European Journal of Internal Medicine xxx (xxxx) xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original article

Pre-operative physical performance as a predictor of in-hospital outcomes in older patients undergoing elective cardiac surgery

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ARTICLE INFO

Keywords:
Older adults
Cardiac surgery
Performance measures

ABSTRACT

Objective: Risk stratification of cardiac surgery patients is usually based on the Society of Thoracic Surgeons (STS) score, that has limited predictive value in older persons. We aimed assessing whether the Short Physical Performance Battery (SPPB) improves, beyond the STS score, assessment of hospital prognosis in older patients undergoing elective cardiac surgery.

Methods: All patients aged 75+ years referred for elective cardiac surgery to Careggi University Hospital (Florence, Italy) from April 2013 to March 2017 were evaluated pre-operatively. Participants were classified according to the STS-Predicted Risk Of Mortality (STS-PROM): low (<4%), intermediate (4 to 8%), and high risk (>8%). Primary study outcomes were hospital mortality and STS-defined major morbidity. Length of hospital stay was an additional outcome.

Results: Out of 235 participants (females: 46.5%; mean age: 79.6 years), 144 (61.3%) were at low, 67 (28.5%) at intermediate and 24 (10.2%) at high risk, based on the STS-PROM. SPPB (mean±SEM) was 8.8 ± 0.2, 7.0 ± 0.5, and 6.0 ± 0.8 in participants at low, intermediate, and high risk, respectively ($p<0.001$). The primary outcome occurred in 62 participants (26.4%). In low-risk participants, the SPPB score predicted the primary endpoint (adjusted OR 0.77, 95% CI 0.66–0.89 per each point increase; $p<0.001$) controlling for STS-Major Morbidity or Operative Mortality (STS-MM) score. This result was not observed in the intermediate-high risk group.

Conclusions: SPPB predicts mortality and major morbidity in older patients undergoing elective cardiac surgery, classified as low risk with the STS risk score. The SPPB, applied preoperatively, might improve risk stratification in older patients undergoing elective cardiac surgery.

1. Introduction

Improved surgical techniques and intensive care management have dramatically reduced perioperative complications and mortality after cardiac surgery over the last two decades [1]. Therefore, indications to cardiac surgery are nowadays increasingly extended to patients aged 80+ years [1], often in the past excluded due to unacceptable risk of death and major morbidity, as estimated by risk assessment scores of

Abbreviations: BADL, basic activities of daily living; CKD, chronic kidney disease; CI, confidence interval; eGFR, estimated glomerular filtration rate; EKG, electrocardiogram; EuroSCORE, *EUROpean* system for cardiac operative risk evaluation; GDS, geriatric depression scale; IDS, index of disease severity; IADL, instrumental activities of daily living; OR, odds ratio; PLOS, prolonged length of stay; SEM, standard erros of the mean; SPPB, short physical performance battery; SPSS, statistical package for social sciences; STS, society of thoracic surgeons; STS-MM, society of thoracic surgeons major morbidity or operative mortality; STS-PROM, society of thoracic surgeons predicted risk of mortality.

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https://doi.org/10.1016/j.ejim.2020.10.021
Received 16 July 2020; Received in revised form 24 September 2020; Accepted 26 October 2020

common use. Despite these remarkable improvements, perioperative complications and mortality, as well as long-term unfavorable outcomes, remain common in older persons [2].

Risk assessment tools, such as the *EUROpean System for Cardiac Operative Risk Evaluation* (EuroSCORE II) [3] and the *Society of Thoracic Surgeons* (STS) score [4], have been shown to improve the accuracy of prognostic assessment in middle-aged individuals, but their validity is suboptimal in older persons [5]. Indeed, surgical risk calculators do not take into account important non-cardiovascular variables, such as cognitive impairment, depression, functional decline, and sarcopenia, neither they are able to capture the "frail phenotype", a powerful, independent predictor of mortality and complications after surgery [6]. Frailty is defined as a reduction in physiological homeostatic reserve, with consequent increased vulnerability to stressful events [7]. Cardiac surgery represents a powerful stressor for vulnerable older adults, in whom the presence of frailty, variously defined, appears as a major prognostic determinant in this setting [8,9].

Physical performance measures have been successfully applied to assess the prognosis of older patients with heart diseases. Gait speed has been tested in patients undergoing cardiac surgery [9], whereas the Short Physical Performance Battery (SPPB) [10] has been shown to predict long-term survival after hospitalization for heart failure exacerbation [11]. The SPPB objectively and quantitatively assesses balance, gait speed, and lower limbs strength (indirectly estimated from repeated chair standing), thus offering a thorough evaluation of lower extremity function, which is crucial to maintain autonomy [10]. Aim of the present study was to assess whether the SPPB can improve the prediction of hospital course (i.e., major clinical events and prolonged hospital stay) in older patients undergoing elective cardiac surgery, above and beyond the prognostic assessment obtained with the STS score.

2. Materials and methods

2.1. Study design

The present study is a prospective, single-center cohort study conducted at Careggi University Hospital, Florence. Institutional Review Board approval was obtained. Before enrolment, participants gave their written informed consent.

2.2. Population

All patients aged 75+ years referred to the Cardiac Surgery Unit of Careggi Hospital for their first elective cardiac surgery procedure via standard sternotomy were screened for enrolment. All types of cardiac surgery (coronary aortic by-pass grafting, valvular surgery, or combined procedures) were initially evaluated, although only participants receiving a procedure considered by the STS calculator were eventually included. Patients undergoing an emergency/urgent procedure or clinically unstable, i.e. with an acute coronary syndrome, acute or worsening heart failure were excluded.

