Monaldi Archives for Chest Disease

eISSN 2532-5264 https://www.monaldi-archives.org/

Monaldi Arch Chest Dis 2022 [Online ahead of print]

To cite this Article:
Vigorè M, Granata N, Callegari G, et al. **Frailty and rehabilitation outcome in older patients with cardiorespiratory disease: Preliminary multidimensional data.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2022.2447

Frailty and rehabilitation outcome in older patients with cardiorespiratory disease: Preliminary multidimensional data

Martina Vigorè[1], Nicolò Granata[2*], Giovanna Callegari[3], Raffaella Vaninetti[2], Simona Conti[2], Roberto Maestri[4], Giancarlo Piaggi[3], Gioele Cremonese[2], Antonia Pierobon[1]

[1]Psychology Unit, ICS Maugeri IRCCS Institute of Montescano, Italy

[2]Department of Cardiac Respiratory Rehabilitation, ICS Maugeri IRCCS Institute of Tradate (VA), Italy

[3]Pulmonary Rehabilitation, ICS Maugeri IRCCS Institute of Montescano, Italy

[4]Department of Biomedical Engineering, ICS Maugeri IRCCS Institute of Montescano, Italy

Corresponding author: Nicolò Granata, Department of Cardiac Respiratory Rehabilitation, ICS Maugeri IRCCS, Via Crotto Roncaccio 16, 21049 Tradate (VA), Italy. Tel. +39.385.247255. E-mail: n.granata05@gmail.com

Acknowledgments: We would like to thank Dr. Silvia Audifreddi for her valuable support in the data collection phase of the research.

Conflict of interest: The authors declare that they have no competing interests, and all authors confirm accuracy.

Funding: This work was supported by the Italian National funding (5x1000): project name "Decadimento cognitivo, fragilità e outcome riabilitativo in pazienti anziani affetti da patologia cardiorespiratoria. DEC_FRAinRIAB" (Grant Agreement Number 2424_20 04 20). MV and NG received a research grant from the project's funder. The funders had no role in the study design, data collection, analysis, decision to publish, or preparation of the manuscript.

Ethics Approval: The study was approved by the Institutional Review Board and Central Ethics Committee of the ICS Maugeri SpA SB (CEC) (approval number: CEC N.2424, 23/04/2020).

Data availability: The dataset generated for this study is available on request to the corresponding author.

Authors Contributions

Conceptualization: Antonia Pierobon
Data curation: Martina Vigorè, Nicolò Granata
Formal analysis: Roberto Maestri
Investigation: Martina Vigorè, Nicolò Granata, Giovanna Callegari, Raffaella Vaninetti, Simona Conti, Giancarlo Piaggi, Gioele Cremonese

Methodology: Roberto Maestri, Antonia Pierobon
Supervision: Giovanna Callegari, Raffaella Vaninetti, Simona Conti, Giancarlo Piaggi, Gioele Cremonese
Writing ± original draft: Martina Vigorè, Nicolò Granata, Antonia Pierobon
Writing ± review & editing: Martina Vigorè, Nicolò Granata, Roberto Maestri, Antonia Pierobon

Abstract

Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are two clinical conditions often associated with cognitive dysfunctions, psychological distress, poor quality of life (QoL), and functional worsening. In addition, since patients suffering from these conditions are often older adults, frailty syndrome represented a further and important issue to be investigated. The present preliminary study aimed to perform a multidimensional assessment of CHF COPD older patients (age ≥65) undergoing cardiac or pulmonary rehabilitation. The characteristics of the included patients (30 CHF and 30 COPD) resulted almost similar, except for the COPD patients' longer duration of illness and better performances in Addenbrooke's cognitive examination III subtests and short physical performance battery (SPPB). No significant differences were found in the frailty evaluation, but a consistent number of patients resulted to be frail (CHF=36.7% *vs* COPD=26.6%). After the rehabilitation program, a significant improvement was found in the whole sample concerning the executive functions (14.34±2.49 *vs* 15.62±2.22, p=0.001), quality of life (58.77±18.87 *vs* 65.82±18.45, p=0.003), depressive and anxious symptoms (6.27±4.21 *vs* 3.77±3.39, p=0.001 and 5.17±3.40 *vs* 3.38±3.21, p=0.001), frailty status [4.00 (3.00,5.00) *vs* 3.00 (3.00,5.00) p=0.035] and functional exercise abilities [SPPB, 7.40±3.10 *vs* 9.51±3.67, p=0.0002; timed up and go test, 14.62±4.90 *vs* 11.97±4.51, p=<0.0001; 6-minute walking test, 353.85±127.62 *vs* 392.59±123.14, p=0.0002]. Preliminary results showed a substantial homogeneity of CHF and COPD older patients' cognitive, psychosocial, frailty, and functional characteristics. Nevertheless, the specific rehabilitation intervention appears promising in both clinical populations. This trial has been registered with the ClinicalTrials.gov, NCT05230927 registration number (clinicaltrials.gov/ct2/show/NCT05230927).

Key words: Chronic heart failure; chronic obstructive pulmonary disease; older; frailty; clinical trial; rehabilitation.

