak to by phone at least once a month [24]. The examples of questions are as follows: How many friends do you have? How many friends do you see at least once a month? How many friends do you have a very close relationship with? How many of them do you speak to by phone at least once a month? Social network questions were not asked about partners as they usually had daily contacts. Response options were "never" (code 1), "rarely" (code 2), "sometimes" (code 3), "frequently" (code 4), and "always" (code 5). The items related to each social tie were summed to give a social contact score, with higher scores indicating higher levels of social networks. The Cronbach's alpha internal consistency estimates for friends, children, siblings, and grandchildren were 0.70, 0.87, 0.75, and 0.74, respectively.
- Social support was measured by the following five items of the IMIAS's social support scale: whether participants felt helpful, loved, listened to, important to, and useful to their social ties, including friends, children, extended family, and partner [24]. The examples of questions are as follows: Do you help your friends from time to time? Do you feel that you are loved and appreciated by friends? Do your friends listen to you when you need to talk about your problems or preoccupations? Do you feel that you play an important role in your friends' lives? Do you feel useful to your friends? The scores ranged from 1 (never) to 5 (always), with a higher score indicating a higher level of social support. The Cronbach's alpha internal consistency estimates for friends, children, extended family, and partner were 0.72, 0.72, 0.70, and 0.73, respectively.
- The absence of social ties: We created a binary variable for social ties to indicate the absence of friends, children, grandchildren, siblings, and partner [25,26]. Accordingly, we dichotomized participants' responses to the presence or absence of social ties into two categories: (a) participants with social ties (score 0) (i.e., having friends) and (b) participants without social ties (score 1) (i.e., having no friends).

2.2.2. Moderator Variable

Frailty: Physical frailty was assessed based on Fried's criteria [13], including weight loss, weakness, exhaustion, slowness, and low physical activity levels. Participants were categorized as physically frail in the presence of three or more of these criteria, as prefrail in the presence of one or two of these criteria, and as robust if none of these characteristics were observed. The detailed measurement methods for each component of frailty in the FRéLE study are provided elsewhere [27]. Frailty is described as a syndrome in the Fried phenotype of frailty. Based on the construct validity measured in the FRéLE study, frailty is a marker and determinant of health outcomes [27].

2.2.3. Dependent Variables–Health Outcomes

- Cognitive function was measured by the Montreal Cognitive Assessment (MoCA), which has high test–retest reliability and internal consistency. The total MoCA scores ranged from 0 to 30 points, with higher scores indicating better cognitive function (≥25) [28]. In the FRéLE's sample population, 66 respondents had a lower cognitive status and were excluded from taking the MoCA. We censored them to the left in our analysis [21].
- Comorbidity was evaluated by the Functional Comorbidity Index (FCI), a validated scale that predicts older adults' physical function [29]. Diagnoses include arthritis, osteoporosis, asthma, chronic obstructive pulmonary disease, coronary artery disease, heart failure, myocardial infarction, neurological diseases, stroke, peripheral vascular disease, diabetes, gastroduodenal pathology, depression, anxiety or panic disorders, visual impairment, hearing impairment, degenerative disc disease, obesity, and cancer. In this study, cancer was added, which was one of the comorbidities in the Cardiovascular Health Study conducted by Fried [13]. The presence of each of these conditions gave one point, with the score ranging from 1 to 19 points, with a high FCI score meaning greater comorbidity. The information on the presence of specific disease was ascertained by physician assessment.
- Disability was measured by the Katz [30] Index of Independence in Activities of Daily Living (ADLs) and the Lawton [31] Instrumental Activities of Daily Living (IADLs) index. ADLs include difficulty in nine self-care activities: bathing, grooming, dressing, eating, toileting, walking, getting out of bed, getting up from a chair, and cutting toenails. IADLs comprise difficulty in the nine following activities: using the telephone, using transportation, shopping, doing errands, cooking, light housekeeping, heavy housekeeping, taking medications, and managing finances. We categorized ADLs or IADLs into two groups: (1) able to perform the activity without help (score 0), and (2) unable to perform the activity (score 1). Participants who reported that they were unable to perform any of the activities were considered to have difficulty in performing ADLs or IADLs.
- Depressive symptoms were measured using the 15-item Geriatric Depression Scale (GDS-15) [32]. The scores ranged from 0 to 15, with greater scores suggesting greater depressive symptoms. The Cronbach alpha reliability estimate for the GDS was 0.75.

2.2.4. Covariates

Covariates included demographic and socioeconomic characteristics (i.e., age, sex, education, and annual income) and life habits (i.e., smoking, alcohol consumption, and sleeping disturbance).

2.3. Statistical Analysis

Descriptive statistics were performed to describe the sample including means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. One-way analysis of variance (ANOVA) and chi-square tests were applied to evaluate differences between frailty groups. According to the Hayes's multi-

categorical moderation model [33], we estimated frailty, a multi-categorical moderator, in the regression models by using a system of coding based on $g - 1$ variables, representing the g categories of frailty ($g = 3$). We thus categorized participants into frail (w1) and prefrail (w2) with reference to the non-frail group. We subsequently conducted a "slope difference test" in the moderation model to examine whether the effects of social isolation on health depended on frailty. This can be described as a test of the difference between two conditional effects of social isolation on health for two different values of frailty, including frail (w1) and prefrail (w2). As suggested by McDonough and Walters [26] and Béland and his colleagues [25], we added a binary variable for the absence of children, friends, grandchildren, siblings, and partner to all equations, considering for having or not having social ties. We performed a series of multivariate regression models to examine the effects of social isolation on frailty and health outcomes and to test whether frailty moderated the effects of social isolation on health, using Mplus version 8 [34]. We added simultaneously all dependent variables into the regression equations. In the first step, we examined our first hypothesis by testing the effects of social isolation on frailty and on adverse health outcomes, including disability, chronic diseases, depression, and cognitive decline. We then investigated our second hypothesis via examination of the interaction effects of social isolation and frailty on health outcomes. We assessed whether frailty improved model fit when added to the final model, using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), adjusted BIC, and chi-square tests. All multivariate regression models were controlled for covariates, and 5000 bootstrapped samples/Monte Carlo integration were performed to calculate 95% confidence intervals. The statistical significance was set at $p \leq 0.05$.

3. Results

3.1. Participants' Characteristics

The mean (SD) age of participants was 78.7 (7.9) years, and 50.2% of respondents were women. Almost 12.6% of participants were classified as being frail, with 38.2% being prefrail, and 49.2% robust. The level of frailty increased significantly with age. There was no gender difference between frailty groups. Frail older adults had higher levels of chronic diseases, disability, depressive symptoms, and cognitive impairment than robust ones. They had lower levels of participation in social activities, fewer social networks, and received less support from social ties. They were less educated, less likely to drink alcohol, and to have sleep disturbances. The percentage of participants who had no friends, children, grandchildren, siblings, and partner were 14.8, 14.7, 22.2, 13, and 45.5, respectively. (Table 1).

Table 1. Characteristics of the participants by frailty status.

Variables	Total (*N* = 1643)	Frail (*n* = 207)	Prefrail (*n* = 628)	Robust (*n* = 808)	*p* Value *
Age, mean (SD)	1643	84.7 (6.7)	80.4 (7.5)	75.6 (7.2)	<0.001
Age groups (%)					<0.001
65–74	536	7.7	23.2	46.3	
75–84	555	27.1	34.4	35	
85+	552	65.2	42.4	18.7	
Gender, (%)					0.451
Male	818	46.9	48.9	51.2	
Female	825	53.1	51.1	48.8	
Education, mean (SD)	1643	4.4 (2.7)	5.2 (2.8)	5.7 (2.8)	<0.001
Income, mean (SD)	1643	4.1 (1.7)	4.1 (1.6)	4.2 (2.7)	0.664
Smoking (%)					0.148
Current smoker	122	6.8	8.8	6.6	
Former smoker	797	44.4	46.3	51.2	
Non-smoker	724	48.8	44.9	42.2	
Alcohol (%)					<0.001
Yes	1166	48.3	67	79.8	
No	477	51.7	33	20.2	
Sleeping disturbance (%)					0.005
Yes	677	50.7	41.9	38.2	
No	966	49.3	58.1	61.8	
ADL (%)					<0.001
No difficulty	1223	32.9	69.7	88.7	
Have difficulty	420	67.1	30.3	11.3	
IADL (%)					<0.001
No difficulty	913	6.8	44.6	76.6	
Have difficulty	730	93.2	55.4	23.4	
Depression, mean (SD)	1635	5.7 (2.9)	3.4 (2.6)	1.8 (1.7)	<0.001
Comorbidity, mean (SD)	1642	4.3 (1.9)	3.6 (1.9)	2.5 (1.7)	<0.001
Cognitive function, mean (SD)	1643	19.1 (8.1)	21.9 (6.9)	24.6 (4.2)	<0.001
Social participation, mean (SD)	1643	12.6 (18.8)	17.3 (20.8)	20.7 (20.2)	<0.001
Friends					
Social network, mean (SD)	1643	12.5 (18.7)	17.3 (20.8)	20.7 (20.2)	<0.001
Social support, mean (SD)	1643	11.7 (10.5)	14.7 (9.3)	16.8 (8.2)	<0.001
No friends (%)	243	26.1	16.4	10.6	<0.001
Children					
Social network, mean (SD)	1643	10.3 (10.4)	9.4 (8.4)	8.4 (7.6)	0.005
Social support, mean (SD)	1643	14.5 (10)	16.9 (9.4)	17.3 (9.7)	<0.001
No children (%)	242	18.4	13.9	14.5	0.273
Extended family					
Social network, grandchildren, mean (SD)	1643	12.2 (14.6)	11.1 (12.8)	9.8 (11.9)	0.031
No grandchildren (%)	365	22.7	23.4	22.2	0.429
Social network, siblings, mean (SD)	1643	5.2 (7.9)	7 (7.4)	9.5 (8.4)	<0.001
No siblings (%)	214	25.1	14	9.2	<0.001
Social support family, mean (SD)	1643	15.3 (5.3)	16.9 (4.9)	17.5 (4.8)	<0.001
Partner					
Social support, mean (SD)	1643	5.3 (12.8)	9 (13.5)	11.2 (13.5)	<0.001
No partner (%)	748	59.9	47.3	40.5	<0.001

* *p* < 0.05.

3.2. Social Isolation, Frailty, and Health Outcomes

Table 2 presents the results of the logistic regression of the association between social isolation and frailty. Older adults who engaged less in social activities (β: 0.595; 95% CI: 0.394, 0.789) and received less social support from children (β: −0.393; 95% CI: −0.622, −0.155) and an intimate partner (β: −0.831, 95% CI: −1.507, −0.099) were more likely to be frail. The absence of siblings (β: 0.651, 95% CI: 0.149, 1.149) was significantly associated with a higher level of frailty. However, older adults with an intimate partner (β: −1.617, 95% CI: −3.072, 0.048) and children (β: −1.297; 95% CI: −2.265, −0.245) were more likely to be frail. Our results revealed that social contacts with friends, receiving social support from friends, and having friends were not associated with frailty. Only the lack of social

contact with siblings was significantly related to prefrailty (β: −0.125, 95% CI: −0.208, −0.042).

Table 2. Logistic regression of social isolation on frailty.

Social Isolation Variables	Frailty					
	Frail			Prefrail		
	Coefficient	CI < 0.95	CI > 0.95	Coefficient	CI < 0.95	CI > 0.95
Intercept	**11.111**	**7.922**	**14.156**	**3.077**	**1.210**	**4.979**
Social participation	**0.595**	**0.394**	**0.789**	**0.079**	**−0.022**	**0.177**
Friends						
Social Network	–	–	–	–	–	–
Social Support	–	–	–	–	–	–
No Friends	–	–	–	–	–	–
Children						
Social Network	–	–	–	–	–	–
Social Support	**−0.393**	**−0.622**	**−0.155**	0.043	−0.126	0.218
No children	**−1.279**	**−2.265**	**−0.245**	0.013	−0.725	0.777
Extended Family						
Social Network— Grandchildren	–	–	–	–	–	–
No Grandchildren	–	–	–	–	–	–
Social Network— Siblings	0.028	−0.140	0.180	**−0.125**	**−0.208**	**−0.042**
No siblings	**0.651**	**0.149**	**1149**	−0.285	−0.625	0.045
Social Support— Family	–	–	–	–	–	–
Partner						
Social Support	**−0.831**	**−1.507**	**−0.099**	−0.437	−0.936	0.051
No partner	**−1.617**	**−3.072**	**0.048**	−1.013	−2.120	0.060

Statistically significant associations are highlighted in bold. Non-statistically significant associations are indicated by two hyphens [–]. Coefficient values in plain numbers are the non-statistically significant coefficient of the categories of statistically significant independent variables. All entries are unstandardized regression coefficients. CI = confidence interval.

Table 3 displays the results of the association between social isolation and frailty with adverse health outcomes. It is evident from this table that frailty was associated with all poor health outcomes, including disability, depression, comorbidity, and cognitive function. Less participation in social activities was notably associated with IADLs, depression, and cognitive decline but not with ADLs and comorbidity. Less social support from children was significantly associated with comorbidity and depression. Likewise, those who received less support from extended family were at greater risk for depression. The absence of friends was associated with depression symptoms and cognitive decline. However, perceived social support from friends and social contact with friends were not linked to poor health outcomes. The presence or absence of siblings and grandchildren was unrelated to adverse health outcomes, while the presence of children was linked to depressive symptoms. Although higher levels of contact with grandchildren were related to better cognitive function; social contacts with children, siblings, and friends were not associated with older adults' health. Further, it appears that older people who had more social contact with their grandchildren experienced a higher level of functional dependence in ADLs. Lastly, older adults who perceived less social support from a partner and had an intimate partner were more likely to be depressed or cognitively impaired.

Table 3. Regression of social isolation and frailty on health outcomes.

Variables	ADL			IADL			Chronic Diseases			Depression			Cognitive Function		
	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95
Intercept	**8.143**	**6.238**	**10.049**	**10.054**	**7.923**	**12.184**	**3.132**	**1.895**	**4.170**	**7.293**	**5.310**	**9.275**	**7.312**	**6.351**	**8.274**
Frailty															
Frail	**1.828**	**1.419**	**2.236**	**2.385**	**1.763**	**3.007**	**1.453**	**1.148**	**1.759**	**2.570**	**2.180**	**2.959**	**−0.567**	**−0.766**	**−0.368**
Prefrail	**0.627**	**0.321**	**0.932**	**0.653**	**0.383**	**0.923**	**0.995**	**0.796**	**1.193**	**1.045**	**0.804**	**1.285**	**−0.312**	**−0.440**	**−0.183**
Social participation	–	–	–	**0.249**	**0.122**	**0.376**	–	–	–	**0.320**	**0.217**	**0.422**	-0.075	-0.131	-0.019
Friends															
Social Network	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Social Support	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
No Friends	–	–	–	–	–	–	–	–	–	**0.434**	**0.135**	**0.733**	-0.274	-0.436	−0.113
Children															
Social Network	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Social Support	–	–	–	–	–	–	**−0.155**	**−0.287**	**−0.024**	**−0.363**	**−0.535**	**−0.191**	–	–	–
No Children*	–	–	–	–	–	–	−0.475	−1.071	0.122	**−1.423**	**−2.174**	**−0.672**	–	–	–
Extended Family															
Social Network Grandchildren	**0.171**	**0.050**	**0.292**	–	–	–	–	–	–	–	–	–	**0.057**	**0.001**	**0.113**
No* Grand-children	0.050	−0.326	0.426	–	–	–	–	–	–	–	–	–	0.028	−0.131	0.186
Social Network siblings	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
No siblings	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

Table 3. *Cont.*

Variables	ADL				IADL				Chronic Diseases				Depression				Cognitive Function			
	Coef.	CI < 0.95	CI > 0.95		Coef.	CI < 0.95	CI > 0.95		Coef.	CI < 0.95	CI > 0.95		Coef.	CI < 0.95	CI > 0.95		Coef.	CI < 0.95	CI > 0.95	
Social Support-Family Partner	–	–	–		–	–	–		–	–	–		–0.207	–0.328	–0.086		–	–	–	
Social Support No Partner	–	–	–		–	–	–		–	–	–		–0.983	–1.453	–0.513		0.275	0.028	0.522	
	–	–	–		–	–	–		–	–	–		–2.007	–3.049	–0.965		0.592	0.042	1.141	

Statistically significant associations are highlighted in bold. Non-statistically significant associations are indicated by two hyphens [–]. * These variables should always enter the equations for considering participants without social ties. ADL: activities of daily living; IADL: instrumental activities of daily living.

3.3. The Moderating Effect of Frailty on Social Isolation and Health Outcomes

Table 4 presents the findings for the final model with interaction terms. Compared to the results of Table 3, when we added the interaction models to the previous model, the first-order coefficients for the absence of friends and the presence of a partner were no longer associated with cognitive function. The other first-order associations remained significant. The inclusion of the interaction terms improved the overall multivariate goodness of fit, according to the reduction in the AIC (from 21,811.26 to 21,794.66), and the significance of the chi-square at the 0.05 level (χ^2 = 32.59). Nonetheless, the BIC and adjusted BIC values increased (from 22,259.81 to 22,286.45 and from 21,996.13 to 21,997.36, respectively), indicating that our moderation models may provide little or no extra information.

The moderation regression models in Table 4 demonstrated that the following interactions with frailty were statistically significant: social participation (β: 0.270, 95% CI: 0.071, 0.469), social support from friends (β: 0.420, 95% CI: 0.166, 0.674), having no friends (β: 1.293, 95% CI: 0.281, 2.305) and no siblings (β: 1.758, 95% CI: 0.566, 2.950). Based on the Hayes moderation model, we conducted a "slope difference test" to compare whether the effect of social isolation on health outcomes varied in different values of frailty. As presented in Table 5, the conditional effect tests showed that the negative effect of having no siblings on ADL limitations was significant for frail older adults (β: 1.242, 95% CI: 0.390, 2.094). As predicted, this effect was not apparent for prefrail and robust older adults. The subsequent conditional effects revealed that the effect of non-participation in social activities on depression was stronger for frail (β: 0.404; 95% CI: 0.119, 0.689) and prefrail (β: 0.464; 95% CI: 0.308, 0.621) older adults compared to robust ones (β: 0.194; 95% CI: 0.057, 0.331). Of importance, this effect was significantly diminished for robust older adults. Additionally, higher levels of perceived social support from friends were protective against cognitive decline for frail older adults (β = 0.323; 95% CI: 0.098, 0.547), but this benefit was significantly attenuated for prefrail and non-frail older adults. Lastly, frail older adults without friends had higher levels of cognitive decline compared to prefrail and non-frail older adults (β = 0.804; 95% CI: −0.059, 1.666). In sum, we observed that associations of having no siblings, receiving less social support from friends, and participating less in social activities with ADL limitations, cognitive decline, and depression were higher for frail older adults than for prefrail and robust ones.

Table 4. Social isolation and frailty on health outcomes with interactions.

Variables	ADL			IADL			Chronic Diseases			Depression			Cognitive Function		
	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95
Intercept	**8.151**	**6.224**	**10.077**	**10.053**	**7.923**	**12.184**	**3.131**	**1.895**	**4.368**	**8.337**	**6.221**	**10.453**	**7.713**	**6.627**	**8.800**
Frailty															
Frail	**1.507**	**1.059**	**1.954**	**2.385**	**1.763**	**3.007**	**1.453**	**1.148**	**1.759**	**2.566**	**2.121**	**3.011**	**−0.702**	**−0.945**	**−0.459**
Prefrail	**0.602**	**0.281**	**0.924**	**0.653**	**0.383**	**0.923**	**0.995**	**0.796**	**1.193**	**1.074**	**0.833**	**1.316**	**−0.361**	**−0.533**	**−0.190**
Social participation	–	–	–	**0.249**	**0.122**	**0.376**	–	–	–	**0.194**	**0.057**	**0.331**	**−0.072**	**−0.129**	**−0.016**
Friends															
Social Network	–	–	–	–	–	–	–	–	–	–	–	–	−0.097	−0.221	0.026
Social Support	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
No Friends	–	–	–	–	–	–	–	–	–	0.415	0.117	0.714	−0.489	−1.026	0.048
Children															
Social Network	–	–	–	–	–	–	−0.155	−0.287	−0.024	−0.361	−0.533	−0.189	–	–	–
Social Support	–	–	–	–	–	–	−0.474	−1.071	0.122	−1.408	−2.157	−0.658	–	–	–
No Children*	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Extended Family															
Social Network Grandchildren	0.169	0.048	0.291	–	–	–	–	–	–	–	–	–	0.061	0.005	0.117
No Grandchildren	0.051	−0.329	0.431	–	–	–	–	–	–	–	–	–	0.032	−0.126	0.190
Social Network sibling	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
No siblings	−0.516	−1.354	0.322	–	–	–	–	–	–	–	–	–	–	–	–
Social Support-Family	–	–	–	–	–	–	–	–	–	−0.207	−0.328	−0.087	–	–	–

Table 4. *Cont.*

Variables	ADL Coef.	CI < 0.95	CI > 0.95	IADL Coef.	CI < 0.95	CI > 0.95	Chronic Diseases Coef.	CI < 0.95	CI > 0.95	Depression Coef.	CI < 0.95	CI > 0.95	Cognitive Function Coef.	CI < 0.95	CI > 0.95
Partner															
Social Support															
No	–	–	–	–	–	–	–	–	–	**−0.998**	**−1.468**	**−0.529**	**0.252**	**0.003**	**0.501**
Partner	–	–	–	–	–	–	–	–	–	**−2.030**	**−3.071**	**−0.990**	0.545	−0.009	1.100
Interactions															
Social Participation															
Frail	–	–	–	–	–	–	–	–	–	0.209	−0.102	0.520	–	–	–
Prefrail	–	–	–	–	–	–	–	–	–	**0.270**	**0.071**	**0.469**	–	–	–
No Siblings															
Frail	**1.758**	**0.566**	**2.950**	–	–	–	–	–	–	–	–	–	–	–	–
Prefrail	0.305	−0.677	1.287	–	–	–	–	–	–	–	–	–	–	–	–
Social Support – Friends															
Frail	–	–	–	–	–	–	–	–	–	–	–	–	**0.420**	**0.166**	**0.674**
Prefrail	–	–	–	–	–	–	–	–	–	–	–	–	0.138	−0.042	0.317
No Friends															
Frail	–	–	–	–	–	–	–	–	–	–	–	–	**1.293**	**0.281**	**2.305**
Prefrail	–	–	–	–	–	–	–	–	–	–	–	–	0.239	−0.527	1.006
Summary of Model fits	LL			Parameters			AIC			BIC			Adjusted BIC		
Model without interaction (LLh0)	−10,822.63			83			21,811.26			22,259.81			21,996.13		
Model with interaction (LLh1)	−10,806.33			91			21,794.66			22,286.45			21,997.36		
−2 (LLh0 −LLh1)	32.59			8			16.6			−26.64			−1.23		

Statistically significant associations are highlighted in bold. Non-statistically significant associations are indicated by two hyphens [–]. Coefficient values in plain numbers are the non-statistically significant coefficient of the categories of statistically significant independent variables. LL: log likelihood; AIC: Akaike's Information Criterion; BIC: Bayesian Information Criterion.

Table 5. Conditional effects of social isolation on health outcomes at different values of frailty.

Social isolation indicators	Moderator levels	ADL			Depression			Cognitive Function		
		Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95	Coef.	CI < 0.95	CI > 0.95
Social Participation	Frail	–	–	–	**0.404**	**0.119**	**0.689**	–	–	–
	Prefrail	–	–	–	**0.464**	**0.308**	**0.621**	–	–	–
	Robust	–	–	–	**0.194**	**0.057**	**0.331**	–	–	–
Social support-Friends	Frail	–	–	–	–	–	–	**0.323**	**0.098**	**0.547**
	Prefrail	–	–	–	–	–	–	0.040	–0.095	0.176
	Robust	–	–	–	–	–	–	–0.097	–0.221	0.026
No Friends	Frail	–	–	–	–	–	–	0.804	–0.059	1666
	Prefrail	–	–	–	–	–	–	–0.250	–0.803	0.303
	Robust	–	–	–	–	–	–	–0.489	–1.026	0.048
No Siblings	Frail	**1242**	**0.390**	**2.094**	–	–	–	–	–	–
	Prefrail	–0.211	–0.733	0.311	–	–	–	–	–	–
	Robust	–0.516	–1.354	0.322	–	–	–	–	–	–

Statistically significant associations are highlighted in bold. Non-statistically significant associations are indicated by two hyphens [–]. Coefficient values in plain numbers are the non-statistically significant coefficient of the categories of statistically significant independent variables.

4. Discussion

Drawing on the Berkman theoretical model of social relationships, we examined the interplay between social isolation, frailty, and health outcomes. Our results partially support our first hypothesis that older adults who engage in leisure activities, have social contacts with siblings, and perceive support from children and an intimate partner are less frail. The current study confirms the prior evidence that frailty is associated with adverse health outcomes [2]. Apart from frailty, our results indicate that actively engaging in social activities may alleviate the impact of IADL limitations, depressive symptoms, and cognitive decline among older adults. This result is consistent with evidence from previous longitudinal research [25,35] and also, is in line with the World Health Organization (WHO) framework on healthy aging [36], emphasizing the importance of social participation in later life, which may, in turn, reinforce the health of older people.

We found that older adults who perceived a shortfall in social support from children and an intimate partner were at greater risk of depression, comorbidity, and cognitive decline. The presence of an intimate partner and children and a relative lack of friends resulted in a higher likelihood of cognitive decline and depression. In this vein, our findings shed further light on the impact of intimate and kin relations on health. This interpretation is in line with previous research that emphasizes children have salient roles on the health status of Spanish and Latin American older adults [37,38]. Evidence in China and Canada yields the beneficial impact of social interactions with friends on the health of older people [37,39]. Relatedly, the findings on the importance of strong social ties for health in old age are in accord with the Berkman theory, illustrating that social ties provide essential emotional and instrumental support at times of illness [40].

Concerning social connections with different types of social ties, our results revealed that only social contacts with grandchildren were related to health outcomes. In this view, social connection with grandchildren was positively linked to better cognitive function. Contrary to expectations, our results showed that more contacts with grandchildren (a continuous variable) were associated with higher levels of independence in ADLs. As suggested by Seeman and colleagues [41], we created a binary variable, comparing those who had 0–2 grandchildren with those who had three or more grandchildren to examine whether the extreme values or gender differences were the cause of this inverse association. We ran a separate univariate analysis for males and females, entering the foregoing binary variable. The results revealed that men who had more contact with grandchildren were less likely to have ADL dependency ($\beta = -0.453$; 95% CI: 0.417, 0.969), albeit this relationship was not significant among women. This association is explained by the fact that male older adults had less functional limitations and more contact with grandchildren compared to female older adults in our sample. This binary variable was no longer significant after adjustment for covariates. The continuous variable remained significant in both univariate and multivariate analyses with a stronger association between social networks and less risk of limitations in ADL in men than in women. The results of the Survey of Health, Aging, and Retirement in Europe (SHARE) study [42] lend support to the sex difference in ADL among older adults in Northern, Eastern, and Western Europe, indicating that female older adults have a higher risk of ADL dependence than male older adults. This relationship needs further investigation in other datasets.

Taken together, our findings suggest that social isolation is linked to depression symptoms and cognitive decline rather than other adverse health outcomes in community-dwelling older adults. This result coheres with a population-based intervention in England [43], indicating that social isolation risk is related to depression and memory decline but not multiple chronic diseases and difficulties in performing ADLs and IADLs. Another longitudinal study from England [44] reached the conclusion that neither structural nor functional aspect of social relationship is associated with ADL limitations over six years. Evidence from several reviews on social isolation and health demonstrated that the most researched outcomes in physical health are mortality and cardiovascular diseases [1,45,46].

In this regard, a rapid review of 40 systematic reviews [46] found strong and consistent evidence for the association between social isolation and cardiovascular disease and depression, albeit evidence is less strong for other physical health conditions. Interventions and research studies on depression and cardiovascular diseases highlighted the absence of social support as an important risk factor for poor health outcomes, emphasizing the pivotal role of the quality of relationships [1,45].

Overall, the weak or moderate association between social isolation, frailty, and poor health outcomes is consistent with the available literature, including a scoping review of 26 studies [2], where each social relation promotes health through different mechanisms. According to this review, few studies support the impacts of both social isolation and frailty on adverse health outcomes.

Our second hypothesis pertains to the potential moderating role of frailty on the pathway from social isolation and health. Importantly, our results confirm our hypothesis that the impact of social isolation on adverse health outcomes differs depending on the frailty status. More specifically, our results revealed that the associations of receiving less support from friends and participating less in social activities with mental and cognitive impairment were stronger in frail than in prefrail and robust older adults. Hence, social isolation does not seem to promote the functional and mental health status of robust older adults but may reduce health decline in frail and prefrail older adults. Based on the recent scoping review [2], only one longitudinal study [47] has investigated the interaction effect of receiving and providing social support and frailty on mortality. The results revealed a lower risk of mortality among robust and prefrail older adults who provided social support to their family ties but not among those who received family support [2,47].

This study was cross-sectional, which limits our understanding of causative relationships between social isolation, frailty, and health outcomes. Future studies with longitudinal methods are warranted to capture developmental changes in social isolation and frailty and their effects on health outcomes over time. In particular, more research is needed to further explore the direction of the association between contact with family members and the likelihood of ADL limitations. Despite these limitations, the present study extends the social isolation domain, focusing on frailty. The notable strengths of the study include the large and population-based sample; the multicenter nature of the study; and the use of validated scales for social isolation, frailty, and health outcomes. To the best of our knowledge, this is the first attempt to focus on frailty as a moderator on the pathway from social isolation to physical and mental health, incorporating the multidimensional measure of social isolation across different types of social ties.

From a public health standpoint, the results of our study elucidate the pivotal role of kin and intimate relationships in old age, and particularly their impacts on mental and cognitive health. In this respect, several public health policies and programs implicitly incorporate social connectedness as mechanisms for enhancing older population health and well-being across the globe. As such, social participation is one of the eight domains of the Global Network of Age-Friendly Cities and Communities (AFCCs) led by the WHO in 2007. The WHO decade of Healthy Aging (2020–2030) is another initiative to promote health and well-being in later life. Several models have been developed in the United States, Canada, and Europe based on the political priorities and needs of older adults. For example, the village models of age-friendly communities [48] in the U.S. foster neighborhood social ties. In Québec, age-friendly cities [49] focus mainly on the social participation of older adults in communities, addressing social determinants of health. Despite these laudable efforts on enhancing social interrelatedness in the communities, there is scant evidence on the effectiveness of these actions and their impacts on the physical or mental health of older adults. Additionally, the current age-friendly policies focus on the physical environment but not so far on the social or mental environment [50]. At this juncture, our results underscore that social isolation influences older adults' mental and cognitive health, though its association with physical health is notably non-statistically significant except in some limited instances. Therefore, healthcare policies and public health initiatives could

benefit from considering explicitly these results in efforts aimed at reducing mental health problems and cognitive decline among vulnerable older populations. In particular, the results of our study are highly relevant for health policymakers in the context of the current coronavirus disease 2019 (COVID-19) pandemic, in which frail older adults are mostly affected by restriction measures imposed by governments all over the world. Ultimately, strategies to prevent or lessen the long-term effect of social isolation on older adults' mental health are of paramount importance post-pandemically.

5. Conclusions

In conclusion, this research study is a novel contribution to the empirical literature on social gerontology by highlighting the key roles of social ties, perceived support, and engagement in social activities on promoting mental health in later life, particularly among frail older adults.

References

1. Holt-Lunstad, J.; Robles, T.F.; Sbarra, D.A. Advancing social connection as a public health priority in the United States. *Am. Psychol.* **2017**, *72*, 517–530. [CrossRef] [PubMed]
2. Mehrabi, F.; Béland, F. Effects of social isolation, loneliness and frailty on health outcomes and their possible mediators and moderators in community-dwelling older adults: A scoping review. *Arch. Gerontol. Geriatr.* **2020**, *90*, 104119. [CrossRef] [PubMed]
3. Landeiro, F.; Barrows, P.; Musson, E.N.; Gray, A.M.; Leal, J. Reducing social isolation and loneliness in older people: A systematic review protocol. *BMJ Open* **2017**, *7*, e013778. [CrossRef]
4. Gilmour, H. Social participation and the health and well-being of Canadian seniors. *Health Rep.* **2012**, *23*, 23–32.
5. Janke, M.C.; Payne, L.L.; Van Puymbroeck, M. The role of informal and formal leisure activities in the disablement process. *Int. J. Aging Hum. Dev.* **2008**, *67*, 231–257. [CrossRef]
6. Okura, M.; Ogita, M.; Yamamoto, M.; Nakai, T.; Numata, T.; Arai, H. The relationship of community activities with cognitive impairment and depressive mood independent of mobility disorder in Japanese older adults. *Arch. Gerontol. Geriatr.* **2017**, *70*, 54–61. [CrossRef]
7. Li, C.-L.; Hsu, H.-C. Cognitive function and associated factors among older people in Taiwan: Age and sex differences. *Arch. Gerontol. Geriatr.* **2015**, *60*, 196–200. [CrossRef]
8. Santini, Z.I.; Jose, P.E.; Cornwell, E.Y.; Koyanagi, A.; Nielsen, L.; Hinrichsen, C.; Meilstrup, C.; Madsen, K.R.; Koushede, V. Social disconnectedness, perceived isolation, and symptoms of depression and anxiety among older Americans (NSHAP): A longitudinal mediation analysis. *Lancet Public Health* **2020**, *5*, e62–e70. [CrossRef]
9. Holt-Lunstad, J.; Smith, T.B.; Baker, M.; Harris, T.; Stephenson, D. Loneliness and social isolation as risk factors for mortality: A meta-analytic review. *Perspect. Psychol. Sci.* **2015**, *10*, 227–237. [CrossRef]

10. Holt-Lunstad, J.; Smith, T.B.; Layton, J.B. Social relationships and mortality risk: A Meta-analytic review. *PLoS Med.* **2010**, *7*, e1000316. [CrossRef] [PubMed]
11. Berkman, L.F.; Krishna, A. Social network epidemiology. In *Social Epidemiology*, 2nd ed.; Berkman, L.F., Kawachi, I., Glymour, M.M., Eds.; Oxford University Press: New York, NY, USA, 2014; pp. 234–289.
12. Clegg, A.; Young, J.; Iliffe, S.; Rikkert, M.O.; Rockwood, K. Frailty in elderly people. *Lancet* **2013**, *381*, 752–762. [CrossRef]
13. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. Ser. A* **2001**, *56*, M146–M156. [CrossRef] [PubMed]
14. Peek, M.K.; Howrey, B.T.; Ternent, R.S.; Ray, L.A.; Ottenbacher, K.J. Social support, stressors, and frailty among older Mexican American adults. *Journals Gerontol. Ser. B* **2012**, *67*, 755–764. [CrossRef]
15. Vaingankar, J.A.; Chong, S.A.; Abdin, E.; Picco, L.; Chua, B.Y.; Shafie, S.; Ong, H.L.; Chang, S.; Seow, E.; Heng, D. Prevalence of frailty and its association with sociodemographic and clinical characteristics, and resource utilization in a population of Singaporean older adults. *Geriatr. Gerontol. Int.* **2017**, *17*, 1444–1454. [CrossRef]
16. Chon, D.; Lee, Y.; Kim, J.; Lee, K.-E. The association between frequency of social contact and frailty in older people: Korean Frailty and Aging Cohort Study (KFACS). *J. Korean Med. Sci.* **2018**, *33*, e332. [CrossRef]
17. Berglund, H.; Hasson, H.; Wilhelmson, K.; Dunér, A.; Dahlin-Ivanoff, S. The impact of socioeconomic conditions, social networks, and health on frail older people's life satisfaction: A cross-sectional study. *Health Psychol. Res.* **2016**, *4*, 5578. [CrossRef] [PubMed]
18. Schnittger, R.I.; Walsh, C.; Casey, A.-M.; Wherton, J.; McHugh, J.E.; Lawlor, B. Psychological distress as a key component of psychosocial functioning in community-dwelling older people. *Aging Ment. Health* **2012**, *16*, 199–207. [CrossRef]
19. Hayashi, T.; Umegaki, H.; Makino, T.; Huang, C.; Inoue, A.; Shimada, H.; Kuzuya, M. Combined impact of physical frailty and social isolation on rate of falls in older adults. *J. Nutr. Health Aging* **2020**, *24*, 312–318. [CrossRef]
20. Hoogendijk, E.O.; Smit, A.P.; Van Dam, C.; Schuster, N.A.; De Breij, S.; Holwerda, T.J.; Huisman, M.; Dent, E.; Andrew, M.K. Frailty combined with loneliness or social isolation: An elevated risk for mortality in later life. *J. Am. Geriatr. Soc.* **2020**, *68*, 2587–2593. [CrossRef]
21. Béland, F.; Julien, D.; Bier, N.; Desrosiers, J.; Kergoat, M.-J.; Demers, L. Association between cognitive function and life-space mobility in older adults: Results from the FRéLE longitudinal study. *BMC Geriatr.* **2018**, *18*, 227. [CrossRef]
22. Provencher, V.; Béland, F.; Demers, L.; Desrosiers, J.; Bier, N.; Ávila-Funes, J.A.; Galand, C.; Julien, D.; Fletcher, J.D.; Trottier, L.; et al. Are frailty components associated with disability in specific activities of daily living in community-dwelling older adults? A multicenter Canadian study. *Arch. Gerontol. Geriatr.* **2017**, *73*, 187–194. [CrossRef]
23. Statistics Canada. *Canadian Community Health Survey (CCHS)- Healthy Aging Questionnaire (2008–2009)*; Statistics Canada: Ottawa, ON, Canada, 2010; pp. 117–120.
24. Ahmed, T.; Belanger, E.; Vafaei, A.; Koné, G.K.; Alvarado, B.; Beland, F.; Zunzunegui, M.V. Validation of a social networks and support measurement tool for use in international aging research: The International Mobility in Aging Study. *J. Cross Cult. Gerontol.* **2018**, *33*, 101–120. [CrossRef] [PubMed]
25. Béland, F.; Zunzunegui, M.-V.; Alvarado, B.; Otero, A.; Del Ser, T. Trajectories of cognitive decline and social relations. *J. Gerontol. Ser. B* **2005**, *60*, P320–P330. [CrossRef]
26. McDonough, P.; Walters, V. Gender and health: Reassessing patterns and explanations. *Soc. Sci. Med.* **2001**, *52*, 547–559. [CrossRef]
27. Béland, F.; Julien, D.; Wolfson, C.; Bergman, H.; Gaudreau, P.; Galand, C.; Fletcher, J.; Zunzunegui, M.-V.; Shatenstein, B.; Kergoat, M.-J.; et al. Revisiting the hypothesis of syndromic frailty: A cross-sectional study of the structural validity of the frailty phenotype. *BMC Geriatr.* **2020**, *20*, 1–13. [CrossRef] [PubMed]
28. Nasreddine, Z.S.; Phillips, N.A.; Bedirian, V.; Charbonneau, S.; Whitehead, V.; Collin, I.; Cummings, J.L.; Chertkow, H. The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *J. Am. Geriatr. Soc.* **2005**, *53*, 695–699. [CrossRef] [PubMed]
29. Groll, D.L.; To, T.; Bombardier, C.; Wright, J.G. The development of a comorbidity index with physical function as the outcome. *J. Clin. Epidemiol.* **2005**, *58*, 595–602. [CrossRef]
30. Katz, S.; Ford, A.B.; Moskowitz, R.W.; Jackson, B.A.; Jaffe, M.W.; White, K.L. Studies of illness in the aged—The index of ADL: A standardized measure of biological and psychosocial functions. *JAMA* **1963**, *185*, 914–919. [CrossRef]
31. Lawton, M.P.; Brody, E.M. Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist* **1969**, *9*, 179–186. [CrossRef]
32. Yesavage, J.A.; Sheikh, J.I. 9/Geriatric Depression Scale (GDS)—Recent evidence and development of a shorter version. *Clin. Gerontol.* **1986**, *5*, 165–173. [CrossRef]
33. Hayes, A.F. *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*; Guilford Press: New York, NY, USA, 2017.
34. Muthén, L.; Muthén, B. *Mplus User's Guide: Statistical Analysis with Latent Variables, User's Guide*, 8th ed.; Muthén & Muthén: Los Angeles, CA, USA, 2017.
35. Wang, R.; Feng, Z.; Liu, Y.; Lu, Y. Relationship between neighbourhood social participation and depression among older adults: A longitudinal study in China. *Health Soc. Care Community* **2019**, *28*, 247–259. [CrossRef]
36. World Health Organization. *Global Strategy and Action Plan on Ageing and Health*; WHO: Geneva, Switzerland, 2017.

37. Belanger, E.; Ahmed, T.; Vafaei, A.; Curcio, C.L.; Phillips, S.P.; Zunzunegui, M.V. Sources of social support associated with health and quality of life: A cross-sectional study among Canadian and Latin American older adults. *BMJ Open* **2016**, *6*, e011503. [CrossRef] [PubMed]

38. Zunzunegui, M.-V.; Béland, F.; Sanchez, M.-T.; Otero, A. Longevity and relationships with children: The importance of the parental role. *BMC Public Health* **2009**, *9*, 351. [CrossRef]

39. Wang, B.; He, P.; Dong, B. Associations between social networks, social contacts, and cognitive function among Chinese nonagenarians/centenarians. *Arch. Gerontol. Geriatr.* **2015**, *60*, 522–527. [CrossRef] [PubMed]

40. Berkman, L.F.; Glass, T.; Brissette, I.; Seeman, T.E. From social integration to health: Durkheim in the new millennium. *Soc. Sci. Med.* **2000**, *51*, 843–857. [CrossRef]

41. Seeman, T.E.; Bruce, M.L.; McAvay, G.J. Social network characteristics and onset of adl disability: MacArthur studies of successful aging. *J. Gerontol. Ser. B* **1996**, *51*, S191–S200. [CrossRef]

42. Scheel-Hincke, L.L.; Möller, S.; Lindahl-Jacobsen, R.; Jeune, B.; Ahrenfeldt, L.J. Cross-national comparison of sex differences in ADL and IADL in Europe: Findings from SHARE. *Eur. J. Ageing* **2020**, *17*, 69–79. [CrossRef]

43. Iliffe, S.; Kharicha, K.; Harari, D.; Swift, C.; Gillmann, G.; Stuck, A.E. Health risk appraisal in older people 2: The implications for clinicians and commissioners of social isolation risk in older people. *Br. J. Gen. Pract.* **2007**, *57*, 277–282.