2.3. Baseline evaluation

Patients scheduled for elective procedures to the Cardiac Surgery Unit of Careggi Hospital and residing in the metropolitan area of Florence are routinely assessed by a multidisciplinary team composed by a cardiac surgeon, a cardiologist and an anesthesiologist. From April 1, 2013, to March 31, 2017 and limited to patients aged 75+ years, geriatricians participated to this evaluation procedure, although only twice a week because of limited resources. No specific criteria dictated assignment of patients to weekdays when the geriatrician was present. Age, weight, height, body mass index, medical history (including current symptoms and New York Heart Association – NYHA - class), EKG, echocardiographic parameters, and laboratory data were recorded, together with educational level, social network, and presence of a primary caregiver. The EuroSCORE II [3] and the STS score [12] were calculated. Participants were stratified into three groups according to their STS Predicted Risk Of Mortality (STS-PROM) score: low risk (STS-PROM <4%), intermediate risk (STS-PROM 4 to 8%), and high risk (STS-PROM >8%).

Comprehensive geriatric assessment was conducted by an expert geriatrician, using the Basic [13] and Instrumental [14] Activities of Daily Living (BADL, IADL) scales for functional status, the MiniCog test with the Seattle algorithm [15] and the 5-item Geriatric Depression Scale (GDS) [16] for cognitive and affective status, respectively. Comorbidity was quantified with Greenfield's Index of Disease Severity (IDS) [17], which records a list of diseases with their corresponding level of severity (0= disease absent; 1= disease asymptomatic; 2= symptoms present but controlled by therapy; 3= symptoms poorly controlled by therapy; 4= symptoms uncontrolled or life-threatening disease). Renal function was evaluated from creatinine value and estimated Glomerular Filtration Rate (eGFR), obtained with the Cockroft-Gault Formula included in EuroSCORE II [3]. Chronic Kidney Disease (CKD) was considered severe when eGFR was $\leq$30 ml/min/1.73 m^2. Anemia was diagnosed from hemoglobin <12 g/dl in women and <13 g/dl in men.

Finally, participants underwent the SPPB, according to standard procedures [10]. Briefly, each of the three performance tests included in the SPPB (balance, gait speed, and repeated chair standing) is scored from 0 (worse) to 4 (best), based upon comparison of test results with normative values from a reference population. A summary score is then calculated, ranging from 0 (severely impaired performance) to 12 (optimal performance). An SPPB score <7 is usually considered as indicative of moderately to severely impaired physical performance [18].

Because the study represented a preliminary phase propaedeutic to routine application of geriatric assessment in the management of older patients prior to a surgical procedure that had already been scheduled, surgeons and anesthesiologists remained blinded towards geriatricians' findings.

2.4. Study outcomes

The primary outcome was a composite endpoint as defined by STS Major Morbidity or Operative Mortality (STS-MM) in STS Risk Model Outcomes [12]: operative mortality, stroke, renal failure, prolonged mechanical ventilation, deep sternal wound infection, and reoperation. Operative mortality was all-cause death occurring during surgery-related hospitalization or within the following 30 days. Permanent stroke was defined according to STS risk score, as any confirmed neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain, persisting $\geq$ 24 h or until death. Acute or worsening renal failure was defined as an increase in serum creatinine up to $\geq$4.0 mg/dl, rising of at least 0.5 mg/dl or with threefold-increase from the most recent preoperative level, or requiring postoperative dialysis. Prolonged ventilation was time until extubation above 24 h, including any additional hours following reintubation. Deep sternal wound infection, defined according to the Centers for Disease Control and Prevention criteria, was taken into account when occurring within 30 days from operation. Reoperation included any intervention for cardiac or non-cardiac reasons.

Secondary outcome was length of stay exceeding 14 days (prolonged length of stay, PLOS), as in the STS risk score model.

2.5. Statistical analysis

Statistical analysis was performed using SPSS® version 25.0 (SPSS, Inc., Chicago, IL). Data distribution was preliminarily observed, to verify whether parametric tests could be applied. Continuous variables are expressed as means ($\pm$SEM) and categorical variables as percentages. Descriptive analyses were conducted to compare baseline characteristics across the three STS-defined risk groups. Continuous variables were

Table 1
Demographic and clinical characteristics according to STS-PROM risk category (low risk: <4%; intermediate risk: 4–8%; high risk: >8%).