Introduction

Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are both globally widespread and they have a considerable burden on healthcare systems and a high impact on morbidity and mortality [1,2]. Specifically, CHF is a chronic condition associated with high rates of hospitalization, re-admissions, severe disability, and a high risk of mortality, and its prevalence varies widely ranging from 1 to 12% of people in the world and it increases with age: from around 1% for people aged <55 years to 10% in those aged 70 years or older[2]. As to COPD, it is a chronic disease, which typical onset is after 55 years old, characterized by a partially irreversible obstruction of lung airflow [1,3]. In 2010, the estimation of the number of COPD cases was around 384 million, with a global prevalence of 11.7% [95% confidence interval (CI) 8.4%-15.0%], and with mortality rates that resulted to be around 3 million people per year[2]. Both clinical conditions present numerous challenges to healthcare providers, in particular, due to the multiple interactions between each other, since both clinical conditions have similar symptoms such as dyspnea and poor exercise tolerance. In addition, COPD is often responsible for delayed diagnosis of CHF and *vice versa* [4].

Beyond specific medical aspects, in the last few years, literature has highlighted that the functional and clinical worsening in patients affected by cardiac and/or respiratory disease/s increases the risk of cognitive deterioration. This impairment principally affects the frontal lobe and subcortical areas of the brain, leading to different deficits concerning executive functions, attention, memory (working memory and learning abilities), and psychomotor speed [5-10]. The clinical, cognitive, and functional worsening appeared to have a high impact on health-related quality of life (HRQoL) that was reported to be low in these clinical populations [11-13]. Moreover, emotional factors, such as anxiety and depression, are of paramount importance since they play an important role in disease adaptation and in the rehabilitation outcome in both cardiac [14,15] and respiratory diseases [16].

Besides cognitive decline and emotional factors, frailty syndrome is an important comorbidity to deal with when it comes to cardiac and respiratory diseases, in particular in the older adult population. Despite the importance and the interest towards frailty, there is no agreement on the definition [17]. In fact, according to the literature, two main theoretical paradigms try to define frailty: the biomedical and bio-psycho-social paradigms. As to the biomedical paradigm, frailty is considered a biological syndrome in which there is an important reduction in the functional reserves and a diminished resistance to stressors. These features result in a cumulative impairment of the multiple physiological systems that cause a state of increased vulnerability and adverse consequences [18]. Conversely, the bio-psycho-social paradigm defines frailty as a dynamic state that affects an individual that loses one or more functional

domains (physical, psychological, and social) due to the influence of different variables that increase the risk of adverse health outcomes [19]. A further definition has been provided by Rockwood and colleagues, that is the operational definition [20]. It is based on the idea that frailty is a state of chaotic disorganization of physiological systems that can be estimated by evaluating certain indexes such as functional status, diseases, physical and cognitive deficits, psychosocial risk factors, and geriatric syndromes.

Despite the differences between the considered paradigms or definitions, a common conclusion could be identified: frailty is associated with the loss of different functional domains, which leads to an increased vulnerability to adverse events such as the risk of falls, hospitalization, disability, and mortality [21].

Indeed, frailty evaluation, both with screening or assessment scales, provides predictive information on the risk of death and length of hospitalization, and it represents a good predictor of acute clinical condition outcomes too [22,23]. In particular, in COPD patients, frailty appears to be a reliable outcome measure, an independent predictor of rehabilitation programs interruption, but it was also described as a reversible condition in the short term after rehabilitation [24,25]. However, as far as we know and according to the most recent literature, frailty is still poorly considered and measured in cardiorespiratory rehabilitation settings [26]. Considering the progressive aging of the population and the promising prognostic use of this index, its assessment could assume a pivotal role in maximizing the clinical outcome.

In this vein, the current study aims to bridge this gap. In particular, this paper presents the preliminary data of an ongoing prospective clinical trial. The first aim is to define the multidimensional profiles (socio-demographic, clinical, and functional characteristics, cognitive impairment, perceived HRQoL, anxiety, depression, and frailty) of two samples of older (age ≥65) CHF or COPD inpatients. The second aim is to compare the profiles of the two samples at admission to the inpatient cardiac or pulmonary rehabilitation program. Finally, the third aim is to evaluate the whole CHF and COPD sample at admission and discharge from the rehabilitation program to evaluate the outcomes.

Methods

Participants

All old inpatients (≥65 years) consecutively admitted to the Cardiac Rehabilitation Department and the Pulmonary Rehabilitation Department of ICS Maugeri – Tradate (Province of Varese) and Montescano (Province of Pavia), Italy, undergoing cardiac or pulmonary rehabilitation, were evaluated for their eligibility in the study. The whole recruiting period was from July 2020

to June 2022, while the period considered in the present study was from July 2020 to January 2021.

In particular, CHF definition is i) signs (e.g. elevated jugular venous pressure, pulmonary crackles, and peripheral edema) and symptoms of HF [New York Heart Association (NYHA) functional class II-IV] in the presence of reduced ejection fraction (LVEF <40%); or ii) signs and symptoms of HF (e.g. elevated brain natriuretic peptides and significant structural heart disease/diastolic dysfunction) with mid-range ejection fraction (LVEF 40–49%) or preserved (LVEF ≥50%) [2].

Furthermore, COPD is defined according to the Global initiative for chronic Obstructive Lung Disease (GOLD) criteria (stage II-IV, C–D). Patients should be in a clinically stable condition (no exacerbations in the last 3 months) with optimized pharmacological therapy (inhalation therapy with long-acting anticholinergic and/or β2-agonists, inhaled corticosteroids when needed) [1].

The exclusion criteria were severe clinical (chronic inflammatory diseases, neoplasia) or psychiatric and neurological (at anamnestic or actual clinical evaluation) conditions, no Italian education, illiteracy or relapse into illiteracy, severe visuo-perceptive deficits, lack of motivation or refusal to undergo the evaluation, and severe cognitive deterioration (Mini-Mental State Examination – MMSE score <18.3) [27].

All the patients included in the study were orally and written informed about all procedures. In addition, all patients signed an informed consent.

