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Comprehensive frailty assessment with multidimensional frailty domains as a predictor of mortality among vascular and cardiac surgical patients

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ABSTRACT

Purpose: The frailty concept has become a fundamental part of daily clinical practice. In this study our purpose was to create a risk estimation method with a comprehensive aspect of patients' preoperative frailty. *Patients and methods:* In our prospective, observational study, patients were enrolled between September 2014 and August 2017 in the Department of Cardiac Surgery and Department of Vascular Surgery at Semmelweis University, Budapest, Hungary. A comprehensive frailty score was built from four main domains: biological, functional-nutritional, cognitive-psychological and sociological. Each domain contained numerous indicators. In addition, the EUROSCORE for cardiac patients and the Vascular POSSUM for vascular patients were calculated and adjusted for mortality. *Results:* Data from 228 participants were included for statistical analysis. A total of 161 patients underwent vascular surgery, and 67 underwent cardiac surgery. The preoperatively estimated mortality was not

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significantly different (median: 2.700, IQR (interquartile range): 2.000–4.900 vs. 3.000, IQR: 1.140–6.000, $P = 0.266$). The comprehensive frailty index was significantly different (0.400 (0.358–0.467) vs. 0.348 (0.303–0.460), $P = 0.001$). In deceased patients had elevated comprehensive frailty index (0.371 (0.316–0.445) vs. 0.423 (0.365–0.500), $P < 0.001$). In the multivariate Cox model an increased risk for mortality in quartiles 2, 3 and 4 compared with quartile 1 as a reference was found (AHR (95% CI): 1.974 (0.982–3.969), 2.306 (1.155–4.603), and 3.058 (1.556–6.010), respectively). *Conclusion:* The comprehensive frailty index developed in this study could be an important predictor of long-term mortality after vascular or cardiac surgery. Accurate frailty estimation could make the traditional risk scoring systems more accurate and reliable.

KEYWORDS

frailty, frailty assessment, frailty score, preoperative risk, risk stratification, vascular surgery, cardiac surgery

INTRODUCTION

Background/rationale

More accurate and reliable risk estimation methods are required for daily practice in medicine. In the surgical field, invasive and non-invasive treatment could have entirely different risks, outcomes and burdens. In elderly patients, aortic valve replacement by a surgical or transcatheter approach is a good example. The choice needs to be guided by multidisciplinary risk estimation to select the best treatment for the patient, which could be challenging and requires multifactorial decisions. To support the decision-making process, different risk calculation methods are used with very different accuracies and predictive values. Traditional risk scores are calculated using basic biological variables and surgical (operative) load/risk but not by taking into account the patients' frailty, which is well proven to be an independent risk factor for postoperative mortality and morbidity [1–4]. A gold standard definition of frailty is missing, but the commonly accepted definition of frailty is a clinical state where patients have a decreased ability to react to physical stress because of reduced physiological reserve and capacity [5]. According to modern frailty conception this clinical syndrome is developing by accumulation of different deficits, including physical, clinical, cognitive, psychological and social problems. An up-to-date review clearly summarizes the evolution of the frailty concept which emphasizes that frailty syndrome is how many ways more complex than e.g. decreased muscle strength. Furthermore, this work from Wleklik et al., highlights the fact that frailty syndrome could be reversible which could directly lead clinicians toward the need for adequate prehabilitation [6]. In this manner correct frailty estimation could be useful selection for prehabilitation and help to make and prove – sometimes difficult – clinical questions. In the literature increasing numbers of evidence and recommendation can be found about the improvement of frailty and the importance of prehabilitation [7, 8].

The general frailty concept is increasingly being accepted and has become a part of daily clinical routine. Currently, we still do not have an exact, comprehensive frailty assessment method for mapping, describing and understanding patients' frailty status. An increasing number of studies have emphasized that frailty status is superior to special surgical risk scores. Using only one or a few parameters from the frailty tools could be misleading [9]. Furthermore, it seems to be the case that frailty is not a good predictor for early postoperative problems but instead has a specific effect on mid- and long-term mortality and morbidity.

When conducting an overview of the literature, the effect of frailty on negative outcomes is clearly identifiable. According to a meta-analysis, the prevalence of frailty is approximately 19–62% in the surgical and intensive care population. The odds ratios for mortality of frail patients ranges from 1.76 to 3.09, and the length of stay (LOS), discharge to other types of care and surgical complications were also elevated. However, the additional benefits of frailty estimation in this field are obvious, and better standardization of the different frailty scores is highly recommended according to the final conclusions of this meta-analysis [10].

The effect of frailty syndrome on mortality and mortality is important to investigate in contrast of currently used risk estimation methods. These methods built up mostly with physiological conditions and each medical discipline has its own routine processes. In cardiac surgery the EuroScore II, in vascular surgery the Vascular POSSUM (V-POSSUM) are the one of the most frequently used risk estimation methods [3, 4].

