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ORIGINAL ARTICLE / ÖZGÜN MAKALE

Which frailty score in cardiac surgery patients?

Kalp cerrahisinde hangi kırılganlık testi?

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ABSTRACT

Background: Frailty assessment for risk prediction is suggested in elderly patients undergoing cardiac surgery. We aimed to compare five different frailty tests.

Methods: Relation of Edmonton Frailty Score (EFS), Fried Frailty Phenotype (FFP), FRAIL (Fatigue, Resistance, Ambulation, Illness, and Loss of weight), Katz and hand grip strength (HGS) tests to each other, postoperative outcomes and mortality rates were evaluated prospectively in 140 consecutive patients aged ≥65 years.

Results: The median follow-up period was 880.5 (range, 0 to 1,237) days with higher EFS and FFP scores in non-survivors (p<0.05). Patients with any complication had higher EFS (p=0.002), FFP (p=0.004) and FRAIL (p=0,006) scores. Compared to non-frail patients, frail patients' NYHA capacity, EuroSCORE II and STS mortality risks were higher; hemoglobin values and HGS were lower with EFS, FFP, and FRAIL tests. Frail patients' hospitalization periods with EFS (p=0.003) and intensive care unit stay with FFP (p=0.029) were longer. No mortality was observed in non-frail patients according to the FFP test. The Kaplan-Meier (KM) log-rank survival curves showed significant differences in favor of non-frail subgroups according to EFS, FFP and HGS tests (p<0.05). Relative risks for mortality in frail and pre-frail patients were between 0.9 and 4. The FFP was the most sensitive test (area under curve=0.721). There was discordance rather than concordance among five different tests (Kappa <0.411).

Conclusion: For patients aged ≥65 years undergoing heart surgery the FFP can be used safely to determine non-frail patients. Although the EFS seems to be promising to identify frail patients, further large-scale studies using various tests are needed to predict an optimal cut-off value for this patient population.

Keywords: Cardiac surgery, elderly, frail, frailty.

ÖZ

Amaç: Yaşlı hastalarda açık kalp cerrahisi riski hesaplanırken kırılganlığın dikkate alınması önerilir. Ancak bu konuda kararlaştırılmış uygun bir test olmadığı için, beş farklı kırılganlık testini karşılaştırmayı amaçladık.

Çalışma planı: Ardışık, 65 yaş ve üzeri, 140 hastada prospektif olarak Edmonton Kırılganlık Ölçeği (EFS), Fried Kırılganlık Fenotipi (FFP), FRAIL, Katz ve el kavrama gücü (HGS) testlerinin birbiriyle, ameliyat sonrası sonuçlarla ve mortaliteyle ilişkisi araştırılmıştır.

Bulgular: Hastalar median 880.5 (dağılım, 0-1237) gün izlenmiş, kaybedilen hastalarda EFS ve FFP skorları, komplikasyon geçiren hastalarda ise EFS (p=0.002), FFP (p=0.004) ve FRAIL skorları (p=0.006) yüksekti. EFS, FFP ve FRAIL testine göre, kırılgan hastalarda New York Heart Association kapasitesi, EuroSCORE II ve STS mortalite riski daha yüksek; hemoglobin değeri, HGS daha düşüktü. Kırılgan altgruplarda EFS testine göre hastanede kalış (p=0.003), FFP testine göre ise yoğun bakım kalış süresi uzundu (p=0.029). Kırılgan olmayan FFP alt grubunda mortalite gözlenmedi. Kaplan-Meier log-rank sağ kalım eğrileri, EFS, FFP ve HGS testlerine göre kırılgan olmayanlar lehine anlamlı farklılık gösterdi (p<0.05). Kırılgan ve kırılganlık öncesi dönemde olan hastalarda mortalite için rölatif risk, 0.9 ile 4.6 arasında değişmekteydi. En duyarlı test FFP skalasıydı (eğri altındaki alan=0.721). Kappa istatistiğine göre beş test arasında uyumdan çok uyumsuzluk vardı (Kappa <0.411).

Sonuç: Açık kalp cerrahisi yapılacak ≥65 yaş hastalarda, kırılgan olmayanların belirlenmesinde FFP testi güvenle kullanılabilir. Kırılgan hastaların belirlenmesinde EFS ümit verici olsa da, bu hasta grubunda optimum bir kesme değeri belirlemek için farklı testlerin kullanıldığı geniş ölçekli başka çalışmalara gereksinim vardır.

Anahtar sözcükler: Kalp cerrahisi, yaşlı, kırılgan, kırılganlık.

Frailty is described as a biological syndrome characterized by a decline in physiological reserve and being more fragile to stressors such as acute or chronic illnesses or surgical procedures with resultant adverse health outcomes.[1,2] Being a great stressor, cardiac surgery deals with more elderly patients with worse clinical profiles, as life expectancy increases. Frailty screening for elderly patients objectively may

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have important aspects for risk reduction by taking preoperative precautions to increase the strength of the patients such as nutritional support, respiratory muscles reinforcement, exercise, and treatment of reversible comorbidities such as hypothyroidism, anemia, or depression. There are numerous frailty tests which differ widely with respect to their evaluation criteria and with no consensus on the most optimal test to be used preoperatively according to cardiac surgery guidelines.[3-6]

The number of studies regarding frailty assessment before cardiac surgery in Turkish literature is extremely limited and there is an unmet need for deciding surgery or otherwise less invasive percutaneous procedures in elderly and seemingly frail patients.[7] In the present study, we aimed to compare five frailty tests with different properties, namely Edmonton Frailty Scale (EFS), Fried Frailty Phenotype (FFP), Fatigue, Resistance, Ambulation, Illness, and Loss of weight (FRAIL), Katz, and hand grip strength (HGS) tests, and to evaluate concordance/discordance between the test pairs. Our secondary objective was to identify the most useful test in cardiac surgery patients for future use.

PATIENTS AND METHODS

Study design and study population

This single-center, prospective study was conducted at Ankara Bilkent City Hospital, Department of Cardiovascular Surgery between September 2021 and February 2023. Patients who were scheduled for cardiac surgery were screened. Inclusion criteria were as follows: age ≥65 years; having coronary artery disease and/or heart valve pathology or ascending and/or aortic arch aneurysm. Exclusion criteria were as follows: emergent cases, age <65 years or having either mental or physical disability precluding the patients from performing the tests. No patient was denied surgery based on detected frailty level and the surgeons were blinded to the test results. Finally, a total of 140 consecutive patients (92 males, 48 females; mean age: 70.0±4.0; range, 65 to 84 years) who met the inclusion criteria were recruited. A written informed consent was obtained from each patient. The study protocol was approved by the Ankara City Hospital Clinical Research (date: 28.04.2021, no: E1-21-1775). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data collection and definitions

Demographics, comorbidities, and pre- and postoperative data were recorded. The European System for Cardiac Operative Risk Evaluation (EuroSCORE II) and Society of Thoracic Surgeons (STS) mortality and morbidity risks (renal failure, cerebrovascular accident, prolonged ventilation, re-operation, morbidity, and prolonged hospitalization) were calculated for each patient.

