The Annals of Thoracic Surgery

Impact of Frailty on Outcomes in Acute Type A Aortic Dissection

--Manuscript Draft--

Manuscript Number:	ANNALS-18-00241R1
Article Type:	STS Poster Presentation (Original Article)
Section/Category:	Adult Cardiac
Keywords:	Acute type A aortic dissection; Frailty; rehabilitation
Manuscript Classifications:	Aortic dissection; Aortic operation; Frailty
Corresponding Author:	Kenji Okada, Ph. D. Shinshu University School of Medicine Matsumoto, Japan
First Author:	Toshihito Gomibuchi, M.D.
Order of Authors:	Toshihito Gomibuchi, M.D.
	Tatsuichiro Seto, MD
	Masaki Komatsu, MD
	Haruki Tanaka, MD
	Hajime Ichimura, MD
	Takateru Yamamoto, MD
	Noburo Ohashi, MD
	Yuko Wada, MD
	Kenji Okada, MD
Manuscript Region of Origin:	JAPAN
Abstract:	Background: Although frailty is used to predict morbidity and mortality, its effect on the outcomes of acute type A aortic dissection (ATAAD) has not been examined. Thus, the objective was to evaluate the role of frailty in predicting postoperative morbidity and mortality in ATAAD. Methods: A retrospective analysis of a prospectively maintained database was undertaken for all patients (310) undergoing aortic surgery between May 2004 and March 2017. Frailty was evaluated using an index consisting of age >70 years, body mass index <18.5 kg/m2, serum creatinine >1.2 mg/dL, anemia, history of stroke, hypoalbuminemia, and the psoas muscle area index. One point was given for each criterion met for a frailty score between 0 to 7. Frailty was defined as a score of ≥3. Results: Of all patients, 106 (34.2%) were defined as frail. In-hospital mortality rates of frail versus non-frail patients were not significantly different (10.4% vs. 8.3%, respectively; P = 0.54). Incidences of postoperative major morbidities without re-exploration for bleeding were also not statistically different. Five-year survival rates were significantly worse for frail patients (57.7% vs. 85.1%; P = 0.0001). A frailty score of ≥ 3 was associated with late mortality and long-term outcomes were clearly stratified by frailty score. Conclusions: Frailty, as defined using a 7-component frailty index, can serve as an independent predictor of the risk of late mortality in patients undergoing an ATAAD. Such frailty markers, all of which are easily assessed preoperatively, may provide valuable information for patient counseling and risk stratification before aortic surgery.

Impact of Frailty on Outcomes in Acute Type A Aortic Dissection

Running Head: Impact of Frailty in Aortic Dissection

Toshihito Gomibuchi, MD, Tatsuichiro Seto, MD, Masaki Komatsu, MD, Haruki Tanaka, MD, Hajime Ichimura, MD, Takateru Yamamoto, MD, Noburo Ohashi, MD, Yuko Wada, MD, Kenji Okada, MD

Department of Cardiovascular Surgery, Shinshu University School of Medicine, Matsumoto, Japan

Corresponding author: Kenji Okada

Department of Cardiovascular Surgery, Shinshu University School of Medicine,

Asahi 3-1-1, Matsumoto, Nagano, 390-8621, Japan

email: keokada@shinshu-u.ac.jp

Key words: acute type A aortic dissection, frailty, rehabilitation

Abstract: 250

Text (including figures, tables and references): 4432

Abstract

Background: Although frailty is used to predict morbidity and mortality, its effect on the outcomes of acute type A aortic dissection (ATAAD) has not been examined. Thus, the objective was to evaluate the role of frailty in predicting postoperative morbidity and mortality in ATAAD.

Methods: A retrospective analysis of a prospectively maintained database was undertaken for all patients (310) undergoing aortic surgery between May 2004 and March 2017. Frailty was evaluated using an index consisting of age >70 years, body mass index <18.5 kg/m^2, serum creatinine >1.2 mg/dL, anemia, history of stroke, hypoalbuminemia, and the psoas muscle area index. One point was given for each criterion met for a frailty score between 0 to 7. Frailty was defined as a score of ≥3.

***Results*:** Of all patients, 106 (34.2%) were defined as frail. In-hospital mortality rates of frail versus non-frail patients were not significantly different (10.4% vs. 8.3%, respectively; P = 0.54). Incidences of postoperative major morbidities without re-exploration for bleeding were also not statistically different. Five-year survival rates were significantly worse for frail patients (57.7% vs. 85.1%; P = 0.0001). A frailty score of ≥ 3 was associated with late mortality and long-term outcomes were clearly stratified by frailty score.

Conclusions: Frailty, as defined using a 7-component frailty index, can serve as an independent predictor of the risk of late mortality in patients undergoing an ATAAD. Such frailty markers, all of which are easily assessed preoperatively, may provide valuable information for patient counseling and risk stratification before aortic surgery.

Acute type A aortic dissection (ATAAD) is a life-threatening cardiovascular event that requires immediate surgical repair (1). In the field of aortic surgery, treatment methods such as surgical techniques, perioperative care, and sealing grafts have improved dramatically over the past decade. Consequently, improved outcomes in hospital mortality from this disease are well described in the recent literature (2). The aging population is rapidly increasing in many countries. However, with increasing life expectancy of the population comes a rise in the incidence of cardiovascular disease, including ATAAD (3). Frailty, defined as a state of increased vulnerability to stressors caused by a deterioration across multiple physiologic systems, is an emerging concept in clinical medicine. Most extensively investigated in community-dwelling geriatric populations, frail patients have been shown to be predisposed to increased falls, hospitalization, institutionalization, and mortality (4-6). Although frailty has been examined as a predictor of morbidity and mortality, its effect on ATAAD outcomes has not been studied. Therefore, the objective of the present study was to evaluate the role of frailty in predicting postoperative morbidity and mortality in patients undergoing aortic surgery.