Objectives

Our aim was to investigate patients' preoperative frailty using a multidomain assessment and modelling of its effect on postoperative mortality. Behind the overall influence, the effect of distinct frailty aspects was also analysed. Comparing and adjusting traditionally used risk estimation methods were also important parts of our work to evaluate the summarized accuracy of both types of scores.

PATIENTS AND METHODS

Study design, setting, participants

In our prospective, observational study, patients were enrolled between September 2014 and August 2017 in the Department of Cardiac Surgery and Department of Vascular Surgery at Semmelweis University, Budapest, Hungary. This study was approved by the local scientific ethics committee (TuKEB 250/2013) and was registered on clinicaltrials.gov (NCT02224222). This current report is a sub-analysis of the database created for the original aim, which was to investigate patients' preoperative risk factors before cardiac and vascular surgery. In cardiac surgical group surgical valve replacement (aortic and mitral valve), coronary artery bypass grafting or ascending aorta reconstruction was performed. In vascular surgical group procedures on arterial system were performed (operations on abdominal aorta, iliac and femoral artery system or carotid artery endarterectomies).

Definitions and measurements (variables and data sources and grouping), study size

The inclusion criteria were age over 18 years and elective surgery. Exclusion criteria were pregnancy and patients with a legal incapacity or considered to have a limited capability of understanding the study procedures and providing informed consent. All enrolled participants were capable of making their own decisions regarding their participation in this study, and accordingly, written consent was obtained. A study nurse, a medical student or a postdoctoral fellow invited patients to participate in this study during their outpatient anaesthesiology visit. All staff members were trained by a psychologist to perform the cognitive mapping and assessments. The baseline questionnaires were completed 30 days before surgery.

Basic anthropometric data, such as height, weight, age, and sex, were collected. Place of residence, education, marital and working status were also recorded. The previous medical history (including past illness and surgeries) was collected, and the frailty indicators were also mapped. In cardiac surgical patients EuroScore II, in vascular surgical patients V-POSSUM was calculated and transformed into predicted mortality percentage.

EuroScore II contains 3 basic domains: 1. the patient related factors (age, sex, renal impairment or insufficiency, respiratory disease, atherosclerosis, poor mobility, previous cardiac surgery, endocarditis, preoperative critical state, diabetes mellitus treated with insulin), 2. cardiac related factors (congestive heart failure, angina severity, current myocardial infarction, left ventricular ejection fraction, pulmonary hypertension) and 3., operation-related factors (urgency, weight of procedures (e.g. valve replacement with coronary artery bypass grafting) and the involvement of thoracic aorta) [4]. The V-POSSUM contains two domains: 1., physiology parameters (age, cardiac failure, respiratory disease, heart rhythm, systolic blood pressure, pulse rate, haemoglobin level, white blood cells, blood urea nitrogen, serum potassium and sodium level, Glasgow Coma Scale level) and 2., operative parameters (operation type, number of procedures, planned blood loss, peritoneal contamination, coexisting malignancy, urgency) [3].

Building a comprehensive frailty score

The comprehensive frailty score was built from four main domains. Each domain contained numerous indicators. All the indicators had values between 0 and 1. For binomial indicators (e.g. atrial fibrillation or diabetes), the presence of the illness scored 1 point. In the case of continuous variables (e.g. self-rated scales), the original score was calculated to obtain a value between 0 and 1. The biological frailty domain was composed of cardiovascular risk factors (congestive heart failure, atrial fibrillation, chronic coronary syndrome, hypertension, previous myocardial infarction or stroke, diabetes) and non-cardiovascular diseases (asthma or chronic obstructive pulmonary disease (COPD), arthritis, degenerative spinal disorders, chronic renal insufficiency, neoplasia). The chronic administration of medications was also considered, and regularly taking more than 5 drugs was identified as a potential risk factor. The functional domain included functional indicators (being able to move heavy objects, engage in sports and housework) and nutritional parameters (body mass index (BMI) lower than 20, serum albumin level lower than 35 g L^{-1} and unintended weight loss (more than 10% during the last 6 months)). The main cognitive and psychological domains were cognitive dysfunction, depression, anxiety and self-reported happiness and satisfaction. The sociological frailty domain included education, living alone, Caldwell Social Support Dimension Scale and self-reported financial problems. The education indicator was clustered into low (elementary and high school) and high levels (college and higher education).

Self-reported physical function tests

In the functional domain, there were self-reported indicators for physical status. Our indicators were derived from the activities of daily living questionnaire, such as transferring heavy objects and performing housework independently. Regarding sports, engaging in more than one exercise session per week was accepted as regular sports activity. Its limitation is that some patients were not able to do any exercises because of their medical conditions (severe lower limb artery stenosis, etc.).