	STS-PROM risk category			p value
	Low (*n* = 144)	Intermediate (*n* = 67)	High (*n* = 24)	
Age, years	78.5 ± 0.3	81.1 ± 0.5	81.7 ± 0.7	<0.001
Male	90 (63)	24 (36)	12 (50)	0.008
BMI, kg/m^2	26.1 ± 0.30	25.7 ± 0.6	25.4 ± 0.8	0.370
Type of surgery				
- CABG	32 (22)	4 (6)	2 (8)	<0.001
- Isolated valve surgery	67 (47)	18 (27)	5 (21)	
- Combined surgery	45 (31)	45 (67)	17 (71)	
EuroSCORE II,%	3.0 ± 0.1	5.9 ± 0.3	12.7 ± 1.6	<0.001
STS-PROM,%	2.4 ± 0.1	5.6 ± 0.1	14.0 ± 2.1	<0.001
STS-MM,%	16.3 ± 0.4	28.3 ± 0.7	49.7 ± 3.2	<0.001
Hypertension	119 (83)	58 (87)	21 (88)	0.410
Type 2 Diabetes	30 (21)	16 (24)	10 (42)	0.052
Insulin-requiring Diabetes	10 (7)	6 (9)	7 (29)	0.004
History of CAD	67 (47)	34 (51)	17 (71)	0.048
Heart failure	76 (53)	46 (69)	22 (92)	<0.001
NYHA class III-IV	50 (35)	31 (47)	19 (79)	<0.001
History of stroke	9 (6)	9 (13)	2 (8)	0.266
Chronic kidney disease	33 (23)	23 (34)	16 (67)	0.001
Atrial fibrillation	27 (19)	24 (36)	7 (29)	0.031
COPD	12 (8)	17 (25)	3 (13)	0.039
PAD	11 (7)	4 (6)	2 (8)	0.905
LVEF	58.7 ± 0.8	55.2 ± 1.3	46.8 ± 3.3	<0.001
TAPSE, mm	22.6 ± 0.4	21.6 ± 0.5	20.1 ± 0.7	0.0043
Hemoglobin, g/dl	12.8 ± 0.1	12.1 ± 0.2	11.5 ± 0.4	<0.001
Anemia	62 (43)	37 (55)	16 (67)	0.014
Creatinine, mg/dl	0.96±0.03	1.14±0.06	1.38±0.11	<0.001
eGFR, ml/min/ 1.73 m^2	69.1 ± 5.3	49.1 ± 2.2	39.5 ± 3.2	0.001
Total SPPB	8.8 ± 0.2	7.0 ± 0.5	6.0 ± 0.8	<0.001
IDS score	8.7 ± 0.3	10.8 ± 0.4	12.0 ± 0.9	<0.001
BADL lost	0.2 ± 0.0	0.3 ± 0.1	0.5 ± 0.1	0.032
IADL lost	0.9 ± 0.1	1.4 ± 0.2	2.4 ± 0.4	<0.001
Abnormal MiniCog	63 (44)	41 (61)	17 (71)	0.002
GDS	1.1 ± 0.1	1.3 ± 0.1	1.4 ± 0.3	0.128
Number of drugs	5.8 ± 0.2	6.6 ± 0.3	8.0 ± 0.4	<0.001

Data are mean (SEM) or n (%).
Abbreviations. BMI: Body Mass Index; CABG: Coronary Artery Bypass Grafting; STS-PROM: Society of Thoracic Surgeons - Predicted Risk Of Mortality; STS-MM: Society of Thoracic Surgeons - Major Morbidity or Operative Mortality; STS-LLS: STS Long Length of stay; CAD: Coronary Artery Disease; NYHA: New York Heart Association; CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Disease; PAD: Peripheral Artery Disease; LVEF: Left Ventricular Ejection Fraction; TAPSE: Tricuspid Annular Plane Systolic Excursion; eGFR: estimated Glomerular Filtration Rate; SPPB: Short Physical Performance Battery; IDS: Index of Disease Severity; BADL: Basic Activities of Daily Living; IADL: Instrumental Activities of Daily Living; GDS: Geriatric Depression Scale 5-item.
P-values are from ANOVA (continuous variables) or chi square (categorical variables) tests for trend.

compared using Student's *t*-test for independent samples or ANOVA, whereas the chi-square test was applied to evaluate differences in proportions; p-values for trend were taken into account as appropriate. In order to identify independent predictors, variables with a significant association with the endpoint in bivariate analyses were entered into multivariable logistic models, with backward deletion (p out >0.1) of redundant variables. The predicted probability of the composite endpoint, obtained from separate logistic regression models, was used to estimate discrimination as the area under the ROC curve. Analyses were conducted in the entire study sample and separately in the two STS-defined groups at low- and intermediate-high risk. Additional analyses tested the predictive ability of each SPPB individual test.

Protection from type I error was set at an α level of 0.05.

Table 2
Hospital outcomes, according to STS risk category, as defined in Table 1.

	STS-PROM risk category			p value
	Low (*n* = 144)	Intermediate (*n* = 67)	High (*n* = 24)	
ICU length of stay, hours	47.2 ± 8.2	50.7 ± 8.1	70.2 ± 11.8	0.288
ICU staying >72 h	15 (10)	10 (15)	8 (33)	0.006
Duration of invasive ventilation, hours	15.9 ± 7.7	13.2 ± 2.8	25.9 ± 9.7	0.723
Invasive ventilation >24 h	6 (4)	4 (6)	7 (29)	<0.001
Length of stay, days	14.3 ± 0.6	15.9 ± 0.8	20.8 ± 3.5	0.001
Prolonged length of stay	58 (41)	33 (49)	14 (58)	0.074
Death	2 (1)	2 (3)	1 (4)	0.306
Stroke	4 (3)	2 (3)	0	0.566
Reoperation	3 (2)	2 (3)	3 (13)	0.030
Acute kidney failure	14 (10)	16 (24)	10 (42)	0.001
Deep sternal wound infection	0	0	0	–
Composite endpoint	27 (19)	23 (34)	12 (50)	<0.001

Data are mean (SEM) or n (%).
Abbreviations. ICU: Intensive Care Unit.
P-values are from ANOVA (continuous variables) or chi square (categorical variables) tests for trend.

3. Results

3.1. Study population

In the enrollment timeframe, 457 patients fulfilled the selection criteria and were eligible for the study. This figure represented approximately 22% of those aged 75+ and scheduled for elective cardiac surgery in the Careggi Hospital Unit, most of whom were not eligible because of a non-STS compatible surgical procedure or residence outside the Florence metropolitan area. Of those eligible, 193 could not be enrolled because their preoperative assessment was scheduled when the geriatrician was unavailable, whereas other 29 were enrolled but could not be considered for the study because of missing data. Thus, the final study sample included 235 participants (51.4% of the eligible patients), whose mean age (±SEM) was 79.6 ± 0.2 years; 105 (44.7%) participants were aged 80+ years and women were 109 (46.4%). Isolated CABG was performed in 38 patients (16.2%), isolated aortic or mitral valve surgery in 90 (38.3%), and combined CABG plus aortic or mitral valve surgery in 107 (45.5%). In comparison to the 235 who were eventually enrolled, the 222 who were not had comparable age (79.8 ± 0.3 years; $p = 0.548$) and proportion of men (62.2%; $p = 0.064$); conversely, more participants received coronary and valve surgery combined (39.0%), compared to isolated CABG (6.8%) and valve surgery (54.2%; $p<0.001$).