Hospital mortality was defined as the mortality occurred during the index hospitalization of the patient even after 30 days. Late mortality was defined as mortality occurring after 30 days following discharge. Complications were defined as prolonged ventilation (mechanical ventilatory support lasting more than 24 h), the presence of deep sternal infection (requiring operative intervention), pneumonia (positive cultures with radiological evidence), psychological (any disorder requiring medical therapy), acute renal failure (new requirement for dialysis), stroke (symptoms not resolving after 24 h), re-operation (surgical re-exploration due to bleeding with or without any cardiac problem), atrial fibrillation, postoperative inotropic medication (lasting more than 24 h with more than one type of inotropic agent), incision complication (any incision requiring debridement or secondary suturing with positive wound culture), sepsis (positive blood culture requiring intense antibiotic therapy).

Frailty tests

The patients were asked to perform EFS, FFP, FRAIL, and Katz questionnaire.[1,2,5,6,8] The term prefrailty or vulnerability is used to define a condition predisposing to frailty. The EFS has 10 domains, two of which measure physical performance (time to get-up, walk 3 m then back and sit down) and cognitive ability. The rest are questions about mood, functional independence, medications, nutrition, social support, continence, and general health status. The score ranges between 0 and 17, with cut-off values for frailty ≥8, pre-frailty 6-7, and non-frailty ≤5 points.[8] The FFP scale has two domains to test upper (hand grip) and lower extremity (walking speed) strength and three questions regarding unintentional weight loss, exhaustion, or low physical activity. Deficiency in ≥3 features is defined as frailty, 1 or 2 features as pre-frailty.[1] Both tests take 10 to 15 min according to the educational and physical capability of the patient. The FRAIL test questions five items; fatigue, resistance, ambulation, illnesses, and weight loss.[2] One or 2 points indicates pre-frailty and ≥3 points frailty. The Katz test is the quickest test to question dependency of the patient about six activities of daily living (ADL; (bathing, dressing,

toileting, transferring, continence, feeding) and ≥1 insufficiency is regarded as dependency.[5] Both tests last less than 5 min. Hand grip strength was performed three times with a digital electronic equipment and the strongest value was recorded (Kyto 2326, Guangdong China). Weakness was defined according to predefined FFP stratified body mass index cut-off values for each sex and patients were grouped as HGS weak or normal.[1]

Statistical analysis

Sample size was calculated based on mortality rates of 14.7% in frail and 4.5% in non-frail patients according to Katz ADL test, and 131 patients for each group were found to be sufficient. Upon reaching 140 patients in total, post-hoc power analysis were 87.9%, 96.8%, 51.6%, 9.2%, and 11.5% for the EFS, FFP, FRAIL, Katz and HGS scores, respectively. As 80% power was exceeded with the EFS and FFP tests we decided to terminate the study.

Statistical analysis was performed using the IBM SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean ± standard deviation (SD) or median (min-max), while categorical data were expressed in number and frequency. Relative risks for mortality were calculated by dividing incidence of a risk variable in non-survivors to that of survivors. Frailty tests in the survivors and non-survivors were analyzed with receiver operating characteristic (ROC) analysis and area under the curve (AUCs) were calculated. Categorical variable distributions were compared in cross tables between the two groups with chi-square and Fisher exact tests. The Mann-Whitney U test was used to compare continuous variables between the two, and the Kruskal-Wallis test for multiple groups. After Kruskal-Wallis tests, significant pairs were identified by Bonferroni post-hoc multiple comparison test. The kappa (κ) statistics were used to test concordance or discordance between pairs of five frailty tests. The Kaplan-Meier test was used for survival analysis and the subgroups were compared by using log-rank test. Correlations between each frailty test, and New York Heart Association (NYHA), STS, or EuroSCORE II were calculated using the Spearman correlation test. A *p* value of <0.05 was considered statistically significant with 95% confidence interval (CI).

RESULTS

The median follow-up was 808.5 (range, 0 to 1,237) days. Isolated coronary artery bypass grafting (CABG) surgery was performed in 58.6% and valve surgery in 21.4% of the patients. Aortic surgery and, CABG with valve surgery, were 10% for each. Demographics, procedures, and pre- and postoperative data are given in Supplement Tables 1 and 2. Fifty-seven patients (40.7%) experienced at least one complication in the postoperative period. Except Katz questionnaire, there were significant differences regarding the median frailty scores between patients with complicated and non-complicated postoperative courses: 4.0 *vs*. 3.0 for EFS (p=0.002), 2.0 *vs*. 1.0 for FFP (p=0.002), and 2.0 *vs*. 1.0 for FRAIL (p=0.002), 6.0 *vs*. 6.0 for Katz (p=0.306), and 25.6 kg *vs*. 29.6 kg for HGS (p=0.025), respectively.

In the present study, frail patients constituted 4.3 to 24.3% of the patients (EFS 4.3%, FFP 24.3%, and FRAIL 23.6%) with more prevalent pre-frail patients (EFS 10.7%, FFP 66.4% and FRAIL 50.7%) according to scales used.

Hospital mortality rate was 5.3% (n=7) and overall mortality was 14.3% (n=13). Owing to enough sample size, EFS and FFP scores both as scale and ordinal, HGS only as ordinal parameter were significantly higher in non-surviving patients compared to survivors (p<0.05 for all) (Table 1). The FRAIL, Katz tests did not reveal any significant difference. Survival rates decreased significantly according to Kaplan-Meier log-rank test, as patients became frailer according to EFS, FFP frailty tests, and HGS test (Figure 1). Relative risks for mortality were between 0.9 and 4.6-fold in frail patients compared to the nonfrail patients (Table 1).

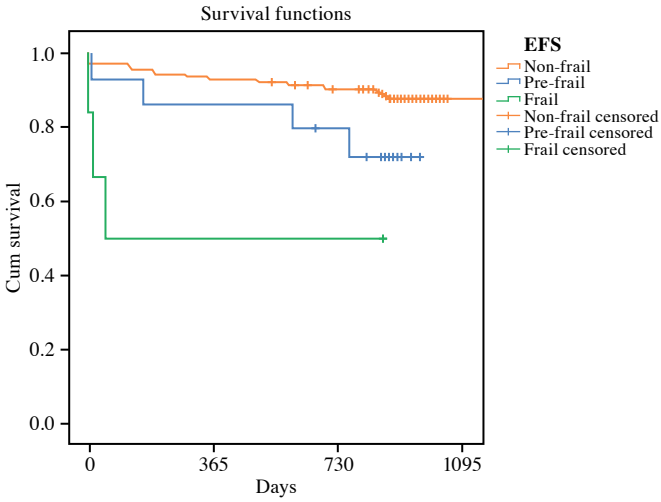
According to EFS and FFP tests, there were statistically significant differences among non-frail, pre-frail, and frail patients regarding preoperative variables (NYHA, hemoglobin, STS and EuroSCORE II risks, and HGS) in favor of non-frail patients. Among postoperative variables, the length of hospital stay in EFS, the length of intensive care unit (ICU) stay, complications, and the need for inotropic support in FFP was also better in non-frail patients (Tables 2 and 3). Although significant differences were observed regarding these preoperative characteristics in patient subgroups according to FRAIL test, no significant difference occurred in the postoperative outcomes (Table 4).