Mini mental state examination

To measure the patients' cognitive performance, the Mini-Mental State Examination (MMSE) was used. However, the MMSE is designed for detecting dementia; it has a high specificity for cognitive impairment, and its clinical relevance has been proven in numerous studies [11]. The test contains questions that map to cognitive function, including language skills, short-term memory and computing abilities. In the current setting, the MMSE was scored as 0, 0.3, 0.7 and 1 according to the original score of 27–30, 24–26, 21–23 and below 21, respectively [12].

Beck depression inventory

The Beck Depression Inventory (BDI) contains 21 multiple-choice questions created by Aaron T. Beck in 1961 [13]. The inventory went through numerous modifications; currently, the BDI-II is used, a version made in 1996. It also has modified cut-off values: 14–19 points are associated with mild depression, 20–28 points with moderate depression and over 29 points with severe depression [14]. In the current study, the definition of depression was 13 points and above on the BDI.

State-Trait Anxiety Inventory

Anxiety was measured by the State-Trait Anxiety Inventory (STAI). It has two axes, trait and state anxiety, which both include 20, 4-point Likert-scale questions [15]. In this study, the trait axis was mapped, and general anxiety was determined as a score of at least 40 points on the STAI-T [16].

Caldwell Social Support Dimension Scale

The Caldwell Social Support Dimension Scale (CSSDS) is a self-report inventory to map patients' social support and social network. It contains aspects about support by family and nonfamily persons [17]. In the current study, the overall social support dimension scale was used.

Other self-reported indicator scales

In the functional, psychological and social domains, simple self-rated questions were used to map happiness, satisfaction, current health status and daily financial problems. The patients were able to choose values on a continuous scale between 1 and 10. The power of the predictive ability for mortality and morbidity of these simple questions was proven in earlier studies [18, 19]. The indicator was calculated as follows: (1-original value/10) (e.g., patients with a self-rated score of 7/10 received 0.3 points, patients with a self-rated score 4/10 received 0.6 points, etc.).

Living alone is a well-proven risk factor for mortality, especially in elderly individuals, and it was used as an indicator in the social frailty main domain [20, 21].

Preoperative surgical risk

For traditional surgical risk estimation in the case of vascular surgical patients, the Vascular POSSUM was used, while for cardiac surgical patients, Euroscore II was used [1, 2, 22]. The original score was translated for estimated mortality in percentages. In the Cox regression model, adjustment of the comprehensive frailty index for estimated mortality was performed.

Outcomes

The primary outcome was mortality during the follow-up. Secondary outcomes were short- and mid-term mortality (at 1, 2 and 4 years of follow-up).

Statistical analysis

Normality was tested with the Kolmogorov–Smirnov test. Normal distributions are described with means and standard deviations. Skewed distributions are described with medians and interquartile ranges (IQR 25–75) and were compared with the Mann–Whitney *U* test and the Wilcoxon rank-sum test. Categorical data are presented as quantities and percentages and were assessed with the chi-square test and Fischer's exact test. A two-sided alpha level of 0.05 was applied.

Multivariable Cox regression models were used as the primary analysis to discover independent risk factors for mortality with adjustment for the Euroscore II and Vascular POSSUM scores. For the comparability of the mortality risk calculation scores, the estimated mortality in percentages was calculated, and this value was used in the adjustment methods. Multivariable two-sided tests with an alpha level of less than 0.05 were considered statistically significant. We used backwards variable elimination to create a model for predicting mortality. We performed our statistical analyses with IBM-SPSS 25.0 software (International Business Machines Corporation, Armonk, New York, United States of America) and jamovi for statistical and graphical tools. Jamovi extensions ClinicoPathDescriptives, deathwatch, felxplot, jjstatsplot, jsurvival, medmod and scatr were used [23].

RESULTS

Participants, descriptive data

Data from 228 participants were included for statistical analysis. A total of 161 patients underwent vascular surgery, and 67 underwent cardiac surgery. The median age of the whole cohort was 68.00 years, and the interquartile range was 60.50–73.00 years. A total of 64.07% were male, and the median BMI was 27.44 (IQR 24.30–29.75). The median follow-up time was 2012 days, IQR 1471–2413 days. Regarding the described parameters, a significant difference was not verified. During the follow-up, 95 patients died (41.667%). The one-, two-, three- and four-year mortality rates were 6.140% (14), 10.088% (23), 18.421% (42) and 23.246% (53), respectively. The incidence of different indicators of the comprehensive frailty score are shown in Table 1.

