A new frailty index as a risk predictor of morbidity and mortality: its application in a Surgery Unit

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Summary. *Background:* It's difficult to explain what *frail patient* means, because universal criteria for its identification and definition have never been drawn up. The whole scientific community is very interested to this issue of the potential effects that fragility may have on surgical and clinical outcomes. For this reason, we try to develop and validate the use of a new surgical frailty index (nsFI) to predict postoperative outcomes and mortality in General Surgery. *Methods:* The study was lead in the General Surgery Department of the "A.O.U. Mater Domini" of Catanzaro. The study was conducted using the database of the patients admitted in 2016. We calculated a score for each patient using data collected from medical records. Items of the Canadian Study of Health and Aging-frailty index (FI) were performed to develop a new frailty index to predict adverse postoperative clinical outcomes. Validation of our index was performed using the notorious mFI of Velanovich et coll., to confirm the proposed index. The resulting population was subdivided into 4 groups: not frail, mild, moderately and severely frail. Subgroups were created using gender, age, site of origin and type of pathology. Morbidity and mortality were evaluated after surgery. *Results:* A total of 481 patients were identified in accordance to inclusion criteria. According to our index 58% of this population was frail and 70% was over the age of 65. Biological frailty is correlated with the patient's origin area, so 61,7% came from rural regions. The percentage of frail men and women was the same. Malignant diseases were found in 71,01% of frail patients. 18,20% developed postoperative complications, while 1.32% died after surgery. This new surgical frailty index demonstrates good discrimination in our cohort (AUROC=0.74) better than previously modified frailty index (AUROC=0.54). *Conclusions:* This new surgical frailty index can be used to guide decision-making when applied on general surgery department. Furthermore, we have identified the identikit of surgical frail patients.

Key words: index, risk predictor, frailty, surgery

Introduction

Pre-operative risk evaluation is a fundamental tool to determine the patient's readiness for surgery, mortality and morbidity. Risk stratification for patients undergoing surgery is necessary for surgical planning, because this assessment permits to take a decision about whether to perform surgery or not, type and timing of the surgery. Moreover, it's useful to recognize patients who need a period of optimization before surgery. Furthermore is essential to forecast any complication and the needed procedures to prevent them (1).

Evaluation of frailty is an important variable for the estimation of perioperative risk in all patients (2-4). Nowadays frailty is considered as a well-characterized and validated method to objectively assess patient's fitness for surgery (5-6).

The World Health Organization in the last *World Report on Ageing and Health*, defines *frailty* as "extreme

vulnerability to endogenous and exogenous stressors that exposes an individual to a higher risk of negative health related outcomes" (7).

It is clear how frailty is consistently associated with adverse outcomes after surgery. The strongest evidences are in the association with increased 30 day, 90 day and 1 year mortality, post-operative complications and length of stay (8). This highlights the importance of early detection of frailty in the surgical diagnostic-therapeutic process. Score systems that are used to estimate the risk of surgery, are designed to predict mortality even if postoperative morbidity has been acknowledged as the major determinant of patient quality of life after surgery (1, 9-10). Traditionally, frailty has been measured by combining a patient's medical history, physical examination, and the assessment of physical and functional status (11-14). Many frailty definition tools were created for this purpose, but there is no one that has universal application. It is therefore necessary to tailor a specific tool for each medical area and especially for each surgical area.

One of the most famous tools in surgical research is that one created by Velanovich and colleagues that mapped the 70 variables included within the frailty index (FI) proposed by the Canadian Study of Health and Aging (CSHA) onto the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database to develop a modified frailty index (mFI) consisting of 11 preoperative variables measuring patient frailty (15).

The limit of this score system is the necessity to retrieve informations from American databases, but not all Countries have an available patient's database. For this reason, we have devised a score based on timely and rapidly detectable data from the patient's clinical record at the time of hospitalization. Moreover, Velanovich score doesn't incorporate surgical-specific informations to stratify patient's risk. For this reason it is not specific to any surgery in particular. In our opinion, this score put more attention on the general clinical problems of the patient, in despite of the surgical variables affecting the outcomes that obviously differ depending on the type of surgery the patient is facing.