According to the Katz ADL questionnaire, the aforementioned baseline parameters, excluding EuroSCORE II mortality risk, were different between dependent or non-dependent patients. Considering postoperative outcomes, only transfused red blood cell

Table 1. Frailty tests between surviving and non-surviving groups and relative risks for mortality

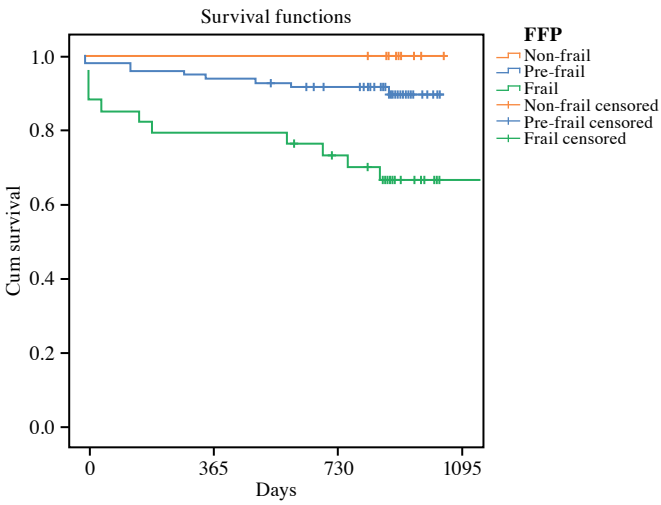
	Non-survivors (n=20)					Survivors (n=120)					Total			
Frailty tests	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	RR	*p*
EFS score			4.9± 2.3	4.5	2-11			3.2±1.9	3.0	0-8				**0.002**
Non-frail (≤5 points)	13[a]	10.9				106	89.1				119	85.0	-	
Pre-frail (6-7 points)	4[b]	26.7				11	73.3				15	10.7	2.4[(b/a)]	**0.010**
Frail (≥8 points)	3[c]	50.0				3	2.5				6	50.0	4.6[(c/a)]	
FFP test			2.6±1.1	3.0	1-5			1.6±1.0	2.0	0-2				**0.001**
Non-frail	0[a]	0.0				13	9.3				13	9.3	*	
Pre-frail	9[b]	9.7				84	70.0				93	66.4		**0.002**
Frail	11[c]	32.4				23	19.2				34	24.3	3.3[(c/b)]	
FRAIL			2.0±1.5	1.5	0-5			1.3±1.1	1.0	0-3				0.057
Non-frail	3[a]	8.3				33	27.5				36	25.7	-	
Pre-frail	9[b]	12.7				62	51.7				71	50.7	1.5[(b/a)]	0.145
Frail	8[c]	24.2				25	20.8				33	23.6	2.9[(c/a)]	
Katz (%)			5.8±0.7	6.0	3-6			5.9±0.3	6.0	5-6				0.888
Independant	18[a]	14.5				106	88.3				124	88.6	-	1.000
Dependant	2[b]	12.5				14	11.7				16	11.4	0.9[(b/a)]	
HGS			26.3±7.0	6.4	14.3-38.4			27.6±7.5	28.3	10.1-41.8				0.459
Normal	7[a]	8.2				78	65.0				85	60.7	-	**0.011**
Weak	13[b]	23.6				42	35.0				55	39.3	2.9[(b/a)]	

SD: Standard deviation; EFS: Edmonton Frail Scale; FFP: Fried Frailty Phenotype; Fatigue; FRAIL: Resistance, Ambulation, Illness, and Loss; HGS: Hand grip strength; * All non-frail patients according to FFP test are alive.

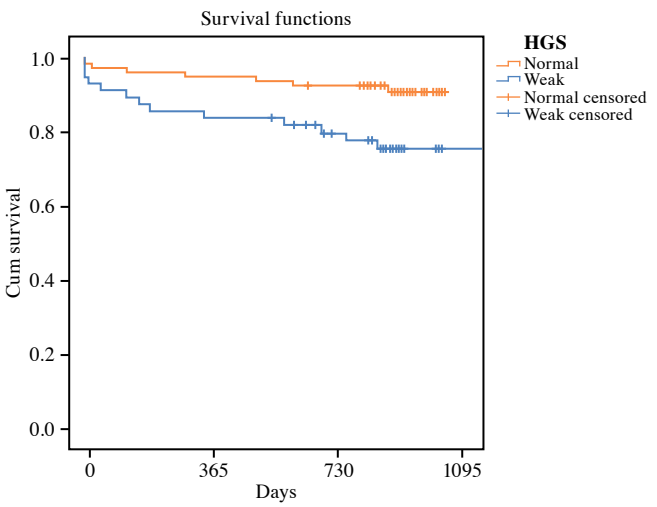


			Mean[a]	
			95% CI	
EFS	Estimate	SE	Lower bound	Upper bound
Non-frail	1137,872	27,229	1084,504	1191,240
Pre-frail	815,048	78,985	660,238	969,859
Frail	443,167	172,720	104,635	781,698
Overall	1101,807	29,376	1044,231	1159,383

CI: Confidence interval; EFS: Edmonton Frailty Scale; SE: Standard error; a: Estimation is limited to the largest survival time if it is censored. LogRank= 14,347; p=0.001<0.01.



Note: No 95% CI statistics are computed because all cases are censored. Log rank= 13,691; p=0.001<0.01.



			Mean[a]	
			95% CI	
HGS	Estimate	SE	Lower bound	Upper bound
Normal	981,534	22,979	936,496	1026,572
Weak	1008,834	58,206	894,750	1122,918
Overall	1101,807	29,376	1044,231	1159,383

CI: Confidence interval; EFS: Hand grip strength; SE: Standard error; a: Estimation is limited to the largest survival time if it is censored. LogRank= 7,047; p=0.008<0.01.

Figure 1. Survival of patients' subgroups according to EFS, FFP scorings and hand grip strength.
(a) Edmonton frailty score (p=0.001). **(b)** FRIED frailty score (p=0.001). **(c)** Hand grip strength (p=0.008)
EFS: Hand grip strength; FFP: Fried frailty phenotype; HGS: Hand grip strength.