44. Shankar, A.; McMunn, A.; Demakakos, P.; Hamer, M.; Steptoe, A. Social isolation and loneliness: Prospective associations with functional status in older adults. *Health Psychol.* **2017**, *36*, 179–187. [CrossRef]

45. Courtin, E.; Knapp, M. Social isolation, loneliness and health in old age: A scoping review. *Health Soc. Care Community* **2017**, *25*, 799–812. [CrossRef]

46. Leigh-Hunt, N.; Bagguley, D.; Bash, K.; Turner, V.; Turnbull, S.; Valtorta, N.; Caan, W. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health* **2017**, *152*, 157–171. [CrossRef] [PubMed]

47. Liao, M.-Y.; Yeh, C.-J.; Liao, C.-C.; Lee, S.-H.; Yang, S.-F.; Lee, M.-C. Effects of receiving and providing family support on mortality in non-frail, pre-frail and frail older adults in Taiwan: A 12-year follow-up longitudinal study. *Eur. Geriatr. Med.* **2018**, *9*, 679–685. [CrossRef]

48. Scharlach, A.E.; Davitt, J.K.; Lehning, A.J.; Greenfield, E.A.; Graham, C. Does the village model help to foster age-friendly communities? *J. Aging Soc. Policy* **2014**, *26*, 181–196. [CrossRef] [PubMed]

49. Garon, S.; Paris, M.; Beaulieu, M.; Veil, A.; Laliberté, A. Collaborative partnership in age-friendly cities: Two case studies from Quebec, Canada. *J. Aging Soc. Policy* **2014**, *26*, 73–87. [CrossRef]

50. Duppen, D.; Lambotte, D.; Dury, S.; Smetcoren, A.-S.; Pan, H.; De Donder, L.; D-SCOPE Consortium. Social participation in the daily lives of frail older adults: Types of participation and influencing factors. *J. Gerontol. Ser. B* **2019**, *75*, 2062–2071. [CrossRef]

Article

Predicting the Severity of Parkinson's Disease Dementia by Assessing the Neuropsychiatric Symptoms with an SVM Regression Model

Haewon Byeon

Department of Medical Big Data, College of AI Convergence, Inje University,
Gimhae 50834, Gyeonsangnamdo, Korea; bhwpuma@naver.com; Tel.: +82-10-7404-6969

Abstract: In this study, we measured the convergence rate using the mean-squared error (MSE) of the standardized neuropsychological test to determine the severity of Parkinson's disease dementia (PDD), which is based on support vector machine (SVM) regression (SVR) and present baseline data in order to develop a model to predict the severity of PDD. We analyzed 328 individuals with PDD who were 60 years or older. To identify the SVR with the best prediction power, we compared the classification performance (convergence rate) of eight SVR models (Eps-SVR and Nu-SVR with four kernel functions (a radial basis function (RBF), linear algorithm, polynomial algorithm, and sigmoid)). Among the eight models, the MSE of Nu-SVR-RBF was the lowest (0.078), with the highest convergence rate, whereas the MSE of Eps-SVR-sigmoid was 0.110, with the lowest convergence rate. The results of this study imply that this approach could be useful for measuring the severity of dementia by comprehensively examining axial atypical features, the Korean instrumental activities of daily living (K-IADL), changes in rapid eye movement sleep behavior disorder (RBD), etc. for optimal intervention and caring of the elderly living alone or patients with PDD residing in medically vulnerable areas.

Keywords: Parkinson's disease dementia; instrumental activities of daily living; clinical dementia rating; convergence rate; neuropsychological tests; neuropsychiatric symptoms

1. Introduction

As the survival rate of patients with Parkinson's disease (PD) has increased and many studies on dementia have been conducted, researchers have become more interested in Parkinson's disease dementia (PDD). Dementia is a common symptom of patients with PD: As PD progresses, seven out of 10 patients with PD suffer from dementia [1,2]. Moreover, compared to PD without dementia, patients with it have a lower survival rate, a higher risk of experiencing depression [3], and are less responsive to treatment with levodopa (L-DOPA) [4]. Since patients with PDD are more susceptible to the side effects of drugs and their functions deteriorate faster than those with PD without dementia, they require a specialist medical attention [5].

Despite the importance of detecting PDD as soon as possible, it is difficult to accurately screen for it due to three reasons. First, it is difficult to determine whether a decrease in instrumental activities of daily living (IADL), an essential item in the diagnosis of dementia, is caused by a cognitive impairment due to dementia or motor dysfunction due to PD [6]. Second, it is difficult to distinguish whether hallucinations or delusions, the main symptom of dementia, are due to the side effects from the drug being administered or the symptoms of PDD. Third, it is difficult to diagnose PDD in the early stages since patients with PD can have autonomic disturbances, emotional disorders, and/or cognitive impairment [4]. Therefore, selecting a highly sensitive screening test that can accurately discriminate PDD-induced cognitive decline is an important issue that medical professionals are interested in [7].

Meanwhile, evaluating the severity of dementia is critical since only once it has been accurately diagnosed can a physician select the appropriate drugs [8], develop a treatment plan [8], explain the patient's current condition and offer appropriate caregiving guidelines [9], and discuss prognosis. The clinical dementia rating (CDR) scale [10] has been widely used worldwide as an effective tool for determining the severity of dementia. Although the CDR scale is a commonly-used gold standard, it has several limitations [11]: (1) It takes a lot of time and effort since it must be evaluated through an interview with the guardian; (2) since the questions (items) used to measure the grade (severity of dementia) are inclusive (over a wide range), it is difficult for the medical professional to obtain all of the relevant information about a patient by asking the caregiver to answer these questions; (3) ambiguity can occur since some of the items are too abstract and in some cases, medical professionals cannot judge the progression of dementia; and (4) it does not reflect fine changes in the patient's condition. Most of all, evaluating the CDR scale results requires a specialist, but elderly people living alone or in medically vulnerable areas often have poor access to medical care [5]. Consequently, if it is possible to predict the CDR scale result for a moderate level of PDD solely using the results of a standardized neuropsychological examination without an interview with the guardian, it will help greatly in identifying the severity of dementia in individuals from medically vulnerable groups such as the elderly living alone.

It has been reported that the severity of dementia is related to demographic factors such as age, the duration of the illness, depression, and motor symptoms such as akinetic-rigidity, and postural instability-gait disturbance, in addition to the neuropsychological profile [12,13]. Therefore, developing a data-mining model that includes these various confounding variables is of great interest and usefulness, and recently, support vector machines (SVMs) have been widely used to explore complex risk factors of diseases [14,15]. The approach has the advantages of less overfitting of probability compared to using decision trees [16] and classifying nonlinear data is possible [17]. Therefore, SVM regression (SVR) was applied to determine the severity of PDD by identifying the convergence rate based on the mean-squared error (MSE) of the standardized neuropsychological test, and baseline data were used to develop a model to predict the severity of PDD.

2. Materials and Methods

2.1. Data Source

Secondary data were used in the study comprising "Patients with Parkinson's Disease Dementia Clinical Epidemiology Data (PDE) registry" conducted by the National Biobank of Korea and the Korean Centers for Disease Control and Prevention (K-CDC). The PDE registry comprises nationwide clinical data collected under the supervision of the K-CDC from 14 university hospitals nationwide including those in Seoul and Busan from January to December 2015. The PDE registry includes demographic factors, disease history, health habits, neuropsychological tests, Parkinson's disease-related motor symptoms, and sleep behavior disorder (SBD) test results (see Byeon et al. [18] for more details). This study was approved by the Research Ethics Review Committee of the National Biobank of Korea and K-CDC (no. KBN-2019-1327; no. KBN-2019-005).

PDD has been designated as idiopathic Parkinson's disease according to the diagnostic criteria of the United Kingdom Parkinson's Disease Society Brain Bank [19]. The diagnostic criteria for probable PDD have been suggested by the Bubois et al. [20]. When causes of cognitive impairment other than PD (e.g., hydrocephalus and vascular Parkinsonism) were found in magnetic resonance imaging (MRI) scans, the subject was excluded from the study. Among 335 patients with PDD who were 60 years or older, we excluded seven patients with missing data (non-response or discontinued testing) from the CDR scale data measured by a neurologist and analyzed 328 patients with PDD. Explanatory variables included rapid eye movement (REM), SBDs, PD-related motor signs, demographic variables, disease history, a family history of PD, the Schwab and England Activities of Daily Living (ADL) score [21], the Korean Montreal Cognitive Assessment (K-MoCA) score [22], the Korean

Mini-Mental State Examination (K-MMSE) score [23], the Korean IADL (K-IADL) score [24], the Unified Parkinson's Disease Rating Scale (UPDRS) motor score [25], the UPDRS total score [26], and Hoehn and Yahr (H&Y) stage [27].

2.2. Methods

The SVM was operated by finding the most optimal hyperplane that separates data into several classes by applying the maximum margin [28]. For a set of training data where x_n is a multivariate set of N observations with observed response values y_n $\{(x_i y_i)\}_i^n$, we apply the regression function $f(x)$ to optimally approximate the given y value as follows:

$$f(x) = \langle w, x \rangle b; w \in X, \ b \in R, \tag{1}$$

w and b in Equation (1) can be optimized via the following transformation:

$$\text{minimize } \frac{1}{2} \|w\|^2 + C \sum_{i=1}^{l} (\xi_i + \xi_i^*) \text{subject to} \begin{cases} y_i - \langle w, x_i \rangle + b \leq \epsilon + \xi_i \\ \langle w, x_i \rangle - b - y_i \leq \epsilon + \xi_i + \xi_i^* \\ \xi_i, \xi_i^* \geq 0 \end{cases}, \tag{2}$$

where C is a compromise between the empirical error and the general term ($\frac{1}{2} \|w\|^2$) and ε is an epsilon tube indicating the tolerance of the error. A general constant is used for empirical error estimation and an increase in C indicates an increase in the relative weight of the empirical error within the total error. Moreover, if ε is too small, it induces overfitting of the regression model.

The regression function in Equation (1) can be expressed by using Lagrangian multipliers and optimal constraints as follows:

$$f(x, a_i, a_i^*) = \sum_{i=1}^{l} (\alpha_i - \alpha_i^*) K(x, x_i) + b, \tag{3}$$

where $K(x, \ x_i)$ is a kernel function. Equation (3) effectively evaluates the nonlinear interrelationship between samples of the training data by expressing them in an internal form [28].

We used the R statistical package (version 4.0.1) for all analyses. To identify the SVR with the best prediction power, we compared the classification performance (convergence rate) of eight SVR models (epsilon-SVR (Eps-SVR) and Nu-SVR with four kernel functions (a radial basis function (RBF), linear algorithm, polynomial algorithm, and sigmoid)). At this time, the convergence rate was determined using the MSE, a loss function based on the mean of the squared error (residual) between the predicted value and the actual value as follows:

$$\frac{1}{n} \sum_{i=1}^{n} (y_i - t_i)^2. \tag{4}$$

This measure allows users to evaluate the similarity between the predicted and actual values to assess the predictive power of the regression model: A smaller value indicates a more accurate model.

3. Results

3.1. The General Characteristics of the Subjects

The results of the descriptive analysis on the general characteristics of the 328 PD subjects show that their mean age was 71.9 years old (standard deviation (SD) = 6.1), the mean education period was 7.2 years (SD = 5.0), and the mean age at the time of the initial PD diagnosis was 70.5 years (SD = 6.2). The results also indicate that 75.9%, 17.7%, 4.3%, and 2.1% of the subjects had a CDR of 0.5 or less, 1.0, 2.0, and 3.0 or higher, respectively. Density plots showing the distribution of the subjects' neuropsychological test results are presented in Figure 1.
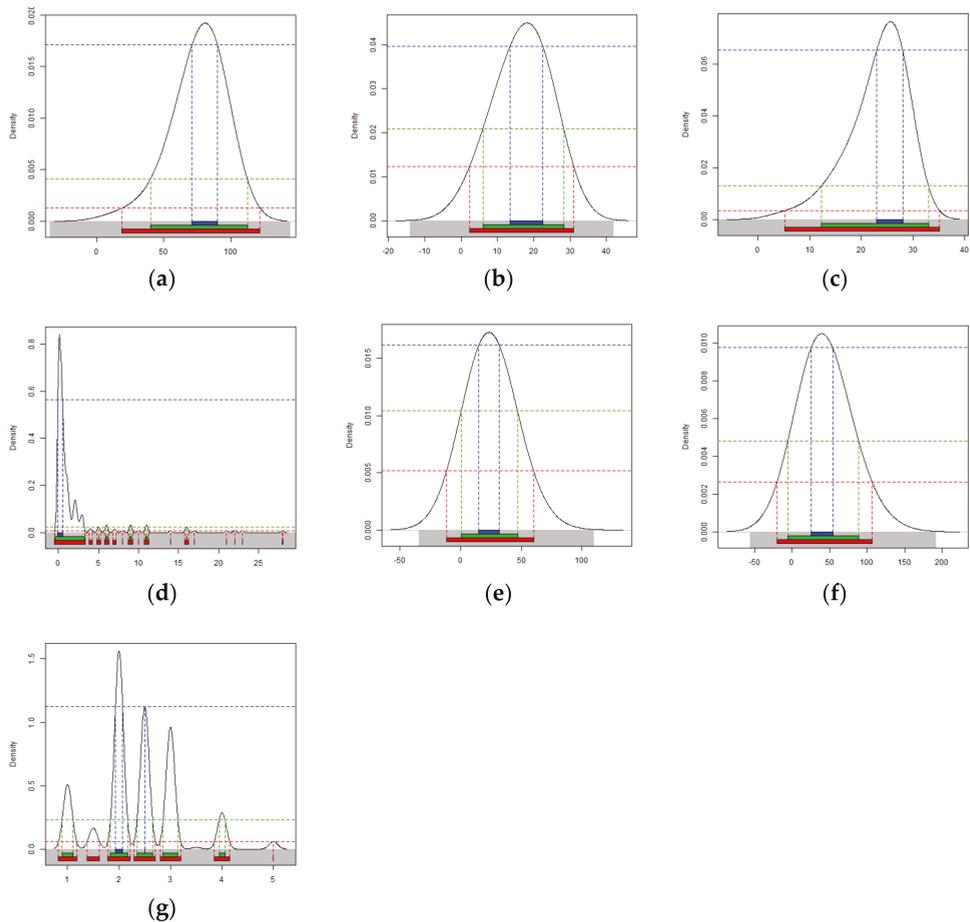
Figure 1. Density plots showing the distribution of the subjects' neuropsychological test results: (**a**) Schwab and England activities of daily living (ADL) score, (**b**) Korean montreal cognitive assessment (K-MoCA) score, (**c**) Korean mini-mental state examination (K-MMSE) score, (**d**) Korean instrumental activities of daily living (K-IADL) score, (**e**) Unified Parkinson's disease rating scale (UPDRS) (motor score), (**f**) UPDRS (total score), and (**g**) Hoehn and Yahr (H &Y) stage. The kernel density curve has a probability of 1 if all are added and the curves have been smoothed. The *x*-axis is the score for each test. Dark blue color = 50% highest density interval (HDI); green color = 95% HDI; red color = 99% HDI.

3.2. Comparing the Convergence Rate of Dementia Severity Prediction Model with the SVR Classification Algorithm

Since the convergence rate (performance) of the predictive model can be affected by the kernel type, we developed predictive models using Eps-SVM and Nu-SVM with four kernel functions (an RBF, linear algorithm, polynomial algorithm, and sigmoid) to measure the convergence rate according to various kernel types. A comparison of the MSEs of the eight SVMs is reported in Table 1 and Figure 2. The analysis results reveal that the MSE of Nu-SVR-RBF was the lowest (0.078) with the highest convergence rate, whereas the MSE of Eps-sigmoid SVR was 0.110 with the lowest convergence rate.

Table 1. Comparison of the convergence rates of the dementia severity predictive model according to the support vector machine regression (SVR) and kernel function.

| SVR | Kernel Function | | | |
	Linear	Polynomial	RBF	Sigmoid
Eps	0.101	0.095	0.079	0.110
Nu	0.079	0.102	0.078	0.091
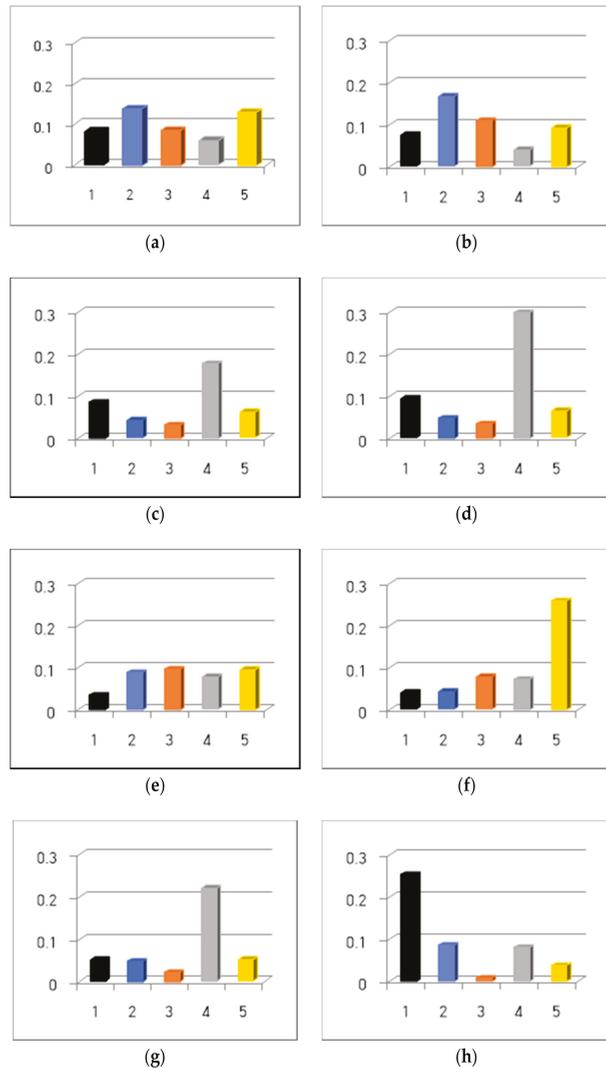
Figure 2. Five-fold cross-validation results of the dementia severity predictive model by the SVR algorithm. (**a**) epsilon-SVR (Eps-SVR)-linear, (**b**) Eps-SVR-polynomial, (**c**) Eps-SVR-radial basis function (RBF), (**d**) Eps-SVR-sigmoid, (**e**) Nu-SVR-linear, (**f**) Nu-SVR-polynomial, (**g**) Nu-SVR-RBF, and (**h**) Nu-SVR-sigmoid.

3.3. Factors Related to the Severity of PDD Using the SVR Models

We determined that Nu-SVR-RBF with the lowest MSE was the optimal model for predicting the severity of PDD. The functional weight values are presented in Figure 3. Although it is not possible to compare the absolute value of the influence of each factor using the functional weight value, it is possible to determine whether the relationship between the factor and the outcome variable is positive (a risk factor) or negative (a preventive factor). Using 22 support vectors, the Nu-SVR-RBF model showed that K-IADL, total UPDRS, motor UPDRS, tremor, postural instability, age, age at diagnosis of PD, education level (high school graduation or higher), a family history of PD, pack year (21–40), coffee drinker, TBI, atrial fibrillation, RBD, and depression had positive relationships with the severity of dementia.
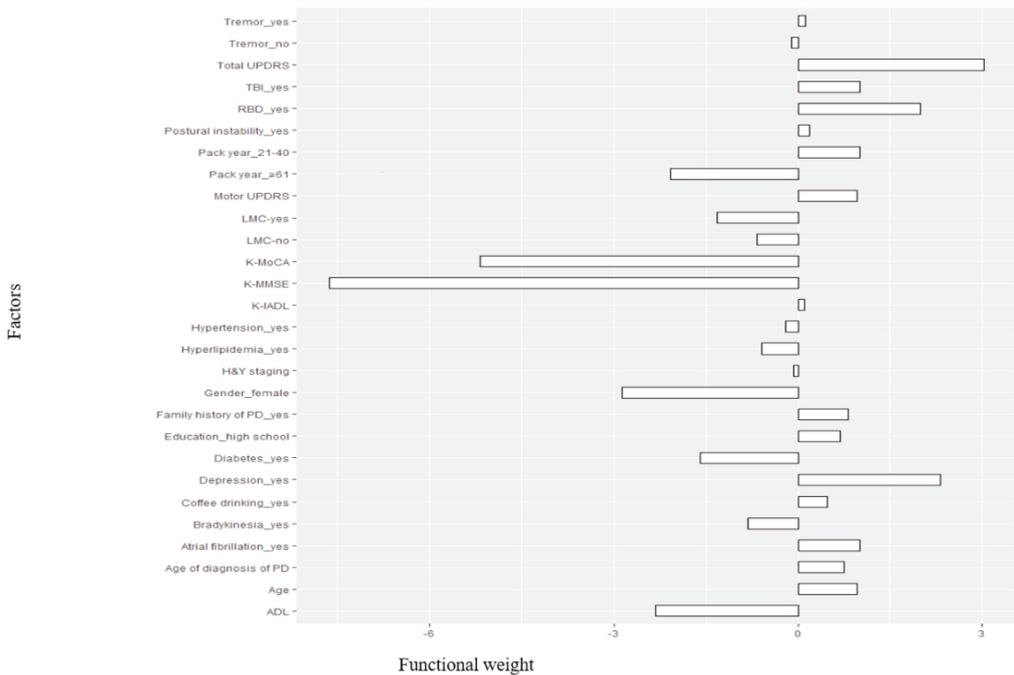

Figure 3. Functional weights of the major variables in the Nu-SVR-RBF model.

4. Discussion

We developed an SVR-based model for predicting the severity of PDD in patients using data from a nationwide clinical data registry. The results of this study showed that K-IADL, total UPDRS, motor UPDRS, tremor, postural instability, age, age at diagnosis of PD, education level above high school graduation, a family history of PD, pack year (21–40), coffee drinker, TBI, atrial fibrillation, RBD, and depression were major predictors of the severity of PDD. The results of previous studies in which the researchers explored the factors related to PDD reveal that major risk factors and influencing factors inducing PDD can be divided into two groups [29,30]. First, older patients had a higher risk of PDD occurrence and severe cognitive impairment. Second, when the trunk shows axial atypical features including the posture and behavior of the patient as phenotypical of PD, the occurrence of PDD and the severity of cognitive impairment increases [31,32]. Our findings also indicate that PD symptoms such as K-IADL and postural instability, as well as socio-demographic factors such as age, gender, and educational level are indicators of

the severity of PDD, which is consistent with the results of [33,34]. Our findings imply that our model could be useful for identifying the severity of dementia by comprehensively examining the axial atypical features, K-IADL, and changes in RBD, etc. for optimal intervention and caring of the elderly living alone or patients with PDD residing in medically vulnerable areas.

PDD, which requires continual treatment, induces a heavy social and economic burden due to caring and medical expenses, and so requires active government support. However, unlike dementia and stroke, the public's perception of PDD is much lower in South Korea than in other countries such as the US and Japan [35]. To make matters worse, there have only been a few epidemiological studies on PD in South Korea [36] and even fewer on evaluating the relationship between PD symptoms, the cognitive level of PDD, and the severity of PD [37]. Therefore, based on the results of the present study, additional longitudinal studies using a large cohort are required to develop an efficient indicator for predicting the severity of PDD.

Another important finding of this study was that the MSE of Nu-SVR-RBF was the lowest among the convergence rates of eight SVR-based predictive models with four kernel functions (linear, polynomial, RBF, and sigmoid). The performance of SVM is largely dependent on the kernel function and the parameters constituting it [28]. Lamorski et al. [38] also created a Nu-SVM-RBF model with high prediction accuracy. They argued that a linear kernel algorithm with SVM is only suitable when the sample size for the training data items is large and recommended using Nu-regression-RBF when the sample size of the training data is small. Therefore, this was implied that when analyzing data on less than 400 people using SVR (such as the PDD clinical data registry used in this study), developing a predictive model using Nu-SVR-RBF has the highest probability of deriving the best convergence rate.

The importance of this study is that we evaluated the severity of PDD by considering various factors such as the neuropsychological profile, demographic factors, disease symptoms, PD motor problems, and depression. The limitations of the study are as follows. First, although we included general cognitive screening tests such as MMSE and K-MoCA, we did not conduct tests for specific cognitive functions. Since [39] reported a relationship between the deficit of a specific cognitive domain and the progress of PDD, future studies are needed to develop a predictive model for the severity of PDD by including tests for specific cognitive functions such as language and executive functions. Moreover, it is necessary to evaluate the relationship between specific cognitive domains. Second, the sample in this study was not collected by systematic sampling since we used data from hospitals across the country. Hence, we must develop a predictive model by sampling subjects systematically to enable generalization of the results. Third, we did not evaluate biomarkers or genomes. To more sensitively predict the severity of PDD, we must develop a predictive model based on a multi-modal approach that includes genomic data and biomarkers in addition to cognitive tests. Fourth, since this was a cross-sectional study, we could not have identified causal relationships even for factors related to PDD. Further longitudinal studies are needed to prove the causal relationships of the risk and influencing factors identified in this study.

5. Conclusions

The CDR scale cannot accurately measure the severity of dementia in the elderly, who have reduced cognitive ability and live alone or in medically vulnerable areas, since it is measured by a specialist based not only by directly interviewing the patient but also collecting the collateral information from the guardian. The results of this study imply that the changes in PD motor symptoms, K-IADL, and RBD could be used as the basis for predicting the severity of PDD. Furthermore, it is necessary to develop a multi-modal screening test that can effectively determine the severity of PDD at an early stage based on the risk and preventive factors derived from the developed predictive model in order to maintain the cognitive health of patients with PD.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of the National Biobank of Korea and Korean Centers for Disease Control and Prevention (protocol code KBN-2019-1327; KBN-2019-005; and date 1 February 2019).

Informed Consent Statement: All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of National Biobank of Korea and Korean Centers for Disease Control and Prevention (KBN-2019-1327; KBN-2019-005).

Data Availability Statement: Restrictions apply to the availability of these data. Data were obtained from the National Biobank of Korea and are available (from the National Biobank of Korea/http://www.nih.go.kr/NIH/cms/content/eng/14/65714_view.html (accessed on 18 February 2021)) with the permission of the National Biobank of Korea.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Papagno, C.; Trojano, L. Cognitive and behavioral disorders in Parkinson's disease: An update. I: Cognitive impairments. *J. Neurol. Sci.* **2018**, *39*, 215–223. [CrossRef] [PubMed]
2. Ascherio, A.; Schwarzschild, M.A. The epidemiology of Parkinson's disease: Risk factors and prevention. *Lancet Neurol.* **2016**, *15*, 1257–1272. [CrossRef]
3. Byeon, H. Development of a depression in Parkinson's disease prediction model using machine learning. *World J. Psychiatr.* **2020**, *10*, 234–244. [CrossRef]
4. Wilczyński, J.; Habik, N. The effect of L-dopa on postural stability in Parkinson's disease patients. *Appl. Sci.* **2019**, *9*, 409–419. [CrossRef]
5. Korczyn, A.D. Dementia in Parkinson's disease. *J. Neurol.* **2001**, *248*, 1–4.
6. Borrione, P.; Tranchita, E.; Sansone, P.; Parisi, A. Effects of physical activity in Parkinson's disease: A new tool for rehabilitation. *World J. Methodol.* **2014**, *4*, 133–143. [CrossRef] [PubMed]
7. Jellinger, K.A. Dementia with Lewy bodies and Parkinson's disease-dementia: Current concepts and controversies. *J. Neural Transm.* **2018**, *125*, 615–650. [CrossRef]
8. Madhusoodanan, S.; Ting, M.B. Pharmacological management of behavioral symptoms associated with dementia. *World J. Psychiatr.* **2014**, *4*, 72–79. [CrossRef] [PubMed]
9. Zheng, X.; Woo, B.K. Association between recognizing dementia as a mental illness and dementia knowledge among elderly Chinese Americans. *World J. Psychiatr.* **2016**, *6*, 233–238. [CrossRef]
10. Choi, S.H.; Na, D.L.; Lee, B.H.; Hahm, D.S.; Jeong, J.H.; Yoon, S.J.; Yoo, K.H.; Ha, C.K.; Han, I.W. Estimating the validity of the Korean version of expanded Clinical Dementia Rating (CDR) scale. *J. Korean Neurol. Assoc.* **2001**, *19*, 585–591.
11. Huang, H.C.; Tseng, Y.M.; Chen, Y.C.; Chen, P.Y.; Chiu, H.Y. Diagnostic accuracy of the Clinical Dementia Rating Scale for detecting mild cognitive impairment and dementia: A bivariate meta-analysis. *Int. J. Geriatr. Psychiatry* **2020**, *36*, 239–251. [CrossRef]
12. Seppi, K.; Ray Chaudhuri, K.; Coelho, M.; Fox, S.H.; Katzenschlager, R.; Perez Lloret, S.; Weintraub, D.; Sampaio, C. The collaborators of the Parkinson's disease update on non-motor symptoms study group on behalf of the movement disorders society evidence-based medicine committee. Update on treatments for nonmotor symptoms of Parkinson's disease—An evidence-based medicine review. *Mov. Disord.* **2019**, *34*, 180–198. [PubMed]
13. Lam, K.; Chan, W.S.; Luk, J.K.; Leung, A.Y. Assessment and diagnosis of dementia: A review for primary healthcare professionals. *Hong Kong Med. J.* **2019**, *25*, 473–482. [CrossRef]
14. Liu, G.Y.; Liu, K.H.; Zhang, Y.; Wang, Y.Z.; Wu, X.H.; Lu, Y.Z.; Pan, C.; Yin, P.; Liao, H.F.; Su, J.Q.; et al. Alterations of tumor-related genes do not exactly match the histopathological grade in gastric adenocarcinomas. *World J. Gastroenterol.* **2010**, *16*, 1129–1137. [CrossRef] [PubMed]
15. Shankar, K.; Lakshmanaprabu, S.K.; Gupta, D.; Maseleno, A.; De Albuquerque, V.H.C. Optimal feature-based multi-kernel SVM approach for thyroid disease classification. *J. Supercomput.* **2020**, *76*, 1128–1143. [CrossRef]
16. Li, D.; Ju, Y.; Zou, Q. Protein folds prediction with hierarchical structured SVM. *Curr. Proteom.* **2016**, *13*, 79–85. [CrossRef]
17. Dolatabadi, A.D.; Khadem, S.E.Z.; Asl, B.M. Automated diagnosis of coronary artery disease (CAD) patients using optimized SVM. *Comput. Methods Programs Biomed.* **2017**, *138*, 117–126. [CrossRef] [PubMed]
18. Byeon, H. Best early-onset Parkinson dementia predictor using ensemble learning among Parkinson's symptoms, rapid eye movement sleep disorder, and neuropsychological profile. *World J. Psychiatr.* **2020**, *10*, 245–259. [CrossRef]

19. Hughes, A.J.; Daniel, S.E.; Kilford, L.; Lees, A.J. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinico-pathological study of 100 cases. *J. Neurol. Neurosurg. Psychiatry* **1992**, *55*, 181–184. [CrossRef]
20. Dubois, B.; Burn, D.; Goetz, C.; Aarsland, D.; Brown, R.G.; Broe, G.A.; Dickson, D.; Duyckaerts, C.; Cummings, J.; Gauthier, S.; et al. Diagnostic procedures for Parkinson's disease dementia: Recommendations from the movement disorder society task force. *Mov. Disord.* **2007**, *22*, 2314–2324. [CrossRef]
21. Schwab, R.S.; England, A.C.J. Projection Technique for Evaluating Surgery in Parkinson's Disease. In *Third Symposium on Parkinson's Disease*; Gillingham, F.J., Donaldson, I.M.L., Eds.; E&S Livingstone: Edinburgh, UK, 1969.
22. Kang, Y.; Park, J.; Yu, K.H.; Lee, B.C. The validity of the Korean-Montreal Cognitive Assessment (K-MoCA) as a screening test for both MCI and VCI. In Proceedings of the 20th Annual Rotman Research Institute Conference, The Frontal Lobes, Toronto, ON, Canada, 22–26 March 2010.
23. Kang, Y.; Na, D.L.; Hahn, S. A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients. *J. Korean Neurol. Assoc.* **1997**, *15*, 300–308.
24. Kang, S.J.; Choi, S.H.; Lee, B.H.; Kwon, J.C.; Na, D.L.; Han, S.H. Korean Dementia Research Group. The reliability and validity of the Korean Instrumental Activities of Daily Living (K-IADL). *J. Korean Neurol. Assoc.* **2002**, *20*, 8–14.
25. Richards, M.; Marder, K.; Cote, L.; Mayeux, R. Interrater reliability of the Unified Parkinson's Disease Rating Scale motor examination. *Mov. Disord.* **1994**, *9*, 89–91. [CrossRef]
26. Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The unified Parkinson's disease rating scale (UPDRS): Status and recommendations. *Mov. Disord.* **2003**, *18*, 738–750. [CrossRef]
27. Hoehn, M.M.; Yahr, M.D. Parkinsonism: Onset, progression and mortality. *Neurology* **1976**, *17*, 427–442. [CrossRef] [PubMed]
28. Smola, A.J.; Schölkopf, B. A tutorial on support vector regression. *Stat. Comput.* **2004**, *14*, 199–222. [CrossRef]
29. Xu, Y.; Yang, J.; Shang, H. Meta-analysis of risk factors for Parkinson's disease dementia. *Transl. Neurodegener.* **2016**, *5*, 11. [CrossRef]
30. Hoogland, J.; Boel, J.A.; de Bie, R.M.A.; Schmand, B.A.; Geskus, R.B.; Dalrymple-Alford, J.C.; Marras, C.; Adler, C.H.; Weintraub, D.; Junque, C.; et al. Validation of Mild Cognitive Impairment in Parkinson Disease. Risk of Parkinson's disease dementia related to level I MDS PD-MCI. *Mov. Disord.* **2019**, *34*, 430–435. [CrossRef] [PubMed]
31. Marinus, J.; Zhu, K.; Marras, C.; Aarsland, D.; van Hilten, J.J. Risk factors for non-motor symptoms in Parkinson's disease. *Lancet Neurol.* **2018**, *17*, 559–568. [CrossRef]
32. Goetz, C.G.; Emre, M.; Dubois, B. Parkinson's disease dementia: Definitions, guidelines, and research perspectives in diagnosis. *Ann. Neurol.* **2008**, *64*, S81–S92. [CrossRef] [PubMed]
33. Takemoto, M. Comparison of early stage clinical symptoms, cognitive, affective and ADL functions between PDD and DLB. *J. Neurol. Sci.* **2017**, *381*, 1021. [CrossRef]
34. Leroi, I.; Pantula, H.; McDonald, K.; Harbishettar, V. Neuropsychiatric symptoms in Parkinson's disease with mild cognitive impairment and dementia. *Parkinsons Dis.* **2012**, *2012*, 308097. [CrossRef] [PubMed]
35. Choi, S.A.; Kim, J.H.; Lee, M.S. Status of Korean patients with Parkinson's disease before diagnosis. *J. Korean Neurol. Assoc.* **2000**, *18*, 687–693.
36. Park, J.H.; Kim, D.H.; Kwon, D.Y.; Choi, M.; Kim, S.; Jung, J.H.; Han, K.; Park, Y.G. Trends in the incidence and prevalence of Parkinson's disease in Korea: A nationwide, population-based study. *BMC Geriatr.* **2019**, *19*, 320. [CrossRef] [PubMed]
37. Llebaria, G.; Pagonabarraga, J.; Kulisevsky, J.; García-Sánchez, C.; Pascual-Sedano, B.; Gironell, A.; Martínez-Corral, M. Cut-off score of the Mattis Dementia Rating Scale for screening dementia in Parkinson's disease. *Mov. Disord.* **2008**, *23*, 1546–1550. [CrossRef]
38. Lamorski, K.; Sławiński, C.; Moreno, F.; Barna, G.; Skierucha, W.; Arrue, J.L. Modelling soil water retention using support vector machines with genetic algorithm optimisation. *Sci. World J.* **2014**, *2014*, 740521. [CrossRef]
39. Pal, A.; Pegwal, N.; Kaur, S.; Mehta, N.; Behari, M.; Sharma, R. Deficit in specific cognitive domains associated with dementia in Parkinson's disease. *J. Clin. Neurosci.* **2018**, *57*, 116–120. [CrossRef] [PubMed]

Article

Exploring Factors for Predicting Anxiety Disorders of the Elderly Living Alone in South Korea Using Interpretable Machine Learning: A Population-Based Study

Haewon Byeon

Department of Medical Big Data, College of AI Convergence, Inje University, Gimhae 50834, Korea; bhwpuma@naver.com; Tel.: +82-10-7404-6969

Abstract: This epidemiological study aimed to develop an X-AI that could explain groups with a high anxiety disorder risk in old age. To achieve this objective, (1) this study explored the predictors of senile anxiety using base models and meta models. (2) This study presented decision tree visualization that could help psychiatric consultants and primary physicians easily interpret the path of predicting high-risk groups based on major predictors derived from final machine learning models with the best performance. This study analyzed 1558 elderly (695 males and 863 females) who were 60 years or older and completed the Zung's Self-Rating Anxiety Scale (SAS). We used support vector machine (SVM), random forest, LightGBM, and Adaboost for the base model, a single predictive model, while using XGBoost algorithm for the meta model. The analysis results confirmed that the predictive performance of the "SVM + Random forest + LightGBM + AdaBoost + XGBoost model (stacking ensemble: accuracy 87.4%, precision 85.1%, recall 87.4%, and F1-score 85.5%)" was the best. Also, the results of this study showed that the elderly who often (or mostly) felt subjective loneliness, had a Self Esteem Scale score of 26 or less, and had a subjective communication with their family of 4 or less (on a 10-point scale) were the group with the highest risk anxiety disorder. The results of this study imply that it is necessary to establish a community-based mental health policy that can identify elderly groups with high anxiety risks based on multiple risk factors and manage them constantly.

Keywords: explainable artificial intelligence; machine learning; stacking ensemble; Self-Rating Anxiety Scale; multiple risk factors

1. Introduction

Anxiety, which is defined as a disorder causing difficulties in daily life due to excess worry, fear, and hyperarousal, is known as one of the most common mental disorders worldwide [1]. It was reported that one in five Americans suffered from anxiety disorders [2] and the lifetime prevalence of anxiety disorders was 9.3% in South Korea [3]. The number of patients with an anxiety disorder is rapidly increasing in South Korea: the number of patients treated for an anxiety disorder increased from 533,619 in 2014 to 690,735 in 2018, a 29.4% increase in five years [3]. Particularly, the incident rate of anxiety disorders by age group showed that the number of treated patients per 100,000 increased the most (15% increase) from 2014 to 2018 in the elderly group ($\geq$60 years old), and the result suggested that the elderly experienced anxiety frequently and that anxiety disorder was a rapidly increasing mental illness.

A number of epidemiologic studies [3–5] have reported that the prevalence of anxiety disorders in the elderly is lower than that of the young/prime-aged. In particular, Gum et al. (2009) [5] examined a community-based epidemiologic survey and showed that the prevalence of anxiety disorders was 20.7% in the 18–44 years old group, 18.7% in the 45–64 years old group, and 7.0% in the 65 years old or older group, indicating that that of the elderly was the lowest. However, it is believed that the actual prevalence of

anxiety disorders in the elderly may be higher than the reported, when considering the fact that the elderly are reluctant to recall and report psychiatric symptoms or often tend to express the symptoms in physical terms [6]. The elderly are at very high risk of experiencing anxiety because (1) they face a lot of social stress such as bereavement, retirement, economic hardship, and abuse from people around them, (2) they are vulnerable to anxiety due to neuro-biological changes in the brain as a result of aging, (3) they are more likely to experience the fear of death in the senescence, and (4) they suffer from more physical diseases than younger people and are taking a lot of drugs [7]. Nevertheless, since the elderly perceive emotional problems such as depression and anxiety as a result of aging and they do not seek medical assistance actively, a small number of them are diagnosed with an anxiety disorder and treated [8]. Anxiety disorders can be treated by drugs, using anti-anxiety drugs such as buspirone, or psychotherapy [9]. Therefore, it is important to identify factors associated with anxiety and detect and manage people who are very vulnerable to anxiety as soon as possible.

It is highly likely that anxiety is affected by social factors as well as the physical and psychological problems of individuals [10]. Therefore, it is necessary to consider environmental factors such as social factors and social networks, in addition to sociodemographic characteristics, when identifying factors related to anxiety. It is unavoidable that the capability to emotionally cope with social and environmental changes is more vulnerable in old age, when people tend to be highly dependent on social factors in terms of economic, physical, and mental health [11,12]. Moreover, the risk factors of anxiety are complex and more likely to cluster with each other [11,12]. Therefore, it is important in public health science to understand the characteristics of anxiety in old age, considering that South Korea is facing a super-aged society. It is clear that the elderly are vulnerable to anxiety and anxiety disorder is a common disease in the elderly. However, only a few studies have evaluated the risk factors of anxiety disorder in old age while considering social factors and social network as well as sociodemographic characteristics and personal characteristics compared to other mental disorders, such as cognitive disorders [7].

Many recent studies [13,14] have used machine learning based on big data to identify the risk factors of a disease while considering multiple risk factors. However, employing a single machine learning technique may show lower prediction performance, depending on the used algorithm, and it is possible to induce errors because the bias existing in each algorithm can affect the prediction result. For example, a decision tree model such as Iterative Dichotomiser 3 (ID3) is very useful for making simple decisions, however, when tree models are complicated, it has lower prediction power and it poses a risk of result instability (possibility of deriving different results in iterated analysis) [15]. As an alternative method to overcome this limitation, many studies have developed predictive models using various machine learning techniques and combined them into a stacking ensemble learning model to reduce the risk of bias that individual models may have [16–18].

On the other hand, when developing a predictive model using medical data, explanatory power (interpretation) of the results is important in addition to accuracy. Recently, one important issue in medical artificial intelligence (AI) is to develop eXplainable Artificial Intelligence (X-AI) that can explain and present decisions made by AI in a form that can be understood by humans [19]. In the case of image classification, which is unstructured data, new methods such as learning deep explanation or gradient-class activation map (Grad-CAM) have been developed and used in various fields [20]. In the case of structured data, such as examination data, Carvalho et al. (2019) [21] and Wang et al. (2019) [22] introduced a method of presenting the key predictors derived from machine learning with decision tree visualization as an alternative way to increase the interpretability of the black box model. This epidemiological study aimed to develop an X-AI that could explain groups with a high anxiety disorder risk in old age. To achieve this objective, (1) this study explored the predictors of senile anxiety using base models and meta models. (2) This study presented decision tree visualization that could help psychiatric consultants

and primary physicians easily interpret the path of predicting high-risk groups based on major predictors derived from final machine learning models with the best performance.

2. Materials and Methods

2.1. Data Source

This study is a secondary data use study using the Korean Psychosocial Anxiety (KPA) Survey, a national survey. The KPA survey was conducted from August to September 2015 under the supervision of the Korea Institute for Health and Social Affairs. This study stratified 17 cities and provinces in South Korea using the population data of the statistical yearbook (complete enumeration) of the Ministry of Safety and Public Administration as of June 2015, and sampled by using the quota sampling method while considering the composition ratios of gender, age, and residential region. This study selected 200 eup, myeon, or dong for sampling sites using the probabilities proportional to size (PPS) method by treating 3552 eup, myeon, or dong in South Korea as the population. This study applied PPS after sorting cities, counties, and districts based on the administrative district code to secure the randomness of the samples. After choosing 200 sample sites, we visited the selected sample sites and chose the fifth household from the community center of each eup, myeon, and dong. As a result, this study surveyed 7000 adults who were 19 years or older. A surveyor who received survey training visited the sample household and conducted a 1:1 survey based on a computer assisted personal interview. This study was approved by the Clinical Research Ethics Committee of University H (No. 20180042). This study analyzed 1558 elderly (695 males, and 863 females) who were 60 years or older and completed the Zung's Self-Rating Anxiety Scale (SAS) [23], which was translated into Korean and standardized.