Considering this background, it is necessary to develop a strong and clinically applicable preoperative frailty model that incorporates procedure-specific information to stratify patient's risk. (12, 16-20).

The aim of the current study was to develop and validate a clinically relevant frailty index using a dataset of patients undergoing general surgery. Additionally, we wanted to compare the predictive power of the proposed new surgical frailty index (nsFI) to existing frailty indices including the mFI.

Moreover our assessment will be performed on a young and old population, because there are several studies that investigate the effect of frailty on clinical and surgical outcomes, but most of them are limited to assessing the fragile elder. Most of the fragile population are over 65 years of age; nevertheless, it is also important to evaluate the effect of fragility on the younger population for the greatest impact they have on society.

Materials and Methods

The study was lead in the General Surgery Department of the "A.O.U. Mater Domini" of Catanzaro. The current analysis was performed using data drawn from clinical records of hospitalized patients from 1st January 2016 until 31st December in General Surgery Department. Among the informations extracted from clinical records, there were basic data such as age, sex, area of origin, type of disease, performed surgery, and post-operative complications. The main interventions considered for this study were surgery of the colon, breast, thyroid, kidney, stomach, pancreas, bile ducts, wall defects. Inclusion criteria were the department of origin and age over 18. For each patient was calculated a new surgical frailty index (nsFI) and modified frailty index (mFi) according to Velanovich. Using the list of 70 items from the Canadian Study of Health and Aging-frailty index (CSHA-FI), we selected the only ones that, according to the Author's experience, have the major impact on comorbidity and mortality after general surgery. We considered only factors that are able to increase the intraoperative risk, the complications and their severity, and the complexity of postoperative intervention and management. The items considered to be of greater value were crossed with data detectable by clinical records. An 11-element system was derived, as shown in Table 1. Each item had equal

Table 1. Items of the new surgical frailty score

Item		Variable	Score
1	Functional state	Independent	0
		Dependent	1
2	ASA class	1-2	0
		3-5	1
3	Presence of ascites	No	0
		Yes	1
4	Disseminated cancer	No	0
		Yes	1
5	Renal insufficiency or dialysis	No	0
		Yes	1
6	Stoma	No	0
		Yes	1
7	Urinary incontinence	No	0
		Yes	1
8	Difficulty in eating	No	0
		Yes	1
9	General mental health problems	No	0
		Yes	1
10	Anti- platelets Therapy	No	0
		Yes	1
11	Multiple drugs	No	0
		Yes	1

weight in the scoring index and it was considered as dichotomous variable, so for each variable could be attributed a score of 1 (yes) or 0 (no). The maximum expected score was 11. Patients were categorized into four groups based on their score: not frail (0 pt), mild (1 pt), moderate (2 pt), high frail (>3 pt).

For each patient was calculated a mFI according to Velanovich et al. The primary outcome of interest was the development of either a postoperative complication or postoperative mortality within 30 days of surgery. Postoperative morbidity was defined using a composite measure for postoperative complications that included surgical site infections, pneumonia, need for intubation, ventilator dependence, venous thromboembolism (pulmonary embolism or deep venous thromboembolism), acute renal failure, urinary tract infections, myocardial infarction, bleeding and sepsis.

Categorical data were reported as whole numbers and percentages and were compared using Pearson's chi-squared test.

Results of the comparison between the two methods were evaluated with area under the receiver operative characteristic curve (AUROC) statistics. Validation of the proposed index was performed using a leave one out cross-validation methodology. Statistical significance was defined by a p value of <0.01. All statistical analyses were performed using XLSTAT statistical software.

A score for linear trend in log odds (18) was used to assess the relationship between FI and postoperative mortality and morbidity.

Results

A total of 536 patient's records were identified in the database of hospitalized patients in 2016; 456 were eligible for the study. When a patient had assigned multiple folders due to different hospitalizations, only the first folder was considered and the others were used for calculating complications and mortality. The folders not included in the study belonged to patients who did not comply with inclusion criteria or did not received surgery. Moreover, we eliminated folders in which important data were missed. The median age of the study population was 62 years (IQR: 48-71) with a slight majority of female (n=254, 55.7%) (Table 2).