The study was approved by the Institutional Review Board and Central Ethics Committee of the ICS Maugeri SpA SB (CEC) (approval number: CEC N.2424, 23/04/2020), and it has been registered on January 28, 2022, with the ClinicalTrials.gov NCT05230927 registration number (clinicaltrials.gov/ct2/show/NCT05230927).

Neuropsychological evaluation

Addenbrooke's Cognitive Examination III (ACE III) is a screening test, designed for the early detection of cognitive deterioration. It is composed of the following five cognitive domains: Attention-Orientation (ACE III-AO = 0-18), Memory (ACE III-M 0 0-26), Verbal Fluency (ACE III-VF = 0-14), Language (ACE III-L = 0-26), and Visuospatial abilities (ACE III-VS = 0-16) [28].

Frontal Assessment Battery (FAB) is a screening test used to assess executive functions. It is divided into the following six sub-tests: conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental dependency [29].

In this research, ACE III scores allow to divide the sample into two subpopulations: patients affected by Mild Cognitive Impairment (MCI) (ACE III-total impaired ≤ 68.68 or borderline = 68.69-75.93 score, or impaired score in at least one subtest: ACE III-AO≤13.2, ACE III-M≤13.04, ACE III-VF≤5.52, ACE III-L≤18.39, and ACE III-VS≤9.97) and patients without cognitive impairment. Furthermore, FAB impaired scores of ≤ 12.03 detect patients with executive dysfunctions.

Health-related quality of life and psychological evaluation

The EQ-5D-5L is a generic quality of life measurement tool which investigates the following five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The second section consists of a visual analogue scale (VAS) where the subject is asked to indicate the level of self-perceived wellness [30].

Generalized anxiety disorder-7 (GAD) is a questionnaire built to measure the severity of anxiety symptoms in the previous two weeks through 7 items organized on a 4-point Likert scale. Scores of 5, 10, and 15 are considered cut-offs for mild, moderate, and severe anxiety, respectively [31]. In this study, we used the Italian version freely downloadable on the PHQ website [32].

Patient Health Questionnaire-9 (PHQ-9) is a scale used to evaluate depressive illnesses. It is divided into nine sub-items identifying depressive symptoms within the last two weeks (following DSM criteria). Scores of 5, 10, and 15 are considered cut-offs for subthreshold, mild major, moderate major, and severe major depression [33,34].

Frailty evaluation

The clinical frailty scale (CFS) is a scale based on clinical judgment only. This scale considers clinical data on the subject's cognition, mobility, functional abilities, and comorbidity, collected through medical history obtained from the patient, the caregiver, and/or other healthcare providers [20]. Frailty index (FI) is a frailty measurement tool that includes variables about mobility, muscle strength, comorbidities, cognitive deficits, mood, anthropometric indices, mini nutritional assessment, and social support. It is made up of 40 items and 17 additional items relating to the social support scale [22].

Functional evaluation

The short physical performance battery (SPPB) is a battery used to investigate the association between physical performance and a self-assessed disability and it is also used as a functional frailty indicator [35,36]. It evaluates the functional capacity of lower limbs and it is composed of three tests.

The timed up and go test (TUG), is a simple test to measure a person's mobility level and requires static and dynamic balancing skills. It measures the time it takes a person to get up from a chair, walk ten feet, turn around, come back to the chair and sit down again [37].
The 6-minute walking test (6MWT) is a self-limited test used to measure functional exercise abilities in people with HF, acute coronary syndrome, and COPD. It is a test in which the person is asked to walk as fast as possible compatible with his clinical condition for a time of 6 minutes, measuring the meters traveled [38].
A summary of the characteristics of measures used for data collection is presented in Table 1.

Data collection

All CHF and COPD inpatients admitted to an inpatient rehabilitation program underwent medical history collection, physical, clinical, and functional examination, exercise testing (SPBB, TUG, 6MWT), educational sessions, exercise training (cycle ergometer/treadmill, arm ergometer, breathing, and strength exercises where indicated, calisthenics exercises), psychological counseling, and metabolic evaluation with a personalized diet when needed. All procedures are in depth explained in the study protocol [39].
The rehabilitation treatment is carried out according to Maugeri's diagnostic therapeutic care pathway following the most recent national and international guidelines [3,40].
The patients included in the study signed informed consent for all procedures and research explanations and underwent an evaluation at three different times that is at the baseline, at the hospital discharge, and at 6 months through a phone follow-up (not described in this preliminary study).

Baseline (T_0)

The first assessment was performed within a maximum of two to four days from the patient's rehabilitation admission or, if necessary, after a therapeutic optimization, by a psychologist (ACE III, FAB, EQ 5D-5L, EQ-VAS, PHQ-9, and GAD-7), by a physiotherapist (SPPB, TUG, and 6MWT), while the cardiologist or pulmonologist will monitor individualized patient's clinical pathway. Concerning frailty screening (CFS) and evaluation (FI) frailty, it was performed by the three aforementioned healthcare professionals and nurses, from an interdisciplinary perspective.

End of hospitalization (T1)

After at least 2-3 weeks from the rehabilitation admission, FAB, EQ 5D-5L, EQ-VAS, CFS, SPPB, TUG, and 6MWT were re-administered as well as the collection of clinical indices related to the disease.