2.2. Measurement and Definition of Variables

The anxiety disorder, an outcome variable, was measured using the Korean version of SAS [23], which is a translated and standardized version of Zung's SAS [24]. SAS is a self-reporting test that encompasses emotional and psychophysiological aspects. It is a widely used standardized screening test that can easily measure anxiety disorders in healthy people [25]. The SAS consists of a 4-point Likert scale composed of 20 items, and the total score is 80 points. A higher score indicates more severe anxiety symptoms. When developing the Korean version of SAS, the Cronbach alpha value, indicating internal consistency, was 0.96, and the overall accurate discrimination rate, discriminating between healthy patients and patients with anxiety, was 93.7% [24]. In this study, the threshold of the anxiety disorder was set as 45 points.

Referring to previous studies [26–30], explanatory variables of this study included age, self-esteem, alcohol use disorder (normal drinker, high-risk drinker, or alcohol use disorder), subjective loneliness (very rare, occasionally lonely, often lonely, or mostly lonely), the experience of suicidal urge over the past year (yes or no), subjective frequency of communication with neighbors and friends (10-point scale; a higher score means more frequent communication), subjective frequency of communication with other family members (10-point scale), subjective satisfaction with help (support) from neighbors (yes or no), regular club activities (yes or no), perceived social support, subjective trust satisfaction with neighbors (yes or no), subjective satisfaction in the safety level of the neighborhood (yes or no), subjective satisfaction in the living environment of the neighborhood (yes or no), subjective satisfaction in the medical service of the region (yes or no), mean monthly household income (<KRW 2 million, ≥KRW 2 million and <KRW 3 million, or ≥KRW 3 million), the highest level of education (middle school graduation or less, or high school graduation or more), residential area (urban or rural), subjective satisfaction with the public transportation environment in the neighborhood, job/income instability (10-point scale), instability of preparation for old age (10-point scale), living safety instability (10-point scale), physical health instability (10-point scale), cognitive health (e.g., dementia) instability (10-point scale), family relationship and dissolution instability (10-point scale),

instability in family support and caregiving (10-point scale), instability in relationship with neighbors (10-point scale), online privacy infringement and personal information leakage instability (10-point scale), instability in the spread of high-risk new infectious disease (e.g., Middle East Respiratory Syndrome and Coronavirus) (10-point scale), economic recession and growth slowdown instability (10-point scale), environmental destruction and natural disaster instability (10-point scale), political and international relations (e.g., North Korea) instability (10-point scale), crime instability such as abuse and violence (10-point scale), social safety net vulnerability instability (10-point scale), low fertility and aging instability (10-point scale), instability in conflicts between classes, groups, and generations (10-point scale), your and your family's experience of being a victim of a crime over the past year (yes or no), awareness of mental health promotion services provided by public health centers and/or mental health promotion centers (yes or no), and experiences of using mental health promotion services provided by public health centers and/or mental health promotion centers (yes or no).

The alcohol use disorders identification test (AUDIT) [31] is an alcohol use disorder screening test developed by the World Health Organization for the purpose of pre-screening drinkers at risk and reducing harmful effects through intervention in diseases that may be caused by excessive drinking as soon as possible. The AUDIT consisted of 10 items (total score is 40 points): 0 to 15 points were classified as normal drinkers, 16 to 19 points were high-risk drinkers, and 20 points or more were classified as alcohol use disorder. Self-esteem was measured using the Self Esteem Scale (SES) [32] developed by Rodenburg (1965). The SES consisted of 10 items (total score is 40 points), and a lower score was interpreted as lower self-esteem.

2.3. Development of Machine Learning Using Stacking Ensemble

This study used SVM and ensemble learning (i.e., random forest, LightGBM, and Adaboost) as the base model (single model). The first goal of this approach was to compare the predictive performance (accuracy) of the single model (base model), because previous studies [13,17,18,21,22,33], which tried to predict diseases using single machine learning, commonly used them and reported them as highly-accurate models. The second goal was to explore the stacking model with the best predictive performance by combining different base models and the meta model.

2.3.1. Base Model: Support Vector Machine (SVM)

SVM is a machine learning algorithm that finds the optimal decision boundary through linear separation that optimally separates the hyperplane [33]. SVM solves the nonlinear problem related to the input space (e.g., 2D) by transforming it into a high-dimensional feature space. For example, A = [a, d] and B = [b, c] are not linearly separable in 2D, however, when they are mapped in 3D, they can have a linearly separable feature. Thus, when adequate nonlinear mapping is conducted to a sufficiently large dimension, data with two classes can always be separated in the maximum-margin hyperplane (Figure 1). This separation boundary maximizes the separation between the two classes, and the training data closest to this boundary is defined as a support vector. Since SVM can model complex nonlinear decision-making domains, it is more accurate than other machine learning techniques and is less likely to cause an overfitting issue, which are advantages of this method [34,35]. This study chose the Gauss function (radial basis function), using parameter C (unit cost), for the SVM's algorithm.
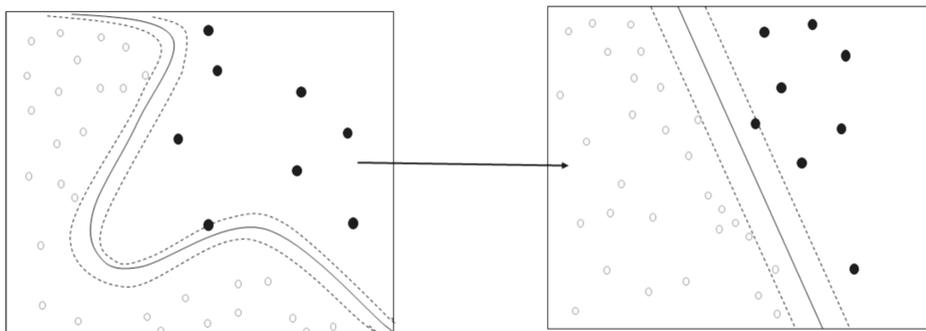
Figure 1. Concept of hyperplane in SVM [35].

2.3.2. Base Model: Random Forest

Random forest is an algorithm that randomly learns multiple decision trees. It repeats random sampling for predictors and observations to create multiple decision trees. After obtaining prediction categories from numerous decision trees, the final category prediction is determined by a majority vote method. It can iteratively build independent decision trees by giving randomness to decision tree formation. This method can reduce prediction errors and it uses bootstrapping for random selection of predictors and observations [36]. In this study, 30 was the number of maximum leaf nodes, 10 was the maximum depth of tree, and 500 was the number of decision trees for fitting that were used as hyperparameters of random forest. The concept of random forest is presented in Figure 2.
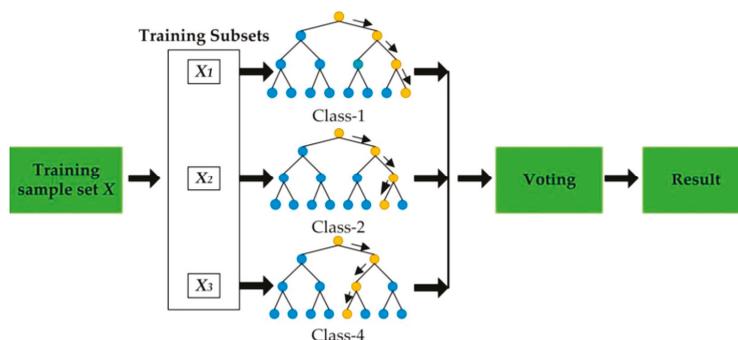

Figure 2. The concept of random forest [37].

2.3.3. Base Model: LightGBM

LightGBM algorithm is a high-performance algorithm based on a decision tree algorithm and is mainly used for machine learning in order to rank or classify. GBM is inefficient in terms of training speed and memory consumption when it is applied to big data containing high-dimensional variables, which is a shortfall. To overcome this disadvantage, Microsoft introduced LightGBM, which rapidly calculates information gain using a portion of the data using Gradient-based One-Side Sampling (GOSS) and reduces features using exclusive feature bundling (EFB), in 2017 [38]. LightGBM splits the tree leaf-wise, unlike other boosting algorithms that split based on the depth or level of trees based on a decision tree algorithm. Therefore, when growing on the same leaf in LightGBM, the leaf-wise algorithm can reduce the loss better than the level-wise algorithm. In this study, learning rate for each lightGBM = 0.3, regularization term on weights = 0.1, colsample,

subsample ratio of columns = 0.8, subsample ratio of the training instances = 0.8 were used as hyperparameters of lightGBM.

2.3.4. Base Model: Adaboost

Adaboost is a learning technique that ultimately generates a strong classifier by iteratively training very weak classifiers using samples from two classes. It trains weak classifiers by giving the same weight to all samples and improves the performance of weak classifiers by increasing the weight of samples that were determined to be misclassified in the basic classifier as the steps progress. The concept of Adaboost's algorithm is presented in Equation (1). In this study, learning rate for each Adaboost = 0.3, regularization term on weights = 0.1, colsample, subsample ratio of columns = 0.8, subsample ratio of the training instances = 0.8 were used as hyperparameters of Adaboost.

Given: $(x_1, y_1), \ldots, (x_m, y_m)$ where $x_i \in \mathcal{X}, y_i \in \{-1, +1\}$.
Initialize: $D_1(i) = 1/m$ for $i = 1, \ldots, m$.
For $t = 1, \ldots, T$:

- Train weak learner using distribution D_t.
- Get weak hypothesis $h_t : \mathcal{X} \to \{-1, +1\}$.
- Aim: select h_t with low weighted error: $\varepsilon_t = Pr_{i \sim D_t}[h_t(x_i) \neq y_i]$.
- Choose $\alpha_t = \frac{1}{2} \ln \left(\frac{1 - \varepsilon_t}{\varepsilon_t} \right)$.
- Update, for $i = 1, \ldots, m$:

$$D_{t+1}(i) = \frac{D_t(i) \exp(-\alpha_t y_i h_t(x_i))}{Z_t}$$

where Z_t is a normalization factor (chosen so that D_{t+1} will be a distribution).

Output the final hypothesis:

$$H(x) = \text{sign} \left(\sum_{t=1}^{T} \alpha_t h_t(x) \right). \tag{1}$$

2.4. Meta Model: XGBoost

This study predicted anxiety disorder in old age through the stacking ensemble technique. The stacking ensemble is better than recent single predictive models in terms of generalization and robustness, and it has been used for classification and prediction in various fields [16–18]. This method generates a new model by combining different various models as if stacking them in multiple layers, and it goes through two stages (base and meta). It improves the performance of the final model by taking the strength of each model and compensating for the weakness of each model [39].

This study used SVM, random forest, LightGBM, and Adaboost for the base model, a single predictive model, while using XGBoost algorithm for the meta model. XGBoost is a method to increase the reliability of the base model while maximizing its stability [40]. Lin et al. (2018) [41] also reported that the accuracy was improved compared to a single predictive model when applying XGBoost to a stacking ensemble model. Thus, this study also used XGBoost as a meta model. In this study, learning rate for each tree = 0.3, regularization term on weights = 0.001, colsample, subsample ratio of columns = 0.8, subsample ratio of the training instances = 0.8, maximum depth of tree = 10 were used as hyperparameters of XGBoost. Finally, this study developed four base models and five stacking ensemble models (SVM + XGBoost, random forest + XGBoost, LightGBM + XGBoost, Adaboost + XGBoost, and SVM + RF + LGBM + AdaBoost + XGBoost) to predict anxiety disorders in old age (Figure 3).
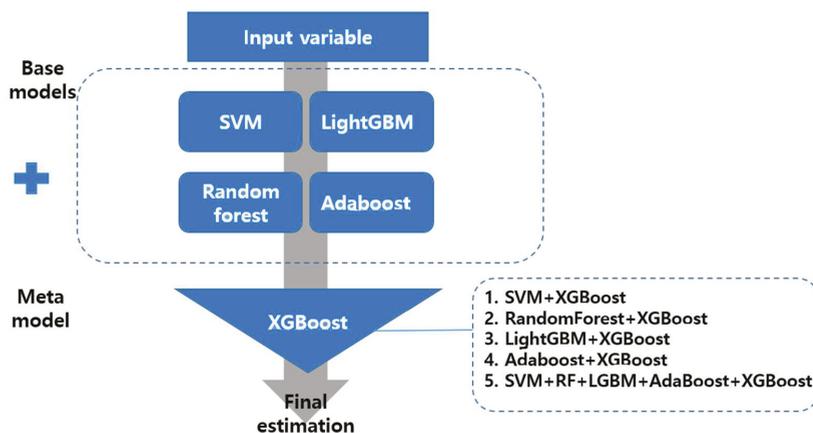
Figure 3. Process flow diagram for predictive models.

2.5. Validation of Model's Predictive Performance

The predictive performance of the nine developed machine learning models was validated using seven-fold cross-validation. This method randomly divides the entire sample into seven groups of equal size, and treats one group as a validation dataset and others as training datasets. It repeats this process seven times to prove the validity of the learning. This study used accuracy, precision, recall, and F1-score as indices to evaluate predictive performance. The calculation formula of each evaluation index is presented in Equation (2).

True positive = It is actually an anxiety disorder, and the predicted outcome
is an anxiety disorder.
False negative = It is actually an anxiety disorder, but the predicted outcome is normal.
False positive = It is actually normal, and the predicted outcome is an anxiety disorder.
True negative = It is actually normal, and the predicted outcome is normal.　　　　　(2)
Recall = TP/(TP + FN)
Precision = TP/(TP + FP)
Accuracy = (TP + TN)/(TP + FP + FN + TN)
F1-score = 2 * (Recall * Precision)/(Recall + Precision)

This study assumed that a model with the highest F1-score was the best predictive performance. If the F1-score was the same, a model with the highest recall was assumed as the best model. All analyses were performed using Python version 3.8.6 (https://www.python.org (accessed on 21 June 2021).

3. Results

3.1. General Characteristics of Subjects

The general characteristics of the subjects are presented in Table 1. The prevalence of the anxiety disorder among the elderly in South Korea was 17.2%. The results of the chi-square test showed that the elderly with a depressive disorder and the elderly without a depressive disorder had significant ($p < 0.05$) self-esteem, subjective loneliness, subjective satisfaction with help from neighbors, subjective satisfaction of the medical service of the region, regular club activities, the experience of suicidal urge over the past year, subjective trust satisfaction with neighbors, subjective frequency of communication with neighbors and friends, alcohol use disorder, subjective satisfaction in the living environment of the neighborhood, subjective satisfaction in the safety level of the neighborhood, age, subjective frequency of communication with other family members, the highest level of education, mean monthly household income, subjective level of discussion and consultation with neighbors and friends, your and your family's experience of being a victim of a crime

over the past year, income instability, instability of preparation for old age, living safety instability, physical health instability, mental health instability, family relationship and dissolution instability, instability in child education, family support, and caregiving, instability in relationship with neighbors, instability in the spread of high-risk new infectious disease, economic recession and growth slowdown instability, crime instability such as violence, social safety net vulnerability instability, low fertility and aging instability, and instability in conflicts between classes, groups, and generations.

Table 1. The general characteristics of the subjects: univariate analysis.

Variables	Anxiety Disorder		*p*
	No (n = 1290)	Yes (n = 268)	
Residential area			0.621
Urban	981 (83.1)	200 (16.9)	
Rural	309 (82.0)	68 (18.0)	
Highest level of education			<0.001
Middle school graduation or less	804 (79.6)	206 (20.4)	
High school graduation or more	486 (88.7)	62 (11.3)	
Mean monthly household income			0.001
<KRW 2 million	739 (80.1)	184 (19.9)	
≥KRW 2 million and <KRW 3 million	248 (84.9)	44 (15.1)	
≥KRW 3 million	303 (88.3)	40 (11.7)	
Subjective loneliness			<0.001
Very rare	653 (95.1)	34 (4.9)	
Occasionally lonely	530 (82.9)	109 (17.1)	
Often lonely	100 (47.6)	110 (52.4)	
Mostly lonely	7 (31.8)	15 (68.2)	
Subjective satisfaction with help from neighbors			<0.001
Yes	915 (85.7)	153 (14.3)	
No	375 (76.5)	115 (23.5)	
Self-esteem, the experience of suicidal urge over the past year			<0.001
Yes	66 (47.1)	74 (52.9)	
No	1224 (86.3)	194 (13.7)	
Subjective trust satisfaction with neighbors			<0.001
Yes	1153 (85.7)	193 (14.3)	
No	137 (64.6)	75 (35.4)	
Alcohol use disorder			<0.001
Normal drinker	685 (83.8)	132 (16.2)	
High-risk drinker	225 (80.9)	53 (19.1)	
Alcohol use disorder	5 (38.5)	8 (61.5)	
Subjective satisfaction of the living environment of the neighborhood			<0.001
Yes	1032 (85.9)	169 (14.1)	
No	258 (72.3)	99 (27.7)	
Subjective satisfaction of the safety level of the neighborhood			<0.001
Yes	1104 (85.9)	181 (14.1)	
No	186 (68.1)	87 (31.9)	
Subjective satisfaction of the medical service of the region			0.007
Yes	947 (84.4)	175 (15.6)	
No	343 (78.7)	93 (21.3)	
Regular club activities			0.001
Yes	421 (87.7)	59 (12.3)	
No	869 (80.6)	209 (19.4)	
Your and your family's experience of being a victim of a crime over the past year			<0.001
Yes	28 (56.0)	22 (44.0)	
No	1206 (84.5)	221 (15.5)	
Awareness of mental health promotion services provided by public health centers and/or mental health promotion centers			0.662
Yes	330 (82.1)	72 (17.9)	
No	960 (83.0)	196 (17.0)	

Table 1. *Cont.*

Variables	Anxiety Disorder		*p*
	No (n = 1290)	Yes (n = 268)	
Experiences of using mental health promotion services provided by public health centers and/or mental health promotion centers			0.372
Yes	95 (79.8)	24 (20.2)	
No	1195 (83.0)	244 (17.0)	
Age, mean ± SD	67.77 ± 5.53	69.01 ± 5.50	0.001
Subjective frequency of communication with other family members, mean ± SD	6.40 ± 1.53	5.22 ± 1.91	<0.001
Subjective frequency of communication with neighbors and friends, mean ± SD	6.18 ± 1.56	5.23 ± 1.79	<0.001
Self esteem scale, mean ± SD	29.28 ± 3.21	26.13 ± 3.35	<0.001
Subjective frequency of communication with neighbors and friends (10 points scale)	5.90 ± 1.54	5.16 ± 1.84	<0.001
Job/income instability (10-point scale)	5.07 ± 1.84	5.86 ± 2.14	<0.001
Instability of preparation for old age (10-point scale)	6.29 ± 2.16	7.27 ± 1.71	<0.001
Living safety instability (10-point scale)	4.66 ± 2.04	5.34 ± 1.87	<0.001
Physical health instability (10-point scale)	6.17 ± 2.14	7.02 ± 2.08	<0.001
Cognitive health instability (10-point scale)	4.86 ± 2.11	6.33 ± 1.95	<0.001
Family relationship and dissolution instability (10-point scale	3.79 ± 2.23	5.31 ± 2.14	<0.001
Instability in family support and caregiving (10-point scale)	3.71 ± 2.28	4.45 ± 2.47	<0.001
Instability in relationship with neighbors (10-point scale)	3.45 ± 2.17	4.27 ± 2.15	<0.001
Online privacy infringement and personal information leakage instability (10-point scale)	3.76 ± 2.37	3.49 ± 2.31	0.094
Instability in the spread of high-risk new infectious disease (10-point scale)	6.35 ± 1.96	6.74 ± 1.66	0.003
Economic recession and growth slowdown instability (10-point scale)	6.42 ± 1.87	6.69 ± 1.80	0.032
Environmental destruction and natural disaster instability (10-point scale)	5.47 ± 1.88	5.66 ± 1.61	0.130
Political and international relations instability	5.63 ± 1.92	5.28 ± 2.02	0.993
Crime instability such as abuse and violence (10-point scale)	5.28 ± 2.02	5.73 ± 2.03	0.001
Social safety net vulnerability instability (10-point scale)	5.37 ± 2.03	5.79 ± 1.97	0.002
Low fertility and aging instability (10-point scale)	5.38 ± 2.12	5.75 ± 2.06	0.010
Instability in conflicts between classes, groups, and generations (10-point scale)	5.03 ± 2.02	5.33 ± 2.01	0.027

3.2. Comparing the Accuracy of Predictive Models for the Anxiety Disorder in Old Age

Figures 4–7 show the predictive performance (accuracy, precision, recall, and F1-score) of nine machine learning models for prediction of the anxiety disorder in old age, respectively. The analysis results confirmed that the predictive performance of the "SVM + RF + LGBM + AdaBoost + XGBoost model (stacking ensemble: accuracy 87.4%, precision 85.1%, recall 87.4%, and F1-score 85.5%)" was the best.
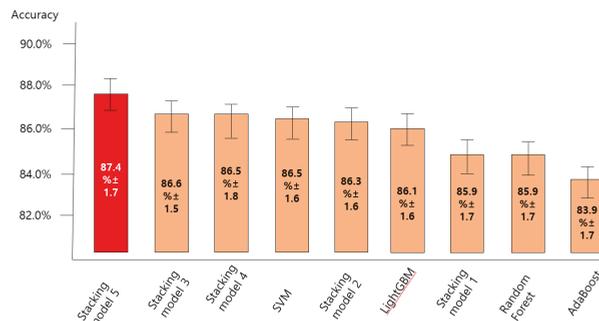

Figure 4. Comparing the accuracy of nine machine learning models for predicting anxiety disorders in old age.

Stacking model 1 = SVM + XGBoost; Stacking model 2 = RandomForest + XGBoost; Stacking model 3 = LightGBM + XGBoost; Stacking model 4 = Adaboost + XGBoost; Stacking model 5 = SVM + RF + LGBM + AdaBoost + XGBoost.
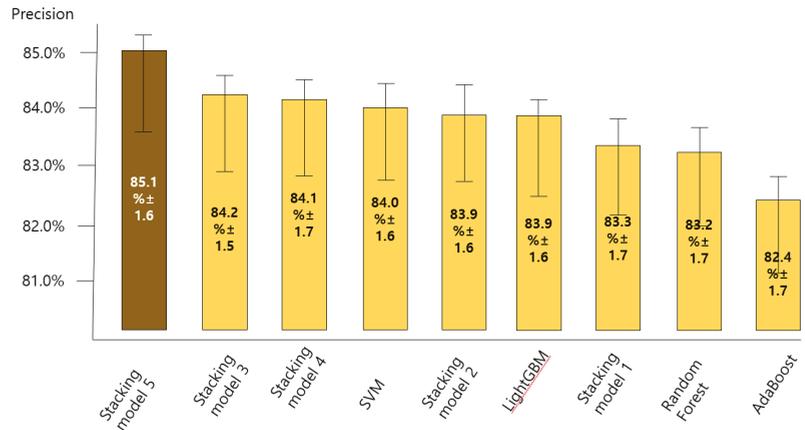
Figure 5. Comparing the precision of nine machine learning models for predicting anxiety disorders in old age.

Stacking model 1 = SVM + XGBoost; Stacking model 2 = RandomForest + XGBoost; Stacking model 3 = LightGBM + XGBoost; Stacking model 4 = Adaboost + XGBoost; Stacking model 5 = SVM + RF + LGBM + AdaBoost + XGBoost.
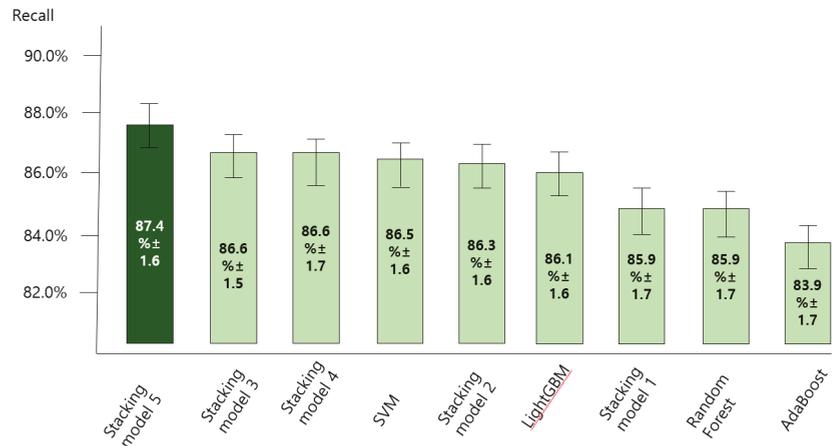

Figure 6. Comparing the recall of nine machine learning models for predicting anxiety disorders in old age.

Stacking model 1 = SVM + XGBoost; Stacking model 2 = RandomForest + XGBoost; Stacking model 3 = LightGBM + XGBoost; Stacking model 4 = Adaboost + XGBoost; Stacking model 5 = SVM + RF + LGBM + AdaBoost + XGBoost.
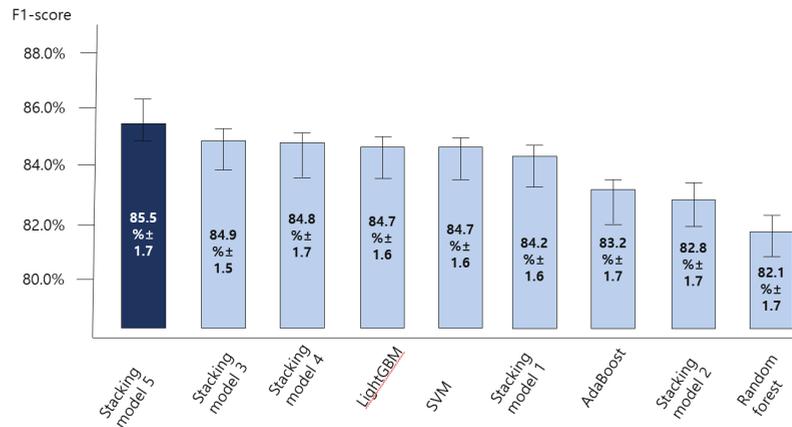
Figure 7. Comparing the F1 score of nine machine learning models for predicting anxiety disorders in old age.

Stacking model 1 = SVM + XGBoost; Stacking model 2 = RandomForest + XGBoost; Stacking model 3 = LightGBM + XGBoost; Stacking model 4 = Adaboost + XGBoost; Stacking model 5 = SVM + RF + LGBM + AdaBoost + XGBoost.

3.3. Exploring Predictors and High-Risk Groups for the Anxiety Disorder in Old Age

The feature importance of the SVM + RF + LGBM + AdaBoost + XGBoost model, the final model for predicting the anxiety disorder in the elderly in South Korea, is presented in Figure 8. In this model, subjective loneliness, SES, subjective family relations, instability in family support and caregiving, subjective frequency of communication with family, family relationship and dissolution instability, and your and your family's experience of being a victim of a crime over the past year were identified as the seven major variables with high weight. Among them, subjective loneliness was the most important factor in the final model.
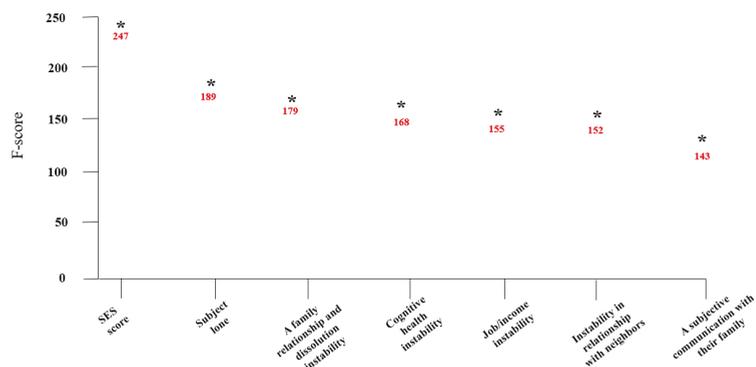
Figure 8. The importance of variables in the prediction model for anxiety disorder in old age (only the top seven variables are presented).

Figure 9 shows a tree plot that presents seven variables with high weight in importance, using the decision tree visualization. The value of the leaf node represents the logistic function probability score (LFP-score). A positive number refers to the probability of having a depressive disorder, and a negative number indicates the probability of not having an

anxiety disorder. There were two paths for predicting anxiety disorder in old age (Table 2). The first path with the highest predictive probability of an anxiety disorder was the elderly who often (or mostly) felt subjective loneliness, had an SES score of 26 or less, and had a subjective communication with their family of 4 or less (on a 10-point scale). The second path was the elderly who sometimes felt subjective loneliness, perceived that they had a bad family relationship (or very bad), and were victims of a crime, or had a family member who was a victim of a crime over the past year.
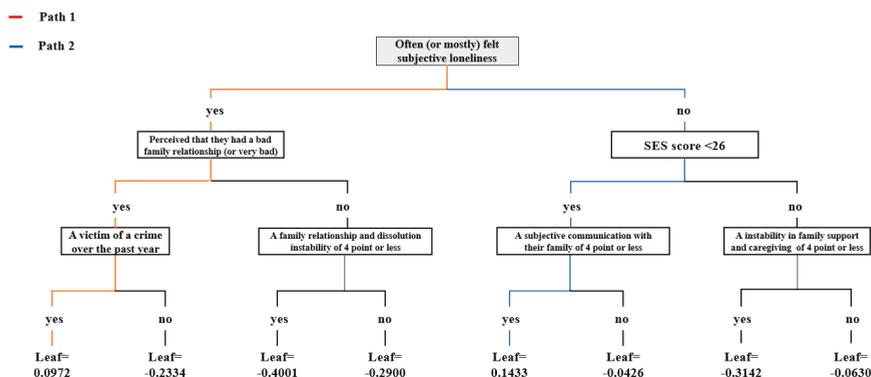
Figure 9. A tree plot that presents seven variables with high weight in the importance using the decision tree visualization.

Table 2. A path for predicting anxiety disorder in old age.

| Path	Characteristics	LFP-Score
1	The elderly who often (or mostly) felt subjective loneliness, had an SES score of 26 or less, and had a subjective communication with their family of 4 or less (on a 10-point scale)	0.14
2	The elderly who sometimes felt subjective loneliness, perceived that they had a bad family relationship (or very bad), and were victims of a crime, or had their family member who was a victim of a crime over the past year	0.09

LEP-score = logistic function probability score.

4. Discussion

This study compared the predictive performance (accuracy) of nine machine learning algorithms to predict anxiety disorders in the elderly in South Korea and confirmed that the SVM + RF + LGBM + AdaBoost + XGBoost model had the best predictive performance. SVM + RF + LGBM + AdaBoost + XGBoost, LightGBM + XGBoost, and Adaboost + XGBoost, among the stacking ensemble models in this study, had higher accuracy, precision, recall, and F1-score than single predictive models. The results agreed with previous studies [42,43], which reported that the root-mean-square error (RMSE) of the stacking ensemble model was lower than that of the single machine learning model. In particular, Byeon (2021) [43] showed that the stacking ensemble model had a higher index of agreement (IA) and variance of errors (Ev), in addition to accuracy, than the single machine learning model, which implied that the predictive performance of the stacking ensemble model could be higher than that of the single predictive model for structured data such as examination data. However, in this study, the F1-score of SVM was 0.5% higher than that of SVM + XGBoost, which suggested that the stacking ensemble model

could perform worse than a single machine learning model depending on the combination of a base model and a meta model. Therefore, futures studies shall explore the stacking ensemble model with the best performance in community examination data by combining various base models and meta models including unsupervised learning (e.g., clustering), in addition to boosting to prove the performance of the stacking ensemble.

Another finding of this study was that subjective loneliness, SES, subjective family relations, instability in family support and caregiving, subjective frequency of communication with family, family relationship and dissolution instability, and your and your family's experience of being a victim of a crime over the past year were independent risk factors for predicting an anxiety disorder in the elderly living in South Korea. Green et al. (2013) [44] conducted a cohort study on Scottish people and reported that socioeconomic differences such as low educational level and low level of income were significantly related to anxiety in old age. However, socioeconomic factors were not significantly related to anxiety in this study, while the effects of family factors such as anxiety about the dissolution of family relations and anxiety due to family support or caregiving were significantly higher. It is believed that the difference from previous studies is due to the characteristics of the elderly of South Korea who value traditional family relationships. The structure and value of family relations have been changed in the past 30 years in South Korea as the traditional family system has been breaking up the nuclear family through the process of rapid industrialization and urbanization [45]. As the range of the elderly's social life has been reduced, their interests and contacts have shifted from society to their families [45]. As a result, family relationships have a significant impact on the psychological health of the elderly [45]. Although it is impossible to conclude that the frequency of communication with family members living together can sufficiently determine the emotional support for the elderly, the results of this study implied that the emotional support obtained from other family members or people around them can alleviate anxiety in old age. Since not enough studies have evaluated factors influencing the anxiety of the elderly, more epidemiological studies are required to understand the characteristics of anxiety in old age.

Previous studies [26–30] that identified factors related to the anxiety of the elderly only tried to identify individual factors of depression using regression analysis. Therefore, they are limited in identifying multiple risk factors for anxiety. This community-based epidemiologic study identified multiple risk factors using the decision tree visualization of the stacking ensemble model. The results of this study showed that the elderly who often (or mostly) felt subjective loneliness, had an SES score of 26 or less, and had a subjective communication with their family of 4 or less (on a 10-point scale) were the group with the highest risk of anxiety disorder.

When people get older, they experience social isolation and loneliness due to separation from their children, retirement from work, and the death of people around them (e.g., spouse, family, and friends). If this loneliness persists, they will be more likely to develop depressive and anxiety disorders [46]. Statistics Korea (2021) [47] forecasted that South Korea will enter a super-aged society in 2026, which means that one in four people will be elderly. It is five years before 2026, and one in five elderly people (17.2%) are suffering from an anxiety disorder. However, there are not sufficient policy measures for identifying anxiety disorders in the elderly soon and managing high-risk groups compared to cognitive disorders such as chronic diseases or dementia. Since early detection and preventive treatment are important for mental disorders such as anxiety, it will be necessary to continuously monitor the elderly who perceive that they have a bad relationship with their family, subjectively experience a lot of loneliness, and frequently feel anxious about family relationships and dissolution to prevent anxiety disorders in old age based on the results of this study from the community level (or primary medical care level). Furthermore, since almost no studies have identified multiple risk factors for anxiety in old age, more epidemiological studies are required to continuously identify multiple risk factors for anxiety in old age.

The importance of this study was that this study analyzed complex factors of anxiety such as individual characteristics, family factors, and social environment using epidemiological data that can represent the elderly living in a local community. When developing a predictive model using medical data, the critical elements are to explain (interpret) the results and to secure high accuracy. This study presented the derived key predictors using decision tree visualization, which added the possibility of explanation. The decision tree visualization technique of the ensemble machine, presented in this study, is meaningful because it presents an application case of interpretable AI using structured data and the grounds of its use. Future studies are needed to develop X-AI or transparent AI using various methods based on structured data in order to explain the judgment of AI in a form that medical personnel can understand based on the interpretable AI case of this study.

The limitations of this study are as follows. First, this study could not identify the detailed types of anxiety disorders due to the nature of the epidemiological investigation using the anxiety disorder screening test. Future studies are needed to classify the types of anxiety disorders into a generalized anxiety disorder, phobia disorder, panic disorder, and obsessive-compulsive disorder using medical diagnosis and to explore risk factors according to the type. Second, although social networks such as the number of close friends to meet are important for anxiety disorder in old age, this epidemiological study did not investigate social networks. Third, this study used a secondary source, the KPA Survey conducted in 2015. Therefore, there is a possibility that there is a difference between the general characteristics of older adults surveyed in 2015 and those of older adults in 2021. Consequently, the results of this study should be interpreted carefully. Fourth, since this study is a cross-sectional study, even if risk factors for anxiety disorder are identified, their causal relationships cannot be argued. Additional longitudinal studies are required to prove the causal relationship between the multiple risk factors for anxiety disorder in old age identified in this study.

5. Conclusions

The results of this study indicated that it will be necessary to continuously monitor subjective loneliness, SES, subjective family relations, instability in family support and caregiving, subjective frequency of communication with family, family relationship and dissolution instability, and your and your family's experience of being a victim of a crime over the past year to prevent and screen anxiety disorders in the elderly living in a local community as soon as possible. Furthermore, it is necessary to establish a community-based mental health policy that can identify elderly groups with high anxiety risks based on multiple risk factors and manage them constantly.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of University (protocol code 20180042 and date: 1 July 2018).

Informed Consent Statement: All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Korea Institute for Health and Social Affairs.

Data Availability Statement: Restrictions apply to the availability of these data. Data was obtained from Korea Institute for Health and Social Affairs and are available [from the Korea Institute for Health and Social Affairs/https://www.kihasa.re.kr/en (accessed on 21 June 2021)] with the permission of Korea Institute for Health and Social Affairs.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Baxter, A.J.; Scott, K.M.; Vos, T.; Whiteford, H.A. Global prevalence of anxiety disorders: A systematic review and meta-regression. *Psychol. Med.* **2013**, *43*, 897. [CrossRef] [PubMed]
2. Kessler, R.C.; Berglund, P.; Demler, O.; Jin, R.; Merikangas, K.R.; Walters, E.E. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch. Gen. Psychiatry* **2005**, *62*, 593–602. [CrossRef]
3. Ministry of Health & Welfare. *National Mental Health Statistics 2019*; Ministry of Health & Welfare: Sejong, Korea, 2020.
4. Remes, O.; Brayne, C.; Van Der Linde, R.; Lafortune, L. A systematic review of reviews on the prevalence of anxiety disorders in adult populations. *Brain Behav.* **2016**, *6*, e00497. [CrossRef]
5. Gum, A.M.; King-Kallimanis, B.; Kohn, R. Prevalence of mood, anxiety, and substance-abuse disorders for older Americans in the national comorbidity survey-replication. *Am. J. Geriatr. Psychiatry* **2009**, *17*, 769–781. [CrossRef]
6. Subramanyam, A.A.; Kedare, J.; Singh, O.P.; Pinto, C. Clinical practice guidelines for geriatric anxiety disorders. *Indian J. Psychiatry* **2018**, *60* (Suppl. 3), S371. [CrossRef]
7. Rangara, J.; Pelissolo, A. Anxiety disorders in the elderly: Clinical and therapeutic aspects. *Psychol. Neuropsychiatr. Vieil.* **2006**, *4*, 179–187.
8. Sable, J.A.; Jeste, D.V. Anxiety disorders in older adults. *Curr. Psychiatry Rep.* **2001**, *3*, 302–307. [CrossRef] [PubMed]
9. Fan, X.; Xie, X.; Zhang, C.; Kong, W.; Zhou, C.; Biao, D.U. Systematic review of tandospirone and buspirone in treatment of patients with generalized anxiety disorder. *Drug Eval. Res.* **2017**, *40*, 400–405.
10. Park, S.A.; Song, J.K. The effect of social anxiety on psychological adaptation. *Korean Psychol. J. Cult. Soc. Issues* **2005**, *40*, 400–405.
11. Kim, C.T. An exploratory study on phenomenological hermeneutics of every day' anxiety of university student. *J. Welf. Adm.* **2013**, *23*, 23–45.
12. Choi, I.; Suh, K.H.; Kim, Y.S. The psychosocial factors affecting suicidal ideation of the elderly. *Health Soc. Sci.* **2009**, *25*, 33–56.
13. Chatterjee, A.; Gerdes, M.W.; Martinez, S.G. Identification of risk factors associated with obesity and overweight—A machine learning overview. *Sensors* **2020**, *20*, 2734. [CrossRef] [PubMed]
14. Byeon, H. Associations between adolescents' earphone usage in noisy environments, hearing loss, and self-reported hearing problems in a nationally representative sample of South Korean middle and high school students. *Medicine* **2021**, *100*, e24056. [CrossRef] [PubMed]
15. Navada, A.; Ansari, A.N.; Patil, S.; Sonkamble, B.A. Overview of use of decision tree algorithms in machine learning. In Proceedings of the 2011 IEEE control and system graduate research colloquium, Shah Alam, Malaysia, 27–28 June 2011; pp. 37–42. [CrossRef]
16. Adhikari, R. A neural network based linear ensemble framework for time series forecasting. *Neurocomputing* **2015**, *157*, 231–242. [CrossRef]
17. Al-Sarem, M.; Saeed, F.; Al-Mekhlafi, Z.G.; Mohammed, B.A.; Al-Hadhrami, T.; Alshammari, M.T.; Alreshidi, A.; Alshammari, T.S. An Optimized Stacking Ensemble Model for Phishing Websites Detection. *Electronics* **2021**, *10*, 1285. [CrossRef]
18. Divina, F.; Gilson, A.; Gomez-Vela, F.; Garcia Torres, M.; Torres, J.F. Stacking ensemble learning for short-term electricity consumption forecasting. *Energies* **2018**, *11*, 949. [CrossRef]
19. Panwar, H.; Gupta, P.K.; Siddiqui, M.K.; Morales-Menendez, R.; Bhardwaj, P.; Singh, V. A deep learning and grad-CAM based color visualization approach for fast detection of COVID-19 cases using chest X-ray and CT-Scan images. *Chaos Soliton Fractals* **2020**, *140*, 110190. [CrossRef]
20. Selvaraju, R.R.; Cogswell, M.; Das, A.; Vedantam, R.; Parikh, D.; Batra, D. Grad-cam: Visual explanations from deep networks via gradient-based localization. *Proc. IEEE Int. Conf. Comput. Vis.* **2017**, 618–626.
21. Carvalho, D.V.; Pereira, E.M.; Cardoso, J.S. Machine learning interpretability: A survey on methods and metrics. *Electronics* **2019**, *8*, 832. [CrossRef]
22. Wang, Y.; Wang, D.; Geng, N.; Wang, Y.; Yin, Y.; Jin, Y. Stacking-based ensemble learning of decision trees for interpretable prostate cancer detection. *Appl. Soft Comput.* **2019**, *77*, 188–204. [CrossRef]
23. Lee, J.H. Development of the Korean Form of Zung's Self-Rating Anxiety Scale. *Yeungnam Univ. J. Med.* **1996**, *13*, 279–294. [CrossRef]
24. Zung, W.W. A rating instrument for anxiety disorders. *Psychosomatics* **1971**, *12*, 371–379. [CrossRef]
25. Julian, L.J. Measures of anxiety. *Arthritis Care Res.* **2011**, *63*. [CrossRef] [PubMed]
26. Carriere, I.; Ryan, J.; Norton, J.; Scali, J.; Stewart, R.; Ritchie, K.; Ancelin, M.L. Anxiety and mortality risk in community-dwelling elderly people. *Br. J. Psychiatry* **2013**, *203*, 303–309. [CrossRef] [PubMed]
27. Clarke, D.M.; Currie, K.C. Depression, anxiety and their relationship with chronic diseases: A review of the epidemiology, risk and treatment evidence. *Med. J. Aust.* **2009**, *190*, S54–S60. [CrossRef] [PubMed]
28. Sami, M.B.; Nilforooshan, R. The natural course of anxiety disorders in the elderly: A systematic review of longitudinal trials. *Int. Psychogeriatr.* **2015**, *27*, 1061. [CrossRef]
29. Bryant, C.; Jackson, H.; Ames, D. The prevalence of anxiety in older adults: Methodological issues and a review of the literature. *J. Affect. Disord.* **2008**, *109*, 233–250. [CrossRef]
30. Domènech-Abella, J.; Mundó, J.; Haro, J.M.; Rubio-Valera, M. Anxiety, depression, loneliness and social network in the elderly: Longitudinal associations from The Irish Longitudinal Study on Ageing (TILDA). *J. Affect. Disord.* **2019**, *246*, 82–88. [CrossRef]

31. Saunders, J.B.; Aasland, O.G.; Babor, T.F.; De LaFuente, J.R.; Grant, M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on earlydetection of persons with harmful alcohol consumption-II. *Addiction* **1993**, *88*, 791–804. [CrossRef]
32. Rosenberg, M. Rosenberg self-esteem scale (RSE). Acceptance and commitment therapy. *Meas. Package* **1965**, *61*, 18.
33. Daneshfaraz, R.; Aminvash, E.; Ghaderi, A.; Abraham, J.; Bagherzadeh, M. SVM performance for predicting the effect of horizontal screen diameters on the hydraulic parameters of a vertical drop. *Appl. Sci.* **2021**, *11*, 4238. [CrossRef]
34. Furey, T.S.; Cristianini, N.; Duffy, N.; Bednarski, D.W.; Schummer, M.; Haussler, D. Support vector machine classification and validation of cancer tissue samples using microarray expression data. *Bioinformatics* **2000**, *16*, 906–914. [CrossRef] [PubMed]
35. Byeon, H. Predicting the swallow-related quality of life of the elderly living in a local community using support vector machine. *Int. J. Environ. Res. Public Health* **2019**, *16*, 4269. [CrossRef]
36. Breiman, L. Random forests. *Mach Learn.* **2001**, *45*, 5–32. [CrossRef]
37. Wu, X.; Gao, Y.; Jiao, D. Multi-label classification based on random forest algorithm for non-intrusive load monitoring system. *Processes* **2019**, *7*, 337. [CrossRef]
38. Ke, G.; Meng, Q.; Finley, T.; Wang, T.; Chen, W.; Ma, W.; Ye, Q.; Liu, T.Y. LightGBM: A highly efficient gradient boosting decision tree. *Adv. Neural Inf. Process. Syst.* **2017**, *30*, 3146–3154.
39. Xiao, Y.; Wu, J.; Lin, Z.; Zhao, X. A deep learning-based multi-model ensemble method for cancer prediction. *Comput. Methods Programs Biomed.* **2018**, *153*, 1–9. [CrossRef] [PubMed]
40. Xie, O.; Liu, Z.T.; Ding, X.W. Electroencephalogram emotion recognition based on a stacking classification model. In Proceedings of the 2018 37th Chinese Control Conference (CCC), Wuhan, China, 25–27 July 2018; pp. 5544–5548. [CrossRef]
41. Lin, F.; Jiang, J.; Fan, J.; Wang, S. A stacking model for variation prediction of public bicycle traffic flow. *Intell. Data Anal.* **2018**, *22*, 911–933. [CrossRef]
42. Yadav, D.C.; Pal, S. To generate an ensemble model for women thyroid prediction using data mining techniques. *Asian Pac. J. Cancer Prev.* **2019**, *20*, 1275–1281. [CrossRef] [PubMed]
43. Byeon, H. Exploring factors associated with the social discrimination experience of children from multicultural families in South Korea by using stacking with non-linear algorithm. *Int. J. Adv. Comput. Sci. Appl.* **2021**, *12*, 125–130. [CrossRef]
44. Green, M.J.; Benzeval, M. The development of socioeconomic inequalities in anxiety and depression symptoms over the lifecourse. *Soc. Psychiatry Psychiatr. Epidemiol.* **2013**, *48*, 1951–1961. [CrossRef] [PubMed]
45. Kim, K.T.; Choi, S.; Park, M.; Park, S.; Go, S.H.; Park, H. The effect of family structures and psycho-social factors on suicidal ideation of senior citizens. *Korean J. Gerontol. Soc. Welfare* **2011**, *52*, 205–228. [CrossRef]
46. Singh, A.; Misra, N. Loneliness, depression and sociability in old age. *Ind. Psychiatry J.* **2009**, *18*, 51–55. [CrossRef] [PubMed]
47. Statistics Korea. *Senior Statistics*; Statistics Korea: Daejeon, Korea, 2021.