Table 2. Demographics, preoperative characteristics, and postoperative results of the patients according to the EFS frailty subgroups

	EFS Frailty Score																
	Non-frail (n=119)					Pre-frail (n=15)					Frail (n=6)						
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*	Different pairs in subgroups (Post hoc Bonferroni)
Age (year)			69.8±3.9*	69.0	65-84			72.6±4.3*	72.0	66-80			68.7±2.7	69.5	65-72	**0.041**	1-2
BMI (kg/m^2)			28.2±4.3	27.8	20.0-43.3			28.8±6.7	27.1	19.3-42.9			26.4±7.7	24.5	17.7-40.4	0.425	-
NYHA			2.1±0.5*	2.0	1-3			2.7±0.5	3.0	2-3			2.8±0.4	3	2-3	**0.000**	1-2; 1-3
LVEF (%)			54.1±8.5	55.0	25-65			54.6±7.5	55.0	40-65			53.3±5.2	55.0	45-60	0.765	-
Hb (g/dL)			13.2±1.6	13.5	8.6-16.2			11.8±2.0	11.6	8.8-15.1			11.3±2.3	11.1	8.9-14.9	**0.004**	1-2; 1-3
Albumin (g/L)			42.1±3.5	42.0	30.2-50.0			40.7±4.6	42.0	30.0-47.0			37.0±6.0	37.5	30-43	0.094	-
EuroSCORE II			2.4±2.0	1.7	0.6-12.8			4.4±4.0	3.1	1.1-15.8			7.2±7.8	3.2	2.4-22.0	**0.001**	1-2; 1-3
STS risk of mortality			1.5±1.5*	1.1	0.3-9.6			3.1±3.6	2.1	0.4-15.3			5.0±4.9	3.9	1.3-14.5	**0.002**	1-2; 1-3
HGS (kg)			28.2±7.3*	29.2	10.1-41.8			23.8±6.6	22.6	12.3-34.5			19.3±3.8*	19.8	15.1-24.0	**0.002**	1-3
Ventilation (h)			6.5±3.7	5.8	1.9-20.6			9.8±5.6	8.2	3.3-25.5			13.9±7.6	13.3	6.0-28.0	0.055	-
ICU stay (h)			43.4±29.9	42.0	14-216			74.6±80.6	48.0	24-336			318.0±556.5	48.0	24-1152	0.091	-
Hospital stay (day)			8.3±6.9	7.0	2.0-63.0			22.4±34.4	10.0	5.0-122.0			15.3±9.0	13.0	7.0-28.0	**0.003**	1-2;1-3
Transfusion (packed red blood cell)			1.6±1.2	1.0	0-5.0			1.5±1.0	2.0	0-3			2.0±1.9	1.0	0-4.0	0.09	-
Chest tube drainage (mL)			582.9±219.7	550.0	150-1350			578.6±295.9	500.0	200-1300			570.0±233.5	700.0	250-800	0.883	-
Survival (day)			836.0±217.1	881.0	1-1237			736.0±282.5	860.0	14-974			440.5+460.6	451.5	0-866	**0.003**	1-3; 2-3
Complications	45	37.8				8	53.3				4	80.0				0.101	-
Inotropic medicine	32	26.9				6	40.0				4	66.7				0.078	-
Mortality	13	10.9				4	26.7				3	50				**0.010**	-

EFS: Edmonton Frailty Scale; SD: Standard deviation; BMI: Body mass index; NYHA: New York Heart Association; LVEF: Left ventricle ejection fraction; Hb: Haemoglobin; EuroSCORE: European System for Cardiac Operative Risk Evaluation; STS: Society of Thoracic Surgeons; HGS: Hand grip strength; ICU: Intensive care unit.

Table 3. Demographics, preoperative characteristics, and postoperative results of the patients according to the FFP frailty subgroups

	FFP Frailty Score																
	Non-frail (n=13)					Pre-frail (n=93)					Frail (n=34)						
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*	Different pairs in subgroups (Post hoc Bonferroni)
Age (year)			68.7±3.8	68.0	65-77			69.9±3.9	70.0	65-84			70.9±4.4	69.5	65-78	0.248	-
BMI (kg/m²)			28.1±4.2	27.7	21.6-36.7			28.6±4.5	28.0	20.0-43.3			26.9±5.5	25.9	17.7-41.0	0.080	-
NYHA			1.9±0.4	2.0	1-2			2.1±0.5	2.0	1-3			2.6±0.6	3	1-3	**0.000**	1-3; 2-3
LVEF (%)			56.5±8.3	60.0	40-65			54.8±7.9	55.0	25-65			51.6±8.8	55.0	30-65	0.056	-
Hb (g/dL)			13.2±1.6	13.5	8.6-16.2			11.8±2.0	11.6	8.8-15.1			11.3±2.3	11.1	8.9-14.9	**0.002**	1-2; 1-3
Albumin (g/L)			43.2±2.8	43.0	40.0-48.0			42.1±3.3	42.0	30.2-49.0			40.2±5.2	40.0	30.0-50.0	0.076	-
EuroSCORE II			1.2±0.5	1.1	0.7-2.5			2.4±2.0	1.7	0.6-15.8			4.8±4.3	3.1	1.1-22.0	**0.000**	1-3; 2-3
STS risk of mortality			0.6±0.4	0.5	0.3-1.5			1.6±1.9	1.2	0.3-15.3			2.9±2.8	2.1	0.7-14.5	**0.000**	1-3; 2-3
HGS (kg)			33.5±6.9	34.3	19.3-41.7			27.9±7.0	28.9	14.3-41.7			23.5±6.9	23.9	10.1-41.8	**0.000**	1-2, 1-3, 2-3
Ventilation (h)			7.8±2.0	7.0	6.0-12.0			15.6±35.5	9.0	4.0-330.0			21.6±38.3	9.8	5.0-192.0	0.059	-
ICU stay (h)			26.9±9.7	24.0	15-48			50.3±43.9	48.0	14-336			81.4±207.4	46.0	18-1152	**0.029**	1-3
Hospital stay (day)			6.9±3.3	5.0	5.0-17.0			10.2±14.0	7.0	3.0-122			10.6±13.7	7.0	2.0-80.0	0.190	
Transfusion (packed red blood cell)			1.0±0.9	1.0	0-3			1.6±1.1	2.0	0-4			1.8±1.5	1.0	0-5	0.174	-
Chest tube drainage (mL)			600.0+124.2	550.0	350-800			585.6+222.3	600.0	200-1300			563.3+276.3	525.0	150-1350	0.644	-
Survival (day)			908.9±61.6	909.0	817-1040			828.3±205.4	881.0	1-1030			715.5+362.3	866.0	0-1237	0.159	-
Complications	2	15.4				35	37.6				20	60.6				**0.010**	-
Inotropic medicine	0	0.0				26	28.0				16	47.1				**0.005**	-
Mortality	0	0				9	9.7				11	32.4				**0.002**	-

FFP: Fried Frailty Phenotype; SD: Standard deviation; BMI: Body mass index; NYHA: New York Heart Association; LVEF: Left ventricle ejection fraction; Hb: Haemoglobin; EuroSCORE: European System for Cardiac Operative Risk Evaluation; STS: Society of Thoracic Surgeons; HGS: Hand grip strength; ICU: Intensive care unit.