Sample size and preliminary analysis

The sample size estimation is extensively described in the study protocol [39]. Instead, concerning preliminary data, descriptive statistics were reported as mean ± standard deviation (SD) for continuous variables and as percent frequency for categorical variables. Between-group comparisons (CHF *vs* COPD) were carried out by Mann-Whitney U-test and by the Chi-square test for continuous and categorical variables respectively. Within-group comparisons (T0 *vs* T1) for continuous variables were carried out by the Wilcoxon signed-rank test. All statistical tests were two-tailed and statistical significance was set at $p<0.05$. All analyses were carried out using the SAS/STAT statistical package, release 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Overall, 92 patients were recruited; out of these, 32 patients were excluded for the following reasons: clinical exacerbation during hospitalization or patient's transferal to another hospital (n=11), illiteracy (n=1), low subjective motivation, or refusal, to undergo the evaluation (n=11), severe neurological diseases (n=4), and severe cognitive impairment (MMSE≤18.3) (n=5). Thus, this preliminary data was referred to 60 patients (Figure 1). The sample was composed of 30 CHF and 30 COPD patients, whose clinical data are presented in Table 2. As for the CHF group, patients were 60% males, 76.7% were retired, 33.3% lives alone, the whole sample had a primary caregiver (43.3% husband/wife/partner, 46.7% son/daughter, 10% other family members), and an actual (6.7%) or past (70%) smoking habit was referred. As for the COPD group, patients were 73.3% males, 90% were retired, 33.3% lives alone, 93.4% had a primary caregiver (46.7% husband/wife/partner, 30.0% son/daughter, 16.7% other family members), and an actual (20%) or past (73.3%) smoking habit.

Table 3 shows the comparison between CHF and COPD concerning socio-demographic and clinical characteristics, cognitive status, quality of life, depressive and anxious symptoms, frailty, and functional variables assessed at baseline. COPD patients' duration of illness (months) resulted to be significantly longer than CHF patients (117.07±87.36 *vs* 53.17±95.93, p=0.001, respectively). Two of the ACE III sub-scales were significantly higher for COPD patients compared to CHF ones (ACE III attention and orientation, 17.54±0.75 vs 16.54±1.86,

p=0.009; ACE III language, 25.66±0.59 *vs* 24.69±2.43, p=0.038, respectively). Finally, SPPB scores were significantly higher for COPD patients (10.21±9.04 *vs* 6.23±3.24, p=0.006).

As further data on cognitive status, ACE III total or at least one subscale score resulted impaired in the 33.3% of the CHF and in the 23.3% of the COPD sample. As for FAB, the percentage of impaired scores is 46.7% in CHF and 36.7% in COPD patients.

Table 4 shows the comparison between the whole CHF and COPD sample at admission (T_0) and discharge from the hospital (T_1). Overall, results indicate that executive functions, quality of life, depressive and anxious symptoms, and functional exercise abilities were significantly improved after the hospitalization.

Concerning frailty scores related to CFS, 36.7% of CHF patients and 26.6% of COPD patients resulted being frail (CFS score≥5). No statistically significant differences emerged between the two clinical conditions considered, instead there are statistically significant differences between T0 and T1 (p=0.035): the score remained unchanged in 51 patients, improved in 8 patients, and worsened in 1 patient.

Discussion

The present multi-center cross-sectional observational preliminary study investigates and compares cognitive impairment, anxiety, depression, and frailty in a population of older CHF or COPD patients at admission and discharge from an inpatient cardiac or pulmonary interdisciplinary rehabilitation program. This study provides a specific focus on older and frail patients with CHF or COPD, contributing to bridging a literature gap. Although there is a growing interest concerning these clinical populations, research data are still lacking, controversial, and need further investigations [26,41-43].

In this research, CHF and COPD patients showed a moderate-severe level of disease severity. The two samples differ in the duration of illness, which resulted to be longer in the COPD sample. To our knowledge, there is no literature regarding the comparison between these chronic conditions. Nevertheless, the majority of the CHF sample was composed of patients with a recent diagnosis of CHF but with a medical history of cardiovascular diseases. This data is consistent with the literature, describing CHF as the result of hereditary defects, systemic diseases, and prior cardiac conditions [44].

As to socio-demographic characteristics, concerning age and education, no statistically significant differences between the two samples emerged. Conversely, the percentage of male patients resulted to be slightly higher in both CHF and COPD patients (60% and 73.3%, respectively). Literature about CHF patients reported that the demographic and clinical characteristics differ considerably between HF with preserved ejection fraction (HfpEF) and

HF with reduced ejection fraction (HFrEF). In particular, HFpEF patients are more likely to be women and older, obese, with a higher NYHA class and both cardiovascular and non-cardiovascular comorbidities; on the other side, HFrEF, mainly a consequence of coronary artery disease, particularly affects males and older patients [45]. Our results appear to be in line with this data since the CHF sample comprehends both HfpEF and HFrEF patients, old and almost equally distributed between males and females. As to COPD, our data is consistent with the results of a recent systematic review and meta-analysis that showed a prevalence of 9.23% (95% CrI: 8.16-10.36%) in men and 6.16% (95% CrI: 5.41-6.95%) in women [46]. The other socio-demographic characteristics (actual work, living conditions, and primary caregiver) resulted to be similar in both samples, except for the actual smoking habit which percentage higher in COPD patients (20% compared to 6.7% of CHF patients). This result is supported by a recent prospective study that followed COPD patients for seven years and the findings showed that two-thirds of the sample (n=572) continued to smoke despite the pulmonary disease and the prescriptions to stop smoking [47].