One hundred forty-four participants (61.3%) were classified by STS-PROM score as low-risk, 67 (28.5%) as intermediate-risk and 24 (10.2%) as high-risk. The SPPB score was 8.0 ± 0.2 in the whole series and increased with decreasing STS-PROM risk status, being 6.0 ± 0.8 in high, 7.0 ± 0.5 in intermediate, and 8.8 ± 0.2 in low-risk participants ($p<0.001$). Sixty-two participants (26.4%) could be defined as more severely impaired because of an SPPB score <7; their prevalence was greater in the high-risk class ($p<0.001$), whose participants were also older, more functionally dependent and with more comorbidities (Table 1).

Five participants died in-hospital, 17 required prolonged invasive ventilation, 8 were re-operated, 40 had acute kidney failure and six a stroke; no deep sternal wound infection or mediastinitis were observed. Overall, 62 participants (26.4%) experienced one or more of the events included in the primary composite endpoint, with a total of 76 major complications as above defined. As shown in Table 2, the composite endpoint, as well as some of the individual complications contributing to

Table 3
Bivariate predictors of the composite endpoint (CE) in the whole study sample and in low risk participants, as defined in Table 1.

	Whole study sample			Low risk		
	CE no (173)	CE yes (62)	p value	CE no (117)	CE yes (27)	p value
Age, years	79.6 ± 0.3	79.5 ± 0.5	0.907	78.8 ± 0.3	77.6 ± 0.5	0.071
Male	88 (51)	38 (61)	0.158	72 (62)	18 (69)	0.620
BMI, kg/m^2	26.0 ± 0.3	25.7 ± 0.4	0.612	26.0 ± 0.3	26.4 ± 0.7	0.573
Type of surgery						
- CABG	33 (19)	5 (8)	0.080	28 (24)	4 (14)	0.405
- Isolated valve surgery	67 (39)	23 (37)		55 (47)	12 (46)	
- Combined surgery	73 (42)	34 (55)		34 (29)	11 (42)	
EuroSCORE II,%	4.2 ± 0.3	6.5 ± 0.7	0.004	2.9 ± 0.1	3.5 ± 0.4	0.157
STS-PROM,%	3.8 ± 0.2	6.8 ± 1.0	0.005	2.4 ± 0.1	2.7 ± 0.1	0.109
STS-MM,%	20.6 ± 0.7	30.0 ± 2.1	<0.001	15.8 ± 0.4	18.3 ± 0.9	0.007
Hypertension	139 (80)	59 (95)	0.006	93 (80)	26 (100)	0.038
Type 2 Diabetes	37 (21)	19 (31)	0.142	22 (19)	8 (31)	0.212
Insulin-requiring Diabetes	14 (8)	9 (15)	0.144	7 (6)	3 (12)	0.345
History of CAD	86 (50)	32 (52)	0.797	55 (47)	12 (46)	0.810
Heart failure	102 (59)	42 (68)	0.223	62 (53)	14 (54)	0.915
NYHA class III-IV	67 (39)	33 (53)	0.051	40 (34)	10 (39)	0.779
History of stroke	10 (6)	10 (16)	0.012	6 (5)	3 (12)	0.247
CKD	44 (25)	28 (45)	0.004	22 (19)	11 (42)	0.014
Atrial fibrillation	38 (22)	20 (32)	0.107	22 (19)	5 (19)	0.973
COPD	20 (12)	12 (19)	0.125	8 (7)	4 (15)	0.176
PAD	8 (5)	9 (15)	0.010	5 (4)	6 (23)	0.002
LVEF,%	57.3 ± 0.8	54.4 ± 1.6	0.105	58.9 ± 0.8	58.0 ± 2.0	0.666
TAPSE, mm	22.3 ± 0.3	21.4 ± 0.5	0.148	22.7 ± 0.4	22.3 ± 0.8	0.663
Hemoglobin, mg/dl	12.6 ± 0.1	11.9 ± 0.2	0.006	12.9 ± 0.1	12.3 ± 0.4	0.122
Anemia	74 (43)	41 (66)	0.002	46 (39)	16 (62)	0.059
Creatinine, mg/dl	1.0 ± 0.0	1.3 ± 0.1	<0.001	0.9 ± 0.0	1.1 ± 0.1	0.043
eGFR, ml/min/1.73 m^2	63.9 ± 4.5	50.4 ± 2.6	0.082	70.9 ± 6.5	61.2 ± 3.9	0.478
SPPB total score	8.5 ± 0.2	6.7 ± 0.5	<0.001	9.3 ± 0.2	7.0 ± 0.7	0.004
IDS score	9.1 ± 0.2	11.3 ± 0.5	<0.001	8.4 ± 0.3	9.9 ± 0.7	0.029
BADL lost	0.3 ± 0.0	0.3 ± 0.1	0.790	0.2 ± 0.0	0.1 ± 0.1	0.193
IADL lost	1.0 ± 0.1	1.7 ± 0.2	0.011	0.7 ± 0.1	1.4 ± 0.4	0.032
Abnormal MiniCog	85 (49)	35 (57)	0.362	51 (44)	12 (46)	0.936
GDS	1.2 ± 0.1	1.3 ± 0.2	0.535	1.0 ± 0.1	1.4 ± 0.3	0.095
Number of drugs	6.1 ± 0.2	6.6 ± 0.3	0.208	5.7 ± 0.2	6.1 ± 0.4	0.376

Data are mean (SEM) or n (%).
Abbreviations as in Table 1.