Article
Hospital Inpatient Falls across Clinical Departments

**Marcin Mikos [1], Tomasz Banas [2,*], Aleksandra Czerw [3,4], Bartłomiej Banas [5], Łukasz Strzepek [6]
and Mateusz Curyło [7]**

1 Department of Bioinformatics and Public Health, Faculty of Medicine and Health Sciences, Andrzej Frycz
   Modrzewski Krakow University, 30-701 Krakow, Poland; mikos@ziz.com.pl
2 Department of Gynaecology and Oncology, Jagiellonian University Medical College, 31-501 Krakow, Poland
3 Department of Health Economics and Medical Law, Medical University of Warsaw, 02-091 Warsaw, Poland;
   ola_czerw@wp.pl
4 National Institute of Public Health NIH—National Research Institute, 00-791 Warsaw, Poland
5 Private Surgical Medical Practice, 31-261 Krakow, Poland; bartek14@wp.pl
6 Department of General Surgery, Regional Public Hospital in Bochnia, 32-700 Bochnia, Poland;
   strzepeklukasz@wp.pl
7 Orthopedic and Posttraumatic Rehabilitation Department, Medical University of Lodz, 90-419 Lodz, Poland;
   mateusz.curylo@azmmedical.pl
* Correspondence: tbanas@mp.pl; Tel.: +48-(12)-424-85-26

Abstract: Background: Inpatient falls are common hospital adverse events. We aimed to determine
inpatient fall rates in an urban public hospital and analyzed their characteristics across clinical
departments. Methods: The study was conducted in a 350-bed urban, multi-specialty public hospital
in the 2013–2019 period. Patient data were retrieved from the hospital's standardized falls reporting
system. Descriptive statistics and statistical tests: chi2 and ANOVA tests with multiple comparison
tests (post-hoc analysis) were used. For fall incidence estimation a joint-point regression was applied.
p-value of 0.05 was considered as statistically significant for all the calculations. Results: The highest
prevalence of falls was reported in the rehabilitation and internal medicine wards (1.915% and 1.181%,
respectively), the lowest in the orthopedic (0.145%) and rheumatology wards (0.213%) ($p < 0.001$).
The vast majority of falls took place in the late evening and during the night (56.711%) and were
classified as bed falls (55.858%). The crude incidence rate (cIR) of falls was 6.484 per one thousand
hospitalizations. In the 2013–2017 period, an increase in total cIR was observed, reaching the peak
value in 2016; it was followed by a slight decline from 2017 to 2019, however, differences in changes
were observed between the wards. Conclusion: Fall rates and trends as well as circumstances of
inpatient falls varied significantly among clinical departments, probably due to differences in patient
characteristics.

Keywords: fall assessment sheet; fall; elderly patients; hospitalization; risk management

1. Introduction

The most widely used definition of a fall occurring within a healthcare setting is the
one proposed by Nitz and Johnston, which describes it as "an unexpected event in which
the participant comes to rest on the ground, floor, or lower level" [1]. Inpatient falls are
the leading cause of hospital adverse events with incidence rate varying from 2.4 in large
tertiary university hospitals to 9.1 in geriatric hospital departments per one thousand
patient-days [1–4]. Two major types of fall risk factors were distinguished: (a) intrinsic
factors comprising age, gender, musculoskeletal disorders, patient's imbalance and using
drugs; (b) extrinsic factors including the weaknesses of the health system in the medical
equipment maintenance and design, human resources, communication, training, and team
work [5].

Age > 85 years, the male sex, a recent fall, gait instability, agitation and/or confusion, new urinary incontinence or frequency, adverse drug reactions and neurological and cardiovascular instability are the predominant risk factors of inpatient falls [6,7]. Chronic diseases including diabetes and hypertension are also risk factors of falls and subsequent fractures [6–8]. Especially elderly patients are more likely to fall, due to balance and coordination deterioration, loss of skeletal muscles strength, as well as many other comorbidities associated with aging [6,7]. Physical activity, therefore, plays essential role in preventing falls. World Health Organization (WHO) recommendations emphasize the importance of physical activity in preventing falls especially among seniors and are consistent with studies showing that systematic movement exercises and balance training can lead to the alleviation of symptoms associated with balance disorders in the elderly, thus reduce the risk of falling [9,10]. Furthermore, 15.4% of patients experience a decline in mobility during hospital stay, particularly women with cognitive impairment and underweight are at high risk of reduced mobility, therefore physical rehabilitation during hospitalization is essential and was proved to reduce the risk of falls [11,12]. Finally, negative interactions between the intrinsic and extrinsic risk factors may lead to serious physical injuries [5].

Up to 42% of falls occur during walking (e.g., to the bathroom), while 7–14% take place during transferring (e.g., standing up, sitting down) or are bed-related (e.g., falling out of bed) [13–16]. Up to 80% of falls, however, occur when patients are not observed, as some patients initiate risky decisions concerning their mobility based on their own judgements, without asking health professionals for help [17,18].

Approximately 30–35% of falls occurring in healthcare facilities result in injury that can cost over USD 14,000 per incident adding, on average, 6.3 days to an individual's length of stay [19]. Adverse outcomes associated with inpatient falls include bruises and fractures, depression and anxiety, prolonged lengths of stay, and even death [20]. Some fall-related incidents may even lead to a medical lawsuit; therefore, fall risk reduction via implementing monitoring and analyzing systems along with nursing care improvement and patients' education have become one of the most important issues in medical safety.

In spite of the fact that most healthcare providers have implemented recommendations to identify patients at increased falls risk, and processes for collecting and reporting fall data, falls continue to occur [21]. Prevention of inpatient falls seems to be crucial for integrity of diagnostic and therapeutic processes. This can be achieved mainly by staff training, implementation of fall risk reduction programs and patient education. The first step in preventing falls is the identification of high-risk patients.

King et al. reported, however, unintended impact of fall prevention messages on nurses and older adult patients. Intense messaging from hospital administration to achieve zero falls resulted in nurses developing a fear of falls, protecting themselves and the unit, and restricting fall risk patients as a way to stop messages and meet the hospital goal [22]. Improperly, an adverse event is often considered as a synonym for "medical error," "medical malpractice," or "treatment failure." However, the term "adverse event" also comprises treatment failures not directly caused by a healthcare provider, and not only by human medical errors [23]. Therefore, depenalization of unintended adverse effects, including inpatient falls, should be strongly considered. Furthermore, creating opportunities for anonymous recording of medical adverse events would significantly improve the number of reported cases. The goal of medical adverse event recording and reporting systems is primarily to identify possible risk factors in order to improve patients' safety. Along with depenalization of unintended medical adverse events, a public insurance system should be established to cover justified patients' claims [23,24].

In this study we aimed to investigate the occurrence of inpatient falls in all wards of a public city hospital in the past seven years, and to analyze the circumstances of these events; additionally, we investigated changes in the incidence of falls.

2. Materials and Methods

2.1. Setting and Sample

This study was conducted in a 350-bed specialist public hospital in the city of Krakow, Poland, after receiving Local Review Board consent. It included all adult inpatients from 1 January 2013 through 31 December 2019, in the clinical departments of internal medicine, rheumatology, rehabilitation, cardiology, neurology and orthopedics. No additional exclusion criteria were applied and all the records in the registry were completed with no missing data. The hospital is localized in a district where the percentage of people in the retirement age is higher than the city average [21]. Therefore, the mean of age in the sample is considerably high and exceeds the value of 75 years old (see Table 1).

Table 1. Characteristics of fallers and circumstances of falls.

Departments	Cardiology	Internal Medicine	Neurology	Orthopedics	Rheumatology	Rehabilitation	*p*
	A	B	C	D	E	F	
Total number of hospitalizations (N)	11980	39811	7517	9673	24849	5536	<0.001 $
Total number of falls (%)	47 (0.39%)	469 (1.18%)	45 (0.60%)	14 (0.15%)	53 (0.21%)	106 (1.92%)	
Females N (%)	18 (38.30%)	256 (54.58%)	17 (37.78%)	8 (57.14%)	43 (81.13%)	81 (76.42%)	A vs. B < 0.008 $ A vs. E = 0.004 $ A vs. F = 0.008 $ C vs. E < 0.001 $ C vs. F < 0.001 $
Males N (%)	29 (61.7%)	213 (45.42%)	28 (62.22%)	6 (42.90%)	10 (18.90%)	25 (23.58%)	
Age (years)	77.94	77.70	77.76	71.29	65.81	72.81	B vs. A < 0.001 $ B vs. C < 0.001 $ B vs. E = 0.004 $ C vs. E = 0.008 $
mean (±SD *; range)	(±10.96; 36)	(±12.08; 73)	(±11.17; 64)	(±8.46; 27)	(±19.07; 63)	(±11.51; 59)	
BMI (kg/m^2) mean (±SD *)	26.57 (±5.01)	27.06 (±5.58)	26.43 (±4.87)	26.24 (±2.89)	26.95 (±4.62)	28.31 (±5.64)	0.083
Length of stay (days)	9	14	9	10	7	22	F vs. A < 0.001 $ F vs. B < 0.001 $ F vs. C = 0.004 $ F vs. D = 0.003 $ F vs. E < 0.001 $ A vs. E < 0.001 $ A vs. B = 0.036 $ B vs. E < 0.001 $
Median; IQR **	IQR **: 3.5	IQR **: 4.0	IQR **: 6.5	IQR **: 5.5	IQR **: 3.0	IQR **: 11.5	
Time of fall							
6:00-12:00	12 (25.53%)	89 (19.98%)	12 (26.67%)	6 (42.86%)	14 (26.42%)	21 (19.81%)	0.018 $
12:00-18:00	15 (31.92%)	91 (19.40%)	12 (26.67%)	0 (0.00%)	17 (32.08%)	29 (27.36%)	
18:00-24:00	11 (23.40%)	123 (26.23%)	11 (24.44%)	4 (28.57%)	9 (16.98%)	31 (29.25%)	
24:00-6:00	9 (19.149%)	166 (35.39%)	10 (22.22%)	4 (28.57%)	13 (24.53%)	25 (23.59%)	
Patient conditions							
Dementia	5 (10.64%)	56 (11.940%)	5 (11.11%)	0 (0.000%)	1 (1.89%)	2 (1.89%)	B vs. E = 0.006 $ C vs. E = 0.012 $
Disorientation	8 (17.02%)	59 (12.58%)	8 (17.78%)	0 (0.00%)	0 (0.00%)	5 (4.72%)	
Psychomotor disorders	2 (4.26%)	19 (4.05%)	2 (4.44%)	3 (21.43%)	0 (0.00%)	4 (3.77%)	
Loss of consciousness	0 (0.00%)	6 (1.28%)	0 (0.000%)	0 (0.00%)	3 (5.66%)	0 (0.00%)	
None	32 (70.15%)	329 (66.67%)	30 (66.67%)	11 (78.57%)	49 (92.45%)	95 (89.62%)	
Place of fall							
Bed	30 (59.92%)	281 (59.92%)	28 (62.22%)	8 (57.14%)	16 (30.19%)	47 (44.34%)	C vs. E < 0.001 $ D vs. E = 0.011 $
Bathroom	11 (22.81%)	107 (22.81%)	11 (24.44%)	0 (0.00%)	14 (26.42%)	19 (17.93%)	
Corridor	6 (12.77%)	81 (17.27%)	6 (13.33%)	6 (42.86%)	23 (43.40%)	40 (37.74%)	

* SD—standard deviation; ** IQR—interquartile range; $ *p* statistically significant. Kruskal–Wallis ANOVA with post hoc multiple cooperation of mean ranks.

Patient data were retrospectively retrieved from the hospital's standardized falls reporting system. Fall report included the following data: (1) clinical department, (2) patient's data, (3) time, (4) location, and (5) circumstances of the fall. In multiple fall cases, only the data of the first fall were analyzed. The hospital policy requires every hospital employee involved in any adverse event such as a patient's fall to fill in a specific form immediately after the event. The form includes fields for entering all information mentioned above. It is then submitted to the Head of Department and its copy is sent to the office of the hospital director's plenipotentiary for quality. The data are then added

to the reporting system. The information is analyzed and appropriate corrective actions are taken.

2.2. Statistical Analysis

The Shapiro–Wilk test was used to determine the distribution of continuous variables. Variables that fit normal distribution were presented as mean values and standard deviation (SD), while those with distribution different from normal as medians and interquartile range (IQR). Analysis of variance (ANOVA) was used to compare more than two groups if variables fit normal distribution and Kruskal–Wallis ANOVA testing was performed if distributions were different from normal. Post-hoc tests were applied if appropriate. To compare the rough number of cases a chi-square test was chosen, and variables were presented as case numbers and percentage (%). The Neuman test was employed to evaluate if the trends of the annual number of admissions and the median hospital stays in the period 2013–2019 were significant. Additionally, Spearman correlation test was used to assess a possible relationship between the annual number of admissions and the annual number of inpatient falls as well as between the median length of hospital stay and the annual number of inpatients falls. Calculations were performed using STATISTICA data analysis software, version 12.0 (TIBCO Software Inc. (2017). Statistica (data analysis software system), version 13. Palo Alto, USA), and MedCalc Statistical Software, version 16.2.1 (MedCalc Software by Ostend, Belgium).

A join-point regression analysis using the Joinpoint Regression program, version 4.8.0.1 April 2020 (Information Management Services Inc., Rockville, MD, USA) was performed to determine the crude incidence rate of falls calculated as the number of falls per 1000 hospitalizations. The analysis included a logarithmic transformation of the rates, standard errors, and a maximum number of five join points with a minimum of 4 years between two join points [22]. The annual percentage change (APC) was subsequently calculated to quantify the trend over a fixed number of years as a geometric weighted average of the trend analysis. *p*-value of 0.05 was considered as statistically significant for all the calculations.

3. Results

In a seven-year period, there were 89,693 hospitalizations and 734 (0.818%) patients' falls were reported. The study group comprised 325 (43.218%) males and 427 (56.782%) females. The mean age of patients who fell was 75.53 ($\pm$13.35) years with an average BMI of 27.08 ($\pm$5.39) kg/m^2, and their median length of hospital stay was 16.5 (IQR: 7.0) days.

Additionally, in the rheumatology ward patients who fell were significantly younger compared to patients admitted to other wards (Table 1). Additionally, significant differences in female to male ratios were identified across the analyzed wards (Table 1). The highest rate of falls of female patients was observed in the rehabilitation ward; it was followed by the orthopedic and internal medicine wards. The lowest rate of falls of female patients was noted down in the neurology unit. There were no significant differences in BMI of fallers across the analyzed departments. Additionally, significant differences in female to male ratios were identified across the wards (Table 1). In the internal ward, the falls were predominately reported in the late evening and at night while in other wards they occurred mostly in the morning and in the afternoon (Table 1). Dementia was diagnosed in 1 in 10 of fallers from the cardiology, internal and neurology wards, while disorientation was recognized in 17% of patients who fell in the neurology and cardiology wards followed by 12% of patients in the internal medicine ward, and the differences between the wards were significant (Table 1). Bed falls were typical for all these wards; however, a rehabilitation and rheumatology corridor was the second most common location where falls occurred contrary to other wards where bathroom falls were more common (Table 1).

The longest hospital stay was reported in the rehabilitation ward followed by the internal medicine and orthopedics wards, while the shortest stay was in the rheumatology

ward and the highest number of annual admissions was to the internal medicine ward while the lowest to the rehabilitation department (Table 1).

In the cardiology department both the trends of the annual admissions and the median length of hospital stay were insignificant (Figure 1). Additionally, no association between the annual number of admissions and the annual number of inpatient falls or a relationship between the median length of hospital stay and the annual number of inpatients falls were proven. Contrary to this, in the internal medicine ward the annual admissions trend increased significantly while the trend of median hospital stay was insignificant (Figure 3). There was also a significant positive association between the annual number of admissions and the annual number of inpatient falls (R = 0.775; p = 0.041) while no correlation between the median length of hospital stay and the annual number of inpatient falls was observed. In the neurology department both the trends of annual admissions and the median length of hospital stay increased significantly (Figure 3). There was a significant positive correlation between the annual number of admissions, the median length of hospital stay and the annual number of inpatient falls (R = 0.982; p = <0.001 and R = −0.908; p = 0.004, subsequently). The annual admissions trend in the orthopedics department increased significantly while the trend of the median hospital stay was insignificant (Figure 3). There was no correlation between the annual number of admissions and the annual number of inpatient falls or between the median length of hospital stay and the annual number of inpatients falls. In the rheumatology department both trends were significant, however, the annual admissions trend was increasing, while the trend of the median hospital stay decreased. Additionally, no correlations between the annual number of admissions and the annual number of inpatient falls or between the median length of hospital stay and the annual number of inpatient falls were found. In the rehabilitation ward only the trend of the median hospital stay decreased significantly, while the annual admissions trend was insignificant. Additionally, there were no correlations neither between the annual number of admissions and the annual number of inpatient falls nor between the median length of hospital stay and the annual number of inpatients.

The crude incidence rate (cIR) of falls was 6.484 per one thousand hospitalizations. In the 2013–2017 period, an increasing trend of total cIR was observed, reaching the peak value in 2016; it was followed by a slight decline from 2017 to 2019 (Figure 2).

Different changes in fall incidence were observed in the analyzed wards. The highest incidence of falls was reported in the rehabilitation ward, where the maximum cIR of 41.06 was noted down while its lowest level for that ward was 2.53 (Figure 3). The second highest cIR of 16.94 falls was observed in the internal medicine ward; here, its lowest value was 2.11 (Figure 3). The lowest cIR of falls was observed in the neurology ward, and it was in the 0.09–1.33 range (Figure 3). In the orthopedics ward, a trend analysis was unavailable due to lack of reported cases in the 2013–2015 and 2018–2019 periods.

In the cardiology department, after a gradual increase in the number of falls from 2013 to 2016, we observe a rapid acceleration of this trend that reached the peak of cIR at the level of 14.11 in 2017; it was followed by a significant decline in the 2017–2019 period (Figure 3). Similarly to the cardiology unit, also in the rehabilitation ward a two-part trend of patient falls was observed. After an initial enormous increase of cIR from 2.53 to 41.06 in the 2013–2017 period, a steep decrease can be seen from 2017 to 2019, with significant APC (Figure 3). In the internal medicine ward, a rapid upward trend was observed from 2013 to 2015, with a significant increase of falls. From the year 2015, however, this trend stabilized, with an insignificant APC, reaching the peak cIR of 16.94 in 2019 (Figure 3).

Contrary to what was mentioned above, we observed a continuous increase of inpatient falls in the neurology and the rheumatology departments, although cIR of falls differed significantly between these two wards (Figure 3). In the neurology ward, after a gentle increase in falls, an acceleration of the trend was observed in the 2013–2017 period; it reached the highest cIR value of 18.48 in the year 2019 and showed a significant APC for the whole analyzed period (Figure 3). In the rheumatology ward, although an upward trend was observed for the entire analyzed period from the years 2013–2019, the reported APC

was insignificant and showed the lowest values of cIR of falls as described above (Figure 3). As we have already mentioned, a trend analysis was unavailable for the orthopedics ward.
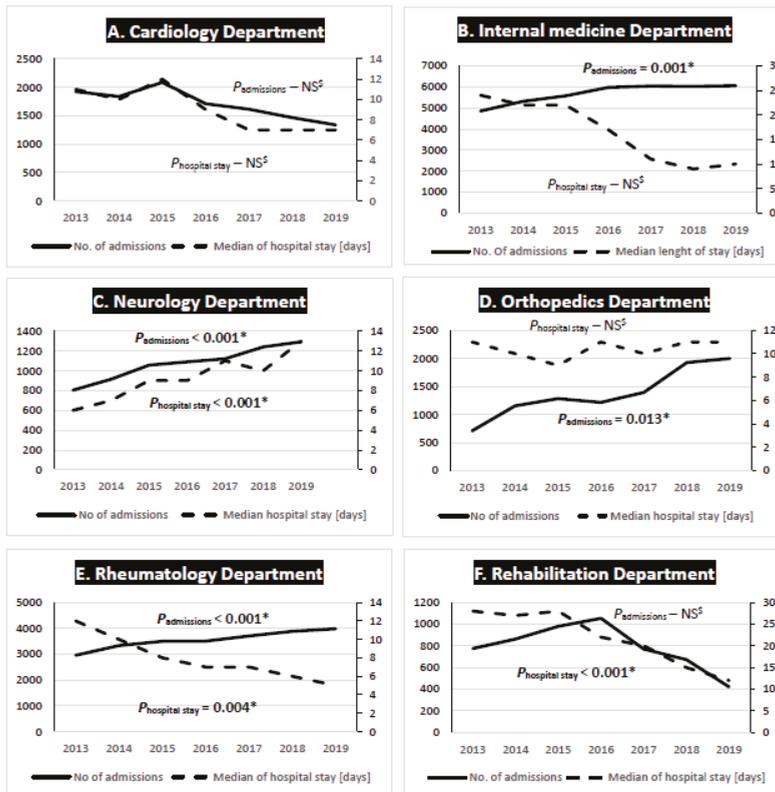
Figure 1. Trends of median hospital stay and annual number of admissions across the analyzed clinical departments. $^\$$ NS—non-significant; * significant *p*-value.
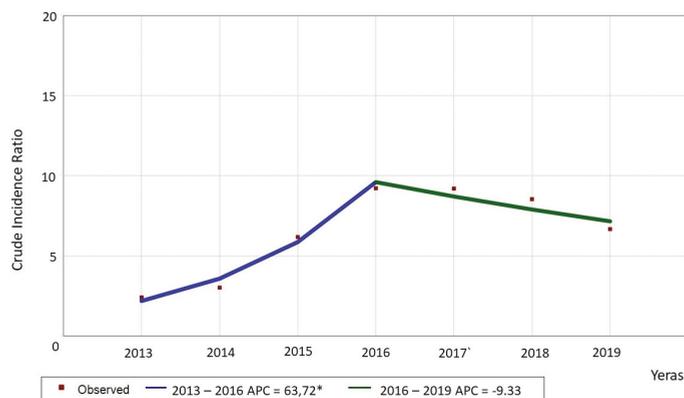

Figure 2. Trend of patient falls (Crude incidence ratio [cIR] per 1000 patients-beds) for all the departments. * please pay attention to a different scale.
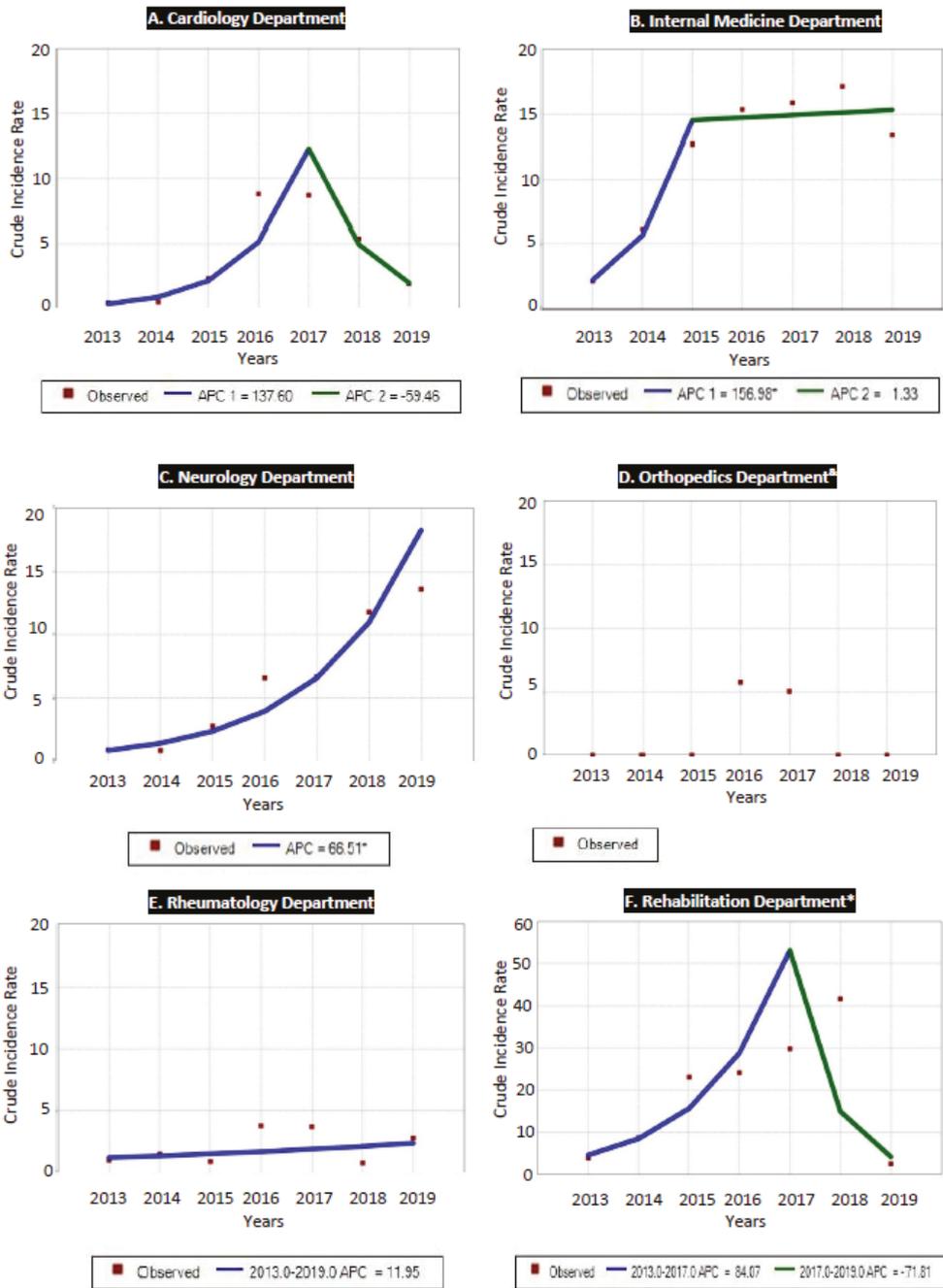
Figure 3. Trends of falls (crude incidence ratio (cIR) per 1000 patient beds) across the analyzed clinical departments; & no trend available due to 0 cases of inpatient falls in several years; * please pay attention to a different scale.

4. Discussion

Our results are consistent with findings of Healey et al., who reported rates of falls per 1000 bed days between 2.1 and 8.4, depending on the hospital profile, and significantly lower than fall rates presented by Schwendimann and colleagues, who showed that 7.2% of hospitalized patients experienced falls [16,22]. Similarly to our findings, they reported significant differences in characteristics of fallers and circumstances of falls; however, they investigated internal medicine, surgical and geriatric departments [22,23]. These significant differences considered patients' age, length of hospital stay as well as comorbidities and the circumstances of falls. They can be easily explained by the fact that in distinct departments patients are diagnosed with different health problems and have individualized treatment. Results presented by Tayabe, however, showed that one fourth of recorded falls were not registered in the incident reporting systems [24]. It is a well-known fact that only a part of the incidents occurring in a hospital is recognized in a voluntary incident reporting systems [25]. Rates of falls recorded based on incident reports, vary remarkably between hospitals and this inconsistency in the rate of falls may be the result of reporting bias of medical staff [25]. Consistently, Healey et al. confirmed that that the rate of falls in acute hospitals varied remarkably between hospitals from 0.2 to 11.5 per 1000 bed days [26]. Reporting bias is a serious problem especially when the precise incidence and detailed information on incidents are required. Epidemiological study of inpatient falls, validation of countermeasures against falls, and development of risk assessment systems for inpatient falls can be effective only if based on truth and verified.

According to our result, the highest fall risk was in the rehabilitation ward followed by internal medicine department, while orthopedics, cardiology and rheumatology patients were at the lowest risk of falls. This knowledge is essential to improve inpatient fall prevention; however, not only a common fall risk in each ward should be evaluated but also an assessment of individual fall risk must be conducted on admission of every patient. There is, however, no consistent evidence that interventions to prevent falls among hospital inpatients are effective [9,10], although many of the published studies were underpowered or methodologically flawed.

Basically, the risk of inpatient falls is positively correlated with the length of hospital stay and rises significantly from the 11th day of hospitalization [27]. Similarly, in intensive care units the risk of inpatient falls increases 9.9 times if the hospitalization exceeds 19 days [28]. A positive and significant correlation between the risk of inpatient falls and hospitalization length was also confirmed in palliative care units [29]. Furthermore, frequent rotations of nursing staff and extensive workload resulted in omitting many important procedures and activities that are directly relevant to patient safety, such as lack of care planning (18.9%), lack of updating medical records (21.7%) and reducing nursing care (23.9%) [29–32].

In the investigated population increases in the incidence of inpatient falls on neurology and rheumatology wards were observed in conjunction with a decrease in the median length of hospital stay and a rise of new admissions.

To the best of our knowledge a very large number of papers evaluated inpatients falls risks but only few studies evaluated changes in the incidence of falls. The novelty of our study is the evaluation of incidence across different clinical departments. In most departments we observed a decrease in the incidence of falls during the last three or five years, except for the internal medicine ward, where this trend was stable. The neurology ward was the only one showing a significant increase in the incidence of inpatient falls. A trend analysis allows to predict potential changes in fall incidence in the future and such information is essential for proper planning of fall prevention activities that should be tailored for each department separately.

We are also aware that our study has some limitations that must be discussed. The major drawback of this data set is lack of description of what medications associated with the risk of falls were being used by patients in which falls occurred. However, the lack

of this analysis does not discredit the results. Secondly, due to the huge number of staff involved in reporting inpatient falls, as well as staff fluctuation during the study period, the quality of data on registered patient falls may vary. Thirdly, falls risk factors were unavailable for the analysis. Finally, we used data from just one hospital which provides treatment for a specific population with the percentage of people in the retirement age higher than the city average. These limitations, however, did not prevent us from achieving the aim of the study and presenting reliable results. The strength of this study is that data were available from patients treated in different clinical departments in a tax-funded healthcare system in public hospital. Furthermore, a comprehensive analysis of inpatient falls in a large sample across clinical departments is the major power of this study. The subject clearly needs meta-analysis based on data from different hospitals functioning in various surroundings, which could provide a more reliable estimate of fall rates. Both characteristics of hospitals and patients treated could be analyzed as potential moderators accounting for differences between results based on separate datasets.

5. Conclusions

Inpatient falls remain the leading cause of adverse events in hospitals. According to the presented results, the prevalence of falls was equal to 0.82%. However, there are significant differences in the incidence of inpatient falls between different wards. The highest fall risk was in the rehabilitation ward followed by internal medicine department, while orthopedics, cardiology and rheumatology patients were at the lowest risk of falls. The falls occurred most frequently between 24:00 and 6:00 and were more prevalent in the group of female patients. Furthermore, in different clinical departments, distinct changes in the incidence of inpatient falls were reported. In our opinion, in order to improve patient safety, not only reporting rough numbers of inpatient falls but also an analysis of changes seem to be crucial, as only this allows to predict potential future changes in falls, which is essential for proper planning of fall prevention activity.

Author Contributions: Conceptualization, M.M. and T.B.; methodology, M.M. and T.B.; software, M.C.; validation, A.C. and Ł.S.; investigation, M.M.; resources, M.M.; data curation, M.M. and M.C.; writing—original draft preparation, M.M., B.B. and T.B.; writing—review and editing, M.M.; visualization, M.C. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to restriction.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Nitz, J.C.; Johnston, V. An argument for a universal definition and method of recording falls. *Phys. Ther. Rev.* **2014**, *19*, 131–135. [CrossRef]
2. Alcee, D. The experience of a community hospital in quantifying and reducing patient falls. *J. Nurs. Care Qual.* **2000**, *14*, 43–53. [CrossRef]
3. Enloe, M.; Wells, T.; Mahoney, J.; Pak, M.; Gangnon, R.; Pellino, T.; Hughes, S.; Leahy-Gross, K. Falls in acute care: An academic medical center six-year review. *J. Patient Saf.* **2005**, *1*, 208–214. [CrossRef]
4. Goodwin, M.B.; Westbrook, J.I. An analysis of patient accidents in hospital. *Aust. Clin. Rev.* **1993**, *13*, 141–149. [PubMed]
5. Stel, V.S.; Smit, J.H.; Pluijm, S.M.F.; Lips, P. Consequences of falling in older men and women and risk factors for health service use and functional decline. *Age Ageing* **2003**, *33*, 58–65. [CrossRef]
6. Halfon, P.; Eggli, Y.; Van Melle, G.; Vagnair, A. Risk of falls for hospitalized patients: A predictive model based on routinely available data. *J. Clin. Epidemiol.* **2001**, *54*, 1258–1266. [CrossRef]

7. Morris, R.; O'Riordan, S. Prevention of falls in hospital. *Clin. Med.* **2017**, *17*, 360–362. [CrossRef] [PubMed]
8. Mathers, L.J.; Weiss, H.B. Incidence and characteristics of fall-related emergency department visits. *Acad. Emerg. Med.* **1998**, *5*, 1064–1070. [CrossRef] [PubMed]
9. WHO. Guidelines on Physical Activity and Sedentary Behaviour, Źródło. Available online: https://www.who.int/publications/i/item/9789240015128 (accessed on 31 May 2021).
10. Gębska, M.; Weber–Nowakowska, K.; Malinowska, J.; Zyzniewska –Banaszak, E. Presbyastasis—Terapia zaburzeń równowagi i kontroli postawy. *Pomeranian. J. Life Sci.* **2016**, *62*, 26–30. [CrossRef] [PubMed]
11. Hall, C.D.; Heusel-Gillig, L.; Tusa, R.J.; Herdman, S.J. Efβicacy of gaze stability exercises in older adults with dizziness. *J. Neurol. Phys. Ther.* **2010**, *34*, 64–69. [CrossRef]
12. Lee, Y.; Lee, H.H.; Uhm, K.E.; Jung, H.J.; Kim, Y.S.; Shin, J.; Choi, J.; Han, S.H.; Lee, J. Early Identification of Risk Factors for Mobility Decline Among Hospitalized Older Patients. *Am. J. Phys. Med. Rehabil.* **2019**, *98*, 699–705. [CrossRef]
13. van Weel, C.; Vermeulen, H.; van den Bosch, W. Falls, a community care perspective. *Lancet* **1995**, *345*, 1549–1551. [CrossRef]
14. Morse, J.M.; Morse, R.M. Calculating fall rates: Methodological concerns. *QRB Qual. Rev. Bull.* **1988**, *14*, 369–371. [CrossRef]
15. Sutton, J.C.; Standen, P.J.; Wallace, W.A. Patient accidents in hospital: Incidence, documentation and significance. *Br. J. Clin. Pract.* **1994**, *48*, 63–66.
16. Morse, J.M.; Tylko, S.J.; Dixon, H.A. Characteristics of the fall-prone patient. *Gerontologist* **1987**, *27*, 516–522. [CrossRef] [PubMed]
17. Tutuarima, J.A.; van der Meulen, J.H.; de Haan, R.J.; van Straten, A.; Limburg, M. Risk factors for falls of hospitalized stroke patients. *Stroke* **1997**, *28*, 297–301. [CrossRef] [PubMed]
18. Staggs, V.S.; Mion, L.C.; Shorr, R.I. Assisted and Unassisted Falls: Different Events, Different Outcomes, Different Implications for Quality of Hospital Care. *Jt. Comm. J. Qual. Patient Saf.* **2014**, *40*, 358–364. [CrossRef]
19. Hill, A.-M.; Hoffmann, T.; Hill, K.; Oliver, D.; Etherton-Beer, C.; McPhail, S.; Brauer, S.; Haines, T. Measuring falls events in acute hospitals—A comparison of three reporting methods to identify missing data in the hospital reporting system. *J. Am. Geriatr. Soc.* **2010**, *58*, 1347–1352. [CrossRef] [PubMed]
20. Schwendimann, R.; Buhler, H.; De Geest, S.; Milisen, K. Falls and consequent injuries in hospitalized patients: Effects of an interdisciplinary falls prevention program. *BMC Health Serv. Res.* **2006**, *6*, 69. [CrossRef]
21. Quigley, P.; White, S. Hospital-based fall program measurement and improvement in high reliability organizations. *Online J. Issues Nurs.* **2013**, *18*, 5.
22. King, B.; Pecanac, K.; Krupp, A.; Liebzeit, D.; Mahoney, J. Impact of Fall Prevention on Nurses and Care of Fall Risk Patients. *Gerontologist* **2018**, *58*, 331–340. [CrossRef]
23. Mikos, M.; Budzowska, J.; Juszczyk, G.; Czerw, A.; Banaś, T.; Urbaniak, M. Conclusions from the analysis of adverse events in the Polish health care system in judicial decisions of civil courts between 2011 and 2013. *Pol. Arch. Intern. Med.* **2017**, *127*, 564–566. [CrossRef]
24. Milisen, K.; Coussement, J.; Flamaing, J.; Vlaeyen, E.; Schwendimann, R.; Dejaeger, E.; Surmont, K.; Boonen, S. Fall prediction according to nurses' clinical judgment: Differences between medical, surgical, and geriatric wards. *J. Am. GeriatrSoc.* **2012**, *60*, 1115–1121. [CrossRef] [PubMed]
25. Loj, A.; Stachanczyk, A. *Statistical Bulletin of the City of Kraków I Quarter 2021*; Statistical Office in Krakow: Krakow, Poland, 2020.
26. Fay, M.P.; Tiwari, R.C.; Feuer, E.J.; Zou, Z. Estimating Average Annual Percent Change for Disease Rates without Assuming Constant Change. *Biometrics* **2006**, *62*, 847–854. [CrossRef] [PubMed]
27. Hill, A.M.; Jacques, A.; Chandler, A.M.; Richey, P.A.; Mion, L.C.; Shorr, R.I. In-Hospital Sequelae of Injurious Falls in 24 Medical/Surgical Units in Four Hospitals in the United States. *Jt. Comm. J. Qual. Patient Saf.* **2019**, *45*, 91–97. [CrossRef] [PubMed]
28. Stevenson, B.; Mills, E.M.; Welin, L.; Beal, K.G. Falls risk factors in an acute-care setting: A retrospective study. *Can. J. Nurs. Res.* **1998**, *30*, 97–111.
29. Goodridge, D.; Marr, H. Factors associated with falls in an inpatient palliative care unit: An exploratory study. *Int. J. Palliat. Nurs.* **2002**, *8*, 548–556. [CrossRef]
30. Healey, F.; Scobie, S.; Oliver, D.; Pryce, A.; Thomson, R.; Glampson, B. Falls in English and Welsh hospitals: A national observational study based on retrospective analysis of 12 months of patient safety incident reports. *Qual. Saf. Heal. Care* **2008**, *17*, 424–430. [CrossRef]
31. Toyabe, S.-I. Characteristics of Inpatient Falls not Reported in an Incident Reporting System. *Glob. J. Heal. Sci.* **2015**, *8*, 17–25. [CrossRef]
32. Sari, A.B.; Sheldon, T.A.; Cracknell, A.; Turnbull, A. Sensitivity of routine system for reporting patient safety incidents in an NHS hospital: Retrospective patient case note review. *BMJ* **2007**, *334*, 79. [CrossRef]

Article

Meaningful Activities and Psychosomatic Functions in Japanese Older Adults after Driving Cessation

Atsushi Nakamura [1,2,*], Michio Maruta [3], Hyuma Makizako [4], Masaaki Miyata [4], Hironori Miyata [2], Gwanghee Han [5], Yuriko Ikeda [4], Suguru Shimokihara [2], Keiichiro Tokuda [6], Takuro Kubozono [7], Mitsuru Ohishi [7] and Takayuki Tabira [4]

[1] National Institute for Minamata Disease, Ministry of the Environment, 4058-18 Hama, Minamata, Kumamoto 867-0008, Japan

[2] Doctoral Program of Clinical Neuropsychiatry, Graduate School of Health Sciences, Kagoshima University, 8-35-1, Sakuragaoka, Kagoshima 890-8544, Japan; 814.miya.418@gmail.com (H.M.); k5848730@kadai.jp (S.S.)