Moving on to multidimensional measures, the two samples are substantially similar except for attention/orientation and language ACE III subtests and SPPB results. This similarity is consistent with previous literature which underlines that these two diseases share decreased functional, psychological, and HRQoL characteristics [48,49]. A review and meta-analysis conducted by Yohannes *et al*. showed that the prevalence of MCI is higher in CHF (35%) and COPD (25%) patients [50] compared to the general older population (10-20%) [51]. Our data strengthen these findings since they provide similar percentages of MCI in the two samples (33.3% and 23.3%, respectively). Additionally, in our study, a specific high percentage of executive impaired scores (46.7% in CHF and 36.7% in COPD patients) was found by a screening battery on procedural dysfunction, which resulted to be pivotal to the study due to the connection with rehabilitation implication and self-care management [9,52].

As to frailty screening results, no statistically significant differences emerged between the two samples. A slight difference in the frailty percentages can be noticed (CHF 36.7% *vs* COPD 26.6%) and these data are consistent with the results of two systematic reviews and meta-analyses on the prevalence of frailty in CHF and COPD patients [53,54]: despite the differences across studies, the overall estimated prevalence of frailty in HF was 44.5% (95% CI, 36.2-52.8%; z = 10.54; p<0.001) [53], while the pooled prevalence of frailty in individuals with COPD was 19% (95% CI, 14-24; I2 = 94.4%) [54].

As for SPPB results, a slightly significant difference was found comparing CHF and COPD patients' performance (6.23±3.24 *vs* 10.21±9.04, p=0.005, respectively). As far as we know, no other studies compared SPPB results between these clinical populations. Nevertheless, by

examining the research addressing only CHF or COPD patients in different studies, our findings are in line with the data distribution of these clinical populations. Specifically, SPPB results appear to be lower in CHF patients than in COPD patients [55,56].

Finally, concerning the comparison between the cognitive, psychological, quality of life, and functional data at admission and discharge, a significant improvement can be observed in all the investigated areas in CHF and COPD patients. The data concerning the benefits of cardiac and pulmonary rehabilitation has been extensively reported in literature in both CHF and COPD patients [41,57-65]. As to CHF, literature shows that cardiac rehabilitation induced significant improvements in physical and psychological parameters in a sample of patients ranging from less than 65 years to 80 years or over [59]. Specifically, results concerning executive functions find support in literature where significant improvements were detected after cardiac rehabilitation [61]. Moreover, another study showed that exercise capacity, assessed by the 6MWT, and HRQoL improved after rehabilitation, regardless of individual patient characteristics [63]. Finally, a recent study showed the potential benefits of cardiac rehabilitation in patients suffering from cardiovascular diseases on frailty as in our CHF sample [62]. Concerning COPD, a recent systematic review, performed on nineteen randomized controlled trials that compared pulmonary rehabilitation groups with usual care groups, showed statistically significant improvements in patient's quality of life [60]. A recent study showed significant improvements in COPD patients' cognitive functions after a rehabilitation program focused on attention, memory, language, visuospatial perception, executive functions, and problem-solving [65]. Moreover, the results of a prospective study in which COPD older patients performed an 8-week pulmonary rehabilitation program, showed a sustained improvement in anxiety and quality of life 2 years after the intervention [64]. In another prospective study COPD patients, after a 5-years multidisciplinary pulmonary rehabilitation maintenance program, showed significant improvements at 4 years for exercise capacity and HRQoL and at 5 years for dyspnea symptoms [58]. Finally, in a recent systematic review, the authors found that frailty could be reversed after specific and tailored pulmonary rehabilitation similarly to our study [41].

The present preliminary study shows a limitation concerning the small sample size that does not allow the generalizability of the findings. Nevertheless, some strengths could be noticed. Firstly, to our knowledge, this study can be considered the first one trying to detect similarities and differences within these chronic conditions. Secondly, the results of cardiac or pulmonary rehabilitation appear to be promising as significant improvements were found in all the investigated areas, and they are substantially consistent with the most recent scientific literature.

Finally, frailty is often considered in rehabilitation settings, but its evaluation is not always performed with standardized methods and measures as in the present research.

Conclusions

The preliminary results of the present study showed a substantial homogeneity of the cognitive, psychosocial, frailty, and functional characteristics of CHF and COPD older patients, with slight differences, which deserve specific attention. Furthermore, our data showed the potential benefits of specific rehabilitation intervention in both samples on the multidimensional spectrum including a frailty measure.

Recruitment of a largest sample size is ongoing since further investigations are necessary to corroborate these findings and to support the fundamental role of cardiac and pulmonary rehabilitation in older chronic patients.

References

1. GOLD. Global Strategy for Prevention, Diagnosis and Management of COPD. 2022. Available from: https://goldcopd.org/2022-gold-reports/
2. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599-26.
3. Singh D, Agusti A, Anzueto A, et al. Global Strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. Eur Respir J 2019;53:1900164.
4. Ostojić J, Pintarić H. Chronic obstructive pulmonary disease and heart failure: Closer than close. Acta Clin Croat 2017;56:269–76.
5. Cannon JA, Moffitt P, Perez-Moreno AC, et al. Cognitive impairment and heart failure: Systematic review and meta-analysis. J Card Fail 2017;23:464–75.
6. ameron J, Gallagher R, Pressler SJ. Detecting and managing cognitive impairment to improve engagement in heart failure self-care. Curr Heart Fail Rep 2017;14:13–22.
7. Kakkera K, Padala KP, Kodali M, Padala PR. Association of chronic obstructive pulmonary disease with mild cognitive impairment and dementia. Curr Opin Pulm Med 2018;24:173–8.
8. Millán-Calenti JC, Maseda A, Rochette S, et al. Mental and psychological conditions, medical comorbidity and functional limitation: differential associations in older adults with cognitive impairment, depressive symptoms and co-existence of both. Int J Geriatr Psychiatry 2011;26:1071–9.
9. Pierobon A, Granata N, Torlaschi V, et al. Psychomotor speed as a predictor of functional status in older chronic heart failure (CHF) patients attending cardiac rehabilitation. PLoS One 2020;15:e0235570.
10. Ilari S, Russo P, Proietti S, et al. DNA damage in dementia: Evidence from patients affected by severe chronic obstructive pulmonary disease (COPD) and meta-analysis of most recent literature. Mutat Res Toxicol Environ Mutagen 2022;878:503499.
11. Moradi M, Daneshi F, Behzadmehr R, et al. Quality of life of chronic heart failure patients: a systematic review and meta-analysis. Heart Fail Rev 2020;25:993-1006.
12. Kharbanda S, Anand R. Health-related quality of life in patients with chronic obstructive pulmonary disease: A hospital-based study. Indian J Med Res 2021;153:459–64.
13. Marcolongo F, Scarlata S, Tomino C, et al. Psycho-cognitive assessment and quality of life