Table 4. Demographics, preoperative characteristics, and postoperative results of the patients according to the FRAIL test frailty subgroups

	FRAIL subgroups																
	Non-Frail (n=36)					Pre-Frail (n=71)					Frail (n=33)						
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*	Different pairs in subgroups (Post hoc Bonferroni)
Age (year)			69.4±3.5	69.0	65-77.0			70.3±4.2	70.0	65.0-84.0			70.3±4.2	69.0	65.0-79.0	0.611	-
BMI (kg/m^2)			28.8±3.8	29.0	20.0-36.7			27.4±3.6	27.1	20.5-37.1			29.1±7.1	27.3	17.7-43.3	0.208	-
NYHA			1.8±0.4	2.0	1.0-2.0			2.21±0.5	2.0	1.0-3.0			2.6±0.6	3.0	1.0-3.0	**0.000**	1-2; 1-3; 2-3
LVEF (%)			55.5±7.3	55.0	40.0-65.0			54.8±7.6	56.0	35.0-65.0			51.4±9.9	55.0	25.0-65.0	0.167	-
Hb (g/dL)			13.9±1.3	13.9	10.1-16.2			12.8±1.6	13.1	8.6-15.7			12.1±2.0	12.0	8.9-15.9	**0.000**	1-2;1-3
Albumin (g/L)			42.6±2.8	42.0	38.0-48.0			42.1±3.8	42.0	30.2-50.0			40.2±4.6	41.0	30.0-47.0	0.080	-
EuroSCORE II			1.9±1.5	1.3	0.7-7.2			2.5±2.4	1.8	0.6-15.8			4.5±4.2	31	1.0-22.0	**0.000**	1-3;2-3
STS risk			0.9±0.6	0.7	0.3-2.6			1.9±2.2	1.2	0.4-15.3			2.7±2.7	2.0	0.5-14.5	**0.000**	1-2;1-3
HGS (kg)			30.9±7.5	33.0	14.7-41.7			27.5±6.7	28.7	14.3-41.8			23.4±7.1	23.8	10.1-40.2	**0.000**	1-3;2-3
Ventilation (h)			9.9±4.1	9.0	6.0-22.0			19.1±42.9	9.5	4.0-330.0			17.3±32.9	9.0	5.5-192.0	0.596	-
ICU stay (h)			40.1±24.3	36.0	15.0-144.0			50.6±48.7	48.0	14.0-336.0			81.9±203.6	48.0	18.0-1152.0	0.699	-
Hospital stay (day)			9.2±10.3	6.5	3.0-63.0			9.9±14.4	7.0	4.0-122.0			11.1±13.9	7.0	2.0-80.0	0.472	-
Transfusion			1.4±1.1	1.0	0.0-4.0			1.6±1.2	1.0	0.0-5.0			1.9±1.5	2.0	0.0-5.0	0.351	-
Chest tube drainage (mL)			617.2±203.4	575.0	250.0-1200.0			619.6±219.9	600.0	300.0-1350.0			481.7±245.5	400.0	150.0-1150.0	**0.014**	1-3;2-3
Survival (day)			809.1±217.7	879.5	1.0-1040.0			838.5±230.0	886.0	4.0-1237.0			742.9±314.0	861.00	0.0-1027.0	0.074	-
Complications	10	27.8				30	42.3				17	53.1				0.101	-
Inotropic support	7	19.4				23	32.4				12	36.4				0.254	-
Mortality	3	8.3				9	12.7				8	24.2				0.145	-

SD: Standard deviation; BMI: Body mass index; NYHA: New York Heart Association; LVEF: Left ventricle ejection fraction; Hb: Haemoglobin; EuroSCORE: European System for Cardiac Operative Risk Evaluation; STS: Society of Thoracic Surgeons; HGS: Hand grip strength; ICU: Intensive care unit.

Table 5. Demographics, characteristics, and postoperative results of the patients according to Katz ADL subgroups

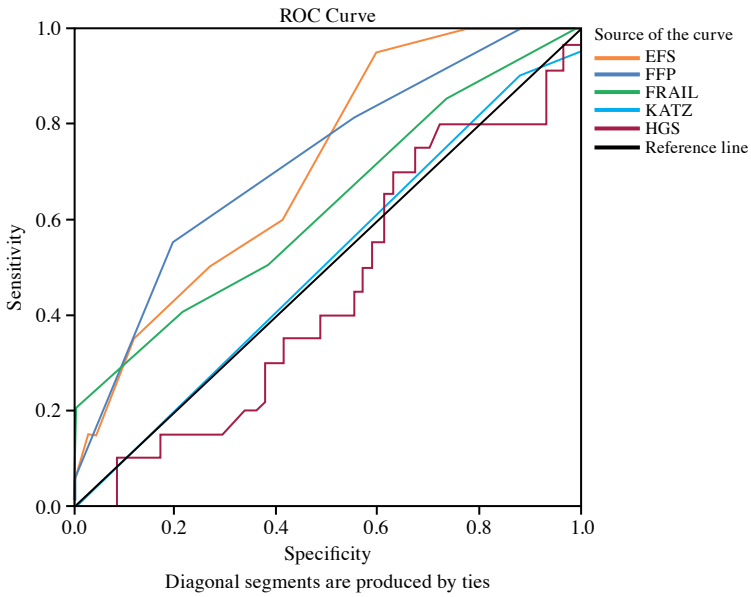
	KATZ Daily Activity Test										
	No dependency (n=124)					≥1 dependency (n=16)					
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*
Age (year)			70.0±4.0	69.0	65.0-84.0			70.6±4.2	70.0	65.0-77.0	0.612
BMI (kg/m^2)			27.9±4.2	27.7	20.0-41.0			29.5±7.9	27.0	17.7-43.3	0.903
NYHA			2.1±0.5	2.0	1.0-3.0			2.7±0.5	3.0	2.0-3.0	**0.000**
LVEF (%)			54.3±8.4	55.0	25.0-65.0			53.2±7.2	55.0	40.0-65.0	0.326
Hb (g/dL)			13.2±1.6	13.5	8.6-16.2			11.2±1.5	11.3	8.9-13.2	**0.000**
Albumin (g/L)			42.1±3.5	42.0	30.0-50.0			39.4±5.6	41.0	30.0-47.0	0.089
EuroSCORE II			2.6±2.4	1.9	0.6-15.8			4.4±5.3	2.6	1.0-22.0	0.056
STS risk of mortality			1.7±1.9	1.2	0.3-15.3			3.0±3.3	2.1	0.7-14.5	**0.005**
HGS (kg)			28.1±7.4	29.2	10.1-41.8			22.0±5.2	22.0	12.3-32.7	**0.002**
Ventilation (h)			17.0±36.5	9.0	4-330.0			10.1±3.9	10.0	5.5-23.0	0.744
ICU stay (h)			56.4±108.2	48.0	14.0-1152.0			40.4±22.6	36.0	19.0-96.0	0.625
Hospital stay (day)			9.6±12.5	7.0	2.0-122.0			13.5±18.7	8.0	5.0-80.0	0.263
Transfusion (packed red blood cell)			1.5±1.2	1.0	0.0-5.0			2.2±1.1	2.0	0.0-4.0	**0.021**
Chest tube drainage (mL)			595.2±228.2	600.0	150.0-1350.0			480.0±198.9	400.0	200.0-850.0	0.062
Survival (day)			807.4±254.1	880.5	1.0-1237			815.8±227.4	878.0	0.0-987.0	0.582
Complications	49	39.5				8	53.3				0.304
Inotropic medicine	37	29.8				5	31.3				1.000
Mortality	18	14.5				2	12.5				1.000