Patients and Methods

The Shinshu University School of Medicine Institutional Ethics Committee approved this study (Permission No. 3989-2018). The need for individual patient consent was waived. From May 2004 to March 2017, 310 consecutive patients underwent an emergency open operation for ATAAD at our institution. Medical records were reviewed for preoperative risk factors, operative records, intraoperative events, and postoperative courses.

Frailty Definition

To classify frailty, a score was created that consisted of seven components previously identified in published data as objective indicators of frailty. The components were: 1) age >70 years (6), 2) body mass index <18.5 kg/m2 (7), 3) serum creatinine >1.2 mg/dL (8), 4) anemia (<12.0 g/dL for women, <13.0 g/dL for men) (9), 5) hypoalbuminemia (<3.5 g/dL) (10), 6) a history of stroke (11), and 7) the psoas muscle area index (12). One point was given for each criterion met to determine a frailty score of between 0 and 7. Frailty was defined as a score of ≥3. Risk models for hospital mortality and long-term survival were calculated using multivariable regression modeling.

The Barthel Index is a popular instrument for assessing the activities of daily living (ADL) (13). The total score ranges from 100 (totally independent patient) to 0 (completely dependent patient) with lower scores representing greater nursing dependency (14).

Definition of Clinical Presentation

Cardiogenic shock was defined as having a preoperative systolic blood pressure less than 80 mmHg or having a need for intravenous inotropic agents. Malperfusion syndromes were defined as signs or symptoms due to disrupted blood flow to end-organ systems such as the central nervous system (CNS), or to the coronary, visceral, or extremities' circulatory systems. CNS disorders caused by malperfusion syndrome were classified as transient or persistent according to the duration of the clinical presentation. Postoperative *de novo* neurologic dysfunction was considered permanent if it persisted at a patient's discharge and was a result of an intraoperative procedure. Transient dysfunction was defined as a temporary loss of orientation, slurred speech, agitation, or poor responses to commands. Neurologic dysfunction caused by preoperative brain malperfusion, deep shock status, cardiopulmonary resuscitation (CPR), requiring preoperative or postoperative supported percutaneous cardiopulmonary support (PCPS), and postoperative atrial fibrillation was excluded from *de novo* neurologic dysfunction. Preoperative independence in ADL was defined as a patient's ability to perform basic activities as follows: light housework, eating, toileting, and walking.

Surgical Protocol

The principal aim of our surgical strategy for treating ATAAD was to excise the primary entry tear. If the primary entry tear was oriented toward the ascending aorta, we performed a ATAAD repair using a hemiarch replacement (HAR) or partial arch replacement (PAR) with an intimal tear exclusion to reduce in-hospital mortality and morbidity in patients older than 70 years. We applied a total arch replacement (TAR) when a HAR or PAR could not exclude the intimal tear. Arterial cannulation sites were determined according to the patient's status, preoperative organ malperfusion, and the preference of the surgeon; however, the femoral artery with the right axial artery was the most frequent choice. A venous cannula was inserted into the right atrium to the superior and inferior vena cava; cardiopulmonary bypass was then established and systemic cooling was initiated. After systemic body hypothermia induced minimal tympanic temperatures below 23°C, and minimal rectal temperatures below 30°C, the ascending aorta was opened, and antegrade selective cerebral perfusion was initiated. A gelatin-impregnated quadfurcated Dacron graft (Gelweave from Vascutek Ltd, Terumo Corporation, Inchinnan, Scotland; or J Graft Shield Neo from Japan Lifeline Co., Ltd., Tokyo, Japan) or Triplex (Terumo Corporation, Tokyo, Japan) was used. After completion of the distal anastomosis of the prosthetic graft, lower body circulation was reinstituted through a branch graft, and the tympanic/rectal temperature was rewarmed early. The proximal anastomosis of the graft was completed, followed by coronary reperfusion. Finally, the aortic arch vessels were reconstructed (15).

Follow-up

Follow-up information on survival, general health status, need for aortic reoperation, rupture, and causes of death were obtained from patients' medical records at our outpatient clinic or by telephoning patients or their relatives.

Statistical Analysis

Data were processed using JMP 12.0 software (SAS Institute Inc, Cary, NC, USA). Continuous values are expressed as the mean ± standard deviation (SD). Data were analyzed by the $\chi 2$ test or Fisher's exact test for categorical variables. Logistic regression analysis was performed to identify the risk factors for hospital mortality. Clinically relevant variables with $P < 0.05$ on univariable analysis were incorporated into multivariable models. Survival was assessed by the Kaplan–Meier method. A Cox proportional hazard analysis, into which all preoperative variables in patient profiles were incorporated, was used to determine the risk factors for late mortality. Differences were considered statistically significant at $P < 0.05$.

Results

Preoperative Patient Characteristics

Of the study patients, 106 (34.2%) were defined as frail (frailty score ≥3). Thirty-six (34.0%) patients of the frail group and 11 (5.4%) patients of the nonfrail group were octogenarians. Age ($P < 0.0001$), cerebrovascular disease ($P < 0.0001$), shock status ($P < 0.0001$), cardiopulmonary resuscitation ($P = 0.0005$), cardiac tamponade ($P < 0.0001$), transient CNS malperfusion ($P = 0.03$) and coma ($P = 0.05$) were significantly more prevalent in the frail group than in the younger group. Body weight ($P < 0.0001$), body mass index ($P = 0.0002$), serum albumin levels ($P < 0.0001$), hemoglobin ($P < 0.0001$), and estimated glomerular filtration rate (eGFR; $P < 0.0001$) were significantly lower in the frail group. Both the EuroSCORE II and JapanSCORE were significantly higher in the frail group ($P < 0.0001$ for both; Table 1).