The most common site of origin was rural area (n=342, 75%), followed by urban area (n=114, 25%). There was quite the same amount of patients with malignancies (n=207, 45,39%) and benign pathologies (n=249 54,6%).

Validation of the nsFI was performed comparing it with mFI for the same group of patients. The nsFI demonstrated a good discrimination with a corresponding AUROC of 0.74 better than mFI, which demonstrated poor discrimination with a corresponding AUROC of 0.54 (p<0.001).

According to nsFi we found that 58,33% of the population of the study could be considered frail; in particular, the 22,59% was mild frail, the 17,32 % was moderate frail and 18,42% strong frail.

The most fragile patients are the older ones, in fact, the 83,2% of the population >65 years is fragile, compared to 48% of those between 50-65 years and

Table 2. Baseline patient and frailty characteristics evaluated with nsFI score

Characteristics	Not frail	Mild frail	Moderate frail	Severe frail
	41,67%	22,59%	17,32%	18,42%
Age				
0-50	80,65%	12,90%	3,23%	3,23%
50-65	52,00%	24,00%	12,00%	12,00%
>65	16,8%	19,57%	20,45%	43,18%
Sex				
Male	42,08%	19,80%	17,33%	20,79%
Female	41,34%	24,80%	17,32%	16,54%
Area				
Urban	51,75%	20,18%	13,16%	14,91%
Rural	38,30%	23,39%	18,71%	19,59%
Pathology				
Benign p.	52,21%	16,87%	15,26%	15,66%
Malignancies	28,99%	29,47%	19,81%	21,74%
Complicances	47,72%	23,06%	14,75%	14,48%
Mortality	33,33%	0,00%	16,67%	50,00%

of the 19,36% of patients under the age <50 (p<0.001; OD: 15).

Rural area is another determinant of frailty; in fact, 48,25% coming from urban area is frail, indeed 61,7% of rural area is frail (p<0.05, OD: 1.72); sex does not affect the determination of frailty as shown by OD: 0.96.

Particularly influential is the nature of the disease. Fragile patients suffer most from cancerous pathologies (71.01%; OD: 2.67).

Complications and mortality were compared among different grades of frailty. The increase of fragility degree was linked to an increase of postoperative complications and mortality.

Frailty is an important risk factor for complications and mortality; 85,54% of frail patients had complications after surgery while just the 14,46% of not frail patients had the same complications, in fact postoperative complications were developed in 20.48% of mild frailty, in 26.51% of moderate frailty and in 38,55% of strong frailty (p<0.001 OD: 5.96). Frail patients had major mortality, in fact 66.66% of death were frail, indeed 33,33% were not frail (p<0.05; OD: 1.45).

Discussion

Fragility is a physiological syndrome characterized by a reduced functional reserve and stress resistance, caused by a cumulative decline in several physiological systems, loss of homeostasis and consequent clinical instability and tendency to worse health manifestations (21).

There is a wide literature on the definition of the frail patient, that comes largely from the geriatric field, because fragility strongly associates with aging.

In the hospital path the detection of fragility is primarily finalized to help the clinician to identify frail patients and consequently stratify them for different levels of risk before surgery. In scientific literature, there are different types of frailty condition index. One of the best known and useful is the Velanovich one, a 11-point modified frailty index (mFI) that use data collected from the ACS-NSQIP to identify patients at risk for adverse postoperative clinical outcomes including postoperative complications, increasing LOS, and postoperative mortality (15). This accumulating deficits model based on patient's history, is a very useful and practical instrument to assess preoperative frailty, but it has several limitations. First of all, this score is applied to a national database; therefore, if clinicians don't have a database and if this is not specific and complete, it can't be used. The selected elements included in the Velanovich index cannot be considered the most important and impactful for general surgery. These are too generic, and could be incorrectly used for a fragile patient evaluation in a precise surgical specialty. Our goal, however, is to create a more specific index that is suitable for the type of surgical procedure conducted and in our case we are talking about surgery related to colon, breast, thyroid, kidney, stomach, pancreas, bile ducts and wall defects surgery.