in older adults with chronic obstructive pulmonary disease-carrying the rs4713916 gene polymorphism (G/A) of gene FKBP5 and response to pulmonary rehabilitation: a proof of concept study. Psychiatr Genet 2022;32:116–24.
14. Sommaruga M, Angelino E, Della Porta P, et al. Best practice in psychological activities in cardiovascular prevention and rehabilitation: Position Paper. Monaldi Arch Chest Dis 2018;88:966.
15. Fattirolli F, Bettinardi O, Angelino E, et al. What constitutes the 'Minimal Care' interventions of the nurse, physiotherapist, dietician and psychologist in Cardiovascular Rehabilitation and secondary prevention: A position paper from the Italian Association for Cardiovascular Prevention, Rehabilitat. Eur J Prev Cardiol 2018;25:1799–810.
16. Pierobon A, Sini Bottelli E, Ranzini L, et al. COPD patients' self-reported adherence, psychosocial factors and mild cognitive impairment in pulmonary rehabilitation. Int J Chron Obstruct Pulmon Dis 2017;12:2059–67.
17. Xue Q-L. The frailty syndrome: Definition and natural history. Clin Geriatr Med 2011;27:1-15. A
18. Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 2004;59:255–63.
19. Gobbens RJJ, Luijkx KG, Wijnen-Sponselee MT, Schols JMGA. In search of an integral conceptual definition of frailty: opinions of experts. J Am Med Dir Assoc 2010;11:338–43.
20. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–95.
21. McCarthy B, Casey D, Devane D, et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2015;(29)CD003793.
22. Abete P, Basile C, Bulli G, et al. The Italian version of the "frailty index" based on deficits in health: a validation study. Aging Clin Exp Res 2017;29:913–26.
23. Strini V, Schiavolin R. [Assessment instruments for frail elders: a literature review].[Article in Italian]. Assist Inferm Ric 2019;38:87–98.
24. Pandey A, Kitzman D, Whellan DJ, et al. Frailty Among older decompensated heart failure patients: Prevalence, association with patient-centered outcomes, and efficient detection methods. JACC Hear Fail 2019;7:1079–88.
25. Maddocks M, Kon SSC, Canavan JL, et al. Physical frailty and pulmonary rehabilitation in COPD: A prospective cohort study. Thorax 2016;71:988–95.
26. Vigorito C, Abreu A, Ambrosetti M, et al. Frailty and cardiac rehabilitation: A call to action from the EAPC Cardiac Rehabilitation Section. Eur J Prev Cardiol 2017;24:577–90.
27. Magni E, Binetti G, Bianchetti A, et al. Mini-mental state examination: a normative study in Italian elderly population. Eur J Neurol 1996;3:198–202.
28. Pigliautile M, Chiesi F, Stablum F, et al. Italian version and normative data of Addenbrooke's Cognitive Examination III. Int Psychogeriatr 2019;31:241-9.
29. Appollonio I, Leone M, Isella V, et al. The frontal assessment battery (FAB): normative values in an Italian population sample. Neurol Sci 2005;26:108–16.
30. EuroQol [Internet]. EQ-5D. Accessed: 2021 Aug 24. Available from: https://euroqol.org/
31. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092–7.
32. Pfizer [Internet]. Patient Health Questionnaire (PHQ) screeners. Accessed: 2022 Nov 25. Available from: https://www.phqscreeners.com/
33. Spitzer RL, Kroenke K, Williams JBW. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient Health Questionnaire. JAMA 1999;282:1737–44.
34. Rizzo R, Piccinelli M, Mazzi MA, et al. The Personal Health Questionnaire: a new screening instrument for detection of ICD-10 depressive disorders in primary care. Psychol