[3] Department of Rehabilitation, Okatsu Hospital, 3-95, Masagohonmachi, Kagoshima 890-0067, Japan; m.maru0111@gmail.com

[4] Graduate School of Health Sciences, Kagoshima University, 8-35-1, Sakuragaoka, Kagoshima 890-8544, Japan; makizako@health.nop.kagoshima-u.ac.jp (H.M.); miyatam@m3.kufm.kagoshima-u.ac.jp (M.M.); yuriko@health.nop.kagoshima-u.ac.jp (Y.I.); tabitaka@health.nop.kagoshima-u.ac.jp (T.T.)

[5] Department of Neuropsychiatry, Kumamoto University Hospital, Kumamoto, 1-1-1 Honjo Chuo-ku, Kumamoto 860-8556, Japan; hans11057@gmail.com

[6] Department of Rehabilitation, Kirameki Terrace Healthcare Hospital, 43-30 Kouraicho, Kagoshima 890-0051, Japan; gomyway.k.t@icloud.com

[7] Department of Cardiovascular Medicine and Hypertension, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima 890-0075, Japan; kubozono@m.kufm.kagoshima-u.ac.jp (T.K.); ohishi@m2.kufm.kagoshima-u.ac.jp (M.O.)

* Correspondence: atsuatsu0323@yahoo.co.jp; Tel.: +81-966-63-3111

Abstract: The purpose of this cross-sectional study was to analyse the differences in meaningful activities and psychosomatic function depending on the driving status of community-dwelling older adults. Data from 594 older adults were obtained, including activities meaningful to individuals and psychosomatic functions, such as grip strength, depression, cognitive function, and ability of activity. Participants were divided into active driving (n = 549) and after driving cessation (n = 45) groups. In addition, the active driving group was operationally divided into three groups: high-frequency group (n = 387), medium group (n = 119), and infrequent group (n = 42). In the after driving cessation group, grip strength, and Japan Science and Technology Agency Index of Competence scores were significantly lower. Furthermore, the proportion of apathy and physical and social frailty was significantly higher in the after driving cessation group. Regarding meaningful activity, domestic life scores in the after driving cessation group were significantly higher than those of the active driving group. Decreased driving frequency in the active driving group was associated with weak muscle strength, lack of interest, and low activity. This study demonstrated that meaningful activity differed based on the driving status. Hence, we should support the activities of older adults who are considering driving cessation.

Keywords: driving cessation; meaningful activities; community-dwelling older adults; psychosomatic functions

1. Introduction

In Japan, the number of driver's license holders aged 75 years and above is increasing, causing many fatal accidents [1]. To resolve this problem in recent years, a supportive environment that involves, for example, driving aptitude consultations and support measures for older drivers considering driving cessation, has been promoted to make it easier for them to return their driver's licenses. However, previous studies on driving cessation have

reported that musculoskeletal and neurological problems, visual problems, and cognitive decline lead to driving cessation in older adults. Furthermore, problems with the musculoskeletal system and vision [2], being a woman, and decline in independence as measured in activities of daily living (ADL) [3] have been reported as reasons for driving cessation in older adults. In contrast, driving cessation in older adults leads to poor health [4]. This is because it decreases physical function and increases the risk of functional limitation [5,6], cognitive decline [7], depressive symptoms, depression [8–10], frailty [11,12], and mortality [13]. Therefore, driving cessation can be caused by diminished physical and psychosomatic function. Further, environmental factors such as financial reasons can also affect driving cessation. In older adults, driving cessation can impair physical and psychosomatic function, and personal factors such as their changing interests. Therefore, considering complex interactions between physical function, activity, participation, environmental and personal factors with respect to driving cessation is necessary. Moreover, it has been reported that driving cessation in older adults negatively impacts life satisfaction, time spent outside [14], networking with friends [15], paid work, and volunteering [16]. Therefore, in addition to creating an environment that makes it easy for older adults to return a license, it is also essential to prevent the deterioration of their physical function and activity that occurs after the suspension of driving.

Tarumizu City (Area: 62.49 square miles), with a population of 14,379 and a low population density, is one of the least populated areas of Japan, and its population aging rate is extremely high. In addition, public transportation is inadequate and driving is necessary to perform various essential life functions. Participation in activities is essential for older adults as it benefits their health and improves their psychological well-being and health-related quality of life [17,18]. In 2002, the World Health Organization developed "Active Aging" to respond to the progress of global aging, and Active Aging places a great deal of emphasis on participation in activities that individuals find meaningful [19]. Quite a few meaningful activities (e.g., cooking meals, dressing, and bathing) are routine, while others include work, caring for others, social activities, and leisure activities [20]. Meaningful activities are those that include personal purposes and values rather than merely indicating the activity [21]. In addition, previous studies have reported a growing recognition for engaging in personally valued activities (meaningful activities) that are also beneficial for the well-being of older adults [22]. Therefore, engaging in meaningful activities is crucial for maintaining good health. Compared to men, women older than 65 years are reported to have a significantly higher self-assessment of their labour in their domestic life [23]. Driving interruptions have been reported to be associated with low levels of out-of-home activities [24] and productive engagement [16]. It has also been reported that, in rural older people, driving is important for the activities they want or need to perform [25]. However, there are no reports regarding the activities that older people, who have stopped driving or drive infrequently, value. Therefore, it is necessary to investigate the content quality, satisfaction, and performance of meaningful activities for older adults who have stopped driving. The reduced frequency of driving may also be associated with reduced activity.

This cross-sectional study aimed to analyse the differences in meaningful activity and mental and physical function between community-dwelling older adults with different driving statuses (driving or not driving, gender, frequency of driving). Understanding how reduced outings and driving affect the physical and mental functioning and activity of older people is useful while considering pre- and post-driving cessation support preparations.

2. Materials and Methods

2.1. Participants

This cross-sectional study used data from the Tarumizu Study 2018. It was a collaborative study undertaken by Kagoshima University, the Tarumizu City office, and Tarumizu Chuo Hospital. This study was conducted from June to December 2018 as a community-based health survey. Reply-paid postcards were mailed to the residents of Tarumizu City

who were aged 40 years or older at the time of examination, and residents were recruited through local newspaper advertisements and community campaigns. The recruitment period was from April to June 2018, and 1385 people participated in the survey. The survey was conducted at public facilities in Tarumizu, and participants attended one of 24 sessions a year.

This study targeted citizens over the age of 65. The exclusion criteria were as follows: Participants whose data regarding the Aid for Decision-making in Occupation Choice (ADOC) (n = 8) and questions about driving (n = 4) were missing; participants who had a history of stroke (n = 36), Parkinson's disease (n = 1), and dementia (n = 8); and participants who had never owned a driver's license (n = 208) in their lifetime.

We questioned the participants about their present driving status and then divided them into two groups: the active driving (n = 549) group and the after driving cessation (n = 45) groups. The active driving group included people with a license, and the after driving cessation group included those who had returned their license (n = 27), who had not renewed their license (n = 2), and who had not returned their license, but were not currently driving (n = 16). In addition, the active driving group was operationally divided into three groups: high-frequency group (n = 387, 6–7 days a week), medium group (n = 119, 3–5 days a week), and infrequent group (n = 42, 2 days or less a week), and their characteristics were compared. Finally, data from 594 community-dwelling older adults (age $\geq$65 years, mean age: 73.5 $\pm$ 5.8, women: 53.2%) were analysed for this study (Figure 1). The ethics committee of Faculty of Medicine, Kagoshima University approved the study protocol (approval number 170351).
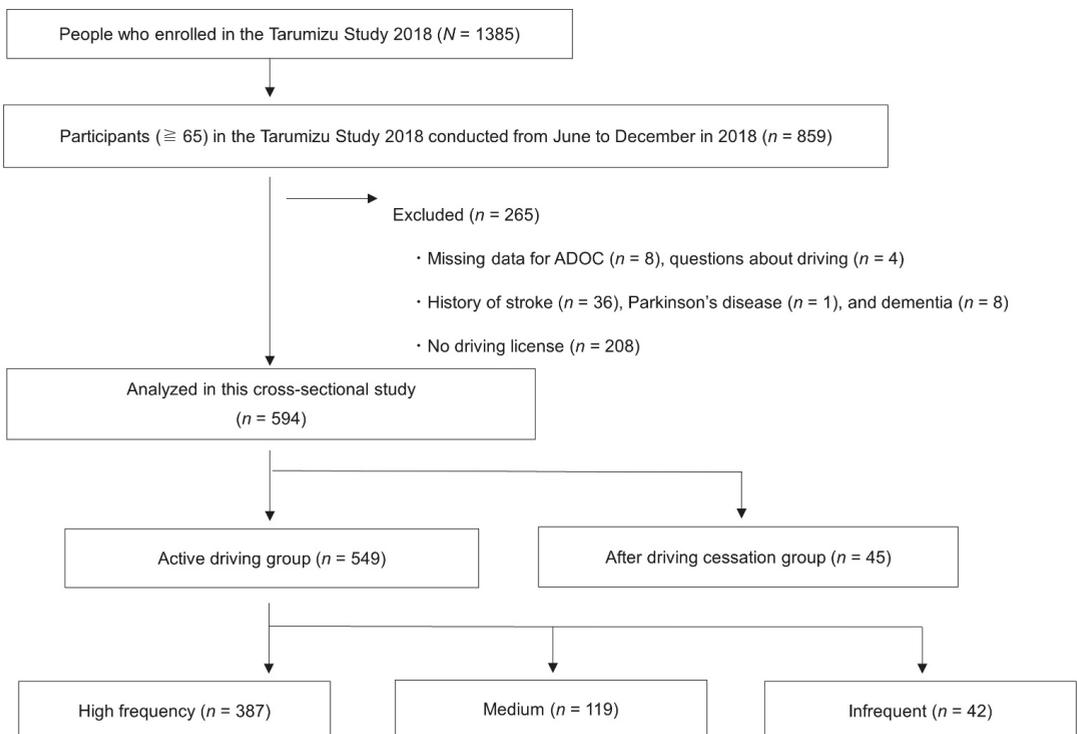

Figure 1. Flowchart of the present study.

2.2. Meaningful Activity

In this study, meaningful activities were operationally defined as "activities that individuals consider important in their daily life" [21]. The ADOC was developed as a meaningful activity choice for clients in rehabilitation [26]. The ADOC consists of eight categories: self-care, mobility, domestic life, work/education, interpersonal interaction, social life, sport, and leisure. The eight categories contain 95 illustrations related to "Activities and Participation", including the International Classification of Functioning, Disability, and Health. Leisure is defined as those activities which produce intrinsic rewards and provide the participant with life-enhancing meaning and a sense of pleasure [27]. The leisure activities in ADOC include 29 items, such as painting, reading, making sweets, gardening, and travelling. An English version has already been developed [28], and the validity of satisfaction in the evaluation has been reported [29]. It is also a preferable tool for focusing on meaningful personal activities [30]. The ADOC has a visually significant effect [31] and is an effective tool for eliciting information about meaningful activities from community-dwelling older adults. Data were collected via a face-to-face survey between the researcher and the subjects. The subjects were shown 95 illustrations of ADOC and asked verbally, "What are the meaningful activities in your daily life?" Therefore, participants were asked to select three to five meaningful activities from the ADOC and then rank the selected activities. Participants evaluated satisfaction using a scale of 1–5 for the selected meaningful activities ranked by ADOC (1 = very dissatisfied, 5 = very satisfied). Furthermore, we also used a scale of 1–10 to assess performance with the selected activity (1: with great difficulty, 10: perfectly). Satisfaction and performance are measures of the individual meaningful activity chosen by them. The researchers in this study were occupational therapists and a few occupational therapy students. Before beginning the study, we conducted two lectures, about two hours each, on the investigation method of meaningful activities. In addition, on the day of the study, we conducted approximately 30 min of practical training before the survey. The study is conducted 24 times a year, and the researchers are engaged multiple times.

2.3. Psychosomatic Functions

Regarding psychosomatic function, we examined the participants' depressive state [8–10], cognitive function [7], frailty [11,12], and apathy [32], which have been reported to be related to driving cessation in previous studies. Their depressive state was evaluated using the Geriatric Depression Scale (GDS-15), and 5 points or more (out of 15) indicated a depressive state [33]. Moreover, among the subordinate items of GDS-15, questions like (1) "Have you dropped many of your activities and interests? (yes)", (2) "Do you prefer to stay at home, rather than going out and doing new things? (Yes)", and (3) "Do you feel full of energy? (No)" were judged as apathy if the answers to these scored ≥ 2 points [34]. Apathy is a behavioural symptom defined as disinterest and loss of motivation [35]. Cognitive function was assessed using a Mini-Cog consisting of a three-word recall task and a clock drawing test [36]. The total scores were the sum of the correct words recalled (0–3) and the drawing of the clock (0 or 2), with a cutoff of <3, which was reported to distinguish between people with and without cognitive impairment [36,37]. Therefore, in this study, a total score of <3 was defined as poor cognitive function.

Frailty is a state of physical and mental decline due to aging, which involves the interaction of physical, cognitive, and social aspects. Physical frailty was evaluated for five items: weight loss, weakness, exhaustion, slowness, and low levels of activity, with reference to the definition of the Cardiovascular Health Study (CHS) [38] and the report by Makizako et al. [39]. Physical frailty was recognised if three or more of the five items applied to participant; pre-frailty was not included in the study. Cognitive frailty is defined as the presence of both physical frailty and cognitive impairment. Cognitive frailty was assessed using the National Centre for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT) to define disability corresponding to the population base. This aspect

included community-dwelling older adults (score >1.5, standard deviations (SD) below the age- and education-specific mean). NCGG-FAT consists of four domains: memory, attention, executive function, and processing speed [40]. Those with either decreased slowness (if <1.0 m/s walking speed regardless of gender and height) or weakness (if <26 kg grip strength for men, if <18 kg grip strength for women), and cognitive impairment were considered cognitively frail [41]. Social frailty considered five questions about social rules, daily social activities, and social relationships: living alone (yes), going out less frequently than last year (yes), visiting friends sometimes (no), wanting to help friends or family (no), and talking with someone every day (no) [42]. If two or more of them were acknowledged, participants were considered socially frail, excluding pre-frailty [42]. The Japan Science and Technology Agency Index of Competence (JST-IC) was used to evaluate the activity's ability. It was developed as an index to evaluate whether older Japanese adults can live independently and greater actively alone [43,44]. It included four areas (16 items): technology usage, information practice, life management, and social engagement. Higher scores reflected higher activity competence (range: 0–16).

2.4. Statistical Analysis

We used Student's *t*-test for continuous variables, Pearson's χ^2 tests for categorical variables, and the Mann–Whitney U-test and Kruskal–Wallis test for ordinal variables. To exclude the effect of gender, we performed the same analysis only in women. In addition, the active driving group was operationally divided into three groups: high-frequency, medium, and infrequent groups, and statistical analysis was performed. We used one-way ANOVA for continuous variables, Pearson's χ^2 tests for categorical variables, and Kruskal–Wallis test for ordinal variables. Meaningful activities were analysed, including all selected activities from the first to fifth place. Further, the representative values of satisfaction and performance were taken as the median score of first to fifth place. All analyses were conducted using IBM SPSS Statistics 24.0 (IBM Corp., Armonk, NY, USA), and *p* values < 0.05 were considered statistically significant.

3. Results

The characteristics of the study participants are listed in Table 1. The 594 participants were divided into two groups: active driving (n = 549) and after driving cessation (n = 45). The age and proportion of women in the after driving cessation group were significantly higher (age: *p* < 0.001, women: *p* < 0.001), while the grip strength and JST-IC scores in the after driving cessation group were significantly lower (grip strength: *p* < 0.001, JST-IC: *p* < 0.001) compared with those in the active driving group. The proportion of those with apathy (*p* = 0.009), physical frailty (*p* = 0.001) and social frailty (*p* = 0.002) in the after driving cessation group was significantly higher compared with those in the active driving group. There was no difference in satisfaction (*p* = 0.266) or performance (*p* = 0.655) of meaningful activities between the two groups. Of the meaningful activity categories selected by the active driving and after driving cessation groups, the ratio that selected leisure was high in both groups (driving: 32.1%, driving cessation: 27.9%) (Figure 2). The work/education in the active driving group was significantly higher than that in the after driving cessation group (active driving: 5.9%, after driving cessation: 1.4 %, *p* < 0.05), while domestic life in the after driving cessation group was significantly higher compared with that in the active driving group (active driving: 16.3 %, after driving cessation: 27.9%; *p* < 0.01) (Figure 2). Regarding specific activities of domestic life, cooking meals (27.0%), collecting information (keeping up to date using newspapers and other news sources) (14.7%), and shopping (14.5%) were often chosen in the active driving group, and cooking meals (36.7%), shopping (11.7%), and laundry (11.7%) were often selected in the after driving cessation group (Table 2). In specific activities of work/education, remunerative employment (56.4%) and non-remunerative employment (38.5%) were often chosen in the active driving group, and remunerative employment (66.7%) was often selected in the after driving cessation group (Table 2).

Table 1. Comparison of characteristics between the active driving and the after driving cessation group in all the participants.

	Group		*p* Value
	Active Driving (n = 549)	**After Driving Cessation (n = 45)**	
Age (Years)	73.1 ± 5.6	77.1 ± 6.5	<0.001 a
Women, n (%)	280 (51.0)	36 (80.0)	<0.001 b
Education (Years)	11.5 ± 2.4	11.0 ± 1.8	0.131 a
Medication (Numbers)	3.56 ± 4.4	5.51 ± 4.3	0.005 a
BMI (kg/m^2)	23.4 ± 3.2	23.3 ± 3.4	0.871 a
Grip strength (kg)	27.0 ± 7.0	21.8 ± 6.8	<0.001 a
JST-IC (Points)	12.1 ± 2.9	9.96 ± 2.7	<0.001 a
GDS (Points)	2.32 ± 2.4	2.95 ± 2.6	0.118 a
Depression, n (%)	80 (14.6)	10 (22.7)	0.147 b
Apathy, n (%)	115 (20.9)	17 (37.8)	0.009 b
Poor Cognition, n (%)	92 (16.8)	7 (15.6)	0.835 b
Living Alone, n (%)	119 (20.9)	18 (40.0)	0.003 b
Physical frailty, n (%)	7 (1.3)	5 (11.1)	0.001 b
Cognitive frailty, n (%)	47 (8.6)	7 (15.6)	0.102 b
Social frailty, n (%)	61 (11.1)	12 (26.7)	0.002 b
Satisfaction with Activity	4.0 (4.0–5.0)	4.0 (3.3–5.0)	0.266 c
Performance of Activity	8.0 (7.0–10.0)	8.0 (7.0–10.0)	0.655 c

Values are mean ± standard deviation (SD) or median (interquartile range); BMI, Body Mass Index; JST-IC, Japan Science and Technology Agency Index of Competence; GDS, Geriatric Depression Scale; a Student's *t*-test, b Pearson's χ^2 test, c Mann–Whitney U-test.
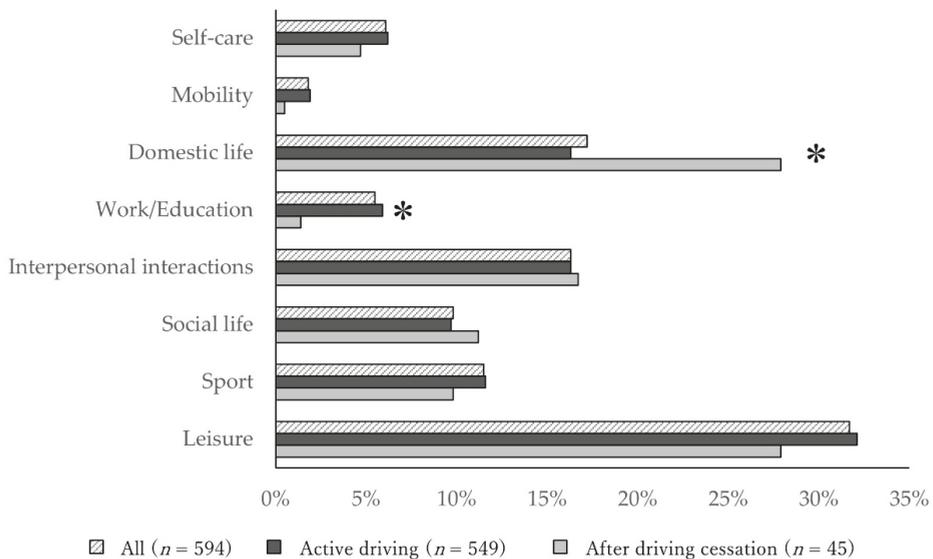
Figure 2. Comparison of the meaningful activities between the active driving group and the after driving cessation group in all participants. * *p* < 0.05, active driving group vs. after driving cessation group.

Table 2. Detail of meaningful activities related to domestic life and work/education in the active driving group and after driving cessation group.

|	No.	Active Driving Group (n = 549)		After Driving Cessation Group (n = 45)
Domestic life	1	Cooking meals (27.0%)	1	Cooking meals (36.7%)
	2	Collecting information (14.7%)	2	Shopping (11.6%)
	3	Shopping (14.5%)		Laundry (11.6%)
	4	Cleaning (11.5%)	4	Cleaning (10.0%)
	5	Laundry (10.6%)	5	Collecting information (8.3%)
	6	Child Care (6.0%)	6	Management of property (6.7%)
	7	Assisting old people/patients (4.0%)	7	Making and repairing clothes (5.0%)
	8	Household maintenance (3.5%)		Child Care (5.0%)
	9	Management of property (3.0%)	9	Household maintenance (1.7%)
	10	Maintaining vehicles/appliances (2.5%)		Assisting old people/patients (1.7%)
	11	Makeup (1.4%)		Barbershop (1.7%)
	12	Making and repairing clothes (0.9%)		
	13	Writing a letter/document (0.2%)		
		Barbershop (0.2%)		
Work/Education	1	Remunerative employment (56.4%)	1	Remunerative employment (66.7%)
	2	Non-remunerative employment (38.5%)	2	Non-remunerative employment (33.3%)
	3	Informal education (4.5%)		
	4	School education (0.6%)		

The activities selected by the older adults are listed in descending order for the items that showed a significant difference in the comparison of meaningful activities.

To determine the effect of gender, we only analysed women. In women, the grip strength ($p < 0.001$) and JST-IC score ($p < 0.001$) were significantly lower, and the proportion of physical frailty ($p = 0.001$) and social frailty ($p = 0.018$) was significantly higher in the after driving cessation group compared with those in the active driving group (Table 3). Furthermore, in women, work/education was significantly higher in the active driving group compared with the after driving cessation group (active driving: 5.7%, after driving cessation: 1.1%; $p < 0.05$), and domestic life in the after driving cessation group was significantly higher than in the active driving group (active driving: 19.8%, after driving cessation: 29.4%; $p < 0.05$) (Figure 3). In contrast, for men only, "Leisure" was the most frequently selected activity for both the active driving group (35.6%, Age: 74.2 ± 6.0) and the after driving cessation group (36.8%, Age: 78.3 ± 6.9). Then, less frequent driving resulted in lower grip strength ($p < 0.007$), and more apathy ($p = 0.001$) and social frailty ($p < 0.025$) (Table 4).

Table 3. Characteristics in the active driving group and the after driving cessation group in women.

	Group		*p* Value
	Active Driving (n = 280)	**After Driving Cessation (n = 36)**	
Age (Years)	72.1 ± 5.0	77.6 ± 6.6	<0.001 a
Education (Years)	11.3 ± 1.9	10.9 ± 1.7	0.243 a
Medication (Number)	3.18 ± 3.5	5.5 ± 4.2	<0.001 a
BMI (kg/m^2)	23.1 ± 3.4	23.8 ± 3.5	0.273 a
Grip strength (kg)	22.3 ± 4.2	19.6 ± 4.1	<0.001 a
JST-IC (Points)	12.6 ± 2.6	10.2 ± 2.5	<0.001 a
GDS (Points)	2.4 ± 2.4	3.0 ± 2.5	0.181 a
Depression, n (%)	43 (15.4)	8 (22.9)	0.256 b
Apathy, n (%)	68 (24.3)	14 (38.9)	0.060 b
Poor Cognition, n (%)	35 (12.5)	4 (11.1)	0.534 b
Living Alone, n (%)	73 (26.1)	14 (38.9)	0.105 b
Physical frailty, n (%)	1 (0.4)	3 (8.3)	0.005 b
Cognitive frailty, n (%)	14 (5.0)	5 (13.9)	0.051 b
Social frailty, n (%)	24 (8.6)	8 (22.2)	0.018 b
Satisfaction with Activity	4.0 (4.0–5.0)	4.0 (3.3–5.0)	0.178 c
Performance of Activity	7.0 (7.0–10.0)	10.0 (8.0–10.0)	0.281 c

Values are mean ± standard deviation (SD) or median (interquartile range); BMI, Body Mass Index; JST-IC, Japan Science and Technology Agency Index of Competence; GDS, Geriatric Depression Scale; a Student's *t*-test, b Pearson's χ^2 test, c Mann–Whitney U-test.
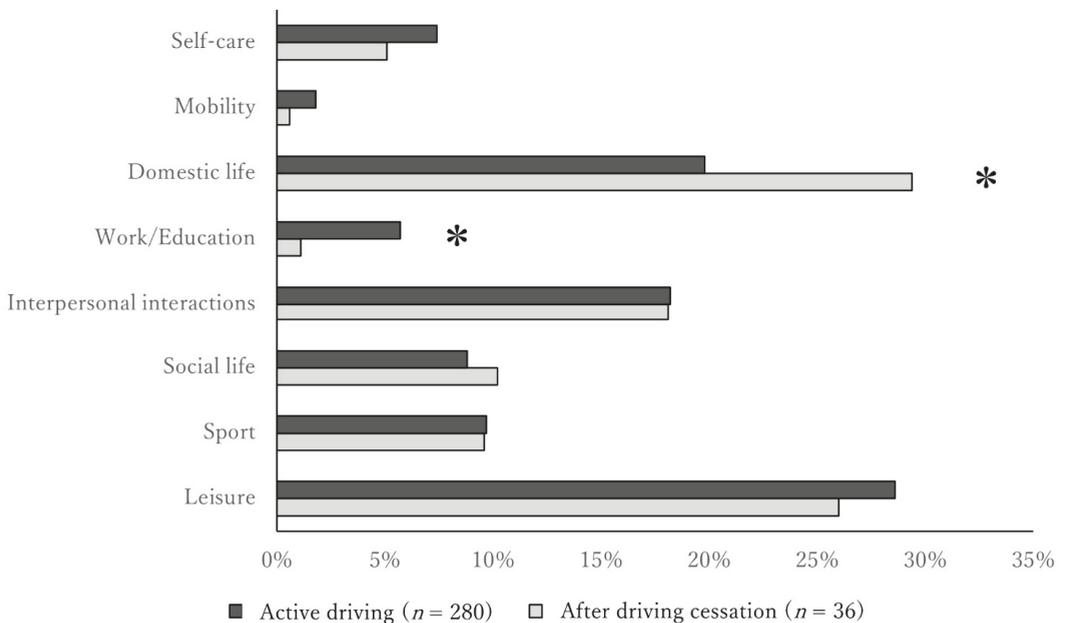
Figure 3. Comparison of meaningful activities between the active driving and the after driving cessation group in women. * *p* < 0.05, active driving group vs. after driving cessation group.

Table 4. Characteristics of differences in the number of driving days per week.

	Group			*p* Value
	High-Frequency (n = 387)	Medium (n = 119)	Infrequent (n = 42)	
Age, mean ± SD (Years)	73.1 ± 5.5	73.2 ± 5.6	73.7 ± 6.5	0.745 a
Women, n (%)	185 (47.8)	70 (58.8)	25 (59.5)	0.057 b
Education, mean ± SD (Years)	11.5 ± 2.4	11.6 ± 2.2	11.6 ± 2.5	0.721 a
Medication ± SD (Number)	3.7 ± 4.8	3.2 ± 3.4	3.0 ± 3.4	0.319 a
BMI, mean ± SD (Kg/m^2)	23.1 ± 3.4	23.8 ± 3.5	23.1 ± 4.0	0.273 a
Grip strength, mean ± SD (Kg)	27.5 ± 7.1	26.0 ± 7.1	25.0 ± 4.7	0.007 a
JST-IC, mean ± SD (Points)	12.1 ± 2.9	12.2 ± 2.8	11.6 ± 3.0	0.445 a
GDS, mean ± (Points)	2.2 ± 2.3	2.6 ± 2.7	2.8 ± 2.4	0.124 a
Depression, n (%)	48 (12.4)	22 (18.5)	10 (23.8)	0.055 b
Apathy, n (%)	66 (17.1)	33 (27.7)	16 (38.1)	0.001 b
Poor Cognition, n (%)	71 (18.3)	15 (12.6)	6 (14.3)	0.309 b
Living Alone, n (%)	81 (20.9)	27 (22.7)	7 (16.7)	0.711 b
Physical frailty, n (%)	4 (1.0)	2 (1.7)	1 (2.4)	0.690 b
Cognitive frailty, n (%)	30 (7.8)	16 (34.0)	1 (2.4)	0.050 b
Social frailty, n (%)	35 (9.0)	17 (14.3)	9 (21.4)	0.025 b
Satisfaction with Activity, Median (IQR)	4.0 (4.0–5.0)	4.0 (4.0–5.0)	4.0 (3.0–5.0)	0.289 c
Performance of Activity, Median (IQR)	8.0 (7.0–10.0)	8.0 (7.0–10.0)	9.0 (7.0–10.0)	0.642 c

SD, standard deviation; BMI, Body Mass Index; JST-IC, Japan Science and Technology Agency Index of Competence; GDS, Geriatric Depression Scale; IQR, interquartile range; a one-way ANOVA, b Pearson's χ^2 test, c Kruskal–Wallis test. High-frequency group (6–7 days a week), Medium group (3–5 days a week), and Infrequent group (2 days or less a week).

4. Discussion

As people get older, they may stop driving due to various reasons, such as deterioration in physical function. However, a driving interruption can be a turning point in their lives. Changes in the living environment due to interruptions in driving are affected by various factors such as physical and psychosomatic functions, personal factors, and environmental factors, and these complex interrelationships can affect daily life. In this study, we examined whether meaningful activities and psychosomatic function of community-dwelling older adults differ due to their driving status. We found that the active driving group valued work/education, while the after driving cessation group attached importance to domestic life. Moreover, the grip strength and JST-IC score were significantly lower in the after driving cessation group than in the active driving group. The proportion of apathy and physical and social frailty were significantly higher in the after driving cessation group than in the active driving group. In the active driving group, grip strength decreased, and social frailty increased as the frequency of driving decreased. As public transport in Tarumizu City is inadequate, it is challenging to live without a private car. Therefore, for older adults considering driving cessation in the future, it is necessary to support them considering their meaningful activities and intervene to maintain their physical activities.

Regarding the psychosomatic functions of the older adults who stopped driving, it was found that their grip strength and activity ability were considerably reduced. Furthermore, the incidences of apathy and physical and social frailty were high. Thus, we think that various daily life activities are restricted by interrupted driving, which may cause a decrease in muscle strength and the ability to be active as well as an increase in apathy in older adults.

Comparing the meaningful activities between both the groups, it was found that the active driving group attached high value to work/education, while the after driving cessation group attached importance to domestic life. As the active driving group was younger and had a higher proportion of men than the after driving cessation group, it was comprised of individuals who were the financial earners in their family. A previous study has reported that older people who retire from their full-time jobs have worse mental

health (GDS-15) and Higher-Level Functional Capacity [45]. Therefore, the active driving group in this study may consider that continuing to work can be effective in terms of health maintenance and social participation. Psychosomatic health and daily and social activity could be maintained by continuing work. In contrast, it has been suggested that increasing the number of social participation activities and increasing participation in sports clubs and neighbourhood associations will prevent physical weakness in older adults [46]. For those who cannot continue their work or have already quit, it may be effective to work in the neighbourhood instead of at their jobs. Conversely, the ratio of women was higher in the after driving cessation group, and many women attached great value to domestic life. Previous studies reported that women were focused on domestic life higher than eight hours a week compared to men [47]. Further, women over the age of 65 also scored significantly higher than men in activities associated with domestic life [22]. There existed 80.0% of women in the after driving cessation group in this study. Domestic life and indoor activities are suggested to be meaningful activities after driving interruption for women. In contrast, women in the active driving group placed greater importance on work/education. Significant differences in activity before and after driving can have a negative impact on life after driving cessation. Therefore, interventions based on social cognitive theory with an emphasis on driving cessation plans and the involvement of friends and family as reported in previous studies may be effective for driving cessation [48].

Previous studies have reported that low mileage while driving [11] and the proportion of car accidents that occur after the age of 60 years are associated with physical frailty [12]. In this study, physical and social frailty were higher in the after driving cessation group than in the active driving group. Therefore, it is suggested that driving cessation may promote a decrease in social and physical activities [15]. Although previous studies have reported the accelerated decrease of cognitive function after driving interruption, there was no significant difference in Mini-Cog and cognitive frailty between the active driving and the after driving cessation groups in our study. This may be because the sample size of the after driving cessation group was small, and the duration after driving interruption was not evaluated in this study. In contrast, the after driving cessation group had increased apathy compared to the active driving group in this study. After driving cessation, they have fewer opportunities to go out, and meaningful outdoor activities are limited; hence, they may develop apathy. The authors acknowledge that the use of the apathy sub-scale of the GDS in this study is complicated by the fact that the items "dropping activities" and "staying home" are directly affected by driving cessation. Highly extensive and longitudinal studies need to be performed to investigate the effect of driving cessation on cognitive function and depressive status.

As drivers drive less frequently, their physical function declines and their social frailty increases. This means that even those who are currently driving are likely to drive less often and experience interruptions, increasing the risk of reduced activity, apathy, and physical frailty. Previous studies have reported that lower Short Physical Performance Battery (SPPB) scores were consistently with lower driving exposure and increased driving cessation [49,50]. However, physical function is a correctable risk factor and an increase in SPPB score can be achieved through fitness interventions [51]. Therefore, meaningful activity, including physical factors, may prevent the decline in physical function due to reduced or interrupted driving exposure. In addition, a decrease in driving frequency may be a sign of decreased activity. Therefore, it is necessary to pay attention to the frequency of operation and prevent the decrease in activity by meaningfully engaging them, in preparation for life after the operation is stopped.

Although driving cessation is associated with psychosomatic function in older citizens, pre-planning for driving cessation has been suggested to influence the quality of life of older persons [52]. Moreover, professionals need to participate in the process as evaluators of driving aptitude [53]. Therefore, occupational therapists should cooperate with driving license centres and communities to support older adults considering driving cessation. The results of this study indicate that we need to consider the meaningful activity of individuals

and take measures to prevent apathy, muscle weakness, and reduction of activity through planning for driving cessation.

This study has several limitations. First, it is a cross-sectional study, and we cannot clarify whether our results are causes or results of driving cessation. Second, this study was carried out in one city, and we cannot deny the selection bias. Therefore, we need to perform high extensive and longitudinal studies to investigate the effect of driving cessation on meaningful activity and physical and social frailty. Third, the percentage of people after driving cessation in the final sample of the study was 8.2%, and the group sizes between active driving and after driving cessation were very different. This means that there is a higher scope for a wide variety of activities in the active driving group. However, in previous studies, the percentage of people who stopped driving was 9.0% [2], 1.4% [5], and 5.2% [6], and the after driving cessation group in this study was the same as or slightly higher. Fourth, we did not determine the factors and details of why older people stopped driving. The reasons to stop driving vary, and we need to analyse these reasons, including physical, social, and psychological frailty, in further studies.

5. Conclusions

In conclusion, we found that meaningful activity differed depending on the driving status; the active driving group valued work/education, while the after driving cessation group attached importance to domestic life. Moreover, in terms of physical and psycho-somatic function, the after driving cessation group may be associated with weak muscle strength, apathy, and physical and social frailty. In addition, infrequent driving in the active driving group may give rise to an increasing number of older adults with social frailty. These results may be helpful in the pre-planning and support of driving cessation in older adults.

Author Contributions: Conceptualization, A.N. and T.T.; methodology, A.N. and T.T.; investigation, A.N., M.M. (Michio Maruta), H.M. (Hyuma Makizako), H.M. (Hironori Miyata), G.H., Y.I., S.S., K.T. and T.T.; writing—original draft preparation, A.N. and T.T.; writing—review and editing, A.N., M.M. (Michio Maruta), M.M. (Masaaki Miyata) and T.T.; supervision, H.M. (Hyuma Makizako) and T.T.; project administration, T.K. and M.O. All authors have read and agreed to the published version of the manuscript.

References

1. About the Characteristics of Traffic Accidents. Available online: https://www.npa.go.jp/publications/statistics/koutsuu/toukeihyo.html (accessed on 28 September 2020).
2. Huisingh, C.; McGwin, G., Jr.; Owsley, C. Association of visual sensory function and higher-order visual processing skills with incident driving cessation. *Clin. Exp. Opt.* **2016**, *99*, 441–448. [CrossRef]
3. Seiler, S.; Schmidt, H.; Lechner, A.; Benke, T.; Sanin, G.; Ransmayr, G.; Lehner, R.; Dal-Bianco, P.; Santer, P.; Linortner, P.; et al. Driving cessation and dementia: Results of the prospective registry on dementia in Austria (PRODEM). *PLoS ONE* **2012**, *7*, e52710. [CrossRef] [PubMed]
4. Edwards, J.D.; Lunsman, M.; Perkins, M.; Rebok, G.W.; Roth, D.L. Driving cessation and health trajectories in older adults. *J. Gerontol. A Biol. Sci. Med. Sci.* **2009**, *64*, 1290–1295. [CrossRef]

5. Shimada, H.; Makizako, H.; Tsutsumimoto, K.; Hotta, R.; Nakakubo, S.; Doi, T. Driving and incidence of functional limitation in older people: A prospective population-based study. *Gerontology* **2016**, *62*, 636–643. [CrossRef] [PubMed]
6. Hirai, H.; Ichikawa, M.; Kondo, N.; Kondo, K. The risk of functional limitations driving cessation among older Japanese adults: The JAGES cohort study. *J. Epidemiol.* **2020**, *30*, 332–337, JE20180260. [CrossRef]
7. Choi, M.; Lohman, M.C.; Mezuk, B. Trajectories of cognitive decline by driving mobility: Evidence from the Health and Retirement Study. *Int. J. Geriatr. Psychiatry* **2014**, *29*, 447–453. [CrossRef]
8. Marottoli, R.A.; de Leon, C.F.M.; Glass, T.A.; Williams, C.S.; Cooney, L.M., Jr.; Berkman, L.F.; Tinetti, M.E. Driving cessation and increased depressive symptoms: Prospective evidence from the New Haven EPESE. *J. Am. Geriatr. Soc.* **1997**, *45*, 202–206. [CrossRef]
9. Chihuri, S.; Mielenz, T.J.; DiMaggio, C.J.; Betz, M.E.; DiGuiseppi, C.; Jones, V.C.; Li, G. Driving cessation and health outcomes in older adults. *J. Am. Geriatr. Soc.* **2016**, *64*, 332–341. [CrossRef]
10. Ragland, D.R.; Satariano, W.A.; MacLeod, K.E. Driving cessation and increased depressive symptoms. *J. Gerontol. A Biol. Sci. Med. Sci.* **2005**, *60*, 399–403. [CrossRef]
11. Crowe, C.L.; Kannoth, S.; Andrews, H.; Strogatz, D.; Li, G.; DiGuiseppi, C.; Hill, L.; Eby, D.W.; Molnar, L.J.; Mielenz, T.J. Associations of frailty status with low-mileage driving and driving cessation in a cohort of older drivers. *Geriatrics* **2020**, *5*, 19. [CrossRef] [PubMed]
12. Lenardt, M.H.; Cechinel, C.; Binotto, M.A.; Kolb Carneiro, N.H.; Lourenço, T.M. Physical frailty and fitness of older driver. *Colomb. Med.* **2017**, *48*, 41–46. [CrossRef]
13. Edwards, J.D.; Perkins, M.; Ross, L.A.; Reynolds, S.L. Driving status and three-year mortality among community-dwelling older adults. *J. Gerontol. A Biol. Sci. Med. Sci.* **2009**, *64*, 300–305. [CrossRef]
14. Al-Hassani, S.B.; Alotaibi, N.M. The impact of driving cessation on older Kuwaiti adults: Implications to occupational therapy. *Occup. Ther. Health Care* **2014**, *28*, 264–276. [CrossRef]
15. Mezuk, B.; Rebok, G.W. Social integration and social support among older adults following driving cessation. *J. Gerontol. B Psychol. Sci. Soc. Sci.* **2008**, *63*, S298–S303. [CrossRef] [PubMed]
16. Curl, A.L.; Stowe, J.D.; Cooney, T.M.; Proulx, C.M. Giving up the keys: How driving cessation affects engagement in later life. *Gerontologist* **2014**, *54*, 423–433. [CrossRef] [PubMed]
17. Eakman, A.M.; Carlson, M.E.; Clark, F.A. The meaningful activity participation assessment: A measure of engagement in personally valued activities. *Int. J. Aging Hum. Dev.* **2010**, *70*, 299–317. [CrossRef] [PubMed]
18. Rantanen, T.; Pynnönen, K.; Saajanaho, M.; Siltanen, S.; Karavirta, L.; Kokko, K.; Karvonen, A.; Kauppinen, M.; Rantalainen, T.; Rantakokko, M.; et al. Individualized counselling for active aging: Protocol of a single-blinded, randomized controlled trial among older people (the AGNES intervention study). *BMC Geriatr.* **2019**, *19*, 5:1–5:14. [CrossRef]
19. W.H.O. *Active Ageing: A Policy Framework*; World Health Organization: Geneva, Swizerland, 2002.
20. Moyers, P.A. The guide to occupational therapy practice. *Am. J. Occup. Ther. Off. Publ. Am. Occup. Ther. Assoc.* **1999**, *53*, 247–322. [CrossRef] [PubMed]
21. Maruta, M.; Makizako, H.; Ikeda, Y.; Miyata, H.; Nakamura, A.; Han, G.; Shimokihara, S.; Tokuda, K.; Kubozono, T.; Ohishi, M.; et al. Associations between depressive symptoms and satisfaction with meaningful activities in community-dwelling Japanese older adults. *J. Clin. Med.* **2020**, *9*, 795. [CrossRef] [PubMed]
22. Eakman, A.M.; Carlson, M.E.; Clark, F.A. Factor structure, reliability and convergent validity of the engagement in meaningful activities survey for older adults. *OTJR (Thorofare N. J.)* **2010**, *30*, 111–121. [CrossRef]
23. Castelblanque, E.M.; Cunat, V.A.; Martinez, J.A. Life-style activities in older people without intellectual impairment: A population-based study. *Rural. Remote Health* **2005**, *5*, 344. [CrossRef]
24. Marottoli, R.A.; de Leon, C.F.M.; Glass, T.A.; Williams, C.S.; Cooney, L.M., Jr.; Berkman, L.F. Consequences of driving cessation: Decreased out-of-home activity levels. *J. Gerontol. B Psychol. Sci. Soc. Sci.* **2000**, *55*, S334–S340. [CrossRef]
25. Strogatz, D.; Mielenz, T.J.; Johnson, A.K.; Baker, I.R.; Robinson, M.; Mebust, S.P.; Andrews, H.F.; Betz, M.E.; Eby, D.W.; Johnson, R.M.; et al. Importance of Driving and Potential Impact of Driving Cessation for Rural and Urban Older Adults. *J. Rural. Health* **2020**, *36*, 88–93. [CrossRef] [PubMed]
26. Tomori, K.; Uezu, S.; Kinjo, S.; Ogahara, K.; Nagatani, R.; Higashi, T. Utilization of the iPad application: Aid for decision-making in occupation choice. *Occup. Ther. Int.* **2012**, *19*, 88–97. [CrossRef]
27. Suto, M. Leisure in occupational therapy. *Can. J. Occup. Ther.* **1998**, *65*, 271–278. [CrossRef]
28. Levack, W.; Tomori, K.; Takahashi, K.; Sherrington, A.J. Development of an English-language version of a Japanese iPad application to facilitate collaborative goal setting in rehabilitation: A Delphi study and field test. *BMJ Open* **2018**, *8*, e018908. [CrossRef] [PubMed]
29. Tomori, K.; Saito, Y.; Nagayama, H.; Seshita, Y.; Ogahara, K.; Nagatani, R.; Higashi, T. Reliability and validity of individualized satisfaction score in aid for decision-making in occupation choice. *Disabil. Rehabil.* **2013**, *35*, 113–117. [CrossRef]
30. Nagayama, H.; Tomori, K.; Ohno, K.; Takahashi, K.; Ogahara, K.; Sawada, T.; Uezu, S.; Nagatani, R.; Yamauchi, K. Effectiveness and Cost-effectiveness of occupation-based occupational therapy using the Aid for Decision Making in Occupation Choice (ADOC) for older residents: Pilot cluster randomized controlled trial. *PLoS ONE* **2016**, *11*, e0150374. [CrossRef]