Our nsFI score is made of robust, easy to use, 11 points index; for its creation We used the CHSA-FI because it easily identifies patient risk factors using just their clinical history. Some elements, such as ASA class, pharmacotherapy, and stoma are not extrapolated from the 70 items of CSHA-FI. These have been introduced into our index because, according to the authors, they have fundamental importance in fragility determination. The novelty of our study is also in the
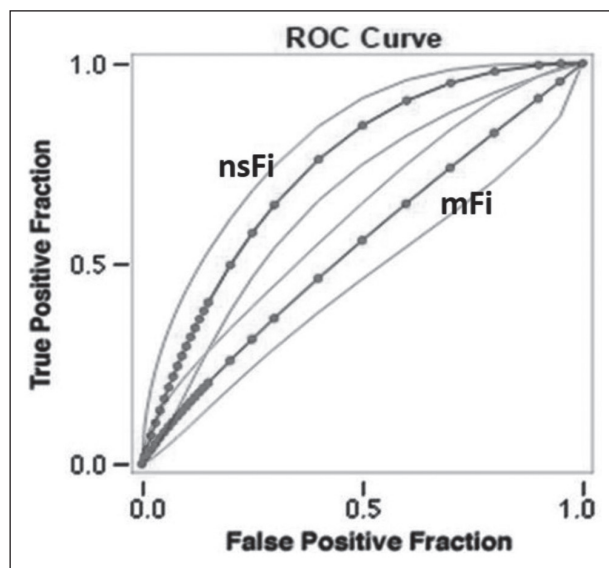
Figure 1. Roc Curve Comparison of the area under the curve of the nsFI (0.74) and the mFI (0.54)

index application, in fact all informations needed to define the score have been obtained from the patient's clinical records.

The study conducted demonstrates that our nsFI shows an improved discrimination and is more accurately able to risk-stratify patients undergoing general surgery when compared with the reference index (mFI). The new index of surgical fragility has demonstrated excellent ability to discriminate biological fragility. Comparing the two AUROCs (Figure 1), it can be seen that the nsFI is a better index than the Velanovich's mFi, which in itself showed little discriminatory ability.

Data suggests that the proposed nsFI is an accurate and easy-to-use risk stratification tool that can be used primarily from clinical folder analysis. Through a preoperative clinical evaluation, it is possible to predict the patient's risk of developing a post-operative adverse clinical outcome after surgery.

Conclusions

The study has shown that the fragile patient phenomenon is very common and important because about half of the patients hospitalized in a general sur-

gery department are fragile. The typical identity of a fragile patient is elderly, coming from rural areas with cancer.

Our study also strengthens the data already found by Velanovich et al. on the fragility of youth; We calculated that a patient of five was frail. The implication here is that although fragility has been studied almost exclusively in older adults, it can be found even in younger adults. This younger and more fragile group has not received much attention in the literature. Further studies will have to be done to better investigate this aspect.

Several studies have analyzed the region impact on fragility but no one has ever focused on defining the effect on surgical outcome (22). Our data is in line with Italian rural realities where there is a smaller amount and less access to health services, and this is accompanied by a lesser awareness of the population living in these areas.

As for the type of pathology, it is easy to understand how malignancies are more complex because they alter the entire homeostasis of the patient. Not least is the effect that the same malignancies produce on the psychological sphere of the patient (23).

This study shows that the evaluation of fragility, based on a simple score determined by the patient's history, is associated with the occurrence of 30-year postoperative morbidity and mortality.

The effects of fragility seem to be more important in postoperative morbidity rather than mortality. The interpretation of all these studies is that fragility is a risk factor for complications and mortality after surgery.

Author contribution

Rosario Sacco, Antonietta Condoluci, Giuseppe Sammarco, Lucia Curto: Concept and design of study, data collection, data interpretation and analysis, drafting, revision, approval of final manuscript.

Michele Ammendola, Roberto Romano, Giuseppina Vescio: Study design, data collection, revision, approval of final manuscript.

Nikolaos Filiotis, Vincenzo Orsini: revision of final English form, critical revision of the entire text.

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