Med 2000;30:831–40.
35. Guralnik JM, Simonsick EM, Ferrucci L, et al. 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:M85–94.
36. Perracini MR, Mello M, de Oliveira MR, et al. Diagnostic accuracy of the short physical performance battery for detecting frailty in older people. Phys Ther 2020;100:90-8.
37. Podsiadlo D, Richardson S. The timed "up & go": A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142–8.
38. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111–7. Erratum in: Erratum: ATS Statement: Guidelines for the Six-Minute Walk Test. Am J Respir Crit Care Med 2016;193:1185.
39. Vigorè M, Granata N, Braga SS, et al. Cognitive impairment, frailty and rehabilitation outcome in older cardiorespiratory patients. DEC_FRAinRIAB: Study protocol. PLoS One 2022;17:e0272132.
40. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representati. Eur Heart J 2016;37:2315–81.
41. Wang Z, Hu X, Dai Q. Is it possible to reverse frailty in patients with chronic obstructive pulmonary disease? Clinics (Sao Paulo) 2020;75:e1778.
42. Fattirolli F, Pratesi A. Cardiovascular prevention and rehabilitation in the elderly: evidence for cardiac rehabilitation after myocardial infarction or chronic heart failure. Monaldi Arch Chest Dis 2016;84:731.
43. Guan C, Niu H. Frailty assessment in older adults with chronic obstructive respiratory diseases. Clin Interv Aging. 2018;13:1513–24.
44. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol 2016;13:368–78.
45. Savarese G, Lund LH. Global public health burden of heart failure. Card Fail Rev 2017;3:7–11.
46. Ntritsos G, Franek J, Belbasis L, et al. Gender-specific estimates of COPD prevalence: a systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2018;13:1507–14.
47. Iribarren ME, Pérez TA, Gómez Punter RM, et al. Smoking habit in COPD patients. Eur Respir J 2019;54:PA4488.
48. Vitacca M, Paneroni M. Rehabilitation of patients with coexisting COPD and heart failure. COPD. England; 2018;15:231–7.
49. Neder JA, Rocha A, Berton DC, O'Donnell DE. Clinical and physiologic implications of negative cardiopulmonary interactions in coexisting chronic obstructive pulmonary disease-heart failure. Clin Chest Med 2019;40:421–38.
50. Yohannes AM, Chen W, et al. Cognitive impairment in chronic obstructive pulmonary disease and chronic heart failure: A systematic review and meta-analysis of observational studies. J Am Med Dir Assoc 2017;18:451.e1-451.e11.
51. Langa KM, Levine DA. The diagnosis and management of mild cognitive impairment: a clinical review. JAMA 2014;312:2551–61.
52. Ranzini L, Schiavi M, Pierobon A, et al. From mild cognitive impairment (MCI) to Dementia in chronic obstructive pulmonary disease. Implications for clinical practice and disease management: A mini-review. Front Psychol 2020;11:337.
53. Denfeld QE, Winters-Stone K, Mudd JO, et al. The prevalence of frailty in heart failure: A systematic review and meta-analysis. Int J Cardiol 2017;236:283–9.
54. Marengoni A, Vetrano DL, Manes-Gravina E, et al. The relationship between COPD and frailty: A systematic review and meta-analysis of observational studies. Chest Uited 2018;154:21-40.

55. Mohan D, Benson VS, Allinder M, et al. Short physical performance battery: What does each sub-test measure in patients with chronic obstructive pulmonary disease? Chronic Obstr Pulm Dis 2020;7:13–25.
56. Zaharias E, Cataldo J, Mackin L, Howie-Esquivel J. Simple measures of function and symptoms in hospitalized heart failure patients predict short-term cardiac event-free survival. Nurs Res Pract 2014;2014:815984.
57. Alosco ML, Spitznagel MB, Cohen R, et al. Cardiac rehabilitation is associated with lasting improvements in cognitive function in older adults with heart failure. Acta Cardiol 2014;69:407-14.
58. Blervaque L, Préfaut C, Forthin H, et al. Efficacy of a long-term pulmonary rehabilitation maintenance program for COPD patients in a real-life setting: a 5-year cohort study. Respir Res 2021;22:79.
59. Deley G, Culas C, Blonde M-C, et al. Physical and psychological effectiveness of cardiac rehabilitation: Age is not a limiting factor! Can J Cardiol 2019;35:1353–8.
60. Dong J, Li Z, Luo L, Xie H. Efficacy of pulmonary rehabilitation in improving the quality of life for patients with chronic obstructive pulmonary disease: Evidence based on nineteen randomized controlled trials. Int J Surg 2020;73:78–86.
61. Kim M, Cho C, Lee C, Kohzuki M. Effects of cardiac rehabilitation on executive function in sedentary older adults. Asian J Hum Serv. 2016;11:98–110.
62. Fonteles Ritt L, Matos e Oliveira F, Santos Pereira Ramos JV, et al. Impact of a cardiovascular rehabilitation program on frailty indicators in elderly patients with heart disease. Eur J Prev Cardiol 2021;28:zwab061.037
63. Taylor RS, Walker S, Ciani O, et al. Exercise-based cardiac rehabilitation for chronic heart failure: the EXTRAMATCH II individual participant data meta-analysis. Health Technol Assess 2019;23:1–98.
64. Yohannes AM, Dryden S, Casaburi R, Hanania NA. Long-term benefits of pulmonary rehabilitation in patients with COPD: A 2-year follow-up study. Chest 2021;159:967–74.
65. Park MO, Oh HS, Seo WS. Effects of a cognitive rehabilitation programme on cognitive function, self-management and quality of life in patients with chronic obstructive pulmonary disease. Int J Nurs Pract 2021;27:e12932.

Table 1. Measures for data collection with related construct and score interpretation.

Measures	Construct	Range	Score interpretation (↗ High, ↘ Low)
Neuropsychological evaluation			
ACE III[a]	Cognitive status (attention, orientation, memory, language, word/semantic fluency, and visuospatial abilities)	0-100	↗ Scores ↗ Cognitive status
FAB[b]	Executive functions	0-18	↗ Scores ↗ Executive functions
Health-Related Quality of Life evaluation			
EQ 5D-5L[c]	Perceived health-related quality of life (questionnaire form)	0-25	↗ Scores ↘ HRQoL
EQ VAS[d]	Perceived health-related quality of life (visual-analogue form)	0-100	↗ Scores ↗ HRQoL
Psychological evaluation			
GAD-7[e]	Anxiety	0-21	↗ Scores ↗ Anxiety symptom
PHQ-9[f]	Depression	0-27	↗ Scores ↗ Depressive symptom
Frailty evaluation			
Frailty Index	Frailty	1-40	↗ Scores ↗ Greater frailty
CFS[g]	Frailty	1-9	↗ Scores ↗ Greater frailty
Functional evaluation			
SPPB[h]	Functional capacity of lower limbs	0-12	↗ Scores ↗ Lower limbs capacity
TUG[i]	Static and dynamic balancing skills	0-…	↗ Scores ↘ Balancing skills
6MWT[l]	Functional exercise abilities	0-…	↗ Scores ↗ Exercise abilities