Table 1. The incidence of different indicators of the comprehensive frailty score among the whole population (a: inverted score, BDI: Beck Depression Inventory, BMI: body mass index, CCS: chronic coronary syndrome, COPD: chronic obstructive pulmonary disease, CSSDS:Caldwell Social Support Dimension Scale, STAI: State-Trait Anxiety Inventory, TIA: transient ischemic attack)

		Count	%	Median	Interquartile range
Biological variables	Atrial fibrillation	25	10.96%		
	Congestive heart failure	23	10.09%		
	CCS	83	36.40%		
	Diabetes mellitus	90	39.47%		
	Hypertension	206	90.35%		
	Myocardial infarction	41	17.98%		
	Stroke (or TIA)	61	26.75%		
	Arthritis	128	56.14%		
	Asthma	6	2.63%		
	Neoplasia in last 5 years	14	6.14%		
	Renal disease	42	20.79%		
	COPD	80	35.09%		
	Degenerative spinal disease	35	15.35%		
	More than 5 regularly used medications	137	60.09%		
Biological domain subindex				0.286	0.214–0.385
Functional and nutritional variables	BMI (≤20 or ≥30)	26	11.40%		
	Unintended weight loss	22	10.05%		
	Current pain/chronic pain	98	44.95%		
	Self-rated health status[a]			0.400	0.400–0.400
	Low albumin level (≤35 g L^{-1})	46	23.71%		
	Lack of sport activities	87	41.23%		
	Unable to doing heavy work around the house	115	50.66%		
	Unable to do housecleaning and home maintenance	96	42.86%		
Functional frailty domain subindex				0.300	0.200–0.425
Cognitive and psychological variables	Cognitive impairment	52	22.81%		
	Self-rated happiness[a]			0.300	0.10–0.50
	Self-rated satisfaction[a]			0.300	0.20–0.50
	STAI (≥40 points)	112	51.61%		
	BDI (≥13 points)	37	18.50%		

(continued)

Table 1. Continued

		Count	%	Median	Interquartile range
Cognitive and psychological frailty domain subindex				0.245	0.10–0.40
Social variables	CSSDS	100	43.86%		
	Living alone	50	21.93%		
	Lower education level	111	48.68%		
	Self-rated financial problems	22	10.00%		
Social frailty domain subindex				0.250	0.25–0.50
Comprehensive frailty index				0.393	0.33–0.46
Ratios	Biological frailty domain			24.950%	18.44–34.79%
	Functional frailty domain			26.759%	19.22–34.51%
	Cognitive and psychological frailty domain			20.703%	11.95–31.13%
	Social frailty domain			23.730%	14.53–32.51%

Outcome data regarding the type of surgery

The mortality during the follow-up time was significantly higher in the vascular surgical group (47.826% vs. 26.866%, $P = 0.003$). The preoperatively estimated mortality was not significantly different (median: 2.700, IQR: 2.000–4.900 vs. 3.000, IQR: 1.140–6.000, $P = 0.266$). The comprehensive frailty index showed significant, remarkable differences (0.400, IQR: 0.358–0.467 vs. 0.348, IQR: 0.303–0.460, $P = 0.001$). The indicators are summarized in Table 2 according to the type of surgery. There were significant differences between the two groups in the biological (0.357, IQR: 0.214–0.429 vs. 0.357, IQR: 0.214–0.429, $P = 0.001$) and functional domains (0.325, IQR: 0.200–0.425 vs. 0.325, IQR: 0.200–0.450, $P = 0.011$).

Main results – long-term mortality regarding differences in preoperative indicators

Patients who died during the follow-up time had significantly higher biological, functional and sociological domain subindex scores. The comprehensive frailty index was also increased (0.371, IQR: 0.316–0.445 vs. 0.423, IQR: 0.365–0.500, $P < 0.001$). However, the cognitive and psychological domain subindex did not differ significantly, and cognitive impairment (16.541% vs. 31.579%, $P = 0.029$) and self-rated happiness (0.200, IQR: 0.000–0.500 vs. 0.300, IQR: 0.100–0.500, $P = 0.045$) were worse in the non-survivor cohort (Table 3).

Comprehensive frailty score and prediction of long-term mortality

For the examination of mortality risk, four subgroups were created according to the comprehensive frailty index quartiles. In univariate Cox regression, an odds ratio of 1.449 (95% CI: 1.199–1.751, $P < 0.001$) was found. After adjusting for traditional surgical risk using the estimated mortality OR = 1.384 (95% CI: 1.140–1.680, $P = 0.001$) was calculated. The adjusted odds ratios calculated according to the comprehensive frailty index quartiles in the multivariate Cox regression are shown in Fig. 1.