Table 4
Multivariable prediction of the composite endpoint, separately in the whole study population and in low risk participants, as defined in Table 1. Logistic regression models with backward deletion of redundant variables.

	Whole study sample		Low-risk participants	
	OR (95% CI)	p value	OR (95% CI)	p value
STS-MM,%	1.05 (1.03–1.08)	<0.001	1.16 (1.04–1.29)	0.007
SPPB total score	0.90 (0.83–0.99)	0.030	0.77 (0.66–0.89)	0.001

Abbreviations as in Table 1.
Variables backward removed from the model in the whole study population: EuroSCORE II, STS-PROM, hypertension, chronic obstructive pulmonary disease, peripheral artery disease, hemoglobin, left ventricular ejection fraction, creatinine, estimated glomerular filtration rate, Index of Disease Severity. Variables backward removed from the model in the low risk population: hypertension, peripheral artery disease, hemoglobin, anemia, creatinine, Index of Disease Severity, Instrumental Activities of Daily Living, chronic kidney disease, Geriatric Depression Scale.

it (prolonged invasive ventilation, reoperation, and acute kidney failure), occurred progressively more often across the three classes of risk defined by the STS-PROM.

In bivariate analyses, many pre-operative variables were associated with the composite endpoint (Table 3). A multivariable logistic regression model was built, which included age, gender, and all the variables that, at bivariate comparisons, were significantly associated with the composite endpoint. In the final model, after backward removal of redundant variables, the SPPB total score resulted an independent predictor of the composite endpoint in the entire study population, controlling for STS-MM score. Using the probability of the composite endpoint, as predicted by this logistic regression model, to estimate discrimination in ROC plots, an area under the ROC curve (AUC) of 0.741 was obtained.

When analyses were repeated separately for participants with STS-PROM indicative of low (<4%) or medium-high risk, the predictive value of SPPB was enhanced in the formers, whereas was lost in the latter. In the first subgroup, for each point increase in the SPPB score, the

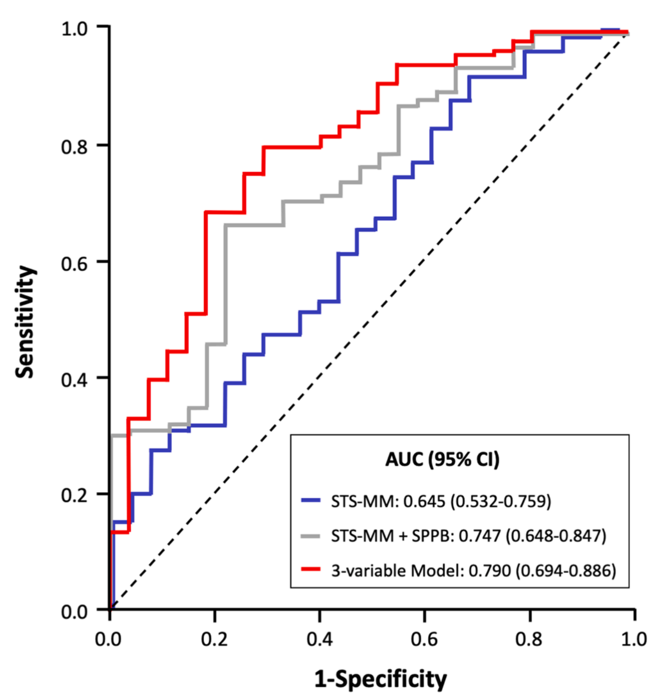

Fig. 1. Area under the ROC curve for composite endpoint in low-risk population based on the predicted probability obtained from STS-Major Morbidity or Operative Mortality (STS-MM), STS-MM and Short Physical Performance Battery and from the 3-variable Model.

Table 5
Bivariate predictors of prolonged length of stay in the whole study sample and in low risk participants (as defined in Table 1).