ADL: Activities of daily living; SD: Standard deviation; BMI: Body mass index; NYHA: New York Heart Association; LVEF: Left ventricle ejection fraction; Hb: Haemoglobin; EuroSCORE: European System for Cardiac Operative Risk Evaluation; STS: Society of Thoracic Surgeons; HGS: Hand grip strength; ICU: Intensive care unit.

Table 6. Demographics, preoperative characteristics, and postoperative results of the patients according to the hand grip strength

	Hand Grip Strength										
	Normal (n=85)					Weak (n=55)					
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*
Age (year)			69.7±4.0	69.0	65.0-84.0			70.7±4.0	70.0	65.0-79.0	0.134
BMI (kg/m^2)			28.7±4.7	27.9	20.0-43.3			27.3±4.7	27.1	17.7-41.0	0.090
NYHA			2.1±0.5	2.0	1.0-3.0			2.2±0.6	2.0	1.0-3.0	0.141
LVEF (%)			55.5±7.3	57.0	35.0-65.0			52.1±9.1	55.0	25.0-65.0	**0.028**
Hb (g/dL)			13.2±1.6	13.6	8.8-16.2			12.5±1.9	12.9	8.6-15.4	**0.042**
Albumin (g/L)			42.4±3.2	43.0	30.2-49.0			40.7±4.7	41.0	30.0-50.0	**0.040**
EuroSCORE II			2.2±2.0	1.6	0.6-15.8			3.9±3.7	2.9	1.0-22.0	**0.000**
STS risk of mortality			1.6±2.0	1.0	0.3-15.3			2.3±2.3	1.5	0.5-14.5	**0.001**
Ventilation (h)			13.6±35.0	9.0	4.0-330.0			20.6±33.6	10.0	5.0-192.0	0.191
ICU stay (h)			45.7±43.4	40.0	14.0-336.0			70.0±158.9	48.0	18.0-1152.0	0.196
Hospital stay (day)			8.4±7.5	7.0	3.0-63.0			12.6±19.1	7.5	2.0-122.0	**0.028**
Transfusion (packed red blood cell)			1.4±1.1	1.0	0.0-4.0			1.8±1.4	2.0	0.0-5.0	0.090
Chest tube drainage (mL)			580.1±198.5	600.0	150.0-1300.0			585.1±273.2	550.0	150.0-1350.0	0.676
Survival (day)			857.4±189.9	897.0	1.0-1040.0			732.7±309.5	865.0	0.0-1237.0	**0.002**
Complications	28	32.9				29	53.7				**0.015**
Inotropic medicine	20	23.5				22	40.0				**0.038**
Mortality	7	8.2				13	23.6				**0.011**

SD: Standard deviation; BMI: Body mass index; NYHA: New York Heart Association; LVEF: Left ventricle ejection fraction; Hb: Haemoglobin; EuroSCORE: European System for Cardiac Operative Risk Evaluation; STS: Society of Thoracic Surgeons; ICU: Intensive care unit.



Area Under the Curve					
				Asymptotic 95% CI	
Test results variable(s)	Area	SE[a]	Asymptotic Sig.[b]	Lower bound	Upper bound
EFS	0.709	0.056	0.003	0.599	0.818
FFP	0.721	0.063	0.002	0.598	0.843
FRAIL	0.626	0.073	0.073	0.483	0.769
KATZ	0.506	0.070	0.933	0.368	0.643
HGS	0.448	0.067	0.459	0.317	0.579

a: Under the nonparametric assumption; b: Null hypothesis: True area=0.5.
The test results variable(s): EFS, FFP, FRAIL, KATZ, HGS has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

Figure 2. ROC analyses of five different frailty tests with AUC, significance and 95%CI.
The test result variable(s): EFS, FREID, FRAIL, KATZ, Hand Grip Strength has at least one tie between the positive actual state group and the negative actual state group.

ROC: Receiver operating characteristic; FRAIL: Fatigue, Resistance, Ambulation, Illness, and Loss of weight; CI: Confidence interval; SE: Standard error; EFS: Hand grip strength; FFP: Fried frailty phenotype; HGS: Hand grip strength.

amount was higher in the dependent group (p=0.021) (Table 5).

In patients with normal HGS, left ventricular ejection fraction, hemoglobin, albumin levels, STS, and EuroSCORE II risks, complication rates, the need for inotropic support, length of hospital stay were significantly different than those with weak HGS (Table 6).

A significant positive correlation was found between each frailty score and patients' NYHA functional class (p<0.001 for all). Other than the Katz ADL questionnaire, frailty scores were positively correlated with EuroSCORE II and STS's predicted mortality risks (p<0.001 for all), and major STS morbidity risk score values (p<0.001 for all), except for deep sternal wound risk.

Considering the concordance rates, we observed discordance between all other pairs (κ<0.200), except for a moderate (0.411) and fair (0.270) concordance between FFP and FRAIL, and FFP and Katz tests, respectively (Supplement Table 3).

According to the ROC curve analysis, the AUC values of five assessment methods reached the highest for FFP scoring with 0.721 (95% CI: 0.598-0.843) (Figure 2).