Table 2. The observed indicators in different frailty domains between surgical groups (a: inverted score, BDI: Beck Depression Inventory, BMI: body mass index, CCS: chronic coronary syndrome, COPD: chronic obstructive pulmonary disease, CSSDS: Caldwell Social Support Dimension Scale, STAI: State-Trait Anxiety Inventory, TIA: transient ischemic attack)

		Vascular surgical patients				Cardiac surgical patients				
		Count	%	Median	Interquartile range	Count	%	Median	Interquartile range	*P*-value
Biological variables	Atrial fibrillation	15	9.320%			10	14.930%			0.217
	Congestive heart failure	17	10.560%			6	8.960%			0.714
	CCS	55	34.160%			28	41.790%			0.275
	Diabetes mellitus	65	40.370%			25	37.310%			0.667
	Hypertension	144	89.440%			62	92.540%			0.471
	Myocardial infarction	35	21.740%			6	8.960%			0.056
	Stroke (or TIA)	57	35.400%			4	5.970%			0.001
	Arthritis	108	67.080%			20	29.850%			0.001
	Asthma	4	2.480%			2	2.990%			0.830
	Neoplasia in last 5 years	11	6.830%			3	4.480%			0.500
	Renal disease	27	19.850%			15	22.730%			0.637
	COPD	58	36.020%			22	32.840%			0.646
	Degenerative spinal disease	15	9.320%			20	29.850%			0.001
	More than 5 regular used medicine	108	67.080%			29	43.280%			0.001
Biological domain subindex				0.357	0.214–0.429			0.214	0.214–0.357	0.001
Functional and nutritional variables	BMI (≤20 or ≥30)	43	26.710%			15	22.390%			0.306
	Unintended weight loss	18	11.840%			4	5.970%			0.183
	Current pain/ chronic pain	85	52.800%			13	22.810%			0.001

(continued)

Table 2. Continued

		Vascular surgical patients				Cardiac surgical patients				
		Count	%	Median	Interquartile range	Count	%	Median	Interquartile range	*P*-value
	Self-rated health status[a]			0.400	0.400–0.400			0.400	0.400–0.600	0.577
	Low albumin level (≤35 g L^{-1})	3	2.360%			43	64.180%			0.001
	Lack of sport activities	67	41.880%			20	39.220%			0.737
	Unable to doing heavy work around the house	97	60.250%			18	27.270%			0.001
	Unable to do housecleaning and home maintenance	68	43.040%			28	42.420%			0.933
Functional frailty domain subindex				0.325	0.200–0.450			0.275	0.175–0.425	0.011
Cognitive and psychological variables	Cognitive impairment	40	24.845%			12	17.910%			0.299
	Self-rated happiness[a]			0.300	0.100–0.500			0.200	0.100–0.500	0.666
	Self-rated satisfaction[a]			0.300	0.200–0.500			0.300	0.200–0.500	0.126
	STAI (≥40 points)	82	50.930%			30	53.570%			0.733
	BDI (≥13 points)	27	17.760%			10	20.830%			0.633
Cognitive and psychological frailty domain subindex				0.260	0.120–0.400			0.200	0.080–0.400	0.098
Social variables	CSSDS	67	41.610%			33	49.250%			0.290
	Living alone	33	20.500%			17	25.370%			0.418
	Lower education level	83	51.550%			28	41.790%			0.179

(continued)

Table 2. Continued

		Vascular surgical patients				Cardiac surgical patients				
		Count	%	Median	Interquartile range	Count	%	Median	Interquartile range	*P*-value
	Self-rated financial problems	20	12.420%			2	3.390%			0.048
Social frailty domain subindex				0.250	0.250–0.500			0.250	0.000–0.500	0.807
Comprehensive frailty index				0.400	0.358–0.467			0.348	0.303–0.460	0.001
Ratios	Biological frailty domain			25.231%	19.582–34.924%			24.829%	17.575–33.944%	0.651
	Functional frailty domain			27.526%	20.000–33.796%			24.623%	17.339–35.233%	0.607
	Cognitive and psychological frailty domain			20.741%	12.516–31.818%			20.664%	8.7363–30.270%	0.348
	Social frailty domain			23.529%	15.953–31.028%			24.87%	0.000–40.698%	0.599
Estimated mortality				2.700	2.000–4.900			3.000	1.140–6.000	0.266

Table 3. The observed indicators in different frailty domains according to long-term mortality (a: inverted score, BDI: Beck Depression Inventory, BMI: body mass index, CCS: chronic coronary syndrome, COPD: chronic obstructive pulmonary disease, CSSDS: Caldwell Social Support Dimension Scale, STAI: State-Trait Anxiety Inventory, TIA: transient ischemic attack)