	Whole study sample			Low-risk participants		
	PLOS no (n = 126)	PLOS yes (n = 104)	p value	PLOS no (n = 83)	PLOS yes (n = 59)	p value
Age, years	79.6 ± 0.3	79.4 ± 0.3	0.722	78.5 ± 0.3	78.6 ± 0.4	0.811
Male	62 (49)	62 (60)	0.115	47 (57)	41 (70)	0.077
BMI, kg/m^2	26.3 ± 0.4	25.5 ± 0.3	0.158	26.6 ± 0.4	25.4 ± 0.4	0.047
Type of surgery						
- CABG	22 (17)	16 (15)	0.002	18 (22)	14 (24)	0.085
- Isolated valve surgery	59 (47)	28 (27)		44 (53)	21 (36)	
- Combined surgery	45 (36)	60 (58)		21 (25)	24 (41)	
EuroSCORE II, %	4.3 ± 0.3	5.4 ± 0.5	0.069	2.8 ± 0.2	3.2 ± 0.2	0.177
STS-PROM,%	4.0 ± 0.3	5.2 ± 0.6	0.079	2.4 ± 0.1	2.5 ± 0.1	0.500
STS-MM,%	21.1 ± 0.9	25.3 ± 1.4	0.011	15.7 ± 0.5	17.0 ± 0.6	0.105
STS-LLS,%	10.0 ± 0.6	13.5 ± 1.2	0.008	6.8 ± 0.5	7.1 ± 0.3	0.612
Hypertension	102 (81)	91 (88)	0.179	67 (81)	50 (85)	0.535
Type 2 Diabetes	25 (20)	30 (29)	0.111	17 (20)	12 (20)	0.983
Insulin-requiring Diabetes	8 (6)	15 (14)	0.042	5 (6)	5 (9)	0.574
History of CAD	49 (39)	66 (63)	<0.001	33 (40)	33 (56)	0.057
Heart failure	76 (60)	63 (61)	0.968	44 (53)	30 (51)	0.799
NYHA class III-IV	46 (37)	50 (48)	0.085	25 (30)	23 (39)	0.271
History of stroke	6 (5)	13 (13)	0.034	3 (4)	6 (10)	0.114
CKD	40 (32)	29 (28)	0.525	19 (23)	13 (22)	0.904
Atrial fibrillation	26 (21)	29 (28)	0.200	13 (16)	13 (22)	0.333
COPD	13 (10)	18 (17)	0.122	6 (7)	5 (9)	0.784
PAD	10 (8)	7 (7)	0.728	6 (7)	5 (9)	0.784
LVEF,%	58.2 ± 0.9	54.6 ± 1.2	0.015	59.8 ± 0.9	57.3 ± 1.3	0.106
TAPSE, mm	22.6 ± 0.4	21.5 ± 0.4	0.060	23.4 ± 0.5	21.2 ± 0.6	0.023
Hemoglobin, mg/dl	12.7 ± 0.2	12.2 ± 0.2	0.041	12.9 ± 0.2	12.6 ± 0.2	0.313
Anemia	53 (42)	57 (55)	0.054	30 (36)	30 (51)	0.080
Creatinine, mg/dl	1.0 ± 0.0	1.3 ± 0.1	0.348	1.0 ± 0.0	1.0 ± 0.0	0.567
eGFR, ml/min/ 1,73m^2	63.5 ± 6.2	57.3 ± 1.	0.374	73.3 ± 9.1	63.3 ± 2.1	0.366
SPPB total score	8.9 ± 0.3	7.1 ± 0.3	<0.001	9.5 ± 0.3	8.1 ± 0.4	0.002
IDS score	9.0 ± 0.3	10.3 ± 0.4	0.008	8.5 ± 0.3	9.0 ± 0.4	0.412
BADL lost	0.3 ± 0.0	0.3 ± 0.1	0.931	0.2 ± 0.1	0.2 ± 0.1	0.747
IADL lost	1.1 ± 0.2	1.2 ± 0.2	0.569	0.8 ± 0.2	1.0 ± 0.2	0.509
Abnormal MiniCog	54 (43)	64 (62)	0.005	29 (35)	32 (54)	0.022
GDS	1.0 ± 0.1	1.3 ± 0.1	0.074	0.8 ± 0.1	1.4 ± 0.2	0.005
Drug number	5.9 ± 0.2	6.6 ± 0.2	0.020	5.5 ± 0.2	6.1 ± 0.3	0.162

Abbreviations: STS-LLS: STS Long Length of stay; other abbreviations as in Table 1.

risk of the composite outcome increased by 23%, controlling for STS-MM score; all the other potential predictors were backward removed as redundant (Table 4). The ROC AUC based on the predicted probability from this logistic regression model was 0.747.

The results of the additional analyses conducted to examine the role of each SPPB individual test are summarized in an online-only Appendix. All the three tests showed significant differences across the three STS-PROM risk categories (Appendix, Table A1), as well between participants who did and did not reach the composite endpoint in bivariate comparisons (Appendix, Table A2). The 4-m walk and the repeated chair standing, but not the balance test, resulted as significant independent predictors of the composite endpoint, both in the entire study sample and in the low-risk subgroup, always together with the STS-MM score (Appendix, Tables A3 and A4).

An alternative model was also tested, where the STS-MM score was not included and peripheral artery disease and creatinine – two variables that contribute to the STS-MM score and that resulted as predictors in our bivariate comparisons – were conversely entered. The SPPB was confirmed as a significant predictor also in this model, with an OR (95% CI) of 0.73 (0.62–0.86) per each unit increase (p<0.001). Peripheral artery disease and creatinine remained significant predictors of the combined outcome, with ORs (95% CI) of 5.81 (1.31–25.3) and 5.46 (1.29–23.15) and p values of 0.023 and 0.019, respectively. Hypertension, hemoglobin, presence of anemia, IDS, GDS and IADL scores, and history of chronic kidney disease, entered in various combinations, were always removed as redundant from the final parsimonious model, which achieved a ROC AUC of 0.790 (3-variable Model; Fig. 1). The SPPB was not associated with the composite endpoint in the medium-high risk group (SPPB mean score 5.0 ± 0.5 vs. 5.5 ± 0.6, p = 0.523), which was predicted only by the STS-MM and IDS scores, creatinine, male gender and presence of anemia.

3.2. *Predictors of prolonged length of stay*

PLOS occurred in 104 (45.2%) participants, without significant differences in the three STS-PROM classes (p = 0.202; Table 2). Many preoperative variables were associated to PLOS in bivariate analyses in the whole series, but only the SPPB and the MiniCog maintained their predictive ability also in the subgroup of low-risk participants (Table 5). Bivariate predictors were entered into a multivariable logistic regression model predicting PLOS, whose final, parsimonious version showed that the SPPB score remained a strong independent predictor (OR 0.84; 95% CI 0.76–0.94; p = 0.002), together with MiniCog (OR 2.02; 95% CI 1.08–3.79; p = 0.027), number of drugs (OR 1.15; 95% CI 1.00–1.31; p = 0.048) and male gender (OR 0.49; 95% CI 0.25–0.95; p = 0.035). When this set of variables was tested in two logistic regression models, separately for participants at low or intermediate-high risk as defined above, the SPPB remained predictive of PLOS in both subgroups: the risk of PLOS was reduced by 20% (OR 0.80; 95%CI 0.67–0.95; p = 0.010) and 13% (OR 0.87; 95% CI 0.76–0.99; p = 0.036) for each point increase in the SPPB score, respectively. Neither STS-long length of stay nor EuroSCORE II predicted this outcome in either subgroup.

