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Review Article

The Impact of Frailty Syndrome on Mortality in Elderly Individuals undergoing Cardiac Surgery: Prospective Cohort

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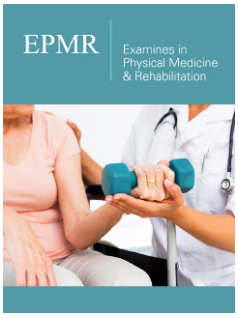

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Abstract

Introduction: Fragility is characterized by vulnerability to stressors, such as cardiac surgery, and can increase the risk of postoperative complications. So, it is necessary to do a broad preoperative evaluation. This study aimed to verify the association between frailty syndrome and mortality, and other clinical outcomes, for a follow-up period of 4 years.

Methods: Cohort study, in which the patients ≥60 years old, who were submitted to cardiac surgery, were evaluated by different instruments, to detect the frailty during the pre and postoperative periods, in 4 years. Frailty was defined through the Fried Frailty Phenotype (FFF)≥3, Clinical Frailty Scale (CFS)≥4, Short Physical Performance Battery (SPPB)≤ 6, Katz Index ≥1, and abnormal values in the Gait Speed (GS) or Handgrip Strength (HGS), indexed by gender and body mass. Clinical outcomes were described and the association between frailty and mortality was verified in 4 years of follow-up.

Result: 137 patients were evaluated in the preoperative periods and 79 were included in the re-evaluation 4 years after the surgery. Thirty-nine (79,6%) were men, with an average age of 72,76±5,96 years old. Among them, 49 were re-evaluated and 30 (38,0%) died in four years, whereas 20 (66,6%) died because of cardiovascular issues and 10 (33,3%) because of other noncardiac causes. Patients who were classified as fragile by FFF, CFS, SPPB, and by the GS and the isolated HGS were associated with the mortality outcome.

Conclusion: The frailty defined by different instruments is associated with long-term mortality, which reinforces the importance of using these tools in the preoperative period, to estimate the risk-benefit of the procedure.

Keywords: Frailty; Cardiac surgery; Mortality; Major adverse cardiac events

Introduction

Frailty is defined as a biological syndrome, characterized by increased vulnerability to stressors, due to the decrease of the physiological reserves, and the dysregulation of the neuroendocrine and immunological systems. It is a multidimensional condition that involves organic systems, physical and cognitive functions, general health conditions, muscular mass, strength, mobility, nutritional status, psychological factors, and social support [1-3].

These stressors are classified as acute and/or chronic illnesses (for example, acute heart attack) or iatrogenic (for example, cardiac surgery), and when exposed to these stress factors, fragile individuals have the risk of marked decompensation, adverse events, complications, prolonged recovery, functional decline, and mortality [4]. In the frailty syndrome, some important clinical signals are observed, such as muscular weakness, decrease in walking speed, difficulty in mobility, fatigue, and involuntary weight loss [2]. There are many instruments to evaluate frailty, through scales or functional tests, for example, but there is not a consensus on which is the most adequate option. This is one of the main reasons frailty is often not evaluated in clinical practice, reported prevalence estimates are so divergent across studies [5]. Evidence suggest an association between Cardiovascular Diseases (CVDs) and the frailty syndrome in the elderly population, as both of the conditions negatively affect health, and decrease the quality of life [6]. The study of Afilalo et al. [7] showed that the prevalence of frailty in the community of elderly people is estimated at 10%, and depending on the population and the instrument for evaluating fragility that is used, it can increase from 10% to 60% in elderly people with CVDs. CVD diagnosis is associated with a three-fold increase in frailty among elderly people [7]. This can be explained through the important relation between inflammatory pathways in the origin of both conditions [5].

In the last years, the number of elderly patients submitted to cardiovascular surgery increased significantly, due to the high life expectancy of the population, and due to the improvements in the clinical and surgical techniques, which enable offering cardiac operations to an elderly population, a more ill and more fragile population [8,9]. However, the number of complications arising from cardiovascular surgery in this population is higher than in young patients. Therefore, it is necessary to carry out a comprehensive preoperative evaluation, to determine the risks and the benefits of the surgery intervention in these individuals [8,10]. Among the existing tools for this evaluation, the European System for Cardiac Operation Risk Evaluation II (EuroSCORE II) is the most commonly used instrument all over the world, in the stratifying of surgical risk and as a predictor of mortality in 30 days in patients submitted to major cardiac surgery [11]. The association between frailty and adverse postoperative events in elderly patients submitted to noncardiac surgery is already broadly described [9]. Fragile patients are at greater risk of developing postoperative delirium, cardiovascular events, and procedure complications, besides a slower recovery, prolonged hospital internment, and association with mortality, with an increase in global medical costs [12,13]. In cardiac surgery, it is associated with a high degree of invasion and iatrogenic stress, and the preoperative risk is significantly greater in fragile patients with a reduced capacity to deal with such suffering, which can compromise the postoperative results [9,14]. Some studies demonstrate the relation of frailty with cardiac surgery, being considered an independent predictor of intra-hospital and medium-length mortality [15].

However, only a few Brazilian studies evaluate the evolution of frailty syndrome in the long-term after cardiac surgery, as well as its association with mortality. So, this study aimed to verify the association between frailty syndrome - measured by different instruments - with mortality, and Major Adverse Cardiac Events (MACCE), which included Acute Myocardial Infarction (AMI), stroke, non-fatal Cardiopulmonary Arrest (CPA), Acute Kidney Injury (AKI), reoperation, need for cardiac catheterization and hospital readmission. Besides that, one of the objectives was to evaluate the evolution of the frailty syndrome in elderly patients submitted to cardiac surgery during a 4-year follow-up.

Methods

Design of the study

A prospective cohort study, in a 4-year postoperative follow-up, developed in the Institute of Cardiology of Rio Grande do Sul - Fundação Universitária de Cardiologia (IC-FUC), in the city of Porto Alegre/RS, in patients with cardiovascular illnesses that were submitted to cardiac surgery between July and December of 2019. The reassessment of postoperative frailty syndrome was carried out in person, 4 years after surgery, at the SUS outpatient clinic of IC-FUC, from April to December of 2023, through prior scheduling via telephone, in which the same preoperative assessments were carried out. This study was approved by the Ethics Committee in Research of IC-FUC (CAAE 87473118.6.0000.5333) and agrees with the principles of the most recent version of the Helsinki Declaration, the Good Clinical Practice Guidelines (ICH-GCP), and the Resolution 466/12.

Participants

In this study, the participants included were elderly people with ischemic and/or valvular heart disease, with an age of ≥60 years old, of both sexes, with an indication of elective cardiac surgery, including valve surgery (replacement or repair), Coronary Artery Bypass Grafting (CABG), associated surgeries (CABG and valve surgery) and aortic surgeries. The criteria of exclusion were the individuals who were submitted to a noncardiac surgery associated with the procedure, patients who need emergent or urgent cardiac surgery, patients who present hemodynamic instability, patients who did not adhere to the Free and Informed Consent Form (FICF), and patients that did not accept to do the reassessment after four years of the postoperative.

Instruments of evaluation

The evaluation of frailty syndrome was made during the period of preoperative hospitalization, on the day before the surgery. Patients were submitted to an evaluation of the frailty according to Fried Frailty Phenotype (FFF), Short Performance Physical Battery (SPPB), Clinical Frailty Scale (CFS) and Katz Index. Besides that, the Gait Speed (GS) and Handgrip Strength (HGS) - which are part of the FFF - were also considered isolated fragility criteria. Firstly, the individuals were submitted to a short interview, through an evaluation form to collect personal information, followed by functional tests. The FFF takes into consideration five factors to evaluate frailty: self-reported non-intentional weight loss (≥4,5kg or ≥5% of the body weight in the last year); self-referred fatigue using two questions in the Depression Scale (CES-D); a decrease

of the hand grip strength with a dynamometer in the dominant hand and adjusted for the gender and Body Mass Index (BMI); level of physical activity measured by the weekly caloric expenditure (Minnesota Leisure Time Activities questionnaire) and adjusted according to the gender; a decrease of the walking speed in seconds (distance of 4,6m adjusted according to the gender and the height). The individuals were considered fragile if they had a punctuation of ≥3 in the FFF [2,16].

The SPPB is an instrument that consists of a brief physical evaluation, composed of three tests that evaluate in sequence, the static balance when standing up, the walking speed, and the muscular strength of the lower members to stand up and to sit in the chair five times. The participants were submitted to the balance test, where they should be able to stay in each position (side-by-side, semi-tandem stand, tandem stand) for 10 seconds, followed by the walking speed, in which the participant was oriented to walk in the habitual speed in a 4 meters distance, and the time wasted to walk this distance was timed. Finally, the test of getting up from the chair was made in a chair without lateral support, in which the patient should get up and sit down five times, without the support of lower members, in the shortest time possible. The punctuation for each test varies on a scale of zero (worst performance) and four points (best performance). The total SPPB score is obtained by the sum of points in each test, which could vary between 0 (worst performance) and 12 points (best performance). The individuals would be considered fragile if they got punctuation ≤6 [17].

CFS, developed by Rockwood et al. [18], is a visual scale composed of nine clinical items, in which the individuals were classified as fragile and nonfragile according to an observation made by the health professional, and with the verification of the information with the patient, being considered nonfragile when the score is ≤ 3 and fragile if the classification was ≥4 [18,19]. The Katz Index is a questionnaire that evaluates the independence of the individual to do basic everyday activities, composed of six items that measure the performance of the individual in the following activities of self-care: nutrition, sphincter control, transference, personal hygiene, the capacity of dressing up and taking a shower. The participants who obtained one point in the Katz Index were considered fragile [20]. For the isolated HGS, criteria already indexed by gender and BMI were used, and for the isolated GS, the criteria that were already indexed by gender and height were used [2], both as shown in (Figure 1).

Gait Speed (GS)			
Female		Male	
High (m)	Time (s)	High (m)	Time (s)
≤ 1,59	≥ 7	≤ 1,73	≥ 7
> 1,59	≥ 6	> 1,73	≥ 6

Handgrip Strength (HGS)			
Female		Male	
BMI (Kg/m²)	HGS (Kg)	BMI (Kg/m²)	HGS (Kg)
≤ 23,0	≤ 17,0	≤ 24,0	≤ 29,0
23,1 – 26,0	≤ 17,3	24,1 – 26,0	≤ 30,0
26,1 – 29,0	≤ 18,0	26,1 – 28,0	≤ 30,0
> 29,0	≤ 21,0	> 28,0	≤ 32,0

Figure 1: Cutoff values for gait speed and handgrip strength [2].

Statistical analysis

Data was collected using the RedCap® platform, posteriorly exported to the Microsoft Excel software, and inserted in the statistic program called SPSS (version 26.0 IBM Corp., Chicago, IL). The quantitative variables were described in mean and standard deviation. The McNemar and Pearson Chi-square tests were used to compare categorical variables. The significance level was set at 5%.

Results

Among the 137 patients evaluated in the preoperatory period in the thesis of Salles FB (2020) [21], 79 were included in this follow-up after 4 years of surgery. Among these, 49 participated of the reassessment, 30 (38% or 21,89%) died in the 4 years follow-up period, 20 (66,6%) died because of cardiovascular issues, and 10 (33,3%) because of other noncardiac causes (Figure 2). The

characteristics of the reevaluated sample are presented in Table 1. The patients considered fragile by the instruments FFF, CFS, SPPB, and the isolated GS had a significant rise in mortality, while the HGS and Katz Index did not show this association (Table 2). Regarding the MACCE after the hospital discharge, the AMI occurred in 1 patient (1,3%), stroke in 2 patients (2,5%), CPA non-fatal, and AKI was not observed in our sample. Among the 49 individuals who were reassessed, 2 (2,5%) needed the reoperation, 7 (8,9%) underwent cardiac catheterization, 22 (27,8%) needed to go to emergency (permanence of <24h), and 19 (24,1%) were hospitalized during an average of 11 days, during 4 years in the follow-up period. The evolution of frailty was evaluated through the comparison of the prevalence according to the results of each instrument used, where only the CFS had a significant rise (p=0,012) among the fragile individuals in the preoperative period and postoperative period (Table 3). None of the instruments showed a decrease in the reduction of fragility during the follow-up period.

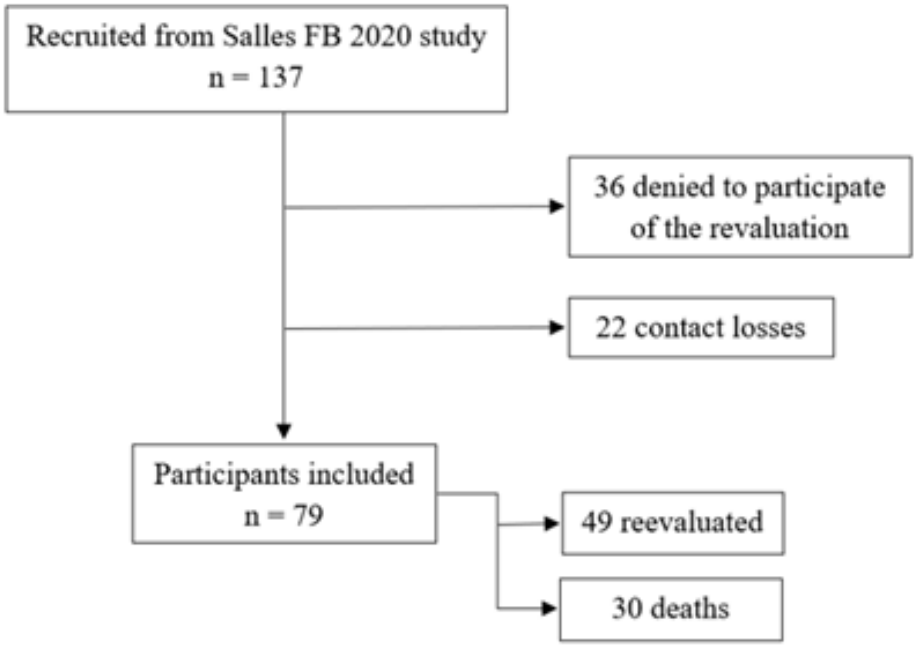

Figure 2: Participant recruitment flowchart.

Table 1: Sample characterization (n=49).

Characteristics	N (%) Mean±DP
Age (years)	72,76±5,96
Sex	
Male	39(79,6%)
Education Level	
Illiterate	0(0%)
Elementary school	27(55,1%)
High School	11(22,4%)
Technical Course	2(4,1%)
Higher Education	7(14,3%)
Graduate studies	2(4,1%)
BMI (Kg/m^2)	28,64±4,31
Surgery Class	
CABG	32 (65,3%)
Valve	12 (24,5%)
CABG+Valve	3 (6,1%)
Aortic	2 (4,1%)

Source: CABG: Coronary Artery Bypass Grafting Surgery; BMI: Body Mass Index.

Table 2: Mortality associated with the Frailty scores (n=79).

Variables	Nonfragile	Fragile	OR (IC 95%)	p (<0,05)
FFF	12 (48)	18 (31)	4,154 (1,579–10,928)	0,003
	25%	58,1%		
CFS	18 (62)	12 (17)	5,867 (1,805–19,066)	0,002
	29%	70,6%		
SPPB	22 (70)	8 (9)	0,057 (0,007–0,487)	0,001
	31,4%	88,9%		
Katz Index	24 (69)	6 (10)	2,813 (0,723–10,944)	0,125
	34,8%	60%		
HGS (kgf)	20 (49)	10 (30)	0,725 (0,281–1,873)	0,506
	40,8%	33,3%		
GS (s)	16 (61)	14 (18)	9,844 (2,823–34,327)	0,001
	26,2%	77,8%		

Source: CFS: Clinical Frailty Scale; FFF: Fried Frailty Phenotype; GS: Gait Speed; HGS: Handgrip Strength; OR: Odds Ratio; SPPB: Short Performance Physical Battery.

Table 3: Evolution of the prevalence of fragility in the preoperative and the postoperative (n=49).

Variables	Preoperative		Postoperative		p (<0,05)
FFF	Nonfragile	Fragile	Nonfragile	Fragile	0,815
	36 (73,5%)	13 (26,5%)	34 (69,4%)	15 (30,6%)	
CFS	Nonfragile	Fragile	Nonfragile	Fragile	0,012
	44 (89,8%)	5 (10,2%)	35 (71,4%)	14 (28,6%)	
SPPB	Nonfragile	Fragile	Nonfragile	Fragile	1,000
	48 (98%)	1 (2%)	47 (95,9%)	2 (4,1%)	
Katz Index	Nonfragile	Fragile	Nonfragile	Fragile	1,000
	45 (91,8%)	4 (8,2%)	46 (93,9%)	3 (6,1%)	
HGS (kgf)	Nonfragile	Fragile	Nonfragile	Fragile	0,804
	29 (59,2%)	20 (40,8%)	27 (55,1%)	22 (44,9%)	
GS (s)	Nonfragile	Fragile	Nonfragile	Fragile	0,146
	45 (91,8%)	4 (8,2%)	39 (79,6%)	10 (20,4%)	

Source: CFS: Clinical Frailty Scale; FFF: Fried Frailty Phenotype; GS: Gait Speed; HGS: Handgrip Strength; SPPB: Short Performance Physical Battery.

Discussion

The current study aimed to verify the association between frailty, evaluated by different validated instruments, mortality and MACCE, in addition to the evaluation of the evolution of the frailty syndrome in elderly patients submitted to cardiac surgery in a follow-up period of four years. The results showed a meaningful rise in mortality in patients considered fragile by the FFF, CFS, SPPB, and the isolated GS. The presence of frailty in the population of this study shows a big divergence, in the preoperative period varied from 2% to 40,8%, and in the postoperative of 4,1% and 44,9%, according to the SPPB and HGS, respectively. This shows the necessity of a consensus about what is the most precise and efficient tool to preview the results in this population. In a Cohort Study [5], the prevalence of frailty through the SPPB was 68% and showed an association with mortality in one year, and a worsening of disability (OR: 1.95; IC 95% 1,41–2,71; p=0,07), similar to our study. However, this study was made only with patients who were submitted to a transcatheter implant of aortic valve or surgery of aortic valve replacement by sternotomy, and the average age was 82 years old. In our current study, the age average was 72,76 years, which can influence the prevalence of frailty by the SPPB. Frailty, defined by the slowness in the GS, was associated with an almost 10 times rise in mortality (OR: 9,844; IC 95% 2,823–34,327, p=0,001), corroborating with the study of Afilalo et al. [22], in which frailty was also associated to a rise in mortality and/or morbidity, in patients submitted to a CABG or valve replacement by standard sternotomy [22], the results of this study are closer to ours, as they have a similar population. In the study of Nguyenhuy et al. [14], the presence of frailty was observed, which was evaluated through the FFF, in patients who underwent cardiac surgery, is associated with an increased risk of mortality for all causes in one year in relation to the nonfragile patients (RR: 2,23; IC 95% 1,17–4,23; p=0,01) [14], which is similar to our study, in which the patients defined as fragile by the FFF also show a higher rate of mortality, but in a long-term follow-up of 4 years. (OR: 4,154; IC 95% 1,579–10,928; p=0,003).

The CFS was the only instrument that showed a significant rise (p=0,012) of the preoperative and postoperative period, which was 10,2% in the preoperatory time, to 28,6% in the post-operatory. This rise in fragility during the postoperative period can be associated with the factor of the advanced age of the participants, and to the low level of physical activity, due to the fear of practicing exercises and doing everyday activities after a cardiac surgery. A Cohort study with 6156 patients showed that CFS could predict mortality in the short and medium term, in patients who were submitted to isolated CABG [23]. In our study, however, it was also observed that this association with the mortality, but in a long-term follow-up. The results of our study show that frailty has a strong association with long-term mortality, besides being one of the only studies with an evaluation time in the long-term period. However, it also has some limitations, such as the number of samples after four years of the first evaluation, due to the difficulty in recruiting all the participants that were part of the initial sample, for not being able to get phone contact, because of logistic questions, and financial issues related to traveling to the reassessment location, resulting in patients being lost to follow-up.

Conclusions

Based on the data, the frailty defined by the instruments FFF, CFS, SPPB, and the isolated GS have an association with the mortality rise in the follow-up period of 4 years in elderly patients submitted to cardiac surgery, which reinforces the importance of using these tools to evaluate frailty syndrome in the preoperative period, to estimate the risk-benefit of the procedure, identifying the patients who are at greater risk, and to identify possible negative outcomes in this population submitted to cardiac surgery.

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