		Survivor (n = 133)				Non-survivor (n = 95)				
		Count	%	Median	Interquartile range	Count	%	Median	Interquartile range	*P*-value
Vascular surgical patients		84	57.174%			77	42.826%			0.003
Cardiac surgical patients		49	73.134%			18	26.866%			
Biological variables	Atrial fibrillation	12	9.023%			13	13.684%			0.267
	Congestive heart failure	8	6.015%			15	15.789%			0.016
	CCS	51	38.346%			32	33.684%			0.471
	Diabetes mellitus	44	33.083%			46	48.421%			0.019
	Hypertension	122	91.729%			84	88.421%			0.404
	Myocardial infarction	22	16.541%			20	21.153%			0.385
	Stroke (or TIA)	29	21.805%			32	33.684%			0.046
	Arthritis	67	50.376%			61	64.211%			0.038
	Asthma	4	3.008%			2	2.105%			0.675
	Neoplasia in last 5 years	11	8.271%			3	3.158%			0.113
	Renal disease	21	17.500%			21	25.610%			0.163
	COPD	40	30.075%			40	42.105%			0.061
	Degenerative spinal disease	20	15.038%			15	15.789%			0.877
	More than 5 regularly used medications	76	57.143%			61	64.211%			0.283
Biological domain subindex				0.286	0.214–0.357			0.357	0.231–0.429	0.002
Functional and nutritional variables	BMI (≤20 or ≥30)	12	9.023%			14	14.737%			0.181
	Unintended weight loss	11	8.594%			11	12.088%			0.397

(continued)

Table 3. Continued

		Survivor (n = 133)				Non-survivor (n = 95)				
		Count	%	Median	Interquartile range	Count	%	Median	Interquartile range	P-value
	Current pain/ chronic pain	51	40.157%			47	51.648%			0.093
	Self-rated health status[a]			0.400	0.200–0.400			0.400	0.400–0.400	0.572
	Low albumin level (≤35 g L^{-1})	31	26.496%			15	19.481%			0.261
	Lack of sport activities	42	35.000%			45	49.451%			0.035
	Unable to doing heavy work around the house	62	46.970%			53	55.789%			0.190
	Unable to do housecleaning and home maintenance	55	41.985%			41	44.086%			0.754
Functional frailty domain subindex				0.300	0.175–0.425			0.343	0.233–0.450	0.018
Cognitive and psychological variables	Cognitive impairment	22	16.541%			30	31.579%			0.029
	Self-rated happiness[a]			0.200	0.000–0.500			0.300	0.100–0.500	0.045
	Self-rated satisfaction[a]			0.300	0.200–0.500			0.300	0.200–0.500	0.142
	STAI (≥40 points)	65	51.587%			47	51.648%			0.993
	BDI (≥13 points)	17	14.912%			20	23.256%			0.132
Cognitive and psychological frailty domain subindex				0.240	0.100–0.375			0.260	0.120–0.480	0.152
Social variables	CSSDS	52	39.098%			48	50.526%			0.086
	Living alone	26	19.549%			24	25.263%			0.304

(continued)

Table 3. Continued

		Survivor (n = 133)				Non-survivor (n = 95)				
		Count	%	Median	Interquartile range	Count	%	Median	Interquartile range	*P*-value
	Lower education level	58	43.609%			53	55.789%			0.070
	Self-rated financial problems	12	9.375%			10	10.870%			0.715
Social frailty domain subindex				0.250	0.000–0.333			0.250	0.250–0.500	0.007
Comprehensive frailty index				0.371	0.316–0.445			0.423	0.365–0.500	<0.001
Ratios	Biological frailty domain			24.829%	18.132–34.924%			25.025%	19.017–34.167	0.828
	Functional frailty domain			28.020%	18.503–35.484%			25.607%	19.958–32.300	0.351
	Cognitive and pychological frailty domain			20.741%	11.523–31.542%			20.108%	12.160–30.894	0.827
	Social frailty domain			22.846%	0.000–32.169%			25.253%	15.709–33.397	0.415
Estimated mortality				2.400	1.700–4.000			3.200	2.300–5.700	<0.001

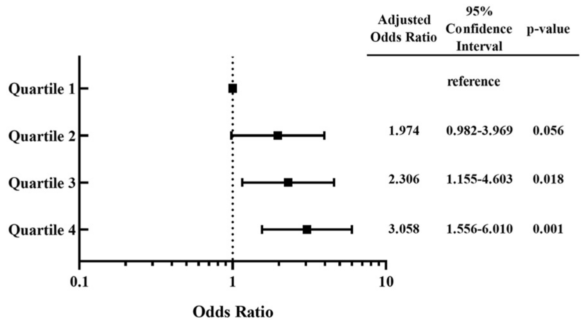

Fig. 1. The adjusted odds ratios for morality according to the comprehensive frailty index quartiles in the multivariate Cox regression model

Kaplan-Meier analysis according to the comprehensive frailty index quartiles showed a significant difference in mortality, as presented in Fig. 2 (Mantel–Cox log-rank test, $P = 0.001$).

Relationship between comprehensive frailty index and surgical risk estimation methods

Between comprehensive frailty index and routinely used surgical risk estimation methods (EuroScore II and V-POSSUM) positive correlation was observed. The predicted mortality was calculated with each specific method and it was analysed in aspect of frailty. The result is showed in Fig. 3.