4. Discussion

In our older participants candidate to elective cardiac surgery, the SPPB improved the short-term risk stratification (morbidity and mortality, PLOS), compared to the STS, in particular in low-risk participants.

Hospital mortality after cardiac surgery has remained unchanged over the years, being nowadays around 5% [1,19]; conversely, serious post-operative complications remain very frequent, possibly because of the increasing age and, hence, growing complexity of patients [20]. In frail older patients, hospitalization is *per se* associated with declining muscle strength and mass [21], incident sarcopenia [22], and loss of functional autonomy [23], especially in the presence of complications and PLOS. Therefore, more than pure survival, disability-free survival and good quality of the residual life are desirable goals of care and of prognostic assessment in these patients [24].

In line with major international reports [1,19], hospital mortality in our sample was as low as 2.1%, with no differences across the three risk groups; conversely, complications contributing to the composite endpoint and PLOS were observed in as many as 26.4% and 45.1% of our participants, respectively. Although STS-PROM was shown to provide good initial risk screening in respect to these important endpoints, other variables added substantial predictive power. In detail, in patients defined as at low-risk by the STS-PROM, the SPPB, creatinine levels and peripheral artery disease improved the prediction of major complications, as shown by the AUC of 0.790.

Robust evidence has been provided that comprehensive geriatric assessment [25], and measures of physical performance in particular [8, 10,11,25], may add clinically valuable predictive information. Physical performance is one of the cornerstones of the frailty framework [13,24]. In a prospective multicenter cohort of patients aged 70+ years, the addition of frailty and disability, defined by gait speed and Nagi score, respectively, improved the prediction of postoperative mortality and major morbidity over STS PROM score, with AOUCs increasing from 0.68 to 0.73 [6]. Among others, gait speed is the most commonly investigated performance measure: a recent original investigation conducted in a large cohort of patients with median age of 71 years demonstrated that each 0.1 m/s reduction in gait speed confers an 11% relative increase in mortality [9]. However, few studies have investigated if pre-operative measures were able to predict the onset of in-hospital complications [20]. Afilalo et al. for the first time demonstrated that preoperatively slow-walker patients (≥6 s to walk 5 m) had an independent higher risk of 30-day mortality and major morbidity for any given levels of STS-Predicted Risk score [9]. The same authors have recently developed and tested, in a large cohort of patients undergoing aortic valve replacement, a frailty score [26] that includes chair standing, a simple cognitive test, hemoglobin, and serum albumin.

The SPPB offers a combined assessment of balance, gait speed, and strength of lower limbs, thus including both the physical performance measures separately tested by Afilalo. Initially shown to predict incident mobility disability in unselected older persons in the community [10], the SPPB has been subsequently used also in the clinical arena, where it was able to predict long-term survival of older patients discharged from the hospital after an episode of acute heart failure, independent of NYHA class, left ventricular ejection fraction, and comorbidity [11]. It therefore appears that the tool reflects thoroughly the burden of functional limitations, due to multimorbidity or to other age-related changes, including sarcopenia [27], whose association with clinical outcomes in non-cardiac surgery has been proven [28].

Our data show that, for each point decrease in SPPB score, the risk of the composite endpoint increased respectively by 10% in the whole study sample and by 23% in the STS-PROM low-risk group. SPPB score was able to predict also PLOS, whose risk increased by 16% in the whole study sample and by 20% in the STS-PROM low-risk group for each 1-point decrease in SPPB score. Walking speed has already been shown to influence length of hospital stay among 1123 older adults admitted to acute care wards [29]; in fact, patients with a gait speed ≥0.8 m/s were less likely to stay in hospital more than ten days. Similarly, SPPB was significantly and inversely associated with length of hospital stay in 90 older patients admitted to acute wards ($b = -0.36$, SEM 0.15, $p = 0.02$) [30]. Therefore, we would offer that SPPB might contribute to better allocate hospital resources, by identifying persons at an increased risk of PLOS.

The lower predictive ability of the SPPB in intermediate-high risk patients seems to suggest that conventional risk stratification is adequate in patients with poor global health status and severe comorbidity, in whom adding assessment of physical performance might offer limited advantage. However, this issue deserves further studies. Older patients deemed to be at a low-risk are the only ones in whom cardiac surgery is strictly recommended, whereas percutaneous procedures are preferable in intermediate- and high-risk patients in the most recent European guidelines [31]. However, an extension of percutaneous techniques to low-risk patients (STS<4) is to be expected in the next future, after the recent PARTNER 3 [32] and Evolut Low Risk [33] trials, in which transcatheter aortic valve replacement was respectively superior and non-inferior to surgery in this subset, for the composite outcome of all-cause mortality, major stroke and re-operation. Thus, our findings on how to improve risk stratification in low-risk patients may provide particularly important information in the choice between the two alternatives, should this new evidence be confirmed and incorporated in updated guidelines. Furthermore, our findings may help select patients in whom pre-habilitation, i.e. structured preoperative programs combining nutritional and physiotherapy interventions [34], may be particularly effective.