DISCUSSION

In the present study, we compared five frailty tests with different properties, namely EFS, FFP, FRAIL, Katz, and HGS tests, and identified the most useful test in cardiac surgery patients for future use. Our study results showed that the NYHA class of frail patients, hemoglobin values, EuroSCORE II and STS risk scores, and HGS values were lower compared to non-frail patients. Frail patients also experienced more postoperative complications (in FFP and HGS), prolonged hospital (in EFS and HGS) or ICU stay (in FFP), compared to non-frail patients. These findings are consistent with the results of previous published series in which frail patients were more likely to have higher STS and EuroSCORE II risk scores and worse postoperative outcomes, and longer length of hospital and ICU stay.[9-13] In a recent meta-analysis, frailty was associated with three-fold greater risk of operative mortality (RR: 2.99, 95% CI: 2.34–3.82, p<0.00001) which differed between 2.9- and 4.6-fold in the present study according to test used.[9]

In a study conducted with FFP test and a similar patient cohort, the prevalence of frailty (23%), postoperative hospital (8 *vs.* 5 days) and ICU stay (54 *vs.* 28 h), and postoperative complications (54% *vs.* 32%) in frail patients compared to the

non-frail patients were similar to the present study; however, this difference regarding postoperative outcomes was not observed after multivariate adjustments.[10] Henry et al.[14] also found no significant difference in adverse clinical outcomes in frail patients other than discharge to home (60.9% *vs*. 85.6%) in contrast to our study.[14] The patient cohort did not permit multivariate analysis in the present study, but the most striking finding for FFP was its ability to discriminate non-frail patients who would benefit from open heart surgery most with 0% mortality rate. Non-frail patients were represented with a relatively small ratio in our cohort (9.3%) compared to other studies (76.5%[10] and 72.5%[14]); however, the study power for mortality calculation in FFP subgroups was (96.8%) enough to arrive at this conclusion. The FFP test evaluates muscle function with objective measurement of HGS with a special instrument and walking speed in addition to questions regarding unintentional weight loss, exhaustion, or low physical activity without any difficulty to the patient. Lower HGS cut-off values were suggested for Turkish population aged ≥59 years in a recent study which may, in part, explain higher prevalence of pre-frail patients in our cohort that might have otherwise been accepted as non-frail.[15]

Several modifications have been proposed which may further increase the discriminating value of the original FFP test at the expense of lengthening and complicating the procedure. Addition of Geriatric Depression Scale and the Montreal Cognitive Assessment frailty revealed 2- to 3.5-fold higher risk of poor functional survival one year after cardiac surgery in frail patients which was 3.3 with simple FFP test in the present study.[16] Being frail was associated with 1.36 times higher risk for mortality or major morbidity according to FFP test with an AUC 0.60 concordant with the present study (AUC=0.743).[17] We believe that simple FFP test may suffice to predict hospital outcomes of particularly non-frail patients by predominantly objective evaluation of upper and lower extremity strength of the patients within a reasonable time frame, as sarcopenia related poor mobilization may have deleterious effects in the early postoperative period. Inclusion of cognitive ability and depression tests may add further value in the longterm, when motivation for self-maintenance requires better cognitive abilities and mood.

A multi-dimensional test with objective assessment of walking performance (Get-Up-and-Go), as well as evaluating mood, medication, nutrition, functional independence, cognitive function, and social support of an individual EFS test was another test with which we had better performance. Lal et al.[11] reported that frail patients according to EFS test were older, had lower preoperative hemoglobin values and longer hospital stay compatible with the present study. With a similar cohort of 309 patients but a higher frailty prevalence (61.3%), Castro et al.[18] also identified reduced survival in one year after surgery. In patients aged ≥75 years and 20% with some degree frailty, EFS was a good predictor for 30-day mortality with an AUC of 0.69 in another study.[19] These values are 15% with an AUC of 0.701 in the present study.

Unlike FFP, the FRAIL test was not commonly used in cardiac surgery, but was reported to predict physical limitation and mortality of older individuals in epidemiological studies.[13] Relying on five-item self-reported queries, it is a rather quick but subjective test. In an epidemiological study in Turkish population aged ≥60 years, the AUC was estimated as 0.672 and 0.588 for the FFP and FRAIL, respectively.[20] The FFP is a stronger predictor than FRAIL scale for mortality in this study, as well (AUC=0.721 *vs*. 0.626).

As a referred frailty assessment tool in 2021 ESC guidelines, the Katz ADL was an independent risk factor for in-hospital mortality in earlier studies.[5,8] Lee et al.[21] reported a higher hospital mortality rate among frail patients compared to non-frail patients (14.7% *vs*. 4.5%). Various complications, transfusion, prolonged length of stay and ventilation were also more common in functionally dependent patients. Only higher blood transfusion requirements were observed postoperatively in dependent patients according to the Katz test in the present study. Odds ratio for in-hospital mortality for Katz was 0.98 and AUC was 0.48 in the aforementioned study, while these values were 0.7 and 0.565, respectively in the present study. However, these results should be interpreted cautiously, as the study power for Katz test in our study was very low (9.2%, n=140) and as it would require more than 3,800 patients for a more powerful study (80%) according to our results.

We believe that muscle function assessment is an essential part of frailty screening. The five-m gait speed, which is a component of FFP and EFS tests, was predictive of both mortality and major morbidity in a multi-center study and offered as a test of frailty in STS Adult Cardiac Database version 2.73.[6,22]

In the EuroSCORE II "poor mobility" was included without any reference to a significant test.[6,23] An indicator of muscle strength and a component of FFP test, HGS may prove useful where joint problems may preclude proper walking speed. Increased HGS was found to be associated with decreased all-cause mortality and ICU length of stay in a study where HGS was evaluated with bioelectrical impedance.[24] In the present study, weaker HGS was linked to longer length of hospital stay, higher complication and mortality rates with decreased survival and higher need for postoperative inotropic medicine.

Frail patients constituted 4.3 to 24.3%, and pre-frail patients constituted 10.7 to 66.4% of our whole cohort according to the test used, indicating a high level of disparity. Since frailty tests differ widely in composition, frailty prevalences also differ in the literature.[4,13,14] Some tests rely only on subjective questions (Katz and FRAIL tests), while others may incorporate objective physical strength measurement or cognitive function tests in varying proportions. There was discordance between most test pairs which may explain the diversity of frailty prevalence found in the present study. As socioeconomic, cultural and educational factors may have implications from patients' perspective during test performance, validation studies for frailty tests are usually carried out in most countries. One of these studies for FFP test found lower HGS cut-off values for Turkish population aged ≥59 years to be in good agreement.[15] Studies conducted according to these national validation test cut-off values in Turkish population may yield more comparable frailty prevalence.

One of the main limitations to the present study is its relatively small sample size and short follow-up period for multivariate analysis. Calculated study powers were 87.9% for EFS score and 96.8% for FFP; therefore, we decided to publish our preliminary results. Of note, thousands of patients were required for the Katz test to reach 80% of study power. Also, studies conducted with validated HGS cut-off values for Turkish population may be more expedient. Studies evaluating validation and reliability of these five tests conducted with patients aged ≥65 years are needed to arrive at an optimum conclusion.