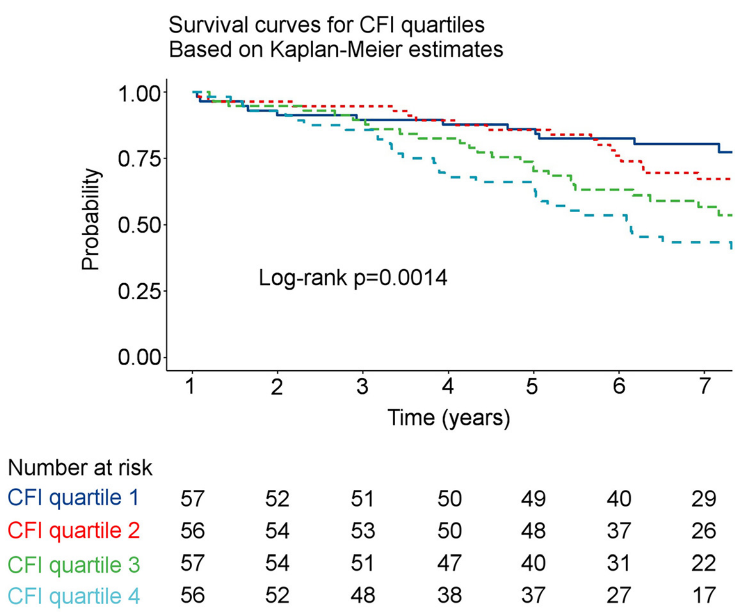

Fig. 2. Kaplan-Meier analysis according to the comprehensive frailty score quartiles

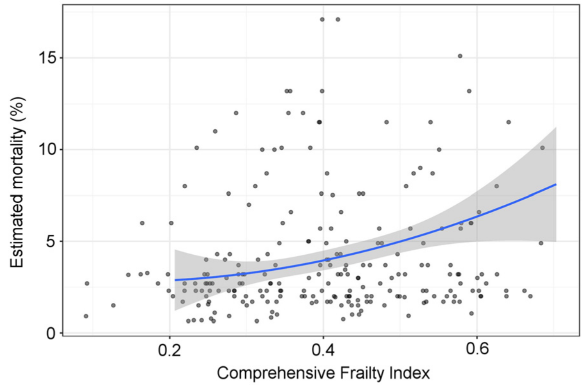

Fig. 3. Scatter plot shows the relationship between comprehensive frailty index and estimated mortality. Trend line was fitted used polynomial method, grey strip represents 95% confidence interval (Pearson $r = 0.262$, $P < 0.001$)

DISCUSSION

Key findings

The current study found that the comprehensive frailty index is an important, independent and reliable indicator for long-term mortality of vascular and cardiac surgical patients. Even a moderate elevation in the patient's frailty index could have consequences. The current frailty index was constructed from biological, functional, sociological, cognitive and psychological elements, and these variables were clustered into 4 main frailty domains.

In conclusion, our current study found a more than 3-fold risk for mortality in the most frail patient population compared to the least frail cohort.

In the studied clinical setting, no evidence for any influence of the comprehensive frailty index on short-term mortality was detected. However, positive correlation was found between comprehensive frailty index and estimated postoperative mortality calculated by using Euro-score II and V-POSSUM.

Relationship to previous studies

Each year, an increasing number of original articles investigate frailty in special subgroups, for example, in vascular surgical and cardiac surgical populations. The basic mechanisms of the general frailty concept are supposed to be widely applicable. In our current study, a comprehensive frailty index was developed based on a comprehensive geriatric assessment [24]. A recently published meta-analysis emphasized the importance of frailty and the preoperative conditions and illnesses that we included in our frailty index [25]. That article clearly showed that frailty significantly increased the risk of mortality among patients undergoing transcatheter aortic valve implantation (TAVI or TAVR) (HR: 2.16, 95% CI: 1.57–3.00). Our current findings confirmed the elevated mortality risk (AHR = 1.384, 95% CI: 1.140–1.680, $P = 0.001$) in our vascular and cardiac surgical population.

Afilalo et al. published an article which studied similar cohort as our current work. In this study authors were compared 7 different frailty tools. The prevalence of frailty was 26%–68% in the cohort that included 1,020 patients underwent transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR) procedure. Among tools the strongest one was the Essential Frailty Tool (EFT) which is similar, multidimensional but simplified method like ours. It was showed heavy influence on one year mortality (adjusted odds ratio [OR]: 3.72; 95% confidence interval [CI]: 2.54–5.45) with a C-statistic improvement of 0.071 ($P < 0.001$) and integrated discrimination improvement of 0.067 ($P < 0.001$) [26].