4.1. Study limitations

This study has several limitations. The sample size was numerically limited, also because we focused on patients who were expected to receive surgical procedures included in STS risk scores calculator, whereas older persons often receive more complex interventions. On the other hand, compared to other studies, mean age of our participants was remarkably high. Testing the prognostic value of geriatric assessment, including the SPPB, in the large share of older patients that receive procedures not suitable to risk stratification with the STS may represent an additional venue of future research. Our limited resources did not allow us to perform geriatric assessment systematically in all potential candidates. However, patients were scheduled for pre-operative surgical evaluation independent of the presence of geriatricians and, indeed, patients who met the inclusion criteria had comparable demographics. The different distribution of surgical procedures between patients enrolled and not enrolled might have, at most, introduced a conservative bias, because our participants more often received combined, more complex procedures. Details on surgical procedures were not consistently available in the database and, therefore, could not be used in the analyses. Finally, only in-hospital endpoints were considered, whereas other outcomes, such as functional and cognitive status after hospital discharge, which are very important in a geriatric perspective, could not be considered.

5. Conclusions

In our cohort of older persons, the SPPB independently predicted hard, short-term outcomes such as mortality, morbidity, and PLOS in patients otherwise considered at low risk, according to standard cardiac surgery stratification systems. Therefore, this tool may provide useful to improve preoperative risk stratification. Further studies are needed to confirm these findings in wider populations and with extended follow-up, to detect changes in independency as well as in functional and cognitive status, which are particularly relevant in a geriatric perspective.

Declaration of Competing Interest

As far as the manuscript entitled “Pre-operative physical performance as a predictor of in-hospital outcomes in older patients undergoing elective cardiac surgery”, which has been submitted to the European Journal of Internal Medicine, all the authors reported below declare no conflict of interest.

Acknowledgements

This paper is dedicated to the memory of our dear friend and colleague, Dr. Alessandra Rossi, prematurely and grimly passed away, whose contribution was crucial to the development and conduction of this study.

With the unconditional support of A.R. Card Onlus Foundation.

Appendix

Tables A1, A2, A3, A4.

Table A1
Comparison of individual SPPB test scores across STS risk categories.

	STS-PROM risk category			p value
	Low ($n = 144$)	Intermediate ($n = 67$)	High ($n = 24$)	
Balance	3.4 ± 0.8	2.8 ± 0.2	2.4 ± 0.3	<0.001
4-m walk	3.3 ± 0.1	2.6 ± 0.2	2.2 ± 0.3	<0.001
Repeated chair standing	2.3 ± 0.1	1.6 ± 0.2	1.5 ± 0.3	0.011

Data are mean (SEM).
P-values are from ANOVA test for trend.

Table A2
Comparison of individual SPPB test scores between participants who did or did not reach the composite endpoint (CE), separately in the whole study population and in low risk participants.

	Whole study sample			Low risk		
	CE no (173)	CE yes (62)	p value	CE no (117)	CE yes (27)	p value
Balance	3.2 ± 0.1	2.9 ± 0.2	0.077	3.5 ± 0.1	3.0 ± 0.3	0.025
4-m walk	3.2 ± 0.09	2.4 ± 0.17	<0.001	3.4 ± 0.8	2.6 ± 0.3	0.004
Repeated chair standing	2.2 ± 0.10	1.4 ± 0.17	<0.001	2.5 ± 0.1	1.4 ± 0.3	<0.001

Data are mean (SEM).
P-values are from *t*-test for independent samples.

Table A3
Multivariable prediction of the composite endpoint, separately in the whole study population and in low risk participants, based on the 4-m walk test score. Logistic regression models with backward deletion of redundant variables.

	Whole study sample		Low-risk participants	
	OR (95% CI)	p value	OR (95% CI)	p value
Gender (F vs. M)	0.47 (0.24–0.94)	0.031	——	NS
Age, years	——-	NS	0.81 (0.67–0.98)	0.026
STS-MM,%	1.05 (1.02–1.08)	0.004	1.16 (1.04–1.29)	0.007
SPPB 4-m walk	0.70 (0.54–0.91)	0.009	0.42 (0.26–0.66)	<0.001

Variables backward removed from the model in the whole study population: age, EuroSCORE II, STS-PROM, hypertension, chronic obstructive pulmonary disease, peripheral artery disease, hemoglobin, left ventricular ejection fraction, creatinine, estimated glomerular filtration rate, Index of Disease Severity. Variables backward removed from the model in the low risk population: anemia, Index of Disease Severity, Instrumental Activities of Daily Living, chronic kidney disease, estimated glomerular filtration rate, Clock Drawing Test score.

Table A4
Multivariable prediction of the composite endpoint, separately in the whole study population and in low risk participants, based on the repeated chair standing score. Logistic regression models with backward deletion of redundant variables.

	Whole study sample		Low-risk participants	
	OR (95% CI)	p value	OR (95% CI)	p value
Gender (F vs. M)	0.47 (0.24–0.94)	0.031	——-	NS
STS-MM,%	1.05 (1.02–1.08)	0.004	1.17 (1.05–1.32)	0.005
Repeated chair standing	0.70 (0.54–0.91)	0.009	0.47 (0.31–0.71)	<0.001

Abbreviations as in Table 1.
Variables backward removed from the model in the whole study population: age, EuroSCORE II, STS-PROM, hypertension, chronic obstructive pulmonary disease, peripheral artery disease, hemoglobin, left ventricular ejection fraction, creatinine, estimated glomerular filtration rate, Index of Disease Severity. Variables backward removed from the model in the low risk population: anemia, Index of Disease Severity, Instrumental Activities of Daily Living, chronic kidney disease, estimated glomerular filtration rate, Clock Drawing Test score.
In logistic regression models with backward deletion of redundant variables, **the balance test did not result as a multivariable predictor of the composite endpoint**, nor in the whole study population neither in low risk participants (data not shown).

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