[a]Addenbrooke's cognitive examination III; [b]frontal assessment battery; [c]EuroQol 5D-5L; [d]EuroQol visual analogue scale; [e]generalized anxiety disorder – 7; [f]patient health questionnaire – 9; [g]clinical frailty scale; [h]short physical performance battery; [i]timed up and go; [l]6 minutes walking test.

Table 2. Clinical values of the CHF and COPD study samples..

Variable	Mean±SD	Range
	CHF (n=30)	
BNP[a] (pg/ml)	556.73±583.63	52-1816
LVEF[b] (%)	44.40±15.15	18-72
Teldia Vol[c] (ml/m2)	58.82±20.79	21-101
TAPSE[d] (mm)	18.88±3.53	10-25
PAPs[e] (mmHg)	40.11±13.80	23-85
	COPD (n=30)	
FEV1[f]	1.23±0.62	0.44-2.44
FEV1%[g]	57.92±21.42	22-101
FEV1/VC%[h]	56.35±19.11	29.9-103
SpO2[i]	94.60±2.91	90-98
Blood pH	7.41±0.02	7.37-7.45

[a]Brain natriuretic peptide; [b]left ventricular ejection fraction; [c]telediastolic volume; [d]tricuspid annulus plane systolic excursion; [e] pulmonary artery pressure; [f] forced expiratory volume in the 1st second; [g]forced expiratory volume in the 1st second%; [h]forced expiratory volume in the 1st second/forced vital capacity; [i]peripheral oxygen saturation.

Table 3. Comparison between CHF and COPD multidimensional variables.

Variables	CHF N (Mean±SD)	COPD N (Mean±SD)	P-value
Socio-demographic and clinical data			
Age	30 (74.87±5.97)	30 (74.10±6.34)	0.53
Education (years)	30 (7.63±3.54)	30 (8.07±3.44)	0.44
Duration of illness (months)	30 (53.17±95.93)	30 (117.07±87.36)	0.001
BMI[a]	30 (26.44±5.40)	30 (26.94±9.22)	0.77
Cognitive status			
ACE III[b] total	30 (88.13±9.97)	30 (93.17±6.23)	0.06
ACE III attention orientation	30 (16.71±1.84)	30 (17.72±0.55)	0.009
ACE III memory	30 (21.30±4.56)	30 (22.75±3.29)	0.21
ACE III fluency	30 (9.69±2.39)	30 (10.01±2.28)	0.42
ACE III language	30 (24.88±2.18)	30 (25.96±0.18)	0.008
ACE III visual-spatial	30 (14.37±2.11)	30 (14.75±1.43)	0.77
FAB[c]	30 (13.91±2.92)	30 (14.77±1.93)	0.51
Quality of life			
EQ 5D-5L[e]	30 (7.77±3.23)	30 (7.20±2.20)	0.83
EQ VAS[f]	30 (61.00±18.96)	30 (56.53±18.83)	0.41
Psychological variables			
GAD7[g]	30 (4.93±3.24)	30 (5.40±3.59)	0.30
PHQ-9[h]	30 (5.63±3.09)	30 (6.90±5.07)	0.55
Frailty			
Frailty index	30 (10.84±5.15)	30 (9.38±5.27)	0.15
Social support	30 (5.20±1.63)	30 (5.77±3.09)	0.86
Functional variables			
SPPB[i]	26 (6.23±3.24)	28 (10.21±9.04)	0.006
TUG[l]	19 (15.29±6.21)	27 (13.73±3.63)	0.66
6MWT[m]	8 (392.88±118.26)	22 (338.68±132.32)	0.44

[a]Body mass index; [b]Addenbrooke's cognitive examination III; [c]frontal assessment battery; [e]EuroQol 5D 5l; [f]EuroQol visual analogue scale; [g]generalized anxiety disorder – 7; [h]patient health questionnaire – 9; [i]short physical performance battery; [l]timed up and go; [m]6 minutes walking test.

Table 4. Comparisons of the whole CHF and COPD sample (n=60) at T_0 and T_1.

Variables	**Mean±SD (T_0)**	**Mean±SD (T_1)**	**Delta**	**p-value**
FAB[a]	14.34±2.49	15.62±2.22	1.28±1.68	<0.0001
EQ VAS[b]	58.77±18.87	65.82±18.45	7.05±17.05	0.003
PHQ-9[c]	6.27±4.21	3.77±3.39	-2.50±3.74	<0.0001
GAD7[d]	5.17±3.40	3.38±3.21	-1.78±3.05	<0.0001
SPPB[e]	7.40±3.10	9.51±3.67	2.11±3.62	0.0002
TUG[f]	14.62±4.90	11.97±4.51	-2.66±3.97	<0.0001
6MWT[g]	353.85±127.62	392.59±123.14	38.74±48.30	0.0002

[a]Frontal assessment battery; [b]EuroQol visual analogue scale; [c]patient health questionnaire – 9; [d]generalized anxiety disorder 7; [e]short physical performance battery; [f]timed up and go; [g]6 minutes walking test.

Figure 1. Flowchart of patients' recruitment.