Intraoperative Data

Supplemental Table E1 shows intraoperative data. Operation and cardiopulmonary bypass times were significantly shorter in the frail group because the mode of surgery was mostly limited to the replacement of the hemiarch aorta in 70 patients (66.0%) of the frail group, but was applied to 73 patients (35.8%) of the younger, nonfrail group (P < 0.0001).

Early Outcomes

Mortality and morbidities rates are shown in Table 2. Overall, hospital mortality in the frail group was 10.4% (11/106); causes of death were low cardiac output syndrome (three patients), sepsis (three patients), multiple-organ failure (two patients), stroke (one patient), rupture of abdominal aortic aneurysms (one patient), and re-dissection of aorta (one patient). The hospital mortality rate in the nonfrail group was 8.3% (17/204); causes of death were low cardiac output syndrome (three patients), stroke (six patients), multiple-organ failure (four patients), sepsis (one patient), re-dissection of aorta (one patient), acute myocardial infraction (one patient), and cardiac tamponade (one patient). A difference in the in-hospital mortality of frail versus nonfrail patients was not noted (P = 0.54). Statistical differences in the incidences of postoperative major morbidities without re-exploration for bleeding was not observed between the two groups. The postoperative Barthel Index was significantly lower in the frail group, with 46 patients (43.4%) transferred to a rehabilitation hospital.

Supplemental Table E2 shows univariable and multivariable analyses of hospital mortality. Preoperative shock (P = 0.002), cardiopulmonary resuscitation (P = 0.0001), overall malperfusion (P = 0.0008), coronary malperfusion (P = 0.004), visceral malperfusion (P < 0.0001), extremities malperfusion (P = 0.03), coma (P = 0.01), concomitant procedure (P < 0.0001), and long duration of cardiopulmonary bypass (≥4 hours, P = 0.04) were identified as risk factors for postoperative hospital mortality by univariable analysis, whereas surgical procedure and age were not. Preoperative shock (odds ratio [OR], 3.07; P = 0.01), and concomitant procedure (OR, 5.66; P < 0.001) were determined to be risk factors for postoperative hospital mortality by multivariable analysis, whereas having a frailty score ≥3 was not.

Late Outcomes

Follow-up was completed in 95.2% of patients, with the mean follow-up period being 44.4 ± 36.7 (range, 1–148, median 38) months. The number of overall late deaths was 38 (frail group, n = 23; nonfrail group, n = 15). Figure 1 shows overall long-term survival assessed by the Kaplan–Meier method. Survival rates at 1, 5 and 10 years after surgery were 85.8%, 57.7% and 27.8% in the frail group, respectively, and 90.4%, 85.1% and 72.9% in the nonfrail group, respectively, with a significant difference noted between the groups (P = 0.0001). The 5-year survival rates in age- and sex-matched general populations in comparison to the frail group were 83.0% (Figures 2, 3). Figure 4 shows that long-term survival was worse across the higher categories of the frailty score. Cox proportional hazard analysis (Table 3) showed that a frailty score ≥3 (hazard ratio [HR], 4.71; P < 0.0001), male (HR, 3.57; P = 0.0005), preoperative ADL independence (HR, 14.39; $P = 0.002$), and overall malperfusion (HR, 2.23; $P = 0.02$) were significant risk factors for long-term mortality according to multivariable analysis

Comment

Life expectancy is steadily increasing in many countries and with it comes a higher incidence of cardiovascular diseases, including ATAAD (16). Surgical outcomes for ATAAD have been improving in Japan (2) as well as the rest of the world (17), with several studies reporting on good results from the surgical repair of ATAAD in elderly patients (3, 18). Bachet reported (19) that age did not provide an objective criterion of any individual's health condition in elderly patients with acute aortic dissection. In this regard, in addition to the usual surgical scores, indices of frailty developed mostly by geriatricians would be of some interest and could better identify those individuals actually at major perioperative risk. The concept of frailty, which is a term widely used to denote a multidimensional syndrome of the loss of reserves such as energy, physical ability, and cognition, as well as increased vulnerability, has recently been established (20). Lee and colleagues (6) reported the first study of frailty in cardiac surgery patients, with frailty a risk for postoperative complications and an independent predictor of in-hospital mortality, institutional discharge, and reduced midterm survival. Fried et al reported cycle of frailty that frailty is consistent with the several clinical markers and represent an adverse, potentially downward spiral of energetics (21). Ganapathi et al defined frailty using a frailty index consisting six components (age, body mass index, anemia, history of stroke, hypoalbuminemia, and total psoas volume). They showed these frailty were associated with discharge to a destination other than home and poorer 30-day and/or in-hospital and 1-year survival after proximal aortic replacement surgery (5). However, these frailty index consisting six components do not contain renal dysfunction. Walker SR et al reported an association of frailty and physical function in patients with non-dialysis CKD (8). Therefore, we classified frailty consisted of seven components previously identified in published data as objective indicators of frailty. Frailty screening improves risk assessments in cardiac surgery patients.

Preoperative clinical severity, such as shock status, CPR, or malperfusion syndrome, deeply affect morbidity and mortality after surgical treatment of ATAAD (22). Patients of the frail group were older and more likely to be female. They were also more likely to have comorbid disease, including a more frequent history of previous stroke, and chronic renal insufficiency. Frail patients were likely to have severe preoperative status, such as shock, cardiopulmonary resuscitation, and transient CNS malperfusion. However, we found that the in-hospital mortality rate was 10.4% for the frail group while the in-hospital mortality or complication rate without re-exploration for bleeding did not differ from those of the nonfrail group. The reason there was no difference in the results might be that we performed a ATAAD repair using a HAR or PAR in frail patients. We previously performed ATAAD repair using HAR or PAR with intimal tear exclusion to reduce rates of in-hospital mortality and morbidity in patients older than 70 years. We found that HAR and PAR with entry tear exclusion reduced deaths associated with ATAAD in elderly patients, without increasing the risk of reoperation and aortic-related death (23). Owing to this, emergent surgery for frail patients with ATAAD showed acceptable mortality.

The Barthel Index at discharge was significantly lower for the frail group. Our study showed that the postoperative ADL for frail patients had deteriorated, meaning that frail patients generally took a lot of time for rehabilitation. Therefore, of the frail patients, 43.4% were transferred to a rehabilitation hospital in response to the increased time needed to recover well after surgery.

The five-year survival rate for the frail group, who were discharged from hospital after treatment for ATAAD, was 57.7% in our study. The frail group had a significantly lower survival rate than the nonfrail group (*P* = 0.0001). The five-year survival rates of a general population that was age- and sex-matched to the frail group were 83.0% in both cases. Cox proportional hazard analysis determined that having a frailty score ≥3 was a risk factor for late mortality according to univariable and multivariable analysis. These findings suggested that patients who were frail have poor long-term outcomes. Furthermore, the long-term outcomes after ATAAD were clearly stratified by frailty score. We think that the adverse prognosis for patients with frail affected the frail itself rather than the postoperative influence. Participation in self-selected exercise activities is independently associated with delaying the onset and the progression of frailty (24). Therefore, regular exercise might be examined as a potential factor in frailty prevention for postoperative patients.

In-hospital mortality of the octogenarian and younger groups were 6.3% and 9.5%, respectively (*P* = 0.49). 5-year survival rates in the octogenarian and younger groups were 52.2% and 80.2%, respectively (*P* = 0.08). 46.8% of octogenarian patients were transferred to a rehabilitation hospital in responds to the increased time for octogenarian patients to recover well after surgery. Emergency surgery for octogenarians with ATAAD showed acceptable mortality. The option of surgical management for ATAAD in octogenarians should not be disregarded solely due to the advanced age of the patients.

We are a policy to perform surgery in any patients. In an emergency clinical setting, aggressive surgical treatment may be a reasonable option for frail patients. However, We are at a loss as to whether to perform surgery on a very high frailty patient such as bedridden. Consult the patient's family, but the family also become confused. Hata and colleagues (25) described how about 20% of their octogenarian patients with ATAAD who underwent surgery became bedridden forcing families to take responsibility for patients who experienced unconsciousness, had dementia, or became bedridden. Consequently, for patients with a severe frailty, there may often be a hesitation about whether to perform surgery. While JapanSCORE and EuroSCORE II are useful for predicting hospital mortality, they are not related to late outcomes. On the other hand, Frailty score is useful for predicting late outcomes. For this reason, frailty markers may provide valuable information when counseling patients and in late mortality risk stratification before surgery.

Physical performance measures, such as gait speed, have also been used as a standard tool to evaluate the preoperative frailty and disabilities of patients (26). However, ATAAD is an emergency event, meaning there is no time to evaluate physical performance. In contrast, such frailty markers are easily assessed preoperatively.

Limitations

The limitations of this investigation included that this was a retrospective study from a single center. In our study, the majority of patients showed preoperative independence in ADL. However, patients with impaired physical activity may not have been transferred to our hospital because of an inoperative condition, and may have been medically treated in another hospital. In addition, the logistic regression analysis for hospital mortality was limited by a small number of events because our surgical approach generally provided satisfactory outcomes. The mean follow-up period was also short (44.4 ± 36.7 months; range, 1–148 months; median, 38 months).

In conclusion, frailty, as defined using a seven-component frailty index, can serve as an independent predictor of late mortality risk in patients undergoing surgery in ATAAD. Such frailty markers, all of which are easily assessed preoperatively, may provide valuable information for patient counseling and risk stratification prior to surgery.

References

1. Omura A, Miyahara S, Yamanaka K, Sakamoto T, Matsumori M, Okada K, et al. Early and late outcomes of repaired acute DeBakey type I aortic dissection after graft replacement. The Journal of thoracic and cardiovascular surgery. 2016;151(2):341-8.

2. Committee for Scientific Affairs Affairs The Japanese Association for Thoracic Surgery, Masuda M, Okumura M, Doki Y, Endo S, Hirata Y, et al. Thoracic and cardiovascular surgery in Japan during 2014 : Annual report by The Japanese Association for Thoracic Surgery. General thoracic and cardiovascular surgery. 2016;64(11):665-97.

3. Omura A, Matsuda H, Minami H, Nakai H, Henmi S, Murakami H, et al. Early and Late Outcomes of Operation for Acute Type A Aortic Dissection in Patients Aged 80 Years and Older. Ann Thorac Surg. 2017;103(1):131-8.

4. Chikwe J, Adams DH. Frailty: the missing element in predicting operative mortality. Semin Thorac Cardiovasc Surg. 2010;22(2):109-10.

5. Ganapathi AM, Englum BR, Hanna JM, Schechter MA, Gaca JG, Hurwitz LM, et al. Frailty and risk in proximal aortic surgery. J Thorac Cardiovasc Surg. 2014;147(1):186-91 e1.

6. Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010;121(8):973-8.

7. Challa S, Sharkey JR, Chen M, Phillips CD. Association of resident, facility, and geographic characteristics with chronic undernutrition in a nationally represented sample of older residents in U.S. nursing homes. The journal of nutrition, health & aging. 2007;11(2):179-84.

8. Walker SR, Gill K, Macdonald K, Komenda P, Rigatto C, Sood MM, et al. Association of frailty and physical function in patients with non-dialysis CKD: a systematic review. BMC nephrology. 2013;14:228.

9. Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood. 2006;107(5):1747-50.

10. Watanabe A. Why albumin now? Let's think about albumin measurement methods, the definition of hypoalbuminemia, and microheterogeneity. Nutrition. 2005;21(11-12):1156-7.

11. Farhat JS, Velanovich V, Falvo AJ, Horst HM, Swartz A, Patton JH, Jr., et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. The journal of trauma and acute care surgery. 2012;72(6):1526-30; discussion 30-1.

12. Ikeno Y, Koide Y, Abe N, Matsueda T, Izawa N, Yamazato T, et al. Impact of sarcopenia on the outcomes of elective total arch replacement in the elderlydagger. Eur J Cardiothorac Surg. 2017;51(6):1135-41.

13. Mahoney FI, Barthel DW. FUNCTIONAL EVALUATION: THE BARTHEL INDEX. Maryland state medical journal. 1965;14:61-5.

14. Quinn TJ, Langhorne P, Stott DJ. Barthel index for stroke trials: development, properties, and application. Stroke. 2011;42(4):1146-51.

15. Okada K, Omura A, Kano H, Sakamoto T, Tanaka A, Inoue T, et al. Recent advancements of total aortic arch replacement. J Thorac Cardiovasc Surg. 2012;144(1):139-45.

16. Olsson C, Thelin S, Stahle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation. 2006;114(24):2611-8.

17. Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A, et al. Presentation, Diagnosis, and Outcomes of Acute Aortic Dissection: 17-Year Trends From the International Registry of Acute Aortic Dissection. J Am Coll Cardiol. 2015;66(4):350-8.

18. Kawahito K, Kimura N, Yamaguchi A, Aizawa K, Misawa Y, Adachi H. Early and Late Surgical Outcomes of Acute Type A Aortic Dissection in Octogenarians. Ann Thorac Surg. 2018;105(1):137-43.

19. Bachet J. Outcomes of limited proximal aortic replacement for type A aortic dissection in octogenarians: What does "age" mean? J Thorac Cardiovasc Surg. 2016;152(2):447.

20. Furukawa H, Tanemoto K. Frailty in cardiothoracic surgery: systematic review of the literature. Gen Thorac Cardiovasc Surg. 2015;63(8):425-33.

21. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M146-56.

22. Kondoh H, Satoh H, Daimon T, Tauchi Y, Yamamoto J, Abe K, et al. Outcomes of limited proximal aortic replacement for type A aortic dissection in octogenarians. J Thorac Cardiovasc Surg. 2016;152(2):439-46.

23. Komatsu K, Takano T, Terasaki T, Wada Y, Seto T, Fukui D, et al. Surgical outcomes of acute type A aortic dissection in elderly patients. Ann Thorac Surg. 2014;97(5):1576-81.

24. Peterson MJ, Giuliani C, Morey MC, Pieper CF, Evenson KR, Mercer V, et al. Physical activity as a preventative factor for frailty: the health, aging, and body composition study. The journals of gerontology Series A, Biological sciences and medical sciences. 2009;64(1):61-8.

25. Hata M, Sezai A, Niino T, Yoda M, Unosawa S, Furukawa N, et al. Should emergency surgical intervention be performed for a octogenarian with type A acute aortic dissection? J Thorac Cardiovasc Surg. 2008;135(5):1042-6.

26. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. Jama. 2011;305(1):50-8.

Table 1. Preoperative status of patients

Variables	Overall n = 310 (%)	Frail n = 106 (%)	Nonfrail n = 204 (%)	*P* value
No. of patients, (%)	310	106 (34.2)	204 (65.8)	
Age, y, mean ± SD	67.5 ± 11.9	76.2 ± 7.9	63.0 ± 11.1	<.0001
Octogenarians	47 (15.2)	36 (34.0)	11 (5.4)	<.0001
Male gender	155 (50.0)	41 (38.7)	114 (55.9)	.006
Body mass index	23.3 ± 3.95	22.1 ± 3.5	23.9 ± 4.1	.0002
Diabetes mellitus	15 (4.8)	8 (7.6)	7 (3.4)	.16
Hypertension	206 (66.5)	79 (74.5)	127 (62.3)	.03
Hemodialysis	10 (3.2)	8 (7.6)	2 (1.0)	.004
Connective tissue disease	11 (3.5)	0	11 (5.4)	.02
Coronary artery disease	15 (4.8)	6 (5.7)	9 (4.4)	.59
Cerebrovascular disease	27 (8.7)	21 (19.8)	6 (2.9)	<.0001
Prior cardiac surgery	12 (3.9)	5 (4.7)	7 (3.4)	.55
Preoperative ADL independence	304 (98.1)	102 (96.2)	202 (99.0)	.19
Preoperative status				
Shock	74 (23.9)	40 (37.7)	34 (16.7)	<.0001
Cardiopulmonary resuscitation	21 (6.8)	15 (14.2)	6 (2.9)	.0005
Cardiac tamponade	69 (22.3)	42 (39.6)	27 (13.2)	<.0001
Organ malperfusion	129 (41.6)	43 (40.6)	86 (42.2)	.81
CNS	71 (22.9)	31 (29.3)	40 (19.6)	.06
Transient	40 (12.9)	20 (18.9)	20 (9.8)	.03
Persistent	24 (7.7)	12 (11.3)	12 (5.9)	.12
Coronary	14 (4.5)	5 (4.7)	9 (4.4)	1.00
Visceral	7 (2.3)	2 (1.9)	5 (2.5)	1.00
Extremities	42 (13.5)	9 (8.5)	33 (16.2)	.08
Coma	11 (3.5)	7 (6.6)	4 (2.0)	.05
Aortic valve insufficiency > III	38 (12.3)	12 (11.3)	26 (12.8)	.86
Albumin (g/dL)	3.6 ± 0.5	3.3 ± 0.5	3.8 ± 0.4	<.0001
Hemoglobin (g/dL)	12.7 ± 1.9	11.3 ± 1.6	13.5 ± 1.6	<.0001
eGFR (mL/min/1.73 m^2)	59.9 ± 23.8	49.4 ± 25.0	65.4 ± 21.3	<.0001
DeBakey classification				
Type I	198 (63.9)	53 (50.0)	145 (71.2)	
Type II	96 (31.0)	49 (46.2)	47 (23.0)	.0002
Type IIIb retrograde	16 (5.2)	4 (3.8)	12 (5.9)	
EuroSCORE II	6.8 ± 6.5	9.3 ± 6.8	5.5 ± 5.8	<.0001
JapanSCORE				

30 days' operative mortality (%)	13.8 ± 10.5	17.8 ± 12.8	11.8 ± 8.3	<.0001
30 days' operative mortality/morbidity (%)	40.4 ± 12.7	46.2 ± 14.3	37.4 ± 10.6	<.0001

SD, standard deviation; ADL, activities of daily living; CNS, central nervous system; eGFR, estimated glomerular filtration rate.

Table 2. Postoperative data

Variables	Overall n = 310 (%)	Frail n = 106 (%)	Nonfrail n = 204 (%)	*P* value
No. of patients, (%)	310	106	204	
Thirty-day mortality	25 (8.1)	11 (10.4)	14 (6.9)	.28
Hospital mortality	28 (9.0)	11 (10.4)	17 (8.3)	.54
New-onset neurologic dysfunction	32 (10.3)	9 (8.5)	23 (11.3)	.56
Temporary neurologic deficit	7 (2.3)	4 (3.8)	3 (1.5)	.24
Permanent neurologic deficit	25 (8.1)	5 (4.7)	20 (9.8)	.13
Renal failure requiring hemofiltration	29 (9.4)	8 (7.6)	21 (10.3)	.54
Re-exploration for bleeding	15 (4.8)	1 (0.9)	14 (6.9)	.02
Tracheostomy	19 (6.1)	8 (7.6)	11 (5.4)	.46
Prolong mechanical ventilation time >48 h	127 (41.0)	44 (41.5)	83 (40.7)	.90
Intensive care unit stay (days)	7.2 ± 8.1	7.8 ± 8.3	6.9 ± 8.0	.35
Hospital stay (days)	36.9 ± 31.0	38.2 ± 32.5	36.3 ± 30.3	.60
Transfer to rehabilitation hospital	94 (30.3)	46 (43.4)	48 (23.5)	.0004
Barthel Index (2010~)	80.3 ± 30.2	70.5 ± 32.7	85.7 ± 27.4	.0006

Table 3. Univariable and multivariable analyses of late mortality (excluding hospital deaths)

	Univariable		Multivariable	
Variables	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Frailty score ≥3	4.21 (2.20–8.27)	<.0001	4.71 (2.32–9.75)	<.0001
Male gender	2.04 (1.06–4.13)	.03	3.57 (1.71–8.00)	.0005
Preoperative transient Neurologic deficit	3.19 (1.51–6.34)	.003		
Shock	2.14 (1.06–4.14)	.04	1.45 (0.67–2.98)	.34
Cardiopulmonary resuscitation	4.85 (1.42–12.6)	.02		
Cardiac tamponade	2.69 (1.36–5.16)	.005		
Malperfusion (overall)	2.41 (1.26–4.78)	.008	2.23 (1.15–4.51)	.02
Cerebral	2.36 (1.18–4.54)	.02		
Kidney	2.83 (1.11–6.27)	.03		
Preoperative ADL independence	14.36 (3.37–42.18)	.002	14.39 (3.01–52.73)	.002

HR, Hazard ratio; ADL, activities of daily living; eGFR, estimated glomerular filtration rate; CI, confidence interval.

Figure legends

Figure 1. Survival curves of frail and nonfrail patients after discharge from hospital.

Figure 2. Survival curves of frail patients who were surgically treated compared with age- and sex-matched general populations.

Figure 3. Survival curves of frail patients after discharge from the hospital compared with age- and sex-matched general populations.

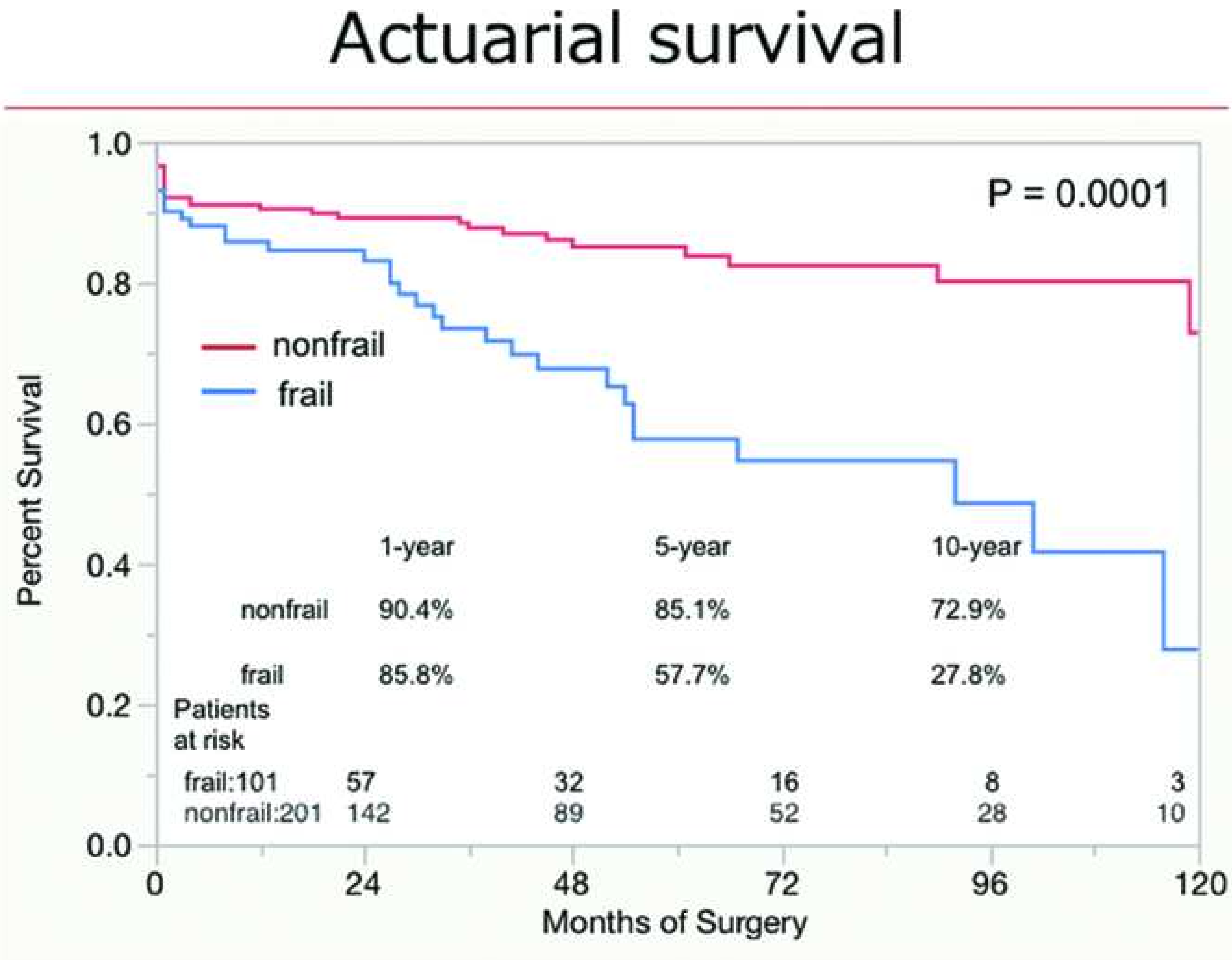
Figure 4. Survival curves across stratified frailty scores (FS).

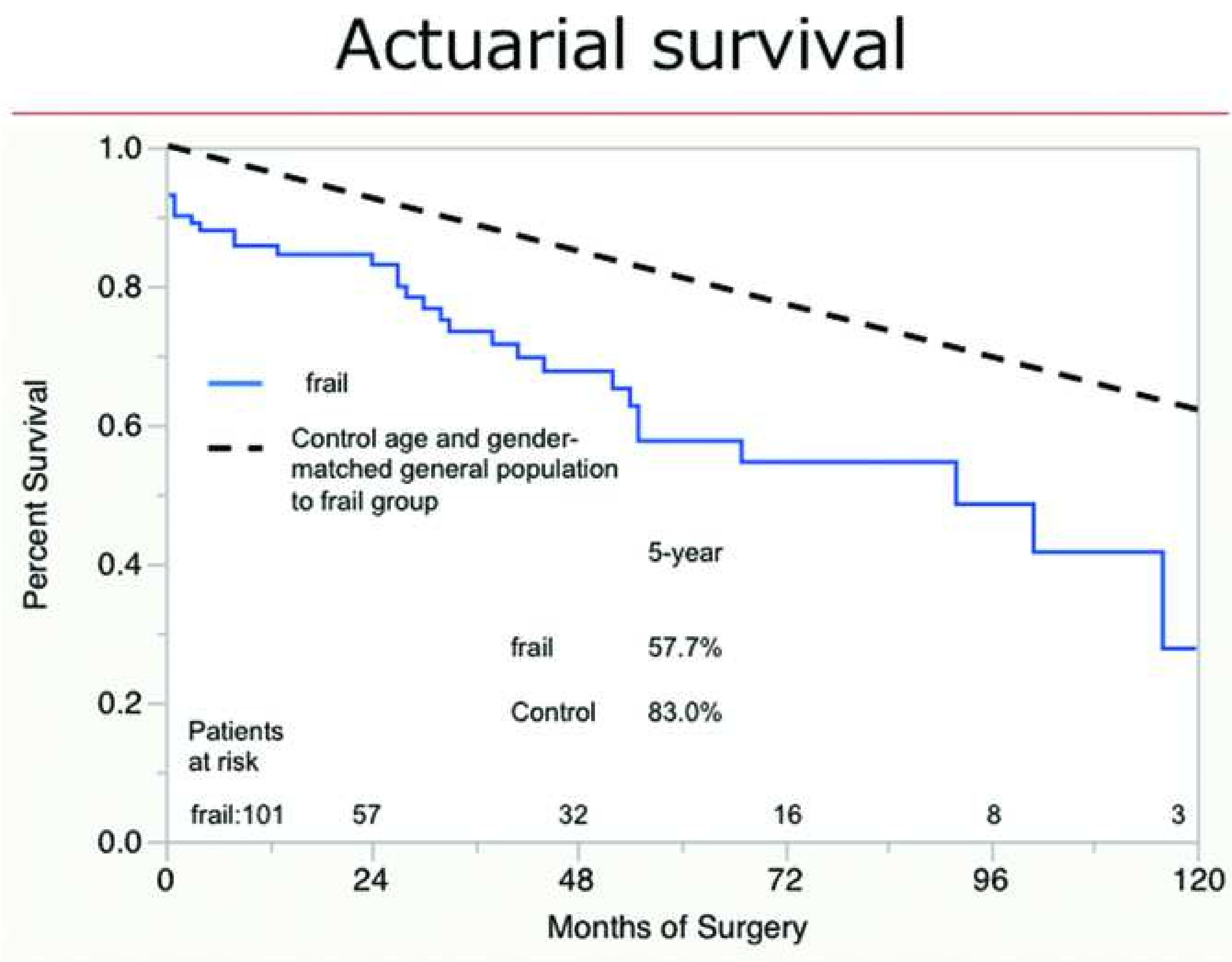
Abbreviations and Acronyms

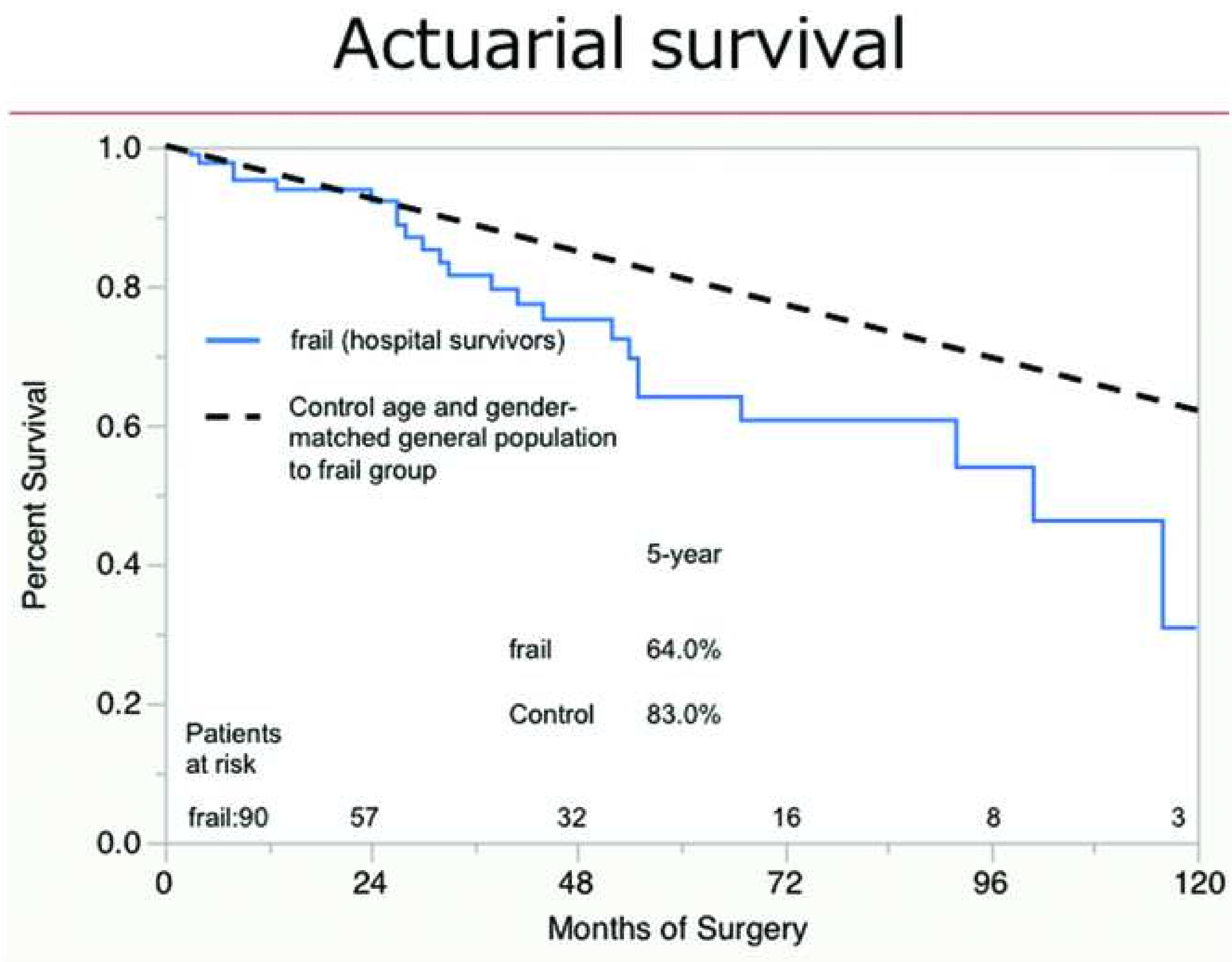
ATAAD	=	acute type A aortic dissection
ADL	=	activities of daily living
CNS	=	central nervous system
CPR	=	cardiopulmonary resuscitation
PCPS	=	percutaneous cardiopulmonary support
HAR	=	hemiarch replacement
PAR	=	partial arch replacement
TAR	=	total arch replacement
SD	=	standard deviation
eGFR	=	estimated glomerular filtration rate
OR	=	odds ratio
HR	=	hazard ratio

FINAL-FIG1