In conclusion, among patients aged 65 years and over undergoing cardiac surgery, frail patients demonstrated higher mortality rates with either more frequent postoperative complications, longer hospital or ICU stay compared to non-frail patients according to the test used. These findings underscore the importance of frailty assessment before cardiac surgery. Among these five tests, the FFP test was the strongest in identifying non-frail patients in univariate analysis and survival comparisons and patients classified as non-frail according to this test can be safely referred to surgery. Since there are components that evaluate muscle strength, it is concluded that FFP and EFS tests may prove useful in detecting frail patients. The Katz, FRAIL, and HGS tests were found to be less powerful with 140 patients to identify either frail or non-frail patients. This difference among these five frailty tests was also corroborated with resultant discordance between each test pair in the present study. Further large-scale studies with more patients using various tests are needed to predict cut-off values to determine frailty in cardiac surgery patient population.

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supplement Table 1. Demographics, characteristics, related procedures and postoperative results of the surviving and non-surviving patients with relative risks

	Non-survivors (n=20)		Survivors (n=120)		Total (n=140)			
	n	%	n	%	n	%	Relative risk (b/a)	*p*
Sex								0.345
Male	15[b]	16.3	77	83.7	92	65.7	16.3/10.4=1.6 (Male)	
Female	5[a]	10.4	43	89.6	48	34.3		
Diabetes mellitus	12	60.0	46	38.3	58	41.4	60.0/38.3=1.6	0.069
Smoking	9	45.0	69	57.5	80	57.1	45.0/57.5=0.8	0.729
COPD	11	55.0	33	27.5	44	31.4	55.0/27.5=2.0	**0.014**
PVD	4	20.0	9	7.5	13	9.3	20.0/7.5=2.7	0.092
NYHA class								**0.000**
I	5	26.3	6	5.0	11	7.9	47.4/26.3=1.8	
II	5	26.3	89	74.2	94	67.6	(NYHA III/II) and	
III	9	47.4	25	20.8	34	24.5	(NYHA III/I	
Solitary life	1	5.0	12	10.0	13	9.3	5.0/10.0=0.5	0.693
Operation groups:								0.056
1. Isolated CABG	10	50.0	72	60.0	82	58.6	50.0/60.0=0.8	
2. Isolated valve	2	10.0	28	23.3	30	21.4	10.0/23.3=0.4	
3. Aortic surgery	3*	15.0	11	9.2	14	10.0	15.0/9.2=1.6	
4. CABG + valve	5**	25.0	9	7.5	14	10.0	25.0/7.5=3.3	
Inotropic support (%)	11	55.0	31	25.8	42	30.0	55.0/25.8=2.1	**0.008**
Complication	13	68.4	44	36.7	57	40.7	68.4/36.7=1.9	**0.009**

COPD: Chronic obstructive pulmonary disease; PVD: Peripheral vascular disease; NYHA: New York Heart Association; CABG: Coronary artery bypass grafting.

Supplement Table 2. Demographics, characteristics, and postoperative results of the surviving and non-surviving patients

	Non-survivors (n=20)			Survivors (n=120)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Age (year)	71.2±3.5	70.0	65-80	69.9±4.1	69.0	65-84	0.097
BMI (kg/m^2)	25.7±3.7	25.7	17.7-33.3	28.5±4.8	27.78	19.3-43.3	**0.017**
Hemoglobin (g/dL)	12.0±2.0	11.8	8.8-14.9	13.1±1.6	13.5	8.6-16.2	**0.019**
Albumin (g/L)	40.4±5.2	42.0	30.0-46.0	42.0±3.6	42.0	30.2-50.0	0.375
EF (%)	49.9±10.0	51.0	30.0-65.0	54.49±7.7	55.0	25-65	**0.017**
EuroSCORE II	6.3±5.8	3.5	0.8-22	2.3±1.5	1.8	0.6-7.2	**0.000**
STS risk of mortality	3.9±4.1	2.9	0.5-15.3	1.5±1.4	1.2	0.3-9.6	**0.002**
STS renal failure risk	3.4±3.2	2.7	0.6-13.9	1.5±1.2	1.1	0.3-7.4	**0.000**
STS stroke risk	2.1±1.7	1.5	0.8-7.3	1.3±0.7	1.2	0.3-5.2	**0.013**
STS prolonged ventilation risk	11.3±6.8	9.2	3.5-28.0	6.5±3.5	5.8	1.9-18.8	**0.000**
DSW infection risk	0.2±0.1	0.2	0.1-0.6	0.3±.0.8	0.2	0.0-6.6	0.647
STS reoperation risk	3.7±1.6	3.3	1.8-7.7	2.9±1.5	2.6	1.3-8.6	**0.010**
STS morbidity risk	18.1±11.8	14.7	5.6-51.7	10.3±4.9	9.2	3.5-29.7	**0.000**
STS prolonged hospitalization risk	8.9±6.1	7.4	2.3-27.1	4.7±3.1	4.1	1.1-19.1	**0.000**
Blood transfusion (packed red blood cell)	2.0±1.6	1.5	0-5	1.5±1.1	1.0	0-4	0.339
CPB (min)	184.4±68.9	167.0	86-362	133.7±43.5	126.0	61-297	**0.001**
CC (min)	116.2±48.5	101.0	53-182	88.1±38.7	78.0	30-236	**0.025**
Ventilatory support (h)	43.8±82.6	13.0	5-330	11.9±14.1	9.0	4-96	**0.014**
ICU stay (h)	136.8±271.6	48.0	18-1152	42.9 ±29.7	40.0	14-216	**0.016**
Hospitalization (day)	15.6±21.3	8.0	2.0-80.0	9.1±11.4	7.0	4-122	0.536

SD: Standard deviation; BMI: Body mass index; EF: Ejection fraction; EuroSCORE: European System for Cardiac Operative Risk Evaluation; STS: Society of Thoracic Surgeons Score; DSW: Deep sternal wound; CPB: Cardiopulmonary bypass. CC: Cross clemp; ICU: Intensive care unit.

Supplement Table 3. Concordance or discordance between pairs of five different frailty tests according to Kappa (κ) statistics*

Tests	FFP	Frail	Katz	HGS
EFS	0.022 poor	0.074 poor	0.270 fair	0.143 poor
FFP		0.411 moderate	–0.001 poor	–0.046 poor
FRAIL			0.020 poor	–0.019 poor
KATZ				0.024 poor

FFP: Fried frailty phenotype; HGS: Hand grip strength; EFS: Edmonton frail scale; * The κ value can be interpreted as; <0.20=poor, 0.21-0.40=fair, 0.41-0.60=moderate, 0.61-0.80=substantial, 0.81-0.99=almost perfect agreement.