It is supposed that the mortality prediction of the comprehensive frailty index becomes stronger as time passes after surgery. As the recently published article described, frailty parameters did not show any association with short- and mid-term mortality after endovascular techniques for aortic repair [27]. Short-term mortality is highly dependent on physical and surgical conditions, being strongly associated with the type of surgery and the perioperative risk factors and postoperative complications.

Shi et al. investigated frailty and the Lee score for their predictive value for mortality and functional decline with severe symptoms among patients who underwent artificial aortic valve implantation [12]. Their frailty index predicted twelve-month mortality in a cohort of patients with transcatheter intervention but did not accurately predict mortality in the surgical group. However, the Lee score had a more accurate predictive value in the surgical population. Furthermore, they reported a slightly higher adjusted hazard ratio for poor outcomes AHR (95% CI) in quartiles 2, 3 and 4 compared to quartile 1 as a reference: 2.7 (0.8–9.5), 2.8 (0.8–10.5), 6.0 (1.5–23.3), $P = 0.010$ compared to our findings AHR (95% CI) in quartiles 2, 3 and 4 compared to quartile 1 as a reference: 1.974 (0.982–3.969), 2.306 (1.155–4.603), and 3.058 (1.556–6.010), respectively.

Among patients with severe aortic stenosis who underwent TAVR or valve replacement surgery, there was no difference in 30-day mortality or complications, but there was in the length of hospital stay and the 1-year all-cause mortality. In this study, clustering for the frail and fit groups was performed, and the frail group had an adjusted hazard ratio of 3.51 (95% CI 1.4–8.5, $P = 0.007$) for mortality. These findings are consistent with our results, especially in our most frail group (the fourth quarter of the comprehensive frailty score) [28].

A similar single-centre prospective cohort study demonstrated similar findings (OR: 3.68 [95% CI 1.21–11.19], $P = 0.02$) using their own comprehensive frailty assessment based on cognitive, psychological, and functional tests in TAVR patients. In addition, they verified a strongly increased risk for 30-day mortality and major adverse cardiovascular and cerebral events (MACCEs) and 1-year MACCEs [29].

Regarding reliability, our models are consistent with findings in the literature. As the accuracy of our unadjusted and adjusted models were checked by receiver operating characteristic (ROC) curves, the c-statistic was found to be between 0.632–0.654. A previous retrospective cohort study with 24,499 patients found almost the same reliability in a general population admitted to the intensive care unit (ICU). They compared different frailty scoring systems regarding 30-, 90- and one-year mortality prediction and found nearly the same accuracy. They compared the Clinical Frailty Score, the Frailty Index – Acute Care and the Changes in Health, End-Stage Disease, Signs, and Symptoms Scale (CHESS) performance using the c-statistic. Their findings were more accurate among ICU patients without a need for mechanical ventilation (c- stat: approx. 0.64) and slightly weaker in the mechanically ventilated group (s- stat: approx. 0.62) [30].

In this study, clustering according to the comprehensive frailty index quartiles was an artificial step. In the literature, exact cut-off values for distinct categories cannot induce the different content of the described indices. However, the categorization helps to describe and understand the differences between the patient's frailty status. On the other hand, we cannot exclude national differences in health care, psychosocial status, etc. Therefore, using quartiles instead of cut-off values in our multidimensional frailty approach can be justified.

Significance of the study findings and what this study adds to our knowledge

Determining patients' frailty is becoming a routine part of risk estimation. Current literature statements and findings suggest that not only are more risk estimation methods being developed but also that clinicians are more often facing a significantly frail population during daily work. Indeed, "eyeball" frailty testing has also been used with great success. As the general population is ageing, the increasing incidence of sarcopenic obesity, diabetes mellitus and cardiovascular diseases is increasing the need for a comprehensive risk estimation method [31]. Complex invasive interventions in the elderly population are also more frequently being performed, and these facts emphasize the importance of our work.

Strengths of this study

The conception of frailty and comprehension of preoperative risk management have increasing relevance in our daily practice. In our current work, the importance of different unconventional risk factors was emphasized and proven in aspects of long-term mortality, and irrespective of the type of cardiovascular surgery.

Limitations of this study

As limitations of this study, its single-centre design and the rather small size of the enrolled population size should be mentioned. Further limitation can be the time-consuming comprehensive frailty estimation process. A presented comprehensive method could take much time depending on each patient's capability, disabilities, and current health status. Further investigation should be conducted to assign the most effective, but enough comprehensive frailty estimation method.

CONCLUSION

A comprehensive frailty index could be a useful and reliable method for estimating long-term mortality among vascular and cardiac surgery patients. An extensive approach to frailty is obligatory for correctly describing patients' frailty status. Using a comprehensive frailty score in parallel with traditional risk estimation methods could be more accurate for calculating the patients' preoperative risk and prognosis, especially their risk of long-term mortality.

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