Changes in frailty status after cardiac surgery. A prospective cohort study.

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Abstract

Background During the last years, the concept of frailty has become increasingly familiar in many surgical specialties, including cardiac surgery. One of the main characteristics of frailty is its potentially reversible nature. With the aim of reducing the incidence of complications after surgery, efforts are being made to preoperatively decrease the level of frailty, however, the effect that the surgery itself may have in the postoperative frailty status is still unknown. **Methods** A prospective cohort of 137 patients aged 70 or more undergoing cardiac surgery with the use of cardiopulmonary bypass were recruited at three university-affiliated hospitals in Spain. Frailty status was assessed preoperatively and six months after surgery using two different validated frailty measurements: The Fried frailty scale and the Clinical Frailty Scale. We analyzed the changes in these frailty scores and the transitions between frailty status after surgery. **Results** Prevalence of frailty was 27.5% with the Fried Frailty Scale and 11% with the Clinical Frailty Scale. Even though frail patients presented a higher incidence of postoperative major complications than their robust counterparts, up to 50% of frail patients improved their frailty status after surgery. The distribution of frailty groups at baseline and six months after surgery changed significantly, decreasing the overall burden of frailty after surgery. Besides, robust patients showed a slightly worsening of their previous frailty scores. **Conclusions** Frailty is a multifactorial and dynamic condition that can be significantly reduced after cardiac surgery, suggesting that cardiac pathology is an important contributor to the preoperative patient's frailty status.

CHANGES IN FRAILTY STATUS AFTER CARDIAC SURGERY. A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background

During the last years, the concept of frailty has become increasingly familiar in many surgical specialties, including cardiac surgery. One of the main characteristics of frailty is its potentially reversible nature. With the aim of reducing the incidence of complications after surgery, efforts are being made to preoperatively decrease the level of frailty, however, the effect that the surgery itself may have in the postoperative frailty status is still unknown.

Methods

A prospective cohort of 137 patients aged 70 or more undergoing cardiac surgery with the use of cardiopulmonary bypass were recruited at three university-affiliated hospitals in Spain. Frailty status was assessed preoperatively and six months after surgery using two different validated frailty measurements: The Fried frailty scale and the Clinical Frailty Scale. We analyzed the changes in these frailty scores and the transitions between frailty status after surgery.

Results

Prevalence of frailty was 27.5% with the Fried Frailty Scale and 11% with the Clinical Frailty Scale. Even though frail patients presented a higher incidence of postoperative major complications than their robust counterparts, up to 50% of frail patients improved their frailty status after surgery. The distribution of frailty groups at baseline and six months after surgery changed significantly, decreasing the overall burden of frailty after surgery. Besides, robust patients showed a slightly worsening of their previous frailty scores.

Conclusions

Frailty is a multifactorial and dynamic condition that can be significantly reduced after cardiac surgery, suggesting that cardiac pathology is an important contributor to the preoperative patient's frailty status.

INTRODUCTION

Frailty is currently considered as a multicausal medical syndrome that is characterized by a diminished strength and endurance. Frailty also implies a reduced physiological reserve, that increases an individual's vulnerability to develop dependency and/or death after different stress situations (1).

This identification of frailty as an increased vulnerability of adverse health outcomes in community-dwelling adults (2–4) led to the characterization of frailty as an independent risk factor for mortality and morbidity in different medical and surgical scenarios(5–7), including cardiac surgery (8–12).

On the one hand, many studies focused on the utility of frailty to predict adverse events after a surgical procedure (9–12). On the other hand, more recent research has focused on the reversible nature of frailty. In this way, it is generally considered that a decrease in the preoperative frailty status will presumably reduce the incidence of postoperative complications. Therefore, efforts are being made to implement specific physical exercises and pharmacological treatments with the aim to reduce the level of frailty during the preoperative period (13,14). This set of preoperative measures has come to be called *prehabilitation* (15–18).

Based also on this dynamic nature of frailty, it would also be interesting to investigate the possibility of changes in frailty status after cardiac surgery. A postoperative improvement in frailty would be expected to the extent that the cardiac pathology was contributing to it. We have recently published that frail patients can improve their quality of life after surgery (19), but postoperative changes in frailty status have not been analyzed. Besides, as a result of the surgical aggression, a postoperative deterioration of the frailty status could also be hypothesized, especially in vulnerable and frail patients. However, there is scarce evidence on this issue and very few studies have addressed it (20,21).

Therefore, the objective of this study was the analysis of the changes of the frailty status that occur six months after a major cardiac surgery with the use of cardiopulmonary bypass.

METHODS

Patient population and study design

Between April 2015 and December 2016, a cohort of patients aged 70 or more undergoing elective cardiac surgery with cardiopulmonary bypass were recruited at three university-affiliated hospital of three different regions of Spain (Madrid, Asturias, and Canary Islands).

Using this cohort of patients, we analyzed the changes in the level of frailty after cardiac surgery with respect to the preoperative ones.

The Institutional Research Ethics Committees at each of the participating hospitals approved the implementation of this study, and every patient provided signed informed consent.

Exclusion criteria were urgent or emergent surgery, off-pump operations, and the absence of the necessary capacity to understand and collaborate in the study. Patients with neurological or physical impairment that could bias the results of the frailty assessment were also excluded.

Frailty was assessed at the time of the hospital admission before the operation, and six months after surgery, using the same frailty assessment tools.

Medical records were used to extract demographic, clinical and surgically related variables.

Frailty assessment

Frailty status was assessed using two validated and widely used scales: The Fried phenotypical frailty scale (2) and the Clinical Frailty Scale (CFS) (22).

Fried frailty scale

This scale works as a scoring system that assigns one point for the presence of each of the following 5 phenotypical manifestations that are commonly found in frail individuals: shrinking (self-report of unintentional weight loss of >4.5 kg in the past year), self-reported exhaustion, weakness (measured with grip strength and standardized by sex and body mass index), slow walking speed (measured as time to walk 4.6 m. at usual pace and standardized by sex and height), and low physical activity (using as cut-off value the consumption of <383 Kcal per week for men and <270 Kcal per week for women). According to the total score obtained, the individuals are classified as robust (0 points), pre-frail (1-2 points) and frail (3-5 points).

Clinical Frailty Scale

This scale was developed using data from the Canadian Study of Health and Aging in Canada. It is based on the interviewer’s clinical judgment and constitutes a more subjective assessment of frailty.

The scale consists of 9 ordinal levels, ranging between 1 “very fit” and 9 “terminally ill”. In order to facilitate the interviewer in classifying patients, the scale shows a short-written description and a figure representing a theoretical silhouette of an individual that would fit in each level.

We considered frail patients those in levels 5-8. Levels 3-4 were considered as pre-frail and levels 1-2 as robust.

Other variables

We collected basal and demographical variables for each patient by direct interview or reviewing medical records. The Charlson index was used to assess comorbidities (23). Clinical and surgical-related variables were also collected.

Operative risk was calculated using the European System for Cardiac Operative Risk Evaluation (EuroSCORE) I and II (24,25). Health-related quality of life (HRQoL) was assessed using the EuroQOL 5D5L questionnaire (26).

Statistical analysis

The patients who died, or did not complete the follow-up period, were excluded from the study as the analysis of the changes in frailty status after surgery was not possible.

Continuous variables are expressed as median and interquartile interval (IQI) or mean and standard deviation (SD), depending on the normality of their distribution as assessed with Shapiro-Wilk normality test. Categorical data are presented as counts and percentages.

Differences among the three ordinal levels of frailty were analyzed considering the presence of a linear trend between categories. The Mantel Haenszel linear trend test was used for categorical variables, and linear regression models were employed for quantitative ones. Concordance between frailty scales was assessed with the Kappa index.

Chi-square test was used to compare the distribution of frailty groups before and after surgery. Changes in the proportion of patients who score a point in each of the components of the frailty phenotype was analyzed using the Mc Nemar’s test for paired proportions.

All the statistical analysis and graphics were performed using Stata/IC 15.0 Software (Statacorp LP, College Station, TX). A significance level $p < 0.05$ was considered as statistically significant.

RESULTS

Study Population

During the study period, 500 patients aged 70 or more were referred for elective surgery in the three participating hospitals. 143 of these patients were initially recruited for the study, but 6 of them were excluded from the analysis because they withdraw the informed consent, or the data was incomplete.

Finally, 137 patients were included in the study and 109 of them completed the 6-month follow-up period. 12 patients (8.8%) died within the study period, and 16 patients were lost during follow-up (**figure 1**).

Figure 1. Enrollment flowchart.

The mean age was 78.1 years (SD 4.1, range 70.1 – 88.1). 47.7% of patients were female. The most frequent surgery performed was isolated valve surgery (78.9%), 11% of patients underwent combined valve and coronary surgery, whereas isolated coronary artery bypass surgery (CABG) was performed in 6.4% of patients. Basal characteristics of the patients are shown in **table 1**.

Table 1. Basal characteristics of the patients

N

Age, yrs

Female

BMI (kg/m²)¹

Comorbidities

HBP²

Dyslipidemia

Diabetes³

Atrial fibrillation⁴

COPD⁵

Cerebrovascular disease⁶

Previous cardiac surgery

Charlson index

NYHA functional class III-IV⁷

Laboratory values

Hemoglobin (mg/dl)

Proteins (mg/dl)

Creatinin (mg/dl)

Preoperative risk

EuroSCORE I

EuroSCORE II

Surgical procedure

CABG⁸

Valvular

CABG + Valvular

Other surgeries

CPB time (min)

N

Cross clamp time

Fried Frailty Scale

Frail

Pre-frail

Robust

CFS⁹

Very fit

Fit

Managing well

Vulnerable

Mildly frail

Moderately frail

CFS (categorized)

Frail

Pre-frail

Robust

Values are expressed as mean $\pm$ SD, median (IQI) or n (%). 1.BMI: Body mass index. 2.HBP: High blood pressure. 3.Patient

Prevalence and clinical profile of frailty

The prevalence of frail patients varied between 27.5% with the Fried scale and 11.0% with the CFS. Pre-frail and robust patients were 48.6% and 23.9% with the Fried scale and 73.4% and 15.6% with the CFS respectively.

The concordance between both scales when classifying individuals as “frail” or “non-frail”, assessed with the kappa index, was only moderate (kappa index 0.52).

As the frailty status increased, there was a significative linear trend towards being female and older age, worse functional status, lower hemoglobin and worse quality of life.

Figure 2 summarizes, for the basal characteristics of the patients, the presence or not of significative linear trend among the three ordinal levels of frailty.

Figure 2. Linear trend among the three ordinal levels of frailty

Changes in frailty status 6-month after surgery

Changes in Frailty prevalence

With both the Fried scale and the CFS, the prevalence of the different frailty groups significantly changed 6 months after surgery with respect to their baseline distribution ($p < 0.01$).

Figure 3 shows the differences in the prevalence of frailty, before and 6 months after surgery. The direction of these changes was towards a decrease in the overall burden of frailty in the entire cohort of patients. In this way, the patients classified as frail with the Fried scale went from 27.5% in the preoperative period to 17% after 6 months of follow-up. On the CFS scale, the most remarkable change occurred in vulnerable patients, who decreased from 39.5 to 22%.

Figure 3. Changes in frailty prevalence after surgery.

Changes in frailty scores after surgery

Figure 4 shows the mean changes in frailty scores for frail, pre-frail and robust patients with both scales. Negative values indicate that patients are less frail 6 months after surgery and positive values indicate a postoperative deterioration of the frailty status.

The most negative change in frailty scores occurred in the group of frail patients. Pre-frail patients showed also negative changes in frailty scores as well, although these changes were less marked than in frail patients. Conversely, robust patients experienced a slightly positive change. This linear trend in the changes of frailty scores that can be graphically appreciated, was also statistically significant ($p < 0.01$) in a linear regression model.

Figure 4. Mean differences in frailty scores after after surgery.

Transitions between frailty status

Changes in frailty scores are also reflected in transitions between the frailty groups between the preoperative level and the one after surgery. These changes, along with the postoperative mortality in each frailty group are shown in **Table 2**.

Although Frail patients had the highest postoperative mortality, up to 50% of them improved their frailty status 6 months after surgery when frailty is assessed with the Fried scale. With the CFS, 39% of frail patients switched to a less frail group. Most robust patients maintained their status after surgery.

Table 2. Transitions between frailty status (values are expressed as percentages).

		6 Months After surgery, %		6 Months After surgery, %	6 Months After surgery, %
Basal Frailty Status	Basal Frailty Status	Frail	Pre-frail	Robust	Frail
Fried Scale	Frail (n=38)	29	50	0	21
	Pre-frail (n=73)	11	48	13.7	27.2
	Robust (n=26)	0	11.5	88.5	0
Clinical Frailty Scale	Frail (n=18)	27.8	38.9	0	33.3
	Pre-frail (n=100)	3	70	7	20
	Robust (n=19)	0	26.3	63.2	10.5

Changes in the components of the Fried frailty phenotype

The most significant changes in the individual domains of the frailty phenotype were found in the group of frail patients (**table 3**). Frail patients improved in all components except gait speed, which remained unchanged. The most marked change was the improvement in the feeling of exhaustion, which went from 93% to 23% ($p<0.01$). In contrast, robust patients showed no changes, remaining practically without deficits in any of the components.

Table 3. Changes in Fried frailty scale domains after surgery.

Changes in Fried frailty scale domains after surgery (n=109)^a

Unexplained weight loss

Weak grip strength

Slow walking speed

Exhaustion

Low physical activity

Values are expressed as n (%)

(a) Patients who died or did not complete de follow-up period have been excluded. (*) p-values for Mc nemar's test for paired

DISCUSSION

The main finding of the present study is that surgery does not have a negative impact on the basal frailty status of patients referred for cardiac surgery. On the contrary, we have shown a significant improvement in the overall burden of frailty 6 months after surgery. This finding is true for both measurements that were employed to assess frailty, the Fried frailty scale and the CFS. In this way, we can confirm the dynamic and partially reversible nature of frailty in patients referred for cardiac surgery.

Changes or transitions among the ordinal levels of frailty is frequent in community-dwelling adults. As we get older, these transitions tend to occur towards a progressively greater degree of frailty. However, in frail patients who suffer a specific pathology for which there is an effective treatment, we could speculate that once this pathology has been treated effectively, the level of frailty will decrease to the extent that this pathology was contributing to it. For example, and focusing on cardiovascular medicine, the presence of heart failure secondary to a certain valve disease promotes a decrease in the level of the patient's activity and energy consumption. These decrease in the individual activity can favor the appearance of a certain degree of sarcopenia, which constitutes a central etiological element in the frailty pathophysiology. These events will have a direct negative impact on each of the items that are evaluated by the Fried Scale, that is to say: slow walking speed, muscle weakness, low physical activity, low resistance to effort and weight loss. Conversely, once the valve disease has been successfully treated and, therefore, the situation of heart failure has been resolved, it is foreseeable that the postoperative scores obtained in the different frailty scales will be improved compared to the preoperative ones.

Our results are consistent with the previous arguments. Frail and pre-frail patients showed a clear improvement in their postoperative scores on four of the five items evaluated by the Fried scale. Conversely, none of the 26 patients classified as robust with the Fried scale presented significant deterioration in the scores evaluated by this scale.

The reversibility of frailty was first shown in studies at community level during the first years of the 21st century (27,28). As an example, in the study of Binder et al. (27), 152 sedentary community-dwelling people, with an average age of 83 years and with a previous screening of mild or moderate frailty, were randomized to perform various strength, balance and resistance exercises during 9 months. The individuals who performed the exercises showed a marked improvement in their previous frailty status, quantified by the modified PPT test (modified Physical Performance Test), and in their functional capacity measured through the basic and instrumental activities of daily life.

In the clinical setting and more specifically in the field of surgery, very few studies have focused on changes in the patient's frailty status after the intervention. In 2015, McAdams et al. (29), with the aim to "study the natural history of frailty after aggressive surgical intervention such as kidney transplantation", analyzed a prospective cohort of 349 patients who were assessed for frailty using the Fried scale before and after kidney transplant surgery. They showed that frailty was increased during the first postoperative month (going from

19.8% to 33%), but it recovered its previous prevalence during the second month and decreased in the third month (17.2%).

In the context of cardiac surgery, Jha et al. (20), published in 2017 a study analyzing the preoperative and postoperative frailty status of 100 patients in whom either a heart transplant was performed, or a ventricular assist device was implanted as a bridge to transplant. Similarly to our study, the authors found that most frail patients who survived the intervention showed a significant improvement in their frailty status two months after surgery.

Therefore, considering our results, we could add a decrease in the previous frailty status to the benefits provided by surgery, besides an improvement in functional capacity and quality of life. This improvement would translate into a lower risk for the occurrence of adverse health-related outcomes, such as falls, disability, need for hospitalization and dependency.

One limitation of the present study is the relatively low number of patients included, however, it has been enough to demonstrate a decrease in the global burden of frailty after surgery. Other limitation of the study is that the follow-up period is limited to 6 months. It would have been interesting to extend this period up to a year or more to see if this improvement in frailty is consolidated or, on the contrary, it tends to return to its preoperative values. As we have previously published (19), frail patients present higher postoperative mortality and morbidity rates. This could have led to a selection bias, as patients who died tend to present higher levels of frailty. However, this trend was only significative when frailty was assessed with the Fried frailty scale.

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