31. Ally, B.A.; Waring, J.D.; Beth, E.H.; McKeever, J.D.; Milberg, W.P.; Budson, A.E. Aging memory for pictures: Using high-density event-related potentials to understand the effect of aging on the picture superiority effect. *Neuropsychologia* **2008**, *46*, 679–689. [CrossRef] [PubMed]
32. Herrmann, N.; Rapoport, M.J.; Sambrook, R.; Hébert, R.; McCracken, P.; Robillard, A. Predictors of driving cessation in mild-to-moderate dementia. *Cmaj* **2006**, *175*, 591–595. [CrossRef]
33. Yesavage, J.A. Geriatric depression scale. *Psychopharmacol. Bull.* **1988**, *24*, 709–711.
34. Bertens, A.S.; Moonen, J.E.F.; de Waal, M.W.M.; Foster-Dingley, J.C.; de Ruijter, W.; Gussekloo, J.; van der Mast, R.C.; de Craen, A.J.M. Validity of the three apathy items of the Geriatric Depression Scale (GDS-3A) in measuring apathy in older persons. *Int. J. Geriatr. Psychiatry* **2017**, *32*, 421–428. [CrossRef] [PubMed]
35. Marin, R.S. Differential diagnosis and classification of apathy. *Am. J. Psychiatry* **1990**, *147*, 22–30. [CrossRef]
36. Borson, S.; Scanlan, J.; Brush, M.; Vitaliano, P.; Dokmak, A. The mini-cog: A cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int. J. Geriatr. Psychiatry* **2000**, *15*, 1021–1027. [CrossRef]
37. Borson, S.; Scanlan, J.M.; Watanabe, J.; Tu, S.P.; Lessig, M. Simplifying detection of cognitive impairment: Comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. *J. Am. Geriatr. Soc.* **2005**, *53*, 871–874. [CrossRef] [PubMed]
38. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M156. [CrossRef]
39. Makizako, H.; Shimada, H.; Doi, T.; Tsutsumimoto, K.; Suzuki, T. Impact of physical frailty on disability in community-dwelling older adults: A prospective cohort study. *BMJ Open* **2015**, *5*, e008462. [CrossRef]
40. Makizako, H.; Shimada, H.; Park, H.; Doi, T.; Yoshida, D.; Uemura, K.; Tsutsumimoto, K.; Suzuki, T. Evaluation of multidimensional neurocognitive function using a tablet personal computer: Test-retest reliability and validity in community-dwelling older adults. *Geriatr. Gerontol. Int.* **2013**, *13*, 860–866. [CrossRef]
41. Shimada, H.; Doi, T.; Lee, S.; Makizako, H.; Chen, L.; Arai, H. Cognitive frailty predicts incident dementia among community-dwelling older people. *J. Clin. Med.* **2018**, *7*, 250. [CrossRef] [PubMed]
42. Makizako, H.; Shimada, H.; Tsutsumimoto, K.; Lee, S.; Doi, T.; Nakakubo, S.; Hotta, R.; Suzuki, T. Social frailty in community-dwelling older adults as a risk factor for disability. *J. Am. Med. Dir. Assoc.* **2015**, *16*, 1003.e7–1003.e11. [CrossRef] [PubMed]
43. Iwasa, H.; Masui, Y.; Inagaki, H.; Yoshida, Y.; Shimada, H.; Otsuka, R.; Kikuchi, K.; Nonaka, K.; Yoshida, H.; Yoshida, H.; et al. Development of the Japan Science and Technology Agency Index of Competence to assess functional capacity in older adults: Conceptual definitions and preliminary items. *Gerontol. Geriatr. Med.* **2015**, *1*, 2333721415609490. [CrossRef]
44. Iwasa, H.; Masui, Y.; Inagaki, H.; Yoshida, Y.; Shimada, H.; Otsuka, R.; Kikuchi, K.; Nonaka, K.; Yoshida, H.; Yoshida, H.; et al. Assessing competence at a higher level among older adults: Development of the Japan Science and Technology Agency Index of Competence (JST-IC). *Aging Clin. Exp. Res.* **2018**, *30*, 383–393. [CrossRef]
45. Minami, U.; Nishi, M.; Fukaya, T.; Hasebe, M.; Nonaka, K.; Koike, T.; Suzuki, H.; Murayama, Y.; Uchida, H.; Fujiwara, Y. Effects of the change in working status on the health of older people in Japan. *PLoS ONE* **2015**, *10*, e0144069. [CrossRef]
46. Abe, T.; Okuyama, K.; Kamada, M.; Yano, S.; Toyama, Y.; Isomura, M.; Nabika, T.; Sakane, N.; Ando, H.; Miyazaki, R. Social participation and physical prefrailty in older Japanese adults: The Shimane CoHRE study. *PLoS ONE* **2020**, *15*, e0243548. [CrossRef]
47. Jolly, S.; Griffith, K.A.; DeCastro, R.; Stewart, A.; Ubel, P.; Jagsi, R. Gender differences in time spent on parenting and domestic responsibilities by high-achieving young physician-researchers. *Ann. Intern. Med.* **2014**, *160*, 344–353. [CrossRef]
48. Windsor, T.D.; Anstey, K.J. Interventions to reduce the adverse psychosocial impact of driving cessation on older adults. *Clin. Interv. Aging* **2006**, *3*, 205–211. [CrossRef] [PubMed]
49. Slims, R.V.; Ahmed, A.; Sawyer, P.; Alman, R.M. Self-reported health and driving cessation in community-dwelling older drivers. *J. Gerontol. A Biol. Sci. Med. Sci.* **2007**, *62*, 789–793. [CrossRef]
50. Gill, T.M.; Gahbauer, E.A.; Murphy, T.E.; Han, L.; Allore, H.G. Risk factors and precipitants of long-term disability in community mobility: A cohort study of older persons. *Ann. Intern. Med.* **2012**, *17*, 131–140. [CrossRef] [PubMed]
51. Mielenz, T.J.; Durbin, L.L.; Cisewski, J.A.; Guralnik, J.M.; Li, G. Select physical performance measures and driving outcomes in older adults. *Inj. Epidemiol.* **2017**, *4*, 14. [CrossRef] [PubMed]
52. Musselwhite, C.B.A.; Shergold, I. Examining the process of driving cessation in later life. *Eur. J. Ageing* **2013**, *10*, 89–100. [CrossRef]
53. Albert, G.; Lotan, T.; Weiss, P.; Shiftan, Y. The challenge of safe driving among elderly drivers. *Healthc. Technol. Lett.* **2018**, *5*, 45–48. [CrossRef] [PubMed]

Article

Assessment of Physical Fitness and Risk Factors for the Occurrence of the Frailty Syndrome among Social Welfare Homes' Residents over 60 Years of Age in Poland

Antonina Kaczorowska [1,*], Katarzyna Szwamel [1], Małgorzata Fortuna [2], Agata Mroczek [1], Ewelina Lepsy [1] and Aleksandra Katan [3]

[1]   Institute of Health Sciences, University of Opole, 45-060 Opole, Poland; katarzyna.szwamel@uni.opole.pl (K.S.); agata.mroczek@uni.opole.pl (A.M.); ewelina.lepsy@uni.opole.pl (E.L.)
[2]   Faculty of Medical Sciences and Technology, The Karkonosze University of Applied Sciences in Jelenia Góra, 58-503 Jelenia Góra, Poland; malgorzata.fortuna@kpswjg.pl
[3]   Rehabilitation Department, District Hospital Nachod, 547 69 Nachod, Czech Republic; akatan@wp.pl
[*]   Correspondence: antonina.kaczorowska@uni.opole.pl

Abstract: The study aimed at assessing physical fitness and occurrence of the frailty syndrome among social welfare homes' residents as well as defining factors which determine the level of frailty and its occurrence. The examination included 198 residents (115 females and 83 males of average age 75.5 ± 10.21) and was carried out with the use of the Short Physical Performance Battery (SPPB) test with the following cut-off points: 0–6—frail, 7–9—pre-frail, 10–12—non-frail. The research additionally collected data regarding age, gender, number of chronic diseases, education level, type of prior work and current physical activity. In addition, the height and weight of the respondents were measured. The frailty syndrome was found in more than a half of the examinees (104; 52.53%), the pre-frailty state in 30.30% ($n = 60$) and 17.17% ($n = 34$) were non-frail. The average result of the SPPB test was 6.52 ± 2.73, which proves a moderate limitation of the sample group's fitness. No significant differences were noted between female and male respondents ($p = 0.27$). The multifactorial linear regression model showed that independent and direct frailty syndrome predicators included age, number of chronic diseases and regular physical activity ($p < 0.05$). In conclusion, promoting and encouraging regular, age and interest-related forms of physical activity among seniors might foster the maintenance of their physiological reservoir and functional efficiency.

Keywords: aging; physical functional performance; nursing homes; frailty syndrome; physical fitness; gait analysis

1. Introduction

Frailty is prevalent among elderly residents living in formal long- term care facilities [1]. One of the reasons of such a situation is that frailty and pre-frailty are significant predictors of nursing home placement among community-dwelling older adults [2]. Unfortunately, frailty syndrome is also an important predictor of mortality among older adults living in nursing homes [3]. Taking the reversible character of frailty into consideration, it is important to take a comprehensive view on frailty and carry out the appropriate interventions to prevent mortality and other adverse outcomes among social welfare homes' residents [1,4].

In Poland in 2020, 67,000 of residents of stationary social welfare institutions were people over 60 years of age. Most of them (25,357 people, 24.1%) stayed in social welfare homes (SWH) [5]. However, an epidemiological study conducted in long-term care facilities in six European countries showed that Poland had one of the highest percentages of residents with poor functional and cognitive status [6].

Population ageing is one of the most significant demographic and social trends of the 21st century. In 2021, more than a fifth of the European Union (EU) population was 65 years of age or older, and this segment is projected to grow to 31.1% by 2100 [7]. Two of the most problematic expressions of population ageing are frailty and multimorbidity [8]. Therefore, promoting physical activity among older people in order to maintain their satisfactory health condition, physical activity and functional fitness and self-reliance has become one of the prioritized strategic areas established by WHO for European countries in 2016–2025 [9].

The prevalence of frailty ranges between 4% and 59% in elderly populations and is higher in women than in men [10]. More than 50% of the European population aged >50 years are pre-frail or frail (the overall prevalence of pre-frailty was 42.9% and frailty was 7.7%). The prevalence of frailty in Europe was estimated at approximately 3–15.6%, and in Poland it was—3.1% [11]. The studies showed that the prevalence of frailty and pre-frailty syndrome was of a higher incidence in inhabitants of formal long-term care (LTC) facilities than in people living in the community [12,13].

Frailty in aging marks a state of decreased reserves, resulting in increased vulnerability to adverse outcomes when exposed to stressors [14]. Functional reserve is essential to avoid stressors impacting function, and when intrinsic capacity and functional reserve are reduced the risk for additional disability is very high [15]. The most common concept of frailty is physical frailty. This concept includes the following criteria: unintentional weight loss (10 lbs in the past year), self-reported exhaustion, weakness (low grip strength), slow walking speed and low physical activity. Having at least three of them classifies as a frailty diagnosis [16]. The most common concept of frailty is physical frailty. This concept includes the following criteria: unintentional weight loss (10 lbs in past year), self-reported exhaustion, weakness (low grip strength), slow walking speed and low physical activity. Having at least three of them classifies one with a frailty diagnosis [16]. Chronic inflammation is likely to play a pivotal role in frailty, both directly and indirectly through other systems, such as the musculoskeletal, endocrine, and neurological systems [17]. Frailty increases health care expenditures and has a negative impact on older adults' quality of life [1,18]. Frail elderly have been predisposed to functional deficits such as comorbidity and mortality because frailty reduces their ability to maintain overall homeostasis [19].

Nursing home residents are a particularly vulnerable to frailty [13,20]. The main determinants of being physically frail in nursing home residents' are: malnutrition [21], vitamin D deficiency [22,23], older age, female, living in a private institution, living with unknown person or living alone, having no regular exercise (≤2 times/week) and sedentary behaviour, poor self-reported health, lower socioeconomic status, lack of educational qualifications, obesity, being a smoker, and pain [24–26].

There is a lot of evidence which has proven that frailty among the elderly may be delayed or reversed. The following actions might prove effective: a multicomponent exercise programme, psychosocial intervention, cognitive stimulation, a combination of resistance exercise and protein supplementation [27–29].

The study aimed at (1) analysing and assessing physical fitness and the occurrence of the frailty syndrome among social welfare home residents as well as (2) defining factors significantly determining the level of the aspects mentioned above in the research group.

2. Materials and Methods

2.1. Study Design and Setting

This was a cross-sectional study from February 2019 to October 2019. The research was conducted in social welfare homes (SWH) in the Lower Silesia, Opolskie and Mazovian voivodships in Poland. The research was carried out in accordance to the Declaration of Helsinki and followed good clinical practice guidelines. The research project was approved by the Bioethics Committee of Opole Medical School (no KB/202/FI/2019). All participants gave written informed consent after explanation of the procedures involved. The STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) were followed.

2.2. Participants

The study used a non-probabilistic sampling method. To calculate the minimal required number of participants for the sample, GUS data was used, which found 67,200 of those over 60 lived in a social welfare home SWH in Poland. With a confidence level of 95% and a margin of error of 5%, $p = 50\%$, the minimum study sample was set at 382 subjects. Therefore, the information about the study and the request for the agreement were sent to 14 social welfare homes. The management of all the 14 facilities gave their consent for the examination. However, 165 out of 1320 residents had medical contraindications, 775 were unable to perform the fitness test, 158 did not comply with the age criterium and 24 did not agree to the examination (Figure 1).
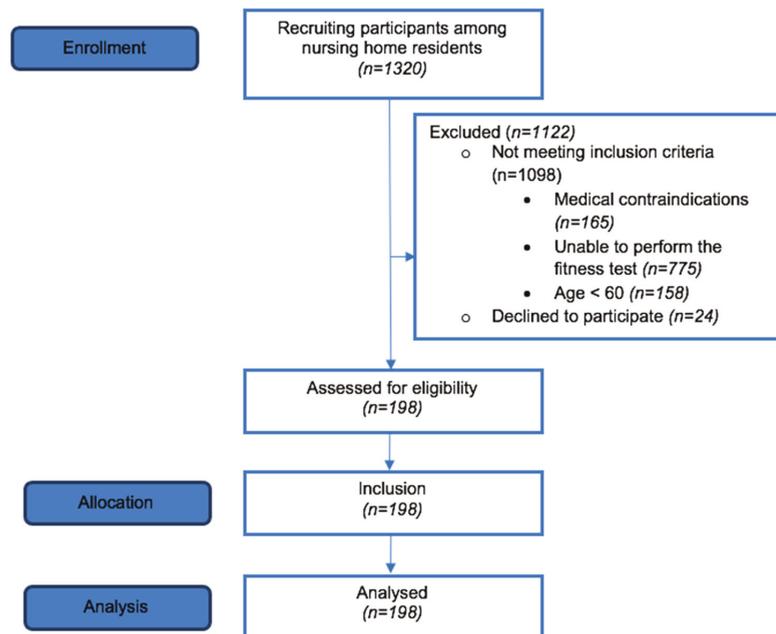

Figure 1. Flow diagram of the study.

Finally, 198 residents were qualified, including 115 women and 83 men aged 60–96. To be included in the study, participants were required to: (1) be of age of 60 years and over, (2) be able to move independently and take the fitness test, (3) not have any medical impediments, (4) be able to communicate verbally, and (5) provide voluntary written consent to participate in the study. The exclusion criteria comprised (1) acute injuries and infections, (2) recent myocardial infarction, (3) other medical impediments to research, (4) the lack of verbal contact, and (5) lack of written consent to participate in the study.

2.3. Measurement Tools

Initially, the respondents filled in the authors' self-written questionnaire to collect data such as age, gender, number of chronic diseases, education, type of prior work and current physical activity. In addition, their height (to the nearest 0.5 cm) and weight (to the nearest 0.5 kg) were measured. Subjects were dressed in light clothing and stood barefoot, upright, and with eyes directed straight ahead when being measured. Body mass index (BMI) was calculated using participants' height (in meters) and mass measurements (mass/height^2). Using the World Health Organization (WHO) criteria (2000), BMI was

used to categorize participants (underweight: <18.5 kg/m^2; normal: 18.5–24.99 kg/m^2; overweight: 25–29.9 kg/m^2; obese: $\geq$30 kg/m^2).

To assess physical condition the SPPB test was applied [30]. The test consists of three trials:

The assessment of strength and endurance of the lower extremities: 5-fold stand-ups off a chair with arms crossed on the chest. The time measured in seconds was recorded.

The assessment of static balance: a respondent is requested to keep their balance in three positions (side-by-side, semi-tandem stand and tandem balance stand). Each next position is performed if no complications with the previous one occur and an examinee is able to withstand it for 10 s.

The assessment of walking speed: walking 4 metres at a normal pace. If examinees walk with some orthopaedic aids, they use it during the examination. The time of the trial was recorded.

The results recorded for each participant were compared with normative data and assigned to 0–4 points for each trial. The overall test score ranged from 0–12 points [30–32]. The SPPB test scoring was used to assess the occurrence of the frailty syndrome. Regarding the threshold score for frailty, older adults who score $\leq$ 9 on the SPPB are most likely to be classified as frail [33], and are at risk of losing the ability to walk 400 m [34] (predictive validity). An SPPB score of $\leq$9 has the most desirable sensitivity (92%), specificity (80%) and greatest area under the curve (AUC = 0.81) for identifying frail adults [35]. In order to classify participants as frail, pre-frail and non-frail, the following cut-offs were used: SPPB 0–6 (frail), SPPB 7–9 (pre-frail), SPPB 10–12 (non-frail) [36]. The measurements and the SPPB test were supervised and performed by the same professionals. They were performed in the morning hours, in SWH common rooms and with the use of a standard chair to assure the same research conditions.

2.4. Statistical Methods

The analysis of the quantitative variables was made by calculating the mean (M), standard deviation (SD), median (Me) and quartiles (Q1, Q3). The qualitative variables' data was assessed by calculating numbers and percentage of occurrence for each value individually. The comparison of qualitative variables' values in groups were counted with the use of a chi-square test (with Yate's correction for 2 $\times$ 2 tables) or a Fisher's test. The comparison of quantitative variables in two groups was carried out with a Mann-Whitney test, while the comparison of quantitative variables' values in three or more groups was counted with Kruskal-Wallis' test. After statistically significant differences had been observed, the post-hoc analysis was applied with the use of Dunn's test to identify statistically and significantly different groups. The comparison between qualitative variables' values in three or more subsequent measurements was calculated with Friedman's test. After statistically significant differences had been revealed, the post-hoc analysis (Wilcoxon's test for related pairs with Bonferroni correction) was applied so as to identify statistically different measurements. The correlations between quantitative variables were made with the use of Spearman's correlation coefficient. The multifactorial analysis of the impact of many variables on one qualitative variable was assessed with the linear regression method. The results were presented in the form of regression model parameter values with a 95% confidence interval. The significance level for the analysis was 0.05. The analysis was calculated in programme R, version 4.1.2 [37].

3. Results

3.1. Descriptive Data

Compared to men, women were statistically significantly older ($p < 0.001$), had more numbers of chronic diseases ($p < 0.001$), and had higher BMI values ($p = 0.028$). Statistically significant differences were also observed between the genders in terms of education ($p = 0.022$) and prior work ($p = 0.007$) (Table 1).

Table 1. The characteristics of a sample group.

Parametr		Gender			*p*
		Women (N = 115)	Men (N = 83)	Total (N = 198)	
Age [years]	M ± SD	77.83 ± 10.17	72.27 ± 9.39	75.5 ± 10.21	*p* < 0.001 *
	Me	80	69	78	
	Q1–Q3	70.5–86	64.5–80.5	66–84	
Number of chronic diseases	M ± SD	2.75 ± 1.09	2.3 ± 0.97	2.56 ± 1.06	*p* = 0.001 *
	Me	3	2	2	
	Q1–Q3	2–3	2–3	2–3	
Education	No	4 (3.48%)	2 (2.41%)	6 (3.03%)	*p* = 0.022 *
	Primary	53 (46.09%)	28 (33.73%)	81 (40.91%)	
	Vocational	13 (11.30%)	25 (30.12%)	38 (19.19%)	
	Secondary	38 (33.04%)	24 (28.92%)	62 (31.31%)	
	High	7 (6.09%)	4 (4.82%)	11 (5.56%)	
Prior work	Physical	68 (59.13%)	67 (80.72%)	135 (68.18%)	*p* = 0.007 *
	Combination of physical and mental	15 (13.04%)	7 (8.43%)	22 (11.11%)	
	Mental	22 (19.13%)	8 (9.64%)	30 (15.15%)	
	No	10 (8.70%)	1 (1.20%)	11 (5.56%)	
Physical activity	No	41 (35.65%)	32 (38.55%)	73 (36.87%)	*p* = 0.275
	Rare	35 (30.43%)	17 (20.48%)	52 (26.26%)	
	Yes	39 (33.91%)	34 (40.96%)	73 (36.87%)	
BMI [kg/m^2]	M ± SD	27.69 ± 5.63	26.01 ± 4.84	26.99 ± 5.37	*p* = 0.028 *
	Me	27.27	25.26	26.3	
	Q1–Q3	23.86–31.56	22.58–28.52	23.2–30.1	
BMI interpretation	Underweight	4 (3.48%)	2 (2.41%)	6 (3.03%)	*p* = 0.156
	Standard	37 (32.17%)	37 (44.58%)	74 (37.37%)	
	Overweight	37 (32.17%)	28 (33.73%)	65 (32.83%)	
	Obesity	37 (32.17%)	16 (19.28%)	53 (26.77%)	

Legend: *p*-Mann-Whitney's test for quantitative variables, Chi-squared or exact Fisher's test for qualitative variables, * statistically significant difference (*p* < 0.05).

3.2. Main Results

The mean of the SPPB test score was 6.52 ± 2.73 and the median was 6, which proves a moderate limitation of the group's fitness. The best statistically significant result was obtained in the walking speed at the 4 m distance trial (2.44 ± 1.07; *p* < 0.001) compared to other trials (Table 2).

Table 2. The statistical characteristics of the SPPB test results.

Trial	N	M	SD	Me	Min	Max	Q1	Q3	*p*
SPPB test	198	6.52	2.73	6	1	12	4.25	9	
Standing off a chair (A)	198	1.95	1.2	2	0	4	1	3	*p* < 0.001 *
Balance test (B)	198	2.13	1.07	2	0	4	1	3	
Walking speed at a 4 m distance (C)	198	2.44	1.07	2	1	4	2	3	C > A.B

Legend: *p*-Friedman's test + post-hoc analysis (Wilcoxon's test for related pairs with Bonferroni correction). * statistically significant difference (*p* < 0.05).

The prevalence of frailty among the residents of SWH was found in over half of the respondents (*n* = 104; 52.53%), both pre-frail (*n* = 60; 30.30%) and non-frail (*n* = 34; 17.17%). There were no statistically significant differences between groups of women and men (Table 3).

Table 3. The proportion of frail, pre-frail and non-frail residents in a sample group.

Frailty Syndrome Ranges	Gender			*p*
	Women (N = 115)	Men (N = 83)	Total (N = 198)	
Frail	66 (57.39%)	38 (45.78%)	104 (52.53%)	*p* = 0.27
Pre-frail	31 (26.96%)	29 (34.94%)	60 (30.30%)	
Non-frail	18 (15.65%)	16 (19.28%)	34 (17.17%)	

Legend: *p*-chi-squared test.

Gender differentiates the results of the SPPB test, however only in a 'walking speed' trial, where the statistically significantly higher score was in men rather than in women (2.65 ± 1.12 vs. 2.29 ± 1.01; $p = 0.022$). The level of activity declared by the respondents also significantly differentiated the results of the SPPB test. The overall SPPB score and trial scores were significantly higher in the physically active group than in all other groups ($p < 0.001$). However, there were no statistically significant differences when taking into account such variables as education or prior work (Table 4).

Table 4. Statistical characteristics of the SPPB test results in correlation to gender, education, prior work and level of physical activity.

Test		Gender		*p*
		Women (N = 115)	Men (N = 83)	
SPPB test	M ± SD	**6.28 ± 2.68**	**6.86 ± 2.78**	*p* = 0.128
	Me	6	7	
	Q1–Q3	4–8	5–9	
Standing off a chair	M ± SD	1.87 ± 1.2	2.06 ± 1.2	*p* = 0.220
	Me	1	2	
	Q1–Q3	1–3	1–3	
Balance test	M ± SD	2.11 ± 1.02	2.16 ± 1.13	*p* = 0.797
	Me	2	2	
	Q1–Q3	1–3	1–3	
Walking speed at a 4 m distance	M ± SD	2.29 ± 1.01	2.65 ± 1.12	*p* = 0.022 *
	Me	2	3	
	Q1–Q3	1–3	2–4	

Test		Education				*p*
		No, primary (N = 87)	Vocational (N = 38)	Secondary (N = 62)	High (N = 11)	
SPPB test	M ± SD	6.41 ± 2.49	6.92 ± 2.84	6.71 ± 2.79	4.91 ± 3.56	*p* = 0.304
	Me	6	7	6	5	
	Q1–Q3	5–8	5–9	5–9	2–7.5	
Standing off a chair	M ± SD	1.93 ± 1.14	2.05 ± 1.18	2.03 ± 1.28	1.27 ± 1.27	*p* = 0.212
	Me	2	2	2	1	
	Q1–Q3	1–3	1–3	1–3	0.5–1.5	
Balance test	M ± SD	2.1 ± 1.01	2.26 ± 1.08	2.19 ± 1.04	1.55 ± 1.51	*p* = 0.356
	Me	2	2	2	2	
	Q1–Q3	1–3	2–3	1–3	0–2	
Walking speed at a 4 m distance	M ± SD	2.36 ± 1.03	2.66 ± 1.07	2.48 ± 1.1	2.09 ± 1.14	*p* = 0.352
	Me	2	3	2.5	2	
	Q1–Q3	2–3	2–4	2–3	1–3	

Table 4. *Cont.*

Test		Physical (N = 135)	Combination of Physical and Mental(N = 22)	Mental (N = 30)	No (N = 11)	*p*
		Prior Work				
SPPB test	M ± SD	6.53 ± 2.5	6.55 ± 2.65	6.47 ± 3.69	6.55 ± 3.01	*p* = 0.997
	Me	6	6	6	6	
	Q1–Q3	5–8	5–9	3–10	4.5–9	
Standing off a chair	M ± SD	1.98 ± 1.15	1.86 ± 1.17	1.87 ± 1.48	2 ± 1.26	*p* = 0.811
	Me	2	1	1	2	
	Q1–Q3	1–3	1–2	1–3	1–2.5	
Balance test	M ± SD	2.1 ± 1.01	2.23 ± 1.11	2.17 ± 1.26	2.27 ± 1.27	*p* = 0.934
	Me	2	2	2	2	
	Q1–Q3	1–3	2–3	1–3	1–3.5	
Walking speed at a 4 m distance	M ± SD	2.46 ± 1.02	2.45 ± 1.1	2.4 ± 1.3	2.27 ± 1.01	*p* = 0.949
	Me	2	2	2.5	2	
	Q1–Q3	2–3	2–3	1–4	1.5–3	

Test		No-A (N = 73)	Rare-B (N = 52)	Yes-C (N = 73)	*p*
		Physical Activity			
SPPB test	M ± SD	5.53 ± 2.38	5.98 ± 2.62	7.89 ± 2.61	*p* < 0.001 *
	Me	5	5.5	8	C > B.A
	Q1–Q3	4–7	4–8	6–10	
Standing off a chair	M ± SD	1.68 ± 1.12	1.67 ± 1.13	2.41 ± 1.21	*p* < 0.001 *
	Me	1	1	2	C > A.B
	Q1–Q3	1–2	1–3	1–4	
Balance test	M ± SD	1.82 ± 0.98	2.02 ± 0.98	2.52 ± 1.11	*p* < 0.001 *
	Me	2	2	2	C > B.A
	Q1–Q3	1–2	1–2	2–3	
Walking speed at a 4 m distance	M ± SD	2.04 ± 0.92	2.25 ± 1.05	2.97 ± 1.01	*p* < 0.001 *
	Me	2	2	3	C > B.A
	Q1–Q3	1–3	1–3	2–4	

Legend: *p*-Mann-Whitney's test (gender), *p*-Kruskal-Wallis test (education, prior work), *p*-Kruskal-Wallis test + post hoc analysis (Dunn's test) (physical activity), * statistically significant difference (*p* < 0.05).

A weak (r = −0.2), but statistically significant negative correlation between age and the overall number of the SPPB test points (*p* = 0.003) and the points at the 'standing off a chair' (*p* < 0.001) and 'walking speed at 4 m distance' trials (*p* = 0.003) were found. It might be concluded that the higher the age, the lower the score at the trials mentioned above. We also found a moderate (r = −0.5) statistically significant negative correlation between number of chronic diseases and SPPB test (*p* < 0.001) and 'walking speed at a 4 m distance' (*p* < 0.001). Another weak statistically significant negative correlation was found between number of chronic diseases and 'standing off a chair' (r = 0.3; *p* < 0.001) and balance test (r = 0.4; *p* < 0.001). The more chronic diseases the residents of SWH suffered from, the lower the scores in all examined aspects (Table 5).

Table 5. Correlations between the SPPB test results and age, number of chronic diseases and BMI.

Variable	Test	Spearman's Correlation Coefficient
Age [years]	SPPB test	r = −0.213. *p* = 0.003 *
	Standing off a chair	r = −0.265. *p* < 0.001 *
	Balance test	r = −0.041. *p* = 0.565
	Walking speed at a 4 m distance	r = −0.211. *p* = 0.003 *

Table 5. *Cont.*

Variable	Test	Spearman's Corellation Coefficient
Number of chronic diseases	SPPB test	r = −0.489. *p* < 0.001 *
	Standing off a chair	r = −0.351. *p* < 0.001 *
	Balance test	r = −0.434. *p* < 0.001 *
	Walking speed at a 4 m distance	r = −0.466. *p* < 0.001 *
BMI [kg/m^2]	SPPB test	r = −0.074. *p* = 0.3
	Standing off a chair	r = −0.041. *p* = 0.569
	Balance test	r = −0.039. *p* = 0.585
	Walking speed at a 4 m distance	r = −0.132. *p* = 0.063

Legend: * statistically significant difference (*p* < 0.05).

The multifactorial model of linear regression showed that significant (*p* < 0.05), independent and direct predictors of the frailty syndrome included age, number of chronic diseases and regular physical activity. Each next year of age decreased the SPPB test score by 0.042 pts. on average (regression parameter −0.042). Each additional chronic disease decreased the SPPB test score by 1.071 pts. on average (regression parameter −1.071), and physical activity increased the score by 2.3 pts. compared to the complete lack of activity (regression parameter 2.3) (Table 6).

Table 6. Direct predictors of the frailty syndrome–the multifactorial analysis.

SPPB Test					
Feature		Parameter	95%CI		*p*
Gender	Women	ref.			
	Men	−0.104	−0.803	0.596	0.771
Age	[years]	−0.042	−0.075	−0.009	0.013 *
Education	No, primary	ref.			
	Vocational	0.057	−0.851	0.965	0.902
	Secondary	−0.783	−1.803	0.237	0.134
	High	−1.037	−2.893	0.82	0.275
Prior work	Physical	ref.			
	Combination of physical and mental	1.045	−0.252	2.342	0.116
	Mental	0.924	−0.331	2.178	0.151
	No	0.101	−1.346	1.548	0.891
Number of chronic diseases		−1.071	−1.395	−0.747	<0.001 *
BMI	[kg/m^2]	0.022	−0.039	0.084	0.477
Physical activity	No	ref.			
	Rare	0.704	−0.107	1.514	0.091
	Yes	2.3	1.553	3.047	<0.001 *

Legend: *p*-multifactorial linear regression, * statistically significant difference (*p* < 0.05).

Age, the number of chronic diseases and regular physical activity proved to be significant (*p* < 0.05), as did direct predictors of the 'standing off a chair' and 'walking speed at 4 m distance' trials, while prior combination work, number of chronic diseases and regular physical activity mattered at the 'balance test' trial. In the 'standing off a chair' trial, each next year of age decreased the trial score by 0.028 pts. on average (regression parameter −0.028), and each additional chronic disease decreased the score by 0.272 pts. on average (regression parameter −0.272) and physical activity increased the score by 0.723 pts. on average compared to the complete lack of activity (regression parameter 0.723). In the 'balance test' trial, prior combination work enhanced the trial score by 0.56 pts. while compared to physical work (regression parameter 0.56), each additional chronic

disease reduced the score by 0.421 pts. on average (regression parameter −0.421), and physical activity increased the score by 0.668 pts. compared to complete lack of activity (regression parameter 0.668). In the 'walking speed at 4 m distance' trial, each next year of age reduced the trial score by 0.015 pts. on average (regression parameter 0.015), and each additional chronic disease reduced the score by 0.38 pts. (regression parameter −0.38), and physical activity increased the score by 0.904 pts. compared to the complete lack of activity (regression parameter 0.904) (Table 7).

Table 7. Direct predictors of 'standing off a chair', walking speed at 4 m distance' and 'balance test' trials.

Standing Off a Chair					
Feature		Parameter	95%CI		*p*
Gender	Women	ref.			
	Men	0.083	−0.197	0.362	0.563
Age	[years]	−0.015	−0.028	−0.002	0.03 *
Education	No, primary	ref.			
	Vocational	0.078	−0.285	0.441	0.674
	Secondary	−0.241	−0.649	0.167	0.249
	High	−0.035	−0.777	0.707	0.926
Prior work	Physical	ref.			
	Combination of physical and mental	0.339	−0.179	0.858	0.201
	Mental	0.202	−0.3	0.704	0.431
	No	−0.035	−0.613	0.544	0.907
Number of chronic diseases		−0.38	−0.51	−0.251	<0.001 *
BMI	[kg/m^2]	−0.002	−0.027	0.023	0.874
Physical activity	No	ref.			
	Rare	0.313	−0.011	0.637	0.06
	Yes	0.904	0.605	1.202	<0.001 *
Balance Test					
Feature		Parameter	95%CI		*p*
Gender	Women	ref.			
	Men	−0.107	−0.402	0.188	0.479
Age	[years]	0.001	−0.013	0.015	0.889
Education	No, primary	ref.			
	Vocational	0.157	−0.226	0.54	0.422
	Secondary	−0.336	−0.766	0.094	0.128
	High	−0.506	−1.289	0.277	0.207
Prior work	Physical	ref.			
	Combination of physical and mental	0.56	0.013	1.107	0.046 *
	Mental	0.468	−0.061	0.997	0.085
	No	0.221	−0.389	0.831	0.479
Number of chronic diseases		−0.421	−0.558	−0.285	<0.001 *
BMI	[kg/m^2]	0.009	−0.016	0.035	0.475
Physical activity	No	ref.			
	Rare	0.267	−0.074	0.609	0.127
	Yes	0.668	0.353	0.983	<0.001 *

Table 7. *Cont.*

Walking Speed at a 4 m Distance					
Feature		Parameter	95%CI		*p*
Gender	Women	ref.			
	Men	0.083	−0.197	0.362	0.563
Age	[years]	−0.015	−0.028	−0.002	0.03 *
Education	No, primary	ref.			
	Vocational	0.078	−0.285	0.441	0.674
	Secondary	−0.241	−0.649	0.167	0.249
	High	−0.035	−0.777	0.707	0.926
Prior work	Physical	ref.			
	Combination of physical and mental	0.339	−0.179	0.858	0.201
	Mental	0.202	−0.3	0.704	0.431
	No	−0.035	−0.613	0.544	0.907
Number of chronic diseases		−0.38	−0.51	−0.251	<0.001 *
BMI	[kg/m^2]	−0.002	−0.027	0.023	0.874
Physical activity	No	ref.			
	Rare	0.313	−0.011	0.637	0.06
	Yes	0.904	0.605	1.202	<0.001 *

Legend: *p*-multifactorial linear regression, * statistically significant difference ($p < 0.05$).

4. Discussion

4.1. Key Results and Interpretation

The primary aim of the research was to analyse and assess physical activity and the occurrence of the frailty syndrome among the SWH residents. The average score of the sample group proves their moderate limitation with regard to fitness. The best scores were noted at the 'walking speed at 4 m distance' trial, whereas the lowest were found at the '5-fold-standing off a chair', which measured the strength and endurance of lower extremities, or the 'balance test'. The overall SPPB test results, 'standing off a chair' and 'balance test' trials' scores in female and male groups did not differ from one another to any significant degree. Male respondents noted significantly better results at the 'walking speed at 4 m distance' trial. Similar results were noted by Guede Rojas et al. They used a senior fitness test and found that the elderly male group achieved better results than the female one in a '2-min marching test' [38]. De Amorim at al. indicated that frailty prevalence is significantly higher among women than men [39].

Such relatively low results achieved by the respondents in the SPPB test might be related to the place of residence, namely SWH. Most physical activity performed by elderly people is connected with their household duties and daily routine. SWH residents lack this kind of daily activity. The performing of daily chores in SWH is highly limited. It is possible that reducing their daily regular activities results in limited physical fitness and significantly lower scores at the 'walking speed' trial, especially among women.

The limitations of opportunities in performing daily duties among the elderly, resulting from low levels of fitness or physical endurance, are closely related to the lack of regular physical activity. According to Fisher et al., a low level of physical activity was connected with the fact of dwelling in a SWH and the level of activity decreased with the age of seniors [40]. Residing in nursing institutions means leading a sedentary lifestyle [41]. Barber et al. assessed SWH residents' daily activity for seven days with the use of an accelerometer. The results showed that the level of activity among the examinees was very low: they spent 79% of the day in a sitting position [42].

Low levels of physical activity in Polish seniors may be related to cultural and social factors as well. The current generation of seniors acquired their habits and behavioural patterns, as well as the ones connected with physical activity, in communist Poland. Polish

and other post-communist countries' seniors lived in a different cultural context than their West European or North American counterparts, where the idea of active aging was thoroughly grounded. In Poland, senility was traditionally considered as the time of well-deserved rest. Also a small fraction of Bohemian seniors take part in sports activities or other forms of physical exercise [43]. The results are collected in the research project entitled 'Bridging the East–West Health Gap', which aimed at examining health condition, attitude and pro-health behaviours in adults from selected Central-Eastern and Western countries, and indicated a huge diversity of physical activity levels in each country. The greatest proportion of physically active respondents was found in West European countries (30.2% Finland, 23.7% Spain) whereas the smallest was in post-communist ones (6.4% Poland, 12.3% Hungary) [44].

Attention ought to be paid to the high proportion of frail and pre-frail respondents found in the self-reported study and the fact that only 17.17% were non-frail. It might be concluded that most of the elderly residents of SWH are at risk of the frailty syndrome. The research by Furtado et al. confirms that institutionalized women, who are found less physically active and not self-reliant, are particularly prone to frailty syndrome occurrence [45]. The issue of frailty in SWH residents was also studied by Kaczorowska et al. The researchers examined 85+ women residing SWH. There was no non-frail individual found among 17 women [20]. The frailty syndrome reduces an elderly person's self-reliance. It leads to an increased vulnerability to unfavourable health-related incidents such as falls, hospitalizations, disability, institutional residence or death [16,46,47]. The correlation between the frailty syndrome and falls in the elderly, assessed on the basis of low SPPB test results, was presented by various authors [47]. Early recognition of the risk of frailty is incredibly crucial, as thanks to the multidirectional prophylaxis there is a possibility to prevent it and improve a patient's condition [48].

More and more research currently makes use of the SPPB test to assess frailty syndrome occurrence. Pritchard et al. examined patients from a geriatric out-patient clinic at the Centre for Healthy Aging in Canada according to Fried's phenotype method with the use of the SPPB test. They achieved similar results to the self-reported ones. After the application of the SPPB test, they found out that 50% of the patients were frail, 35% were pre-frail and 15% were non-frail. Taking into account the Fried's phenotype method, 35% were frail, 57% pre-frail and 7% were non-frail. There was fair to moderate agreement between methods for determining which participants were frail and pre-frail [48]. Danilowich et al. researched seniors in a care home in Illinois with the same test and free online calculator, SHARE-FI. Their online results also resembled the self-reported ones: 45% of the respondents were found to be frail, 35% were pre-frail and 20% were non-frail. The results of the SPPB test revealed that 69% were frail, 28% were pre-frail and 3% were non-frail patients. There was fair to moderate, but statistically significant agreement between these measures [49]. A Spanish study was conducted among over 65year-olds and those respondents living independently. The frailty syndrome was diagnosed with the use of the Frailty Trail Scale (FTS) and physical fitness was assessed with the SPPB test. The authors found a significantly adverse correlation between the results of both measures. A lower score on the SPPB test was related to a higher score on the FTS test and higher intensity of frailty syndrome [50].

The following aim of the study was to determine the factors importantly influencing the level of physical fitness and the occurrence of the frailty syndrome in the research group. It was revealed that demographic variables affected the SPPB test results. Gender was statistically determinant only in the 'walking speed at 4 m distance' trial, although men achieved slightly better results in all trials as well. Other demographic variables, such as education or prior work experience, did not affect physical fitness to any significant degree. Some authors, however, report that frailty prevalence is significantly higher among those having a low educational level and those whose job was predominantly physical. These findings may suggest that work factors could explain the incidence of frailty syndrome [39]. This was not confirmed by the results of our analyses. This would require further research. On the other hand, the factor that significantly differentiated the results was physical

activity. The respondents who declared being physically active achieved higher overall scores as well as in each individual trial than those who rarely or never undertook physical activity. Taking into consideration correlations between age, number of chronic diseases and BMI, the first two variables correlated adversely with the level of fitness. The multifactorial model of linear regression also showed that age, number of chronic diseases and regular physical activity were independent and direct predictors of frailty. The research by other authors found some other variables as strong predictors, namely advanced age elderly, osteoarticular disease, as well as history of hospitalization and falls in the last twelve months [51]. The research by Miller et al. showed that a lower score at the SPPB test was linked to higher age, falls and chronic diseases such as diabetes, sight disorders and kidney issues [52].

The decline of physical activity and functional fitness related with age among elderly men and women was confirmed in the study by Milanovic et al. [53] in which young elderly (60–69 years of age) achieved better results than old elderly (70–80) in almost all the trials of physical fitness assessed with the use of the Senior Fitness Test. Moreover, the study concluded that the decrease of physical activity and functional fitness is caused by a natural aging process. The research of Delbari at al. shows that only the age predictor variable has a statistically significant effect on the occurrence of frailty and, indeed, the frequency of frail older adults significantly increases with age. This result was supported by other studies [29,54,55]. We know that frailty risk increases in association with age, which could be due to the biological rather than the chronological age of individuals. There is consequently an erosion of the homeostatic reserve and vulnerability to disproportionate changes in health status after relatively minor stress events. There is a continuous loss of strength and aerobic resistance, which causes a decrease in functional independence and makes the older adult frail. In general, frailty is superior to age in identifying at-risk older people [56,57].

A vast number of researchers highlight the importance of physical activity and its direct influence on the level of fitness in the elderly as well as the occurrence of the frailty syndrome. The differences in scores of physical fitness between sedentary and active lifestyle groups were confirmed by the study of Silva et al. [58]. The data related to the correlation between sedentary lifestyle or the level of physical activity and physical fitness among elderly patients revealed that the active group achieved higher scores on the Senior Fitness Test than the inactive group. The authors concluded that future prospective research ought to assess the level of physical activity more objectively and discover the causal links between the level of physical activity and fitness in the elderly. To maximize the benefits of physical activity, older people should be encouraged to break down their daily sedentary routine and avoid long-lasting sedentary periods. According to the research by Silva et al., the frailty syndrome is more common among older people who are insufficiently active and spend most of their time sitting, even when considering socio-demographic factors [59].

The scientific data acknowledges that the level of physical activity usually decreases with age and is connected with the decline of functional fitness [52]. It confirms the assumption that the level of physical activity is affected by the aging process and leads to the reduction of functional fitness. The level of physical activity influences the maintenance and the increase of physical fitness [60], and every form of physical activity is better than none [61,62]. The research [63] also noted that lifestyle behaviours such as physical activity may help manage the level of frailty. Adversely, a sedentary lifestyle is connected with frailty regardless of physical activity. Prolonged sitting comes with higher risks of mortality in frail elderly people. Conversely, the research by Billot et al. into the mobility behaviours in the frail elderly suffering from sarcopenia revealed that one of the most common features of aging is the decline of functional skills. Physical frailty and sarcopenia are characterised by weakness, slowness and reduced muscle mass with maintained independent walking skills. One of the strategies which showed some benefits in fighting the mobility loss and its consequences in the elderly is physical activity [64]. Sarcopenia and frailty have mutual aetiology, but aging is connected with a changed signalization of redox in the skeletal

muscles. Modifiable risk factors improve protein synthesis and prevent muscle loss with age. Therefore, physical activity plays a crucial role in preventing these processes [65].

The profession and previous type of work affect the accumulated cognitive reserves. In everyday life, we use only a small part of our cognitive resources. With age, the intellectual abilities are impaired, and this reserve is activated and allows for the compensation of the emerging deficits, which guarantees the maintenance of good cognitive functioning until old age [66]. Our own research showed that the type of prior work and physical activity were important independent direct predictors of the result of the static equilibrium test. A prior combination of physical and mental work and systematic physical activity has a positive effect on balance. Research by Yokoyama et al. showed that two-task cognitive-motor training was more beneficial than just motor training in improving cognitive functions in sedentary elderly people [67]. Similarly, in the studies by Hagovska and Olkeszyova, significant relationships between balance, walking speed and cognitive functions were recorded among the elderly with cognitive impairment who participated in cognitive-motor training [68].

To conclude, aging results in the body fat, reduction of muscle strength, and lower levels of flexibility, agility, and endurance. However, the process of aging is natural and inevitable, and an appropriate level of physical activity might slow down the loss of functional and physical skills and help maintain healthy lifestyles in the elderly [69].

4.2. Strenghts of the Study

The standardized testing tool, the SPPB test, was used, which is highly sensitive at identifying frail individuals and correlates well with other methods which assess the phenomenon, such as Fried's phenotype method, the free online calculator SHARE-FI and the Frailty Trait Scale.

4.3. Limitations

This research has some limitations. As we mentioned in the methodology section, our study lasted from February 2019 to October 2019. In this period we analyzed 198 participants. We are aware that ultimately we should examine 382 participants. Following previous research by Hamilton et al. [70] and Mizumoto et al. [71] we decided to intentionally suspend our research during the winter period. These authors have reported that the activity range for adults decreases during the winter season compared with that reported during the summer season [70,71]. If we were to continue the research in the winter of 2019/2020, we could have obtained much worse results in the SPPB test. We wanted to continue our research in March 2020, but the first cases of patients with COVID-19 in Poland were reported at that time. From 4 March to 30 April 2020, a total of 12,877 laboratory-confirmed COVID-19 cases were registered in Poland. The highest rates for COVID-19 were recorded in the Lower Silesia Province, Silesia and Mazovia [72]. This was the area of our research. As Raciborski et al. reported, the main setting of SARS-CoV-2 transmission was nursing homes (outbreaks of infection in long-term care facilities) [72]. Therefore, we have not obtained consent to continue our research on the forms of the management of social welfare homes. Therefore, we finally decided to analyze the data from 198 participants.

The second limitation of the study was the fact that the nutrition style in SWH was not taken into account, and no standardized measure was applied to assess the examinees' physical activity. A further limitation may stem from the fact that the correlation between place of residence of seniors and the level of their fitness may be adverse. There is a strong need for further research to determine the factors affecting frailty syndrome occurrence in institutionalized people.

5. Conclusions

Functional fitness of elderly SWH residents was limited to a moderate degree. Limiting physical fitness causes a decrease in independence in everyday activities. Systematic physical activation of the inhabitants of nursing homes would limit this unfavorable phe-

nomenon. A large proportion of the SWH seniors were frail or pre-frail, which proves their susceptibility to disability, lower immunity to stressors and decreased adaptational or physiological body reservoirs. The consequence of the frailty syndrome is disability and frequent hospitalizations. Therefore, prophylaxis and activities aimed at improving the condition of people diagnosed as frail should be introduced in social welfare homes.

Direct risk factors of the frailty syndrome were age, number of chronic diseases and low level of physical activity. Proper treatment of chronic diseases as well promoting regular, age and interest-related forms of physical activity among seniors as well as encouraging SWH residents to take part in physical activity classes may facilitate physiological and functional fitness reservoirs' maintenance.

References

1. Wang, H.; Wang, J.; Xie, B.; Liu, B.; Wang, J. Multi-dimensional frailty and its risk factors among older residents in long-term care facilities in Shanghai, China. *Int. J. Nurs. Sci.* **2021**, *5*, 298–303. [CrossRef]
2. Kojima, G. Frailty as a Predictor of Nursing Home Placement Among Community-Dwelling Older Adults: A Systematic Review and Meta-analysis. *J. Geriatr. Phys. Ther.* **2018**, *41*, 42–48. [CrossRef] [PubMed]
3. Zhang, X.; Dou, Q.; Zhang, W.; Wang, C.; Xie, X.; Yang, Y.; Zeng, Y. Frailty as a predictor of all-cause mortality among older nursing home residents: A systematic review and meta-analysis. *J. Am. Med. Dir. Assoc.* **2019**, *20*, 657–663.e4. [CrossRef] [PubMed]
4. Ebina, J.; Ebihara, S.; Kano, O. Similarities, differences and overlaps between frailty and Parkinson's disease. *Geriatr. Gerontol. Int.* **2022**, *22*, 259–270. [CrossRef] [PubMed]
5. Główny Urząd Statystyczny. Zakłady Stacjonarne Pomocy Społecznej w 2020 r. Available online: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&cad=rja&uact=8&ved=2ahUKEwjo8rOn19T2AhUq-yoKHfg-Dq0QFnoECAgQAQ&url=https%3A%2F%2Fstat.gov.pl%2Fobszary-tematyczne%2Fwarunki-zycia%2Fubostwo-pomoc-spoleczna%2Fzaklady-stacjonarne-pomocy-spolecznej-w-2020-roku%2C18%2C5.html&usg=AOvVaw1r_ncUfCl3q2AFj-4DIyeW (accessed on 20 March 2022).
6. Honinx, E.; Van Dop, N.; Smets, T.; Deliens, L.; Van Den Noortgate, N.; Froggatt, K.; Gambassi, G.; Kylänen, M.; Onwuteaka-Philipsen, B.; Szczerbińska, K.; et al. PACE. Dying in long-term care facilities in Europe: The PACE epidemiological study of deceased residents in six countries. *BMC Public Health* **2019**, *19*, 1199. [CrossRef]
7. Eurostat Statistics Explained. Population Structure and Ageing. Available online: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population_structure_and_ageing (accessed on 20 March 2022).
8. Piotrowicz, J.; Soll, A.; Kielar, U.; Zwiefka, A.; Guligowska, A.; Pigłowska, M.; Kostka, T.; Kurpas, D. ICT and environmental support for patients with frailty syndrome: CareWell Project, Focus Project and SUNFRA IL Project. *Med. Sci. Pulse* **2017**, *11*, 37–43. [CrossRef]
9. World Health Organization; Regional Office for Europe. Physical Activity Strategy for the WHO European Region 2016–2025. Available online: https://www.euro.who.int/en/publications/abstracts/physical-activity-strategy-for-the-who-european-region-20162025 (accessed on 20 March 2022).

10. Rohrmann, S. Epidemiology of Frailty in Older People. *Adv. Exp. Med. Biol* **2020**, *1216*, 21–27.

11. Manfredi, G.; Midão, L.; Paúl, C.; Cena, C.; Duarte, M.; Costa, E. Prevalence of frailty status among the European elderly population: Findings from the Survey of Health, Aging and Retirement in Europe. *Geriatr. Gerontol. Int.* **2019**, *19*, 723–729. [CrossRef]

12. Muszalik, M.; Kotarba, A.; Borowiak, E.; Puto, G.; Cybulski, M.; Kędziora-Kornatowska, K. Socio-Demographic, Clinical and Psychological Profile of Frailty Patients Living in the Home Environment and Nursing Homes: A Cross-Sectional Study. *Front. Psychiatry* **2021**, *12*, 736804. [CrossRef]

13. Kojima, G. Prevalence of frailty in nursing homes: A systematic review and meta-analysis. *J. Am. Med. Dir. Assoc.* **2015**, *16*, 940.e5. [CrossRef]

14. Fried, L.P.; Cohen, A.A.; Xue, Q.L.; Walston, J.; Bandeen-Roche, K.; Varadhan, R. The physical frailty syndrome as a transition from homeostatic symphony to cacophony. *Nat. Aging* **2021**, *1*, 36–46. [CrossRef] [PubMed]

15. Angulo, J.; El Assar, M.; Álvarez-Bustos, A.; Rodríguez-Mañas, L. Physical activity and exercise: Strategies to manage frailty. *Redox Biol.* **2020**, *35*, 101513. [CrossRef] [PubMed]

16. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, 146–157. [CrossRef] [PubMed]

17. Motta, F.; Sica, A.; Selmi, C. Frailty in Rheumatic Diseases. *Front. Immunol.* **2020**, *11*, 576134. [CrossRef]

18. Liotta, G.; Gilardi, F.; Orlando, S.; Rocco, G.; Proietti, M.G.; Asta, F.; De Sario, M.; Michelozzi, P.; Mancinelli, S.; Palombi, L.; et al. Cost of hospital care for the older adults according to their level of frailty. A cohort study in the Lazio region, Italy. *PLoS ONE* **2019**, *14*, e0217829. [CrossRef]

19. Dedeyne, L.; Deschodt, M.; Verschueren, S.; Tournoy, J.; Gielen, E. Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: A systematic review. *Clin. Interv. Aging* **2017**, *12*, 873–896. [CrossRef]

20. Kaczorowska, A.; Sebastjan, A.; Kołodziej, M.; Kozieł, S.; Tomczak, M.; Ignasiak, Z. Functional capacity and risk of frailty syndrome in 85-year-old and older women living in nursing homes in Poland. *Anthropol. Rev.* **2021**, *84*, 395–404. [CrossRef]

21. Rizka, A.; Indrarespati, A.; Dwimartutie, N.; Muhadi, M. Frailty among Older Adults Living in Nursing Homes in Indonesia: Prevalence and Associated Factors. *Ann. Geriatr. Med. Res.* **2021**, *25*, 93–97. [CrossRef]

22. Kojima, G.; Tanabe, M. Frailty is Highly Prevalent and Associated with Vitamin D Deficiency in Male Nursing Home Residents. *J. Am. Geriatr. Soc.* **2016**, *64*, e33–e35. [CrossRef]

23. Arnljots, R.; Thorn, J.; Elm, M.; Moore, M.; Sundvall, P.D. Vitamin D deficiency was common among nursing home residents and associated with dementia: A cross sectional study of 545 Swedish nursing home residents. *BMC Geriatr.* **2017**, *17*, 229. [CrossRef]

24. Liu, W.; Puts, M.; Jiang, F.; Zhou, C.; Tang, S.; Chen, S. Physical frailty and its associated factors among elderly nursing home residents in China. *BMC Geriatr.* **2020**, *20*, 294. [CrossRef] [PubMed]

25. Kendhapedi, K.K.; Devasenapathy, N. Prevalence and factors associated with frailty among community-dwelling older people in rural Thanjavur district of South India: A cross-sectional study. *BMJ Open* **2019**, *9*, e032904. [CrossRef] [PubMed]

26. Niederstrasser, N.G.; Rogers, N.T.; Bandelow, S. Determinants of frailty development and progression using a multidimensional frailty index: Evidence from the English Longitudinal Study of Ageing. *PLoS ONE* **2019**, *14*, e0223799. [CrossRef] [PubMed]

27. Travers, J.; Romero-Ortuno, R.; Bailey, J.; Cooney, M.-T. Delaying and reversing frailty: A systematic review of primary care interventions. *Br. J. Gen. Pract.* **2019**, *69*, e61–e69. [CrossRef] [PubMed]

28. Hsieh, T.-J.; Su, S.-C.; Chen, C.-W.; Kang, Y.-W.; Hu, M.-H.; Hsu, L.-L.; Wu, S.-Y.; Chen, L.; Chang, H.-Y.; Chuang, S.-Y.; et al. Individualized home-based exercise and nutrition interventions improve frailty in older adults: A randomized controlled trial. *Int. J. Behav. Nutr. Phys. Act.* **2019**, *16*, 119. [CrossRef]

29. Apóstolo, J.; Cooke, R.; Bobrowicz-Campos, E.; Santana, S.; Marcucci, M.; Cano, A.; Vollenbroek-Hutten, M.; Germini, F.; D'Avanzo, B.; Gwyther, H.; et al. Effectiveness of interventions to prevent pre-frailty and frailty progression in older adults: A systematic review. *JBI Database Syst. Rev. Implement. Rep.* **2018**, *16*, 140–232, Erratum in *JBI Database Syst. Rev Implement. Rep.* **2018**, *16*, 1282–1283. [CrossRef]

30. Guralnik, J.M.; Simonsick, E.M.; Ferrucci, L.; Glynn, R.J.; Berkman, L.F.; Blazer, D.G.; Scherr, P.A.; Wallace, R.B. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *J. Gerontol.* **1994**, *49*, 85–94. [CrossRef]

31. Zasadzka, E.; Pawlaczyk, M. Short Physical Performance Battery test as a tool useful for the assessment of physical function in elderly. *Gerontol. Pol.* **2013**, *4*, 148–153.

32. Guralnik, J.M.; Ferrucci, L.; Simonsick, E.M.; Salive, M.E.; Wallace, R.B. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N. Engl. J. Med.* **1995**, *322*, 556–562. [CrossRef]

33. Bandinelli, S.; Lauretani, F.; Boscherini, V.; Gandi, F.; Pozzi, M.; Corsi, A.M.; Bartali, B.; Lova, R.M.; Guralnik, J.M.; Ferrucci, L. A randomized, controlled trial of disability prevention in frail older patients screened in primary care: The FRASI study. Design and baseline evaluation. *Aging Clin. Exp. Res.* **2006**, *18*, 359–366. [CrossRef]

34. Vasunilashorn, S.; Coppin, A.K.; Patel, K.V.; Lauretani, F.; Ferrucci, L.; Bandinelli, S.; Guralnik, J.M. Use of the short physical performance battery score to predict loss of ability to walk 400 meters: Analysis from the InCHIANTI study. *J. Gerontol. A Biol. Sci. Med. Sci.* **2009**, *64*, 223–229. [CrossRef] [PubMed]

35. Da Camara, S.M.; Alvarado, B.E.; Guralnik, J.M.; Guerra, R.O.; Maciel, A.C. Using the short physical performance battery to screen for frailty in young-old adults with distinct socioeconomic conditions. *Geriatr. Gerontol. Int.* **2013**, *13*, 421–428. [CrossRef] [PubMed]
36. Subra, J.; Gillette-Guyonnet, S.; Cesari, M.; Oustric, S.; Vellas, B.; Platform, T. The integration of frailty into clinical practice: Preliminary results from the Gerontopole. *J. Nutr. Health Aging* **2012**, *16*, 714–720. [CrossRef]
37. R Core Teem R: A language and Environment for Statistical Computing. R Foundation For Statistical Computing: Vienna, Austria, 2021. Available online: https://www.R-project.org/ (accessed on 13 January 2022).
38. Guede Rojas, F.A.; Chirosa, L.J.; Fuentealba, S.; Vergara, C.A.; Ulloa, D.L.; Salazar, S.E.; Márquez, H.A.; Barboza, P.A. Anthropometric characteristics and functional fitness of Chilean community-dwelling older adults. *Nutr. Hosp.* **2017**, *34*, 1319–1327. [PubMed]
39. De Amorim, J.S.C.; Da Silva, S.L.A.; Viana, J.U.; Trelha, C.S. Factors associated with the prevalence of sarcopenia and frailty syndrome in elderly university workers. *Arch. Gerontol. Geriatr.* **2019**, *82*, 172–178. [CrossRef]
40. Fisher, K.L.; Harrison, E.L.; Bruner, B.G.; Lawson, J.A.; Reeder, B.A.; Ashworth, N.L.; Sheppard, M.S.; Chad, K.E. Predictors of Physical Activity Levels in Community-Dwelling Older Adults: A Multivariate Approach Based on a Socio-Ecological Framework. *J. Aging Phys. Act.* **2018**, *26*, 114–120. [CrossRef]
41. Furtado, H.L.; Sousa, N.; Simao, R.; Pereira, F.D.; Vilaca-Alves, J. Physical exercise and functional fitness in independently living vs. institutionalized eldery women: A comparison of 60-to 79-year-old city dwellers. *Clin. Interv. Aging* **2015**, *10*, 795–801.
42. Barber, S.E.; Forster, A.; Birch, K.M. Levels and Patterns of Daily Physical Activity and Sedentary Behavior Measured Objectively in Older Care Home Residents in the United Kingdom. *J. Aging Phys. Activ.* **2005**, *23*, 133–143. [CrossRef]
43. Mudrak, J.; Stochl, J.; Slepicka, P.; Elavsky, S. Physical activity, self efficacy and quality of life in older Czech adults. *Eur. J. Ageing* **2016**, *13*, 5–14. [CrossRef]
44. Drygas, W.; Kwaśniewska, M.; Szcześniewska, D.; Kozakiewicz, K.; Głuszek, J.; Wiercińska, E.; Wyrzykowski, B.; Kurjata, P. Ocena poziomu aktywności fizycznej dorosłej populacji Polski. Wyniki programu WOBASZ. *Kardiol. Pol.* **2005**, *63*, 6.
45. Furtado, G.; Patrıcio, M.; Loureiro, M.; Teixeira, A.N.; Ferreira, J.P. Physical Fitness and Frailty Syndrome in Institutionalized Older Women. *Percept. Mot. Ski.* **2017**, *124*, 754–776. [CrossRef] [PubMed]
46. Skalska, A. Frailty—Zespół słabości. *Geriatr. Opieka Długoterminowa* **2016**, *4*, 1–4.
47. Lauretani, F.; Ticinesi, A.; Gionti, L.; Prati, B.; Nouvenne, A.; Tana, C.; Meschi, T.; Maggio, M. Short-Physical Performance Battery (SPPB) score is associated with falls in older outpatients. *Aging Clin. Exp. Res.* **2019**, *31*, 1435–1442. [CrossRef] [PubMed]
48. Pritchard, J.M.; Kennedy, C.C.; Karampatos, S.; Ioannidis, G.; Misiaszek, B.; Marr, S.; Patterson, C.; Woo, T.; Papaioannou, A. Measuring frailty in clinical practice: A comparison of physical frailty assessment methods in a geriatric out-patient clinic. *BMC Geriatr.* **2017**, *17*, 264. [CrossRef]
49. Danilovich, M.K.; Diaz, L.; Johnson, C.; Holt, E.; Ciolino, J.D. Evaluating frailty in Medicaid Home and Community-based Services clients: A feasibility and comparison study between the SHARE-FI and SPPB. *Pilot Feasibility Stud.* **2019**, *5*, 48. [CrossRef]
50. Rodríguez-Gómez, I.; Mañas, A.; Losa-Reyna, J.; Alegre, L.M.; Rodríguez-Mañas, L.; García-García, F.J.; Ara, I. Relationship between Physical Performance and Frailty Syndrome in Older Adults: The Mediating Role of Physical Activity, Sedentary Time and Body Composition. *Int. J. Environ. Res. Public Health* **2021**, *18*, 203. [CrossRef]
51. Carneiro, J.A.; Cardoso, R.R.; Durães, M.S.; Guedes, M.C.A.; Santos, F.L.; Costa, F.M.D.; Caldeira, A.P. Frailty in the elderly: Prevalence and associated factors. *Rev. Bras. Enferm.* **2017**, *70*, 747–752. [CrossRef]
52. Miller, D.K.; Wolinsky, F.D.; Andresen, E.M.; Malmstrom, T.K.; Miller, J.P. Adverse outcomes and correlates of change in the Short Physical Performance Battery over 36 months in the African American health project. *J. Gerontol. A Biol. Sci. Med. Sci.* **2008**, *63*, 487–494. [CrossRef]
53. Milanović, Z.; Pantelić, S.; Trajković, N.; Sporiš, G.; Kostić, R.; James, N. Age-related decrease in physical activity and functional fitness among elderly men and women. *Clin. Interv. Aging* **2013**, *8*, 549–556, Erratum in *Clin. Interv. Aging* **2014**, *9*, 979.
54. Delbari, A.; Zanjari, N.; Momtaz, Y.A.; Rahim, F.; Saeidimehr, S. Prevalence of frailty and associated socio-demographic factors among community-dwelling older people in southwestern Iran: A cross-sectional study. *J. Diabetes Metab. Disord.* **2021**, *20*, 601–610. [CrossRef]
55. Kidd, T.; Mold, F.; Jones, C.; Ream, E.; Grosvenor, W.; Sund-Levander, M.; Tingström, P.; Carey, N. What are the most effective interventions to improve physical performance in pre-frail and frail adults? A systematic review of randomised control trials. *BMC Geriatr.* **2019**, *19*, 184. [CrossRef] [PubMed]
56. Walston, J.; Buta, B.; Xue, Q.-L. Frailty screening and interventions: Considerations for clinical practice. *Clin. Geriatr. Med.* **2018**, *34*, 25–38. [CrossRef] [PubMed]
57. National Researcher Council. *Preparing for an Aging World: The Case for Cross-National Research*; National Academies Press: Washington, DC, USA, 2001.
58. Silva, M.F.; Petrica, J.; Serrano, J.; Paulo, R.; Ramalho, A.; Lucas, D.; Ferreira, J.P.; Duarte-Mendes, P. The Sedentary Time and Physical Activity Levels on Physical Fitness in the Elderly: A Comparative Cross Sectional Study. *Int. J. Environ. Res. Public Health* **2019**, *16*, 3697. [CrossRef]

59. Da Silva, V.D.; Tribess, S.; Meneguci, J.; Sasaki, J.E.; Garcia-Meneguci, C.A.; Carneiro, J.A.O.; Virtuoso, J.S., Jr. Association between frailty and the combination of physical activity level and sedentary behavior in older adults. *BMC Public Health* **2019**, *19*, 709. [CrossRef] [PubMed]

60. Riebe, D.; Blissmer, B.J.; Greaney, M.L.; Garber, C.E.; Lees, F.D.; Clark, P.G. The relationship between obesity, physical activity, and physical function in older adults. *J. Aging Health* **2009**, *21*, 1159–1178. [CrossRef] [PubMed]

61. Brach, J.S.; Simonsick, E.M.; Kritchevsky, S.; Yaffe, K.; Newman, A.B. The association between physical function and lifestyle activity and exercise in the health, aging and body composition study. *J. Am. Geriatr. Soc.* **2004**, *52*, 502–509. [CrossRef]

62. Simons, R.; Andel, R. The effects of resistance training and walking on functional fitness in advanced old age. *J. Aging Health* **2006**, *18*, 91–105. [CrossRef]

63. Kehler, D.S.; Theou, O. The impact of physical activity and sedentary behaviors on frailty levels. *Mech. Ageing Dev.* **2019**, *180*, 29–41. [CrossRef]

64. Billot, M.; Calvani, R.; Urtamo, A.; Sánchez-Sánchez, J.L.; Ciccolari-Micaldi, C.; Chang, M.; Roller-Wirnsberger, R.; Wirnsberger, G.; Sinclair, A.; Vaquero-Pinto, N.; et al. Preserving Mobility in Older Adults with Physical Frailty and Sarcopenia: Opportunities, Challenges, and Recommendations for Physical Activity Interventions. *Clin. Interv. Aging* **2020**, *15*, 1675–1690. [CrossRef]

65. Nascimento, C.M.; Ingles, M.; Salvador-Pascual, A.; Cominetti, M.R.; Gomez-Cabrera, M.C.; Viña, J. Sarcopenia, frailty and their prevention by exercise. *Free Radic. Biol. Med.* **2019**, *132*, 42–49. [CrossRef]

66. Gabrylewicz, T.; Mandecka, M. Effects of physical activity on cognitive functions in older adults and the course of Alzheimer's disease. *Aktualn. Neurol.* **2013**, *13*, 56–61.

67. Yokoyama, H.; Okazaki, K.; Imai, D.; Yamashina, Y.; Takeda, R.; Naghavi, N.; Ota, A.; Hirasawa, Y.; Miyagawa, T. The effect of cognitive-motor dual-task training on cognitive function and plasma amyloid β peptide 42/40 ratio in healthy elderly persons: A randomized controlled trial. *BMC Geriatr.* **2015**, *15*, 60. [CrossRef] [PubMed]

68. Hagovska, M.; Olekszyova, Z. Relationships between balance control and cognitive functions, gait speed, and activities of daily living. *Z. Gerontol. Geriatr.* **2016**, *49*, 379–385. [CrossRef] [PubMed]

69. Haider, S.; Grabovac, I.; Dorner, T.E. Effects of physical activity interventions in frail and prefrail community-dwelling people on frailty status, muscle strength, physical performance and muscle mass-a narrative review. *Wien. Klin. Wochenschr.* **2019**, *131*, 244–254. [CrossRef]

70. Hamilton, S.L.; Clemes, S.A.; Griffiths, P.L. UK adults exhibit higher step counts in summer compared to winter months. *Ann. Hum. Biol.* **2008**, *35*, 154–169. [CrossRef]

71. Mizumoto, A.; Ihira, H.; Makino, K.; Saitoh, S.; Ohnishi, H.; Furuna, T. Physical activity changes in the winter in older persons living in northern Japan: A prospective study. *BMC Geriatr.* **2015**, *15*, 43. [CrossRef]

72. Raciborski, F.; Pinkas, J.; Jankowski, M.; Sierpiński, R.; Zgliczyński, W.S.; Szumowski, Ł.; Rakocy, K.; Wierzba, W.; Gujski, M. Dynamics of the coronavirus disease 2019 outbreak in Poland: An epidemiological analysis of the first 2 months of the epidemic. *Pol. Arch. Intern. Med.* **2020**, *130*, 615–621.

Article

The Effectiveness of a Hybrid Exercise Program on the Physical Fitness of Frail Elderly

Ziyi Wang [1,†], Deyu Meng [1,†], Shichun He [1], Hongzhi Guo [2,3], Zhibo Tian [4], Meiqi Wei [1], Guang Yang [1,*] and Ziheng Wang [1,3,5,*]

1   Chinese Center of Exercise Epidemiology, Northeast Normal University, Changchun 130024, China
2   Graduate School of Human Sciences, Waseda University, Tokorozawa 169-8050, Japan
3   AI Group, Intelligent Lancet LLC, Sacramento, CA 95816, USA
4   College of Physical Education and Health, Guangxi Normal University, Guilin 541006, China
5   Advanced Research Center for Human Sciences, Waseda University, Tokorozawa 169-8050, Japan
*   Correspondence: yangg100@nenu.edu.cn (G.Y.); wangzh654@nenu.edu.cn (Z.W.)
†   These authors contributed equally to this work.

Abstract: Background: Frailty is a serious physical disorder affecting the elderly all over the world. However, the frail elderly have low physical fitness, which limits the effectiveness of current exercise programs. Inspired by this, we attempted to integrate Baduanjin and strength and endurance exercises into an exercise program to improve the physical fitness and alleviate frailty among the elderly. Additionally, to achieve the goals of personalized medicine, machine learning simulations were performed to predict post-intervention frailty. Methods: A total of 171 frail elderly individuals completed the experiment, including a Baduanjin group (BDJ), a strength and endurance training group (SE), and a combination of Baduanjin and strength and endurance training group (BDJSE), which lasted for 24 weeks. Physical fitness was evaluated by 10-meter maximum walk speed (10 m MWS), grip strength, the timed up-and-go test (TUGT), and the 6 min walk test (6 min WT). A one-way analysis of variance (ANOVA), chi-square test, and two-way repeated-measures ANOVA were carried out to analyze the experimental data. In addition, nine machine learning models were utilized to predict the frailty status after the intervention. Results: In 10 m MWS and TUGT, there was a significant interactive influence between group and time. When comparing the BDJ group and the SE group, participants in the BDJSE group demonstrated the maximum gains in 10 m MWS and TUGT after 24 weeks of intervention. The stacking model surpassed other algorithms in performance. The accuracy and precision rates were 75.5% and 77.1%, respectively. Conclusion: The hybrid exercise program that combined Baduanjin with strength and endurance training proved more effective at improving fitness and reversing frailty in elderly individuals. Based on the stacking model, it is possible to predict whether an elderly person will exhibit reversed frailty following an exercise program.

Keywords: frail; Baduanjin; strength training; endurance training; Explainable Artificial Intelligence

1. Introduction

Frailty is a physical illness that increases with age [1,2] and may be accompanied by psychiatric problems such as cognitive impairment [3]. Meanwhile, elderly people who are frail carry a higher risk of falls, hospitalizations, and care home admissions. Frailty has five clinical features, including unexplained body mass loss, fatigue, idleness, slow movement, and weakness, and frailty is diagnosed when three or more of these characteristics are simultaneously present [4,5]. Elderly people who are frail not only carry a higher risk of falls, hospitalizations, and care home admissions [6], but also higher rates of morbidity, mortality, and failure to rescue after major procedures across surgical specialties [7–18]. Furthermore, frailty also shows negative effects on health systems and the social economy;

nearly half of Medicare spending is attributed to frailty [19]. In the USA, the Netherlands, and Australia, the frail elderly have an average annual healthcare cost that ranges between USD 7500 and 17,500 [20–22]. Thus, given the high financial and emotional burden on the families and healthcare systems, affordable treatments for the core diagnostic symptoms of frailty represent a severe unmet medical need.

Fortunately, frailty is reversible and can be prevented, delayed, or even restored to health through specific interventions and personalized health strategies [23–25]. An exercise program is an efficient means to enhance the strength of skeletal muscles, improve neuromuscular control, and boost the body's immunity, which in turn helps the body to recover from frailty [26–28]. In terms of type, both strength training and endurance training were shown to be efficient in enhancing neuromuscular control and have a positive impact on cardiorespiratory fitness [29]; as a low-intensity aerobic exercise and Chinese traditional exercise, Baduanjin can improve physical health by working from the inside out [30], and a systematic review has shown its benefits for quality of life, sleep quality, balance, handgrip strength, trunk flexibility, systolic and diastolic blood pressure, and resting heart rate [31]. Moreover, Baduanjin involves soft, slow, simple, and safe movements, which are remarkably suitable for the frail elderly. In addition, since previous research demonstrated that proper training techniques may promote exercise habits in elderly individuals, practices integrating Baduanjin might be considered more successful in inspiring elderly individuals to continue exercising [32].

Although good results were achieved with the frail elderly in the works mentioned above, approximately 42.4–56.3% of them did not experience restored health after the exercise program [33,34]. Fortunately, multi-component exercise has been proven in several studies to have a better effect on frail elderly [25,35–39]. These studies, which incorporate strength training, endurance training, and balance training, were used to improve frailty in older adults. In addition, we proposed a mixed training program of Tai Chi, strength, and endurance that was effective in improving strength, walking speed, and endurance in frail older adults in one of our previous studies [40]. This result raises great confidence that hybrid exercise can better improve the health of the frail elderly. Inspired by previous studies [25,35–40], we hypothesized that a hybrid exercise training incorporating Baduanjin could benefit frail older adults by compensating precisely for strength and endurance requirements. Therefore, with the main target of correcting frailty and restoring the physical state in elderly individuals, we added Baduanjin to strength and endurance exercises.

There is a great expectation that personalized medicine will aid in delivering medical care that is more suitable to the individual. However, institutions face difficulties in designing the most appropriate exercise programs due to the complex interaction mechanisms of the human body; in this context, the Explainable Artificial Intelligence (XAI) that we chose to use simulates the clinical treatment process and elucidates its underlying mechanisms of action. Its interpretability could ensure the understanding and trustworthiness of the system [41,42]. Meanwhile, artificial intelligence plays an important role in frailty diagnosis and care [43,44]. Machine learning has also been shown to be effective in screening for frailty and predicting readmission risk in frail individuals [45,46]. Thus, we constructed nine classical models incorporating the characteristics of the frail elderly's physical fitness status and type of intervention to forecast their frailty after the intervention and thus build exercise regimens for them.

To summarize, the goal of this study was to improve physical fitness and reverse frailty in elderly individuals through constructing a hybrid exercise plan that includes Baduanjin, strength, and endurance training. In addition, we utilized nine machine learning models to forecast frailty according to basal physical fitness and distinct interventions. We established the following study hypotheses based on the findings of past investigations: (1) initial physical fitness and intervention programs can be predictive of frailty overcome results; (2) a hybrid exercise program that integrates Bajuanjin, strength, and endurance training can enhance physical fitness and overcome frailty in the elderly.

2. Materials and Methods

2.1. Participants

In order to ensure the safety of procedures and to avoid bias in results, participants were included in this study who met the criteria as follows: Inclusion Criteria: (1) age over 65 years old; (2) meet criteria for frailty, as defined by Fried et al. [5]; (3) no other training within 6 months. Exclusion Criteria: (1) a history of neurological or muscular disorders; (2) having joint discomfort and significant muscle and bone injuries that prevent them from walking normally; (3) having a heart or respiratory illness; and (4) practising any other training courses frequently during the time of the trial. The determination of the sample size was supported by previous intervention research on elderly people who were frail [40]. This study had an effect size of 0.53, and it had 80% power with an alpha level of 0.01. Additionally, it had a dropout frequency of 20%.

2.2. Study Design

2.2.1. Experimental Arrangement

This experiment was performed in a randomized, double-blinded fashion, focusing on the frail elderly to enhance their physical fitness and reverse the frailty. The experiment and application system are shown in Figure 1. Experiments were carried out every Monday, Wednesday, and Friday for a total of 24 weeks. Two Baduanjin instructors were employed: one was a nationwide societal professional coach with more than 8 years of experience as a training instructor; the other instructor was a specialist Baduanjin coach who had obtained a national Baduanjin instructor industry accreditation. All subjects for the study were recruited from the community in Changchun, China. We used the random number table method to randomly assign participants. Subjects were randomized into three groups: the Baduanjin intervention group (BDJ), the Baduanjin, strength, and endurance group (BDJSE), or the strength and endurance group (SE). In March of 2019, after the review and approval of the study protocol by the Ethical Committee of Northeast Normal University, each participant provided their signature on a permission form, indicating that they had read and understood the study's procedures (approval number: NC2018091504). Between the 1st of March and the 30th of September, 2019, measurements and data collection were carried out. It was requested that the subjects avoided engaging in any type of physical exercise other than their typical routine of training.
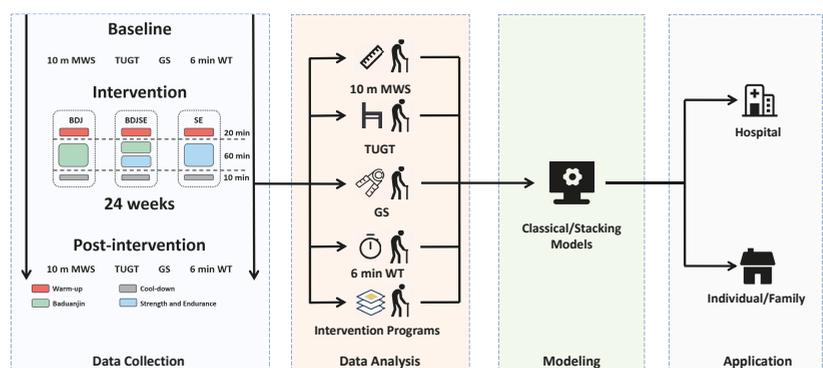
Figure 1. System design; all of the subjects were randomly assigned to one of three intervention groups: BDJ, BDJSE, or SE. At the beginning of the study and at 24 weeks, the subjects' 10-meter maximum walk speed (10 m MWS), timed up-and-go test (TUGT), grip strength, and 6 min walk test (6 min WT) were evaluated.

2.2.2. Intervention

The subjects participated in three separate intervention programs, which comprised endurance training, strength training, and Baduanjin. At the beginning of the intervention, each group spent 20 min warming up with various exercises. The Baduanjin training in the BDJ group lasted for 60 min, whereas the Baduanjin training in the BDJSE group lasted for 30 min and then continued for 30 min of strength and endurance exercise. The SE group completed a strength and endurance workout that lasted for 60 min. Ahead of the end point of the intervention, there was a 10-min cool-down period for all groups. The following is an outline of the training procedure.

(1) Baduanjin: The exercise regimen of Baduanjin was divided into two phases: the first phase continued for 8 weeks, while the second phase continued for 16 weeks. During the first phase of the project, one group was assigned to perform the intervention three times, while another group, the BDJSE group, was assigned to perform the exercise only once. In the next stage, the number of replicates was three and two for the BDJ and BDJSE groups, respectively.

(2) Strength Training: This consisted of three training phases and included five exercises to improve cardiorespiratory fitness and muscle strength [47]. The five movements included three upper-body movements and two lower-body movements. The three upper-body movements were seated rowing, reverse grip curls, and bicep curls, and the two lower-body movements were calf lifts when seated and hip adduction exercises. Elastic bands were utilized in each and every one of the strength workouts. The intensity of the exercise could be determined by the elastic band color. The training consisted of three distinct phases that were repeated every 8 weeks. Phase I aimed to better acclimate subjects to the high-intensity exercise in Phases II and III by using light loads (40–60% of 1RM) and high repeats (12–20), while simultaneously increasing muscle power and muscle endurance by accomplishing 2–4 rounds of training workouts. The second phase of the program was designed to induce muscle growth and improve the muscle mass to fat mass ratio by continuously raising the load to ultimate capacity (60.0–80.0% of 1RM) with 5–12 repeats and 2–4 rounds. The training protocols were intended to achieve these goals. The third phase was intended to optimize the development of strength and also encourage the growth of muscular tissue by utilizing a greater load (70–85% of 1RM) for 5–8 repeats over 2–4 rounds. The SE group would finish four rounds, while the BDJSE group would finish two rounds, with a break of between 2 and 3 min after each round.

(3) Endurance Training: We monitored the subjects' heart rates during the exercise period using a heart rate monitor (MYZONE MZ-3, China). The exercise was conducted via continuous walking on an artificial track. In this investigation, the target heart rate was adapted separately for each subject based on the baseline measure. Exercise level was progressively elevated from 50% of baseline heart rate capacity (first 12 weeks) to 80% (the following 12 weeks) [48]. The SE group undertook 30 min of endurance walking exercise, while the BDJSE group accomplished 15 min. In all exercises, at least two medical staff accompanied the training, and the training was promptly terminated if the subjects became uncomfortable.

2.3. Assessment of Frailty

Fried frailty assessment criteria is widely used in the Asia-Pacific region. One previous study showed that this criterion has better validity and feasibility among older adults in the Chinese community [49]. Thus, the Fried frailty criteria [5] were employed in this work to identify all levels of perceived frailty. According to these criteria, aged people are considered to have frailty when at least three of the following five phenotypic characteristics exist.

(1) Unconscious weight loss: Participants were asked whether their weight had decreased by more than 4.5 kg (or 5% of body weight) without intention in the past year.

(2)   Self-reported fatigue: Participants were asked how often they were too exhausted to participate in any activity that required their full engagement for more than 2 days in a week.

(3)   Grip strength: Subjects' grip strengths were determined by utilizing a calibrated Jamar Hydraulic Hand Dynamometer (model SH5001, Saehan Corp, Masan, Korea, 2017). Every person was given three chances to be evaluated, and their highest score was counted. The grasp was examined to determine if males weighed less than 26 kg and females weighed less than 18 kg.

(4)   The walking speed: The 10 meter walk speed of the subjects was recorded. Older people were judged frail if their walking speed was lower than or equal to 1 m/s.

(5)   Low level of physical activity: The level of physical activity of individuals was determined by the Physical Activity Scale for the Elderly in the Chinese population (PASE-C) [50]. Low physical activity was defined in men as a cut-off value of less than 383 calories per week and in women of less than 270 calories per week, respectively.

2.4. Assessment of Physical Fitness

The physical performance of the participants was evaluated pre- and post-intervention by utilizing the 10-meter maximum walk speed (10 m MWS), the timed up-and-go test (TUGT), grip strength, and the 6 min walk test (6 min WT). Following the collection of primary information, we computed the split-half reliability of the participants' initial testing values to assess reliability. The findings indicated that all four test techniques were reliable ($r = 0.82$, $p < 0.001$; half-score reliability). It was discovered that the 10 m MWS had strong validity in older persons since there was a significant correlation between the item and alterations in frailty [51]. The TUGT is an easy test that requires no specialized device and was proven to have a high degree of validity for assessing agility ($r = 0.63$) [52]. An increased risk of impairment, mortality, and illness is associated with lowering grip strength, which is a feature of frailty in old age [53,54]. The research conducted by Syddall et al. indicated that grip strength was significantly related to measures of frailty and precisely mirrored overall muscle strength ($r = 0.69$) [55]. In older people, frailty can be indicated by multiple variables, including low levels of fitness and stamina, as well as decreased neuromuscular function. The 6 min WT was found to have excellent validity ($r = 0.77$) in assessing indirectly the endurance quality (maximal oxygen consumption) of elderly individuals [56]. The following describes the test's features:

(1)   10 m MWS: Subjects performed two 50-m walking exercises as quickly as possible in a calm testing setting, and the time to cover 2.5 to 12.5 m was calculated to ensure the steady status of data. The highest value was utilized in the study.

(2)   TUGT: Subjects were seated in a conventional chair 45 cm in height and, when prompted by the research assistant, stood up and performed a 3 meter circumference walk around the room as quickly as possible before returning to their seat.

(3)   Grip strength: Grip strength was measured utilizing a calibrated Jamar Hydraulic Hand Dynamometer (model SH5001, Saehan Corp, Masan, Korea, 2017). In a standing position, subjects conducted three grip strength assessments, and the best score was considered the test result.

(4)   6 min WT: The 6 min WT was utilized to evaluate the endurance of the subjects. The test was conducted on a 30-m, enclosed, level promenade. Along the promenade, signs were set every 3 meters, and turn signals were established at each end. Individuals were urged to cover the greatest distance possible along the promenade.

Prerequisites for any examination of a participant's motor abilities included, firstly, that the test participants be attired in appropriate athletic clothing and footwear. They each carried out the test on their own. Second, each subject was required to become familiar with the procedure involved in the experiment in preparation; third, the subjects were required to perform a warm-up to prevent injuries; ultimately, if the subject experienced

bodily distress, stress connected to body posture, or ecologic discomfort, they were asked to notify the researchers. The test could be canceled at any moment.

2.5. Data Analyses

When attempting to determine the post-experimental frailty state of elderly individuals who were already frail, researchers used a total of eight classical machine learning classification models. The 10 m MWS, grip strength, TUGT, 6 min WT, and three intervention types before the intervention were utilized as characteristics in the creation of the data. Labels for the dataset included whether or not the subjects were feeble after the intervention. The effectiveness of the testing measures was judged according to their levels of accuracy, recall, and prediction, as well as their areas under the curve (AUC). In order to obtain an accurate assessment of the performance of the model, we carried out the stratified 10-fold cross-validation 100 times. In the beginning, traditional machine learning modeling was carried out with the assistance of the LightGBM Classifier (LGBM) [57], Gradient Boosting Classifier (GBC) [58], XGBoost Classifier (XGB) [59], Extra Tree Classifier (ETC) [60], Decision Tree Classifier (DT) [61], Random Forest Classifier (RF) [62], Linear Discriminant Analysis (LDA) [63], and Logistic Regression (LR) [64]. Following this, the three models that had the best overall effectiveness within these records were chosen for stacking modeling. For this particular investigation, the process of stacking was carried out by integrating multiple classifiers that were produced by various learning algorithms $L_1, \ldots, L_n$ on a single dataset S. This dataset comprised examples that had the form $S_i = (x_i, y_i)$, where x_i represents the characteristic vectors and y_i represents the classifications. In the initial step of the process, a group of base-level classifiers known as C_1, C_2, and C_3 were developed, with $C_i = L_n (S)$. The second stage consisted of learning a meta-level classifier that comprised the outcomes of the base-level classifiers. To produce a training set for the purpose of learning the meta-level classifier, a cross-validation process was carried out, in which each of the base-level learning algorithms was applied to the whole dataset. We retained only one sample for examination, such as $\forall i = 1, \ldots, n : \forall k = 1, \ldots, N : C_k^i = L_k(S - s_i)$, and then used the learned classifiers to create projections for S_i, as in Equation (1):

$$\hat{y}_i^k = C_k^i(x_i),\tag{1}$$

where the meta-level dataset comprised examples of the form $((\hat{y}_i^1, \ldots, \hat{y}_i^n), y_i)$, the characteristics were the expectations of the base-level classifiers, and the class was the appropriate category for the example considered. By calculating SHAP values (SHapley Additive exPlanations) [65], we were able to determine which characteristic provided the maximum anticipation of change in frailty. SHAP is a game-theoretic method to interpret the outcome of any machine learning model. SHAP values could measure the impact that each feature provides to the estimate provided by the model, as in Equation (2):

$$\phi_j = \sum_{S_F \subseteq F \backslash \{j\}} \frac{|S_F|!(|F| - |S_F| - 1)!}{|F|!} \left[f_{S_F \cup \{j\}} \left(x_{S_F \cup \{j\}} \right) - f_{S_F} \left(x_{S_F} \right) \right],\tag{2}$$

where x indicates input features' value, j denotes a certain feature (out of total features F), S_F is entire subsets without j, and $|S_F|$ indicates the dimension of S_F. In this study, the SHAP "TreeExplainer" algorithm was used to evaluate the feature contribution of predicting reversing frailty, the model $f_{S_F \cup \{j\}}$ was trained with feature j present, and another model F_{S_F} was trained with feature j withheld. Data analysis and visualization used Python 3.8.1 in this study.

2.6. Statistical Analyses

We used SPSS 25.0 to analyze the demographic variables of participants at the baseline and the effectiveness of the three intervention programs on participant improvement. The Shapiro–Wilk test was employed to examine whether the distribution was normal,

and logarithmic transformation was performed for data that lacked a normal distribution. The mean ± standard deviation (SD) were computed, and values were applied to express continuous variables, whereas other values were used to express categorical variables. At the beginning of the study, the demographic factors of the subjects were examined utilizing chi-square tests and one-way ANOVA. The two-way repeated-measures ANOVA was used to determine how much of an impact each of the three intervention regimens had on the individuals' improvements in their 10 m MWS, TUGT, grip strength, and 6 min WT. When multiple comparisons were made, Bonferroni post-hoc testing was employed. When $p < 0.05$, the result was deemed statistically significant.

3. Results

3.1. Participants

In this study, 103 females and 100 males out of a total of 271 individuals passed the selection process to become one of the 203 subjects who were chosen. The research was finished with the participation of 171 people (92 females and 79 males). There were a total of 15 people who dropped out of the training by their own choice, while 17 people dropped out of the training because of illness. The demographic profile of the subjects at the start of the study is presented in Table 1. The results of the Shapiro–Wilk test showed that age ($p = 0.334$), stature ($p = 0.452$), and body mass ($p = 0.165$) were normally distributed in the three groups. In terms of demographics, the groups showed no significant differences from one another.

Table 1. Baseline demographic characteristics of the participants.

Items	BDJ [1] ($n = 57$)	BDJSE [2] ($n = 57$)	SE [3] ($n = 57$)	*p* Value
Sex (male/female)	28/29	27/30	25/32	0.736
Age (years)	71.84 ± 3.77	70.65 ± 3.73	70.74 ± 3.52	0.163
Stature (cm)	165.83 ± 6.77	163.41 ± 7.58	165.54 ± 8.22	0.182
Body mass (kg)	64.53 ± 5.59	62.97 ± 7.11	63.05 ± 6.88	0.378

[1] Baduanjin group; [2] Baduanjin, strength, and endurance group; [3] strength and endurance group.

3.2. Two-Way Repeated-Measures ANOVA Results for Physical Fitness

Figure 2 and Table 2 illustrate the starting and post-intervention findings. The results of the Shapiro–Wilk test showed that 10 m MWS ($p = 0.517$), grip strength ($p = 0.184$), and TUGT ($p = 0.257$) were normally distributed in the three groups. However, 6 min WT demonstrated a non-normal distribution in the three groups. When logarithmic transformation was applied to it, the data showed a normal distribution. Two-way repeated-measures ANOVA data confirmed that there was a significant interaction impact of group × time in 10 m MWS ($p < 0.001$, partial $\eta^2 = 0.259$) and TUGT ($p = 0.011$, partial $\eta^2 = 0.117$). Simple effects analysis revealed that 10 m MWS and TUGT were significantly enhanced following the intervention. Post-hoc testing demonstrated that individuals in the BDJSE group had significantly better 10 m MWS than the BDJ group ($p < 0.001$) and SE group ($p < 0.001$) and better TUGT than the BDJ group ($p = 0.019$) and SE group ($p = 0.038$) in 24 weeks. Nevertheless, we observed no significant interaction influence of grouping time on grip strength and 6 min WT. The major effect demonstrated that, before and after the intervention, the grip strength and 6 min WT experienced a significant increase.
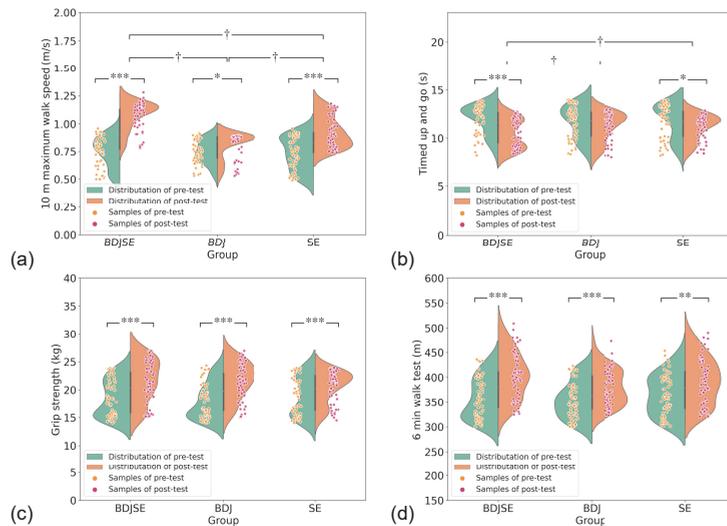
Figure 2. The scatter plot with a rotated kernel density plot on every side. It illustrates the physical capability of the frail elderly at the start and after the intervention. (**a**) 10 m MWS, (**b**) timed up-and-go test, (**c**) grip strength, (**d**) 6 min WT. BDJ denotes Baduanjin group; BDJSE denotes Baduanjin, strength, and endurance group; SE denotes strength and endurance group. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. For the significance of intragroup variations, † shows a significant difference among groups († < 0.05).

Table 2. Two-way repeated-measures ANOVA results for each group at baseline and 24 weeks for the test metrics.

Parameters	BDJ [1] ($n = 57$)		BDJSE [2] ($n = 57$)		SE [3] ($n = 57$)		Group × Time [#]
	Baseline	24 Weeks	Baseline	24 Weeks	Baseline	24 Weeks	*p*-Value
10 m MWS (m/s)	0.75 ± 0.11	0.82 ± 0.12 [†,*]	0.75 ± 0.14	1.08 ± 0.12 [†,***]	0.73 ± 0.13	0.93 ± 0.14 [†,***]	0.000
TUGT (s)	11.76 ± 1.67	11.21 ± 1.48 [†]	12.01 ± 1.50	10.47 ± 1.51 [†,***]	11.90 ± 1.65	11.19 ± 1.29 [†,*]	0.041
grip strength (kg)	18.69 ± 3.50	20.60 ± 2.77 ***	18.44 ± 3.28	21.58 ± 3.82 ***	17.93 ± 3.14	21.63 ± 3.26 ***	0.080
6 min WT (m)	355.25 ± 37.02	380.06 ± 36.55 ***	357.75 ± 42.01	403.21 ± 47.61 ***	365.07 ± 42.11	392.45 ± 47.49 **	0.154

Means × SD are used to depict all the data; [#] analysis of two-way repeated-measures ANOVA; [†] significant difference between groups ($p < 0.05$); * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ significant difference between baseline and post-intervention. [1] Baduanjin group; [2] Baduanjin, strength, and endurance group; [3] strength and endurance group.

3.3. Results of Machine Learning Model Classification

In addition, we reassessed the participants' frailty status at 24 weeks. The results showed that 25 participants (30.1%) in the BDJ group progressed from a frail condition to a non-frail condition, 33 participants (39.8%) in the BDJSE group progressed from a frail condition to a non-frail condition, and 25 participants (30.1%) in the SE group progressed from a weak condition to a non-frail condition, for a total of 83 participants (48.5%).

We used intervention types and participants' 10 m MWS, TUGT, grip strength, and 6 min WT at baseline as features and frailty and non-frailty at 24 weeks as the label. We used eight classical machine learning models and selected three of them with the best performance for stacking. The three classification models, Linear Discriminant Analysis, Logistic Regression, and Random Forest Classifier were stacked to create the first layer mode to construct the super features. In the second layer, we used Logistic Regression, inputting the super features and labels into the second layer model for training. The stacking model obtained the best accuracy as $75.5 \pm 10.0\%$ and best precision as $77.1 \pm 12.3\%$, as shown in

Table 3. However, Linear Discriminant Analysis had the best F1-score (71.3 ± 10.8%) and best recall (73.7 ± 15.1%).

Table 3. Model performance evaluation results.

Models	Accuracy	Precision	Recall	F1
Decision Tree (%)	66.3 ± 11.2	65.4 ± 12.8	65.3 ± 16.2	65.1 ± 12.1
GDB Classifier [1] (%)	66.7 ± 10.6	66.7 ± 13.2	65.5 ± 16.3	64.5 ± 12.5
XGB Classifier [2] (%)	68.8 ± 10.9	70.5 ± 13.2	65.1 ± 15.4	66.7 ± 12.2
LGBM Classifier [3] (%)	69.2 ± 10.6	70.4 ± 13.2	68.0 ± 15.6	68.0 ± 11.9
Extra Tree Classifier (%)	69.7 ± 10.2	70.5 ± 12.4	68.1 ± 15.6	68.0 ± 12.0
RF Classifier [4] (%)	70.3 ± 10.5	71.5 ± 13.4	66.7 ± 16.3	67.4 ± 12.2
Logistic Regression (%)	73.7 ± 10.3	74.9 ± 12.5	71.3 ± 16.0	72.1 ± 11.1
LDA Classifier [5] (%)	75.3 ± 10.3	76.2 ± 12.3	**73.7 ± 15.1**	**74.0 ± 11.6**
Stacking (%)	**75.5 ± 10.0**	**77.1 ± 12.2**	72.8 ± 15.0	73.9 ± 11.3

[1] Gradient Boosting Classifier, [2] XGBoosting Classifier, [3] LightGBM Classifier, [4] Random Forest Classifier, [5] Linear Discriminant Analysis.

When we compared the effectiveness of the various models, we found that the stacking model provided the greatest results in terms of accuracy and precision. The first layer of the stacking model consisted of Linear Discriminant Analysis, Logistic Regression, and Random Forest Classifier. The second layer of the stacking model consisted of Logistic Regression.

In addition, we evaluate the model performance using a confusion matrix and Receiver Operating Characteristic (ROC) curve. The confusion matrix showed the model's anticipation of the frailty state, and the normalized confusion matrix could visualize the prediction accuracy of the model. The elements of the sub-diagonal line in Figure 3a for the confusion matrix indicated the number of predicted categories that were the same as the true category and the elements of the sub-diagonal in Figure 3b. The mean precision of the model's estimation for every label, as indicated by the normalized confusion matrix, was 78%, with 73% being the value for the other label. The ROC curve of the model for estimating the performance of the model is depicted in Figure 3c. The horizontal coordinate demonstrates the false positive frequency, while the vertical coordinate demonstrates the frequency of true positives. The model with the best (AUC) was the Linear Discriminant Analysis model, which had a value of 0.835.
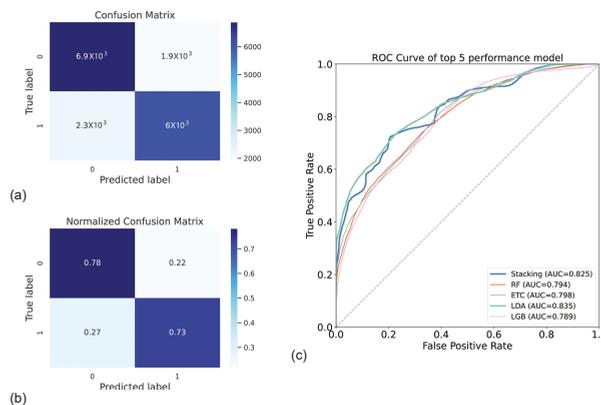

Figure 3. The confusion matrix and the ROC curve of stacking. (**a**) The confusion matrix; (**b**) the normalized confusion matrix. The performance of the model to determine whether a participant is an elderly individual at risk of frailty is displayed in the figure. (**c**) The Receiver Operating Characteristic (ROC) curve of the five best-performing models. Random Forest Classifier (RF), Extra Tree Classifier (ETC), Linear Discriminant Analysis (LDA), and LightGBM Classifier (LGB) are the abbreviations for other classification methods.

3.4. Contribution of Each Feature

Figure 4 demonstrates the contribution of each feature by SHAP values. It is possible to utilize the SHAP value of a characteristic to describe the model since it indicates the value that each feature contributes to the model. Figure 4d clearly illustrates this, as grip strength showed the greatest contribution to physical fitness and SE showed the greatest contribution in the three intervention types. The features could interact with each other, as shown in Figure 4b. Clearly, we were able to find the best combination of features to optimize the model performance by utilizing different combinations of features.
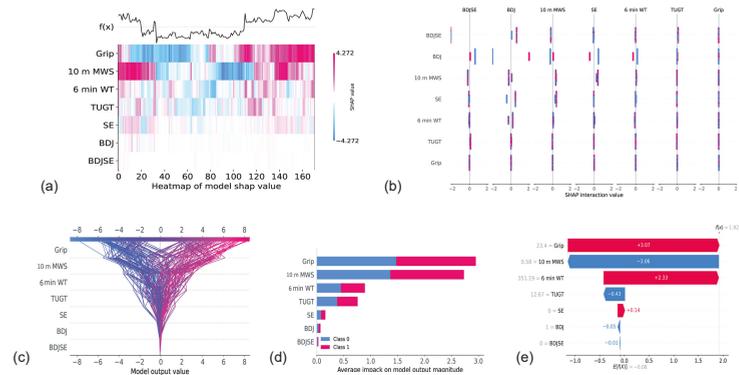
Figure 4. A plot that provides an overview of the SHAP values for every feature. The various characteristics are denoted along the *y*-axis. (**a**) illustrates the heat map of the various characteristic SHAP values, in which the *x*-axis depicts the series of the sample, red denotes a positive effect, blue denotes a negative effect, and the darker the color, the greater the extent to which it has an effect. The output is denoted by the function $f(x)$ (before activation function). It is shown in the figure that the greatest essential characteristic shows a positive impact if the output also appears positive, and it demonstrates a clear boundary (threshold) in the characteristics; (**b**) shows the interaction SHAP values for various characteristics; (**c**) provides an outline of the characteristics that are highly essential to the model and the manner in which the model learned the outcome of every characteristic for each sample, with the *x*-axis denoting the model predicted values; (**d**) demonstrates the mean absolute SHAP value of each characteristic, with the *x*-axis denoting the average SHAP value; (**e**) depicts characteristics that have a role in displaying the model result from the fundamental value of a specific sample, with the SHAP value denoted along the *x*-axis. According to the previous situation, the grip strength demonstrated the most positive effect for predicting the frailty state and the 10 m MWS demonstrated a negative effect for predicting the frailty state.

4. Discussion

This study is unique in considering the use of combined physical activities that address the characteristics of the frail elderly by integrating Baduanjin exercises with strength and endurance training programs and predicting frailty pre- and post-intervention in a clinical trial by using AI. The results showed that all of the experimental groups exhibited some degree of physical progress in terms of their strength, velocity, and endurance after 24 weeks of training. Among them, the mixed-exercise program group showed the best physical improvement in subjects in the 10 m MWS and TUGT.

In addition, the combined workout regimen had the best effectiveness in counteracting frailty, with 46.5% of frail elderly individuals recovering from a non-frail status as a result of participating in the program.

In addition, we incorporated XAI into this study. The stacking model obtained an average accuracy of 75.5% by simulating clinical application scenarios, with physical ability at baseline and intervention type as model attributes used as inputs, and frailty reversed

was used as a result. Additionally, we found that 10 m MWS and grip strength have high contributions and identifiability: elderly individuals who are frail and have higher 10 m MWS and grip strength have a greater chance of recovering from frailty. As a result, increasing the grip strength and 10m distance of elderly individuals who are frail may be able to maximize the efficacy of the intervention.

There was a significant interaction effect in 10 m MWS, as 1.08 m/s (BDJSE) > 0.93 m/s (SE) > 0.82 m/s (BDJ), and TUGT, as 11.21 s (BDJ) > 11.19 s (SE) > 10.47 s (BDJ), at 24 weeks. This is consistent with several previous studies in which multicomponent exercise improved gait capacity and agility in frail older adults [35,38]. The reasons that a combined training schedule had the best effectiveness in 10 m MWS and TUGT are as follows. A multi-component exercise program is a good approach because it allows aged people who are frail to benefit from a variety of training modalities to address any weaknesses they may have. This is a useful method since aged individuals are more likely to experience frailty while they age [28]. Second, the Baduanjin exercise can help participants to improve the sensorimotor ability of their legs [66], and it also has additional benefits for the strength of the muscles in the legs [31]. Both of these benefits can be gained from performing the exercise. As a consequence, the endurance training that is performed in the style of walking compensates for the comparatively slow movement attributes of Baduanjin and assists in improving the participants' capacity to walk under natural settings. Ultimately, DBJSE hybrid exercise enhanced the walking speed and Baduanjin could effectively improve the lower balance function [66]. Therefore, participants in the BDJSE group had significantly better 10 m and grip strength than those in the other two groups.

In this study, participants' grip strength was significantly improved at 24 weeks, but the interaction effect was not significant. This is consistent with a previous study in which the intervention protocol consisted of strength training, endurance training, and balance training [35]. Participants in the SE group had the greatest average grip strength (21.63 kg (SE) > 21.58 kg (BDJSE) > 20.60 kg (BDJ)) and maximum improvement ((3.70 kg (SE) > 3.14 kg (BDJSE) > 1.91 kg (BDJ)). Although Baduanjin can improve grip strength, it seems to be more effective for young people [66]. The BDJSE group included the training content of the SE group, but the overall load was only half that of the SE group, so participants in the BDJSE group showed less improvement.

The 6 min WT also did not show a significant interaction, but, fortunately, all three groups of subjects showed a significant increase. This is consistent with a previous study showing that multicomponent exercise improves aerobic capacity in frail older adults [67]. A possible reason is that Baduanjin can increase lung capacity and lower the resting heart rate [31], and, by combining endurance training with walking as a form of exercise, the endurance improvement effect was increased.

Our study had the desired effect of reversing frailty and improving the exercise capacity of frail older adults through a 24-week mixed exercise program. In the future recovery of frail older adults, a mixed exercise program may be more effective in improving health, such as the Baduanjin exercise hybrid strength and endurance training proposed in this study.

Although our study yielded promising results, limitations still remain. First, we did not classify the severity of frailty, and, in future studies, we will further refine the intervention content. Second, we did not have strict control over the intensity, only controlling the duration of the training. Finally, we strongly believe that there is a potential correlation between physical fitness and frailty reversal in frail aged people. Based on this relationship, in future studies, we will integrate more data to accomplish more precise medical clinical assistance.

5. Conclusions

Our findings indicate that a combined exercise regime that combines Baduanjin, strength training, and endurance training could effectively increase physical performance, particularly 10 m MSW and TUGT, as well as reverse frailty in the frail elderly. Additionally, the stacking model had the best performance to predict the reversal of frailty.

References

1. To, T.L.; Doan, T.N.; Ho, W.C.; Liao, W.C. Prevalence of Frailty among Community-Dwelling Older Adults in Asian Countries: A Systematic Review and Meta-Analysis. *Healthcare* **2022**, *10*, 895. [CrossRef] [PubMed]
2. He, B.; Ma, Y.; Wang, C.; Jiang, M.; Geng, C.; Chang, X.; Ma, B.; Han, L. Prevalence and risk factors for frailty among community-dwelling older people in China: A systematic review and meta-analysis. *J. Nutr. Health Aging* **2019**, *23*, 442–450. [CrossRef] [PubMed]
3. Guo, C.Y.; Sun, Z.; Tan, C.C.; Tan, L.; Xu, W. Multi-Concept Frailty Predicts the Late-Life Occurrence of Cognitive Decline or Dementia: An Updated Systematic Review and Meta-Analysis of Longitudinal Studies. *Front. Aging Neurosci.* **2022**, *14*, 855553. [CrossRef]
4. Cesari, M.; Calvani, R.; Marzetti, E. Frailty in Older Persons. *Clin. Geriatr. Med.* **2017**, *33*, 293–303. [CrossRef] [PubMed]
5. Fried, L.; Tangen, C.; Walston, J.; Newman, A.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.; Burke, G.; et al. Frailty in Older Adults Evidence for a Phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M156. [CrossRef]
6. Clegg, A.; Young, J.; Iliffe, S.; Rikkert, M.O.; Rockwood, K. Frailty in elderly people. *Lancet* **2013**, *381*, 752–762. [CrossRef]
7. Kim, S.w.; Han, H.S.; Jung, H.w.; Kim, K.i.; Hwang, D.W.; Kang, S.B.; Kim, C.H. Multidimensional frailty score for the prediction of postoperative mortality risk. *JAMA Surg.* **2014**, *149*, 633–640. [CrossRef]
8. McIsaac, D.I.; Bryson, G.L.; van Walraven, C. Association of frailty and 1-year postoperative mortality following major elective noncardiac surgery: A population-based cohort study. *JAMA Surg.* **2016**, *151*, 538–545. [CrossRef]
9. McIsaac, D.I.; Taljaard, M.; Bryson, G.L.; Beaulé, P.E.; Gagné, S.; Hamilton, G.; Hladkowicz, E.; Huang, A.; Joanisse, J.A.; Lavallée, L.T.; et al. Frailty as a predictor of death or new disability after surgery: A prospective cohort study. *Ann. Surg.* **2020**, *271*, 283–289. [CrossRef]
10. Shah, R.; Attwood, K.; Arya, S.; Hall, D.E.; Johanning, J.M.; Gabriel, E.; Visioni, A.; Nurkin, S.; Kukar, M.; Hochwald, S.; et al. Association of frailty with failure to rescue after low-risk and high-risk inpatient surgery. *JAMA Surg.* **2018**, *153*, e180214. [CrossRef]
11. Joseph, B.; Phelan, H.; Hassan, A.; Jokar, T.O.; O'Keeffe, T.; Azim, A.; Gries, L.; Kulvatunyou, N.; Latifi, R.; Rhee, P. The impact of frailty on failure-to-rescue in geriatric trauma patients: A prospective study. *J. Trauma Acute Care Surg.* **2016**, *81*, 1150–1155. [CrossRef] [PubMed]

12. Arya, S.; Kim, S.I.; Duwayri, Y.; Brewster, L.P.; Veeraswamy, R.; Salam, A.; Dodson, T.F. Frailty increases the risk of 30-day mortality, morbidity, and failure to rescue after elective abdominal aortic aneurysm repair independent of age and comorbidities. *J. Vasc. Surg.* **2015**, *61*, 324–331. [CrossRef] [PubMed]

13. Saxton, A.; Velanovich, V. Preoperative frailty and quality of life as predictors of postoperative complications. *Ann. Surg.* **2011**, *253*, 1223–1229. [CrossRef] [PubMed]

14. Augustin, T.; Burstein, M.D.; Schneider, E.B.; Morris-Stiff, G.; Wey, J.; Chalikonda, S.; Walsh, R.M. Frailty predicts risk of life-threatening complications and mortality after pancreatic resections. *Surgery* **2016**, *160*, 987–996. [CrossRef] [PubMed]

15. Farhat, J.S.; Falvo, A.J.; Horst, M.H.; Swartz, A.; Velanovich, V.; Patton, J.H.; Rubinfeld, I.S. Are the frail destined to fail? Frailty index as a predictor of surgical morbidity and mortality in the elderly. *J. Trauma Acute Care Surg.* **2011**, *213*, S65. [CrossRef]

16. Suskind, A.M.; Walter, L.C.; Jin, C.; Boscardin, J.; Sen, S.; Cooperberg, M.R.; Finlayson, E. Impact of frailty on complications in patients undergoing common urological procedures: A study from the American College of Surgeons National Surgical Quality Improvement database. *BJU Int.* **2016**, *117*, 836–842. [CrossRef]

17. Adams, P.; Ghanem, T.; Stachler, R.; Hall, F.; Velanovich, V.; Rubinfeld, I. Frailty as a predictor of morbidity and mortality in inpatient head and neck surgery. *JAMA Otolaryngol. Head Neck Surg.* **2013**, *139*, 783–789. [CrossRef]

18. George, E.M.; Burke, W.M.; Hou, J.Y.; Tergas, A.I.; Chen, L.; Neugut, A.I.; Ananth, C.V.; Hershman, D.L.; Wright, J.D. Measurement and validation of frailty as a predictor of outcomes in women undergoing major gynaecological surgery. *BJOG* **2016**, *123*, 455–461. [CrossRef]

19. Figueroa, J.F.; Joynt Maddox, K.E.; Beaulieu, N.; Wild, R.C.; Jha, A.K. Concentration of potentially preventable spending among high-cost Medicare subpopulations: An observational study. *Ann. Intern. Med.* **2017**, *167*, 706–713. [CrossRef]

20. Martínez-Reig, M.; Aranda-Reneo, I.; Peña-Longobardo, L.M.; Oliva-Moreno, J.; Barcons-Vilardell, N.; Hoogendijk, E.O.; Abizanda, P. Use of health resources and healthcare costs associated with nutritional risk: The FRADEA study. *Clin. Nutr.* **2018**, *37*, 1299–1305. [CrossRef]

21. Robinson, T.N.; Wu, D.S.; Stiegmann, G.V.; Moss, M. Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. *Am. J. Surg.* **2011**, *202*, 511–514. [CrossRef] [PubMed]

22. Goldfarb, M.; Bendayan, M.; Rudski, L.G.; Morin, J.F.; Langlois, Y.; Ma, F.; Lachapelle, K.; Cecere, R.; DeVarennes, B.; Tchervenkov, C.I.; et al. Cost of Cardiac Surgery in Frail Compared With Nonfrail Older Adults. *Can. J. Cardiol.* **2017**, *33*, 1020–1026. [CrossRef] [PubMed]

23. Gill, T.; Gahbauer, E.; Allore, H.; Han, L. Transitions Between Frailty States Among Community-Living Older Persons. *Arch. Intern. Med.* **2006**, *166*, 418–423. [CrossRef] [PubMed]

24. Zhang, J.; Liu, Z.; Liu, Y.; Ye, L. Exercise interventions for older people at risk for frailty: A protocol for systematic review and meta-analysis. *Medicine* **2021**, *100*. [CrossRef] [PubMed]

25. Chittrakul, J.; Siviroj, P.; Sungkarat, S.; Sapbamrer, R. Multi-System Physical Exercise Intervention for Fall Prevention and Quality of Life in Pre-Frail Older Adults: A Randomized Controlled Trial. *Int. J. Environ. Res. Public Health* **2020**, *17*, 3102. [CrossRef]

26. Kasim, N.F.; Veldhuijzen van Zanten, J.; Aldred, S. Tai Chi is an effective form of exercise to reduce markers of frailty in older age. *Exp. Gerontol.* **2020**, *135*, 110925. [CrossRef]

27. Cadore, E.L.; Casas-Herrero, A.; Zambom-Ferraresi, F.; Idoate, F.; Millor, N.; Gómez, M.; Rodriguez-Mañas, L.; Izquierdo, M. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. *Age* **2013**, *36*, 773–785. [CrossRef]

28. Bray, N.W.; Smart, R.R.; Jakobi, J.M.; Jones, G.R. Exercise prescription to reverse frailty. *Appl. Physiol. Nutr. Metab.* **2016**, *41*, 1112–1116. [CrossRef]

29. Cadore, E.; Pinto, R.; Bottaro, M.; Izquierdo, M. Strength and Endurance Training Prescription in Healthy and Frail Elderly. *Aging Dis.* **2014**, *5*, 183. [CrossRef]

30. Liao, Y.; Lin, Y.; Zhang, C.; Xue, X.L.; Mao, Q.X.; Zhang, Y.; Dai, J.g.; Wang, T.F. Intervention Effect of Baduanjin Exercise on the Fatigue State in People with Fatigue-Predominant Subhealth: A Cohort Study. *J. Altern. Complement. Med.* **2015**, *21*, 554–562. [CrossRef]

31. Zou, L.; Sasaki, J.; Wang, H.; Xiao, Z.; Fang, Q.; Zhang, M. A Systematic Review and Meta-Analysis of Baduanjin Qigong for Health Benefits: Randomized Controlled Trials. *Evid. Based Complement. Alternat. Med.* **2017**, *2017*, 4548706. [CrossRef] [PubMed]

32. Devereux-Fitzgerald, A.; Powell, R.; Dewhurst, A.; French, D.P. The acceptability of physical activity interventions to older adults: A systematic review and meta-synthesis. *Soc. Sci. Med.* **2016**, *158*, 14–23. [CrossRef] [PubMed]

33. Liao, Y.Y.; Chen, W.; Wang, R.Y. Effects of Kinect-based exergaming on frailty status and physical performance in the prefrail and frail elderly: A randomized controlled trial. *Sci. Rep.* **2019**, *9*, 9353. [CrossRef] [PubMed]

34. Kim, H.; Suzuki, T.; Kim, M.; Kojima, N.; Ota, N.; Shimotoyodome, A.; Hase, T.; Hosoi, E.; Yoshida, H. Effects of Exercise and Milk Fat Globule Membrane (MFGM) Supplementation on Body Composition, Physical Function, and Hematological Parameters in Community-Dwelling Frail Japanese Women: A Randomized Double Blind, Placebo-Controlled, Follow-Up Trial. *PLoS ONE* **2015**, *10*, e0116256. [CrossRef]

35. Sadjapong, U.; Yodkeeree, S.; Sungkarat, S.; Siviroj, P. Multicomponent exercise program reduces frailty and inflammatory biomarkers and improves physical performance in community-dwelling older adults: A randomized controlled trial. *Int. J. Environ. Res. Public Health* **2020**, *17*, 3760. [CrossRef]

36. Tarazona-Santabalbina, F.J.; Gómez-Cabrera, M.C.; Pérez-Ros, P.; Martínez-Arnau, F.M.; Cabo, H.; Tsaparas, K.; Salvador-Pascual, A.; Rodriguez-Mañas, L.; Viña, J. A multicomponent exercise intervention that reverses frailty and improves cognition, emotion, and social networking in the community-dwelling frail elderly: A randomized clinical trial. *J. Am. Med. Dir. Assoc.* **2016**, *17*, 426–433. [CrossRef]
37. Fernández-García, Á.I.; Gómez-Cabello, A.; Gómez-Bruton, A.; Moradell, A.; Navarrete-Villanueva, D.; Pérez-Gómez, J.; González-Gross, M.; Ara, I.; Casajús, J.A.; Vicente-Rodríguez, G. Effects of multicomponent training and detraining on fitness of older adults with or at risk of frailty: Results of a 10-month quasi-experimental study. *Eur. J. Sport Sci.* **2022**, 1–29. [CrossRef]
38. Cadore, E.L.; de Asteasu, M.L.S.; Izquierdo, M. Multicomponent exercise and the hallmarks of frailty: Considerations on cognitive impairment and acute hospitalization. *Exp. Gerontol.* **2019**, *122*, 10–14. [CrossRef]
39. Dun, Y.; Hu, P.; Ripley-Gonzalez, J.W.; Zhou, N.; Li, H.; Zhang, W.; Chen, M.; Zheng, Q.; Cui, N.; Wu, S.; et al. Effectiveness of a multicomponent exercise program to reverse pre-frailty in community-dwelling Chinese older adults: A randomised controlled trial. *Age Ageing* **2022**, *51*, afac026. [CrossRef]
40. Meng, D.; Guo, H.; Liang, S.; Tian, Z.; Wang, R.; Yang, G.; Wang, Z. Effectiveness of a Hybrid Exercise Program on the Physical Abilities of Frail Elderly and Explainable Artificial-Intelligence-Based Clinical Assistance. *Int. J. Environ. Res. Public Health* **2022**, *19*, 6988. [CrossRef]
41. Shirwaikar, R.D.; Acharya U, D.; Makkithaya, K.; M, S.; Srivastava, S.; Lewis U, L.E.S. Optimizing neural networks for medical data sets: A case study on neonatal apnea prediction. *Artif. Intell. Med.* **2019**, *98*, 59–76. [CrossRef] [PubMed]
42. Vellido, A. The importance of interpretability and visualization in machine learning for applications in medicine and health care. *Neural Comput. Appl.* **2020**, *32*, 18069–18083. [CrossRef]
43. Hassan, A.; Hassan, M.; Hassan, M.; Ellahham, S. The Role of Artificial Intelligence in Revolutionizing Frailty Diagnosis and Patient Care. *Gerontol. Geriatr. Res.* **2021**, *7*, 1055.
44. Kouroubali, A.; Kondylakis, H.; Logothetidis, F.; Katehakis, D.G. Developing an AI-Enabled Integrated Care Platform for Frailty. *Healthcare* **2022**, *10*, 443. [CrossRef]
45. Oliosi, E.; Guede-Fernández, F.; Londral, A. Machine Learning Approaches for the Frailty Screening: A Narrative Review. *Int. J. Environ. Res. Public Health* **2022**, *19*, 8825. [CrossRef]
46. Mohanty, S.D.; Lekan, D.; McCoy, T.P.; Jenkins, M.; Manda, P. Machine learning for predicting readmission risk among the frail: Explainable AI for healthcare. *Patterns* **2022**, *3*, 100395. [CrossRef] [PubMed]
47. Karavirta, L.; Häkkinen, A.; Sillanpää, E.; García-López, D.; Kauhanen, A.; Haapasaari, A.; Alen, M.; Pakarinen, A.; Kraemer, W.J.; Izquierdo, M.; et al. Effects of combined endurance and strength training on muscle strength, power and hypertrophy in 40–67-year-old men. *Scand. J. Med. Sci. Sport.* **2011**, *21*, 402–411. [CrossRef] [PubMed]
48. Kallinen, M.; Sipilä, S.; Alen, M.; Suominen, H. Improving cardiovascular fitness by strength or endurance training in women aged 76–78 years. A population-based, randomized controlled trial. *Age Ageing* **2002**, *31*, 247–254. [CrossRef]
49. HAN, J.; WANG, J.; XIE, B.; WANG, Y. Comparison of consistency and validity of Fried frailty phenotype, Frail scale and Edmonton frailty scale for frailty screening among community-dwelling older adults. *Chin. Gen. Pract.* **2021**, *24*, 2669.
50. Ngai, S.; Cheung, R.; Lam, P.; Chiu, J.; Fung, E. Validation and reliability of the Physical Activity Scale for the Elderly in Chinese population. *J. Rehabil. Med.* **2012**, *44*, 462–465. [CrossRef]
51. Rothman, M.; Leo-Summers, L.; Gill, T. Prognostic Significance of Potential Frailty Criteria Comment. *J. Am. Geriatr. Soc.* **2009**, *56*, 2211–2216. [CrossRef] [PubMed]
52. Wickstrom, R.J.; Wang, Y.C.; Wickstrom, N.E.; Smith, R.L.; Dunning, K.K. A new two square agility test for workplace health—reliability, validity and minimal detectable change. *J. Phys. Ther. Sci.* **2019**, *31*, 823–830. [CrossRef] [PubMed]
53. Syddall, H.; Westbury, L.; Dodds, R.; Dennison, E.; Cooper, C.; Aihie Sayer, A. Mortality in the Hertfordshire Ageing Study: Association with level and loss of hand grip strength in later life. *Age Ageing* **2016**, *46*, 407–412. [CrossRef] [PubMed]
54. Dodds, R.M.; Syddall, H.E.; Cooper, R.; Kuh, D.; Cooper, C.; Sayer, A.A. Global variation in grip strength: A systematic review and meta-analysis of normative data. *Age Ageing* **2016**, *45*, 209–216. [CrossRef]
55. Syddall, H.; Cooper, C.; Martin, F.; Briggs, R.; Aihie Sayer, A. Is grip strength a useful single marker of frailty? *Age Ageing* **2003**, *32*, 650–656. [CrossRef]
56. Jones, S.; Tillin, T.; Williams, S.; Coady, E.; Chaturvedi, N.; Hughes, A. Assessment of Exercise Capacity and Oxygen Consumption Using a 6 min Stepper Test in Older Adults. *Front. Physiol.* **2017**, *8*, 408. [CrossRef]
57. Ke, G.; Meng, Q.; Finley, T.; Wang, T.; Chen, W.; Ma, W.; Ye, Q.; Liu, T.Y. LightGBM: A Highly Efficient Gradient Boosting Decision Tree. In Proceedings of the NeurIPS Proceedings, Montreal, QC, Canada, 3–8 December 2018.
58. Friedman, J.H. Greedy function approximation: A gradient boosting machine. *Ann. Stat.* **2001**, *29*, 1189–1232. [CrossRef]
59. Chen, T.Q.; Guestrin, C. XGBoost: A Scalable Tree Boosting System. In Proceedings of the 22nd ACM SIGKDD International Conference, San Francisco, CA, USA, 13–17 August 2016; pp. 785–794.
60. Abhishek, L. Optical Character Recognition using Ensemble of SVM, MLP and Extra Trees Classifier. In Proceedings of the 2020 International Conference for Emerging Technology (INCET), Belgaum, India, 5–7 June 2020; pp. 1–4.
61. Li, L.; Zhang, X. Study of data mining algorithm based on decision tree. In Proceedings of the 2010 International Conference On Computer Design and Applications, Qinhuangdao, China, 25–27 June 2010; Volume 1, pp. V1-155–V1-158.
62. Breiman, L. Random Forests. *Mach. Learn.* **2001**, *45*, 5–32. [CrossRef]

63. Szostak, D.; Walkowiak, K.; Włodarczyk, A. Short-Term Traffic Forecasting in Optical Network using Linear Discriminant Analysis Machine Learning Classifier. In Proceedings of the 2020 22nd International Conference on Transparent Optical Networks (ICTON), Bari, Italy, 19–23 July 2020; pp. 1–4.

64. Kumar, R.; Naik, S.M.; Naik, V.D.; Shiralli, S.; V.G, S.; Husain, M. Predicting clicks: CTR estimation of advertisements using Logistic Regression classifier. In Proceedings of the 2015 IEEE International Advance Computing Conference (IACC), Banglore, India, 12–13 June 2015; pp. 1134–1138.

65. Lundberg, S.; Lee, S.I. A Unified Approach to Interpreting Model Predictions. In Proceedings of the 31st International Conference on Neural Information Processing Systems, Long Beach, CA, USA, 4–9 December 2017; pp. 4768–4777.

66. Zou, L.; Wang, C.; Chen, X.; Wang, H. Baduanjin Exercise for Stroke Rehabilitation: A Systematic Review with Meta-Analysis of Randomized Controlled Trials. *Int. J. Environ. Res. Public Health* **2018**, *15*, 600. [CrossRef]

67. Binder, E.F.; Schechtman, K.B.; Ehsani, A.A.; Steger-May, K.; Brown, M.; Sinacore, D.R.; Yarasheski, K.E.; Holloszy, J.O. Effects of Exercise Training on Frailty in Community-Dwelling Older Adults: Results of a Randomized, Controlled Trial. *J. Am. Geriatr. Soc.* **2002**, *50*, 1921–1928. [CrossRef]

MDPI