

# Prognostic impact of frailty in elderly cardiac surgery patients

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## Abstract

Over the past few decades, the progressive aging of the population combined with the resulting increase in cardiovascular disease and the marked improvement of technologies applied to surgery justify the marked increase of the elderly patients requiring cardiovascular surgery. This claims a highly skilled perioperative management, which should be aimed at treating cardiac disease without increasing risk of hospitalization-related harmful events. Current preoperative assessment for cardiac surgery, such as the European System for Cardiac Operative Risk Evaluation II (EUROSCORE II) and the Society of Thoracic Surgeons (STS) risk score, are limited in their ability to predict perioperative outcomes in older patients. This is because patients' chronological age should not be considered as the only tool to identify the surgical risk. In recent years, indeed, several studies have highlighted the role of frailty syndrome in determining the prognosis of elderly patients undergoing cardiac surgery. Particularly, some functional aspects, such as gait speed seem to have a high sensitivity and specificity in this regard. Therefore, further research is needed in order not only to identify a unique, fast and easy to use tool aimed to recognize frailty syndrome, but chiefly resulting able to give us information about the effectiveness of focused preoperative interventions. Finally, we need to have scientific data on the role that surgical, percutaneous and transcatheter procedures have on outcome in elderly patients in terms of perioperative mortality, postoperative quality of life and regarding the possible reversibility of frailty. Cardiovascular surgery is to date a "moving target", due to changing face of patients and changing face of technical requirements and perioperative management should reflect such changes.

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## Introduction

The progressive aging of population justifies the increase in the average age of patients undergoing cardiac surgery. In the last 15 years, the average age of cardiac surgery patients has increased from 56 years to 69 years, with a proportion of octogenarians of 10% [1]. Nowadays the operative risk assessment must go beyond the simple mortality estimate, since it should give information on the risk of disability and on the overall quality of life. Moreover, the gradual expansion of percutaneous transcatheter approach and techniques for coronary and valvular disease, focuses even more attention on the stratification of surgical risk in order to identify the best therapeutic strategy. Over the past decades, the improvement of surgical techniques, extracorporeal circulation, anesthesiological management has favored a reduction of mortality and morbidity in cardiac surgery [2]. Although scientific evidences in the last years testify prognostic improvement in elderly subjects undergoing cardiac surgery, it has long been recognised a correlation between age, mortality and morbidity risk. If correctly selected, older patients may achieve substantial benefits from cardiac surgery. Unfortunately, neither guidelines exist on perioperative management of elderly patients candidate to cardiac surgery, nor elderly-specific risk score models have been designed for the prognostic risk stratification.

There are several scores aimed to assess the risk for perioperative cardiac surgery. Two risk score are those more widely used: the European system for cardiac operative risk evaluation (EuroSCORE) and Society of Thoracic Surgeons (STS) score [3-4]. Notably, these scores are known to poorly perform in the elderly: the EuroSCORE seems to overestimate mortality at lower score levels ( $\leq 6$ ) and underestimate mortality at higher score levels ( $> 13$ ) while the STS score seems to slightly underestimate perioperative risk. One disadvantage common to both risk scores is that they mainly predict perioperative mortality rather than major morbidity since they are based on the list of the individual diseases without taking account of the overall patient's biological state, which should also be focused on the research of the frailty syndrome and on the weight of comorbidities. In the last decades is emerging that frailty and comorbidities are better predictors of mortality and morbidity than chronological age. Indeed, the trend over time shows an increase in the complexity of elderly patients chiefly related to comorbidities and the frailty. The identification and assessment of frailty may facilitate identification of vulnerable surgical patients so that appropriate operative and perioperative management can be implemented [5].

## Frailty syndrome

Frailty is a geriatric syndrome of impaired resiliency to stressors (*i.e.* cardiac surgery) that has been delineated in the geriatric literature and more recently in the cardiovascular literature. It is characterized by a

reduced ability to ensure the maintenance of homeostatic balance sheet in presence of adverse environmental events. This reduction in homeostatic reserve, known as homeostenosis, results from impairment in multiple, interrelated, different organs and systems, resulting not specific to an organ or disease [5,6].

Although experienced clinicians may feel able to recognize frailty by end-of-bed assessment, the “eyeball” method tends to be subjective and not reproducible among different observers. Indeed, labelling a patient as too frail to heart surgery, relying only on an “eyeball” assessment is an anachronistic expression of ageism, which perpetuates a nihilistic attitude that fits badly to define in scientific terms the patient’s health status and the resulting prognostic implications [6]. Currently there are two main methods of measuring frailty. In the “phenotype” model proposed by Fried, core components of frailty include five determinants: slowness, exhaustion, weakness, weight loss and inactivity. Patients who have three or more of these five features are deemed frail, while those who have none of the features are non-frail. Patients who display one or two of the five features are “pre-frail” [7]. The second model is the Frailty Index (FI), or the cumulative deficit model, developed by Rockwood *et al.* in the Canadian Study of Health and Aging (CSHA). According to this model ageing is considered as a sum of deficits and interprets the frailty as the whole multidimensional result of deficits without focusing on the nature of the health problems. This method is based on the identification of nine categories of patients, based on the degree of self-sufficiency and the degree of activity of diseases and their influence in restricting the activities of daily living. According to this score we can identify the vulnerable state and four levels of frail patients (mildly, moderately, severely and very severely frail). The deficits encompass co-morbidities, physical and cognitive impairments, psychosocial risk factors and common geriatric syndromes [8].

### Association of frailty with postoperative outcomes in patients undergoing cardiac surgery

In the last years, it has emerged a number of scientific evidences that testify to a correlation between frailty and adverse clinical outcomes in patients undergoing cardiac surgery (Table 1).

Recognizing frailty is important to predict the ability of a patient to overcome acute stress in cardiac surgery. Moreover, it is also important to predict the patient’s future path since frailty is associated with multiple adverse health outcomes. Several reports, in recent years, have highlighted that frailty is progressively increasing in elderly subjects undergoing cardiac surgery [6,9]. Recent reports analyzed a time span of about 10 years showing that the prevalence of frailty is more than doubled in this time frame. The same data highlighted that frail subjects have a perioperative mortality tripled, as well as a doubled risk to remain in intensive care unit for a period exceeding 72 hours and a four-fold increased risk of institutionalization in comparison to non-frail patients [6, 9-11].

A recent study involving 3826 patients undergoing cardiac surgery has analyzed the in-hospital and mid-term mortality rates, correlating them to frailty syndrome expressed by parameters of self-sufficiency, gait and previous diagnosis of dementia. The results showed that patients recognized frail had a 1.5 fold increased risk of mortality compared to those not deemed as frail [12].

Sundermann analyzed the association between frailty and 1-year mortality and major adverse cardiac and cerebrovascular events in a cohort of 400  $\geq$  74-years old patients undergoing cardiac surgery. Even this study, using the Comprehensive Assessment of Frailty method, showed that frailty was independently associated with reduced 1 year survival following cardiac surgery [13].

Afilalo in a previous report used four different scales to evaluate frailty: the 7-item expanded Cardiovascular Health Study Frailty Scale, the 5-item Cardiovascular Health Study Frailty Scale, the 4-item Mac Arthur Study of Successful Aging and Gait Speed. In this study, only gait speed was significantly related to mortality and major morbidity after cardiac surgery. The reduction in 5-metres gait speed was associated with a 2- to 3-fold increase in risk [14].

On this basis, in a subsequent study, the authors focused their attention on the relationship between the 5-m gait speed and perioperative outcome in a much higher number of elderly patients undergoing cardiac surgery. Indeed It was performed a prospective study lasted about three years which involved a cohort of 15,171 elderly patients (mean age 71 years) undergoing cardiac surgery. The study results showed a progressive increase in operative mortality in relation

Table 1. Frailty and cardiac surgery.

Author	Population	N.	Frailty indices	Outcomes	Results
Lee (2010)	Pts undergoing cardiac surgery	3826	Katz Index of ADL, deambulation, dementia	In-hospital and midterm mortality, Institutionalization, secondary in-hospital outcomes	Frailty was related to increase in-hospital and midterm mortality, institutionalization, and unadjusted in-hospital outcomes
Sundermann (2011)	Pts $\geq$ 74 yrs undergoing cardiac surgery	400	Simplified CAF	1-y all-cause mortality and MACCE	Frailty has proven reliable in predicting 1-year mortality
Afilalo (2012)	Pts $\geq$ 70 yrs undergoing CABG and/or valve surgery	152	5-item CHS 7-item CHS 4-item MSSA Gait speed	Postoperative mortality or major morbidity	Only gait speed was significantly associated to postoperative mortality/morbidity
Afilalo (2016)	Pts $\geq$ 60 yrs undergoing CABG and/or valve surgery	15,171	5-meters gait speed	All-cause mortality during the first 30 days after surgery, a composite outcome of mortality or major morbidity during hospitalization	Gait speed was independently predictive of operative mortality as well as of the composite outcome of mortality or major morbidity

ADL: activity daily living; CAF: comprehensive assessment of frailty; MACCE: major adverse cardiac and cerebrovascular events; CABG: coronary artery bypass graft; CHS: cardiovascular health study frailty scale; MSSA: Mac Arthur study of successful aging.

to the reduction of the gait speed: in fact, compared to patients in the fastest gait speed tertile (>1.00 m/s), those in the middle tertile (0.83-1 m/s) and those belonging to the lowest speed tertile (<0.83 m/s) showed an increased operative mortality with an odds ratio of 1.77 and 3.16 respectively.

Even after adjustment for STS score, every 0.1-meters/s decrease in gait speed corresponded to an 11% increase in 30-day mortality, irrespectively of left ventricle ejection fraction and serum creatinine, two well known risk factors for mortality. Patients having the slowest gait speed have a 35% higher mortality rate than those at normal gait speed. Reduced gait speed was also predictive of the composite outcome of mortality and major morbidity [15].

Even the studies of elderly patients undergoing transcatheter aortic valve replacement (TAVR) have shown a close correlation between frailty and major adverse cardiac and cerebrovascular events. These studies have even shown, in spite of a less invasive strategy, a higher risk compared to patients undergoing cardiac surgery. This apparent discrepancy is justified by the fact that the TAVR is reserved for older patients who are deemed inoperable [6].

## Conclusions and future directions

To date, no definite indications have been elaborated on how to perform an “elderly-oriented” cardiac surgery. Recent advancements in surgical techniques allow to both reduce tissue trauma and duration and invasiveness, thus providing better results in the elderly. Data in the literature mentioned above have highlighted the role of frailty as an important determinant in the prognosis of cardiac surgery. However, simultaneously, they have focused attention on the lack of uniqueness in the use of tools to assess this syndrome [6]. Indeed, there is significant heterogeneity in the criteria for frailty and in the ascertainment of postoperative outcomes. In an elderly-oriented cardiac surgery, survival alone is not enough to measure outcome. Frail patients suffer a rapid loss of function after even short hospital stays, and recovering from sternotomy may take more than 6 months [11]. Moreover, some complications, such as stroke, are accompanied by unfavourable sequelae, that are commonly considered worse than death. Thus, functional decline and QOL need to be comparatively evaluated. Therefore, current literature reveals the need for further studies to validate a unique tool to assess frailty, possibly both easy to handle and quick in use. Although recent studies highlighted the role of gait speed, as well as of physical function tests and sarcopenia measurements as important tools both in recognition of frailty and in the assessment of cardiac surgery risk in the elderly, further large prospective studies should be done to directly compare these functional measures to other frailty parameters in the prediction of relevant clinical outcomes after cardiac surgery [6,15].

Once the best tool for frailty assessment has been identified, it will have to be able to guide us not only in selecting patients suitable for cardiac surgery, but also in obtaining data about which pre- and post-operative actions to perform in order to improve the outcome of highest risk patients. On the first point, the risk assessment is essential for two main reasons. First it should deal with the question whether the anticipated risks of the procedure are outweighed by the anticipated benefits in terms of survival and quality of life. Second, in the age of transcatheter and percutaneous approaches to coronary artery disease and valve disease, risk stratification has important implications for selecting safer approach to treat cardiovascular condition. In fact, it is one thing to show that a tool to measure frailty is able to identify the outcomes of patients at risk. But it is another thing whether these tools

may be able to identify patients who may benefit from less invasive procedures even at the cost of a sub-optimal technical result [6].

Moreover, we need more literature data that allow us to identify those patients in which the degree of frailty may improve after a cardiovascular procedure *versus* those destined to a progressive deterioration despite a technically successful cardiovascular procedure and peri-procedural intervention.

In the absence of specific guidelines and taking into account the wide spectrum of underlying diseases, the decision to intervene and the choice of perioperative path should come from a comprehensive and multidisciplinary evaluation. At present the Heart Team-based approach is crucial in identifying patients who might benefit from a surgical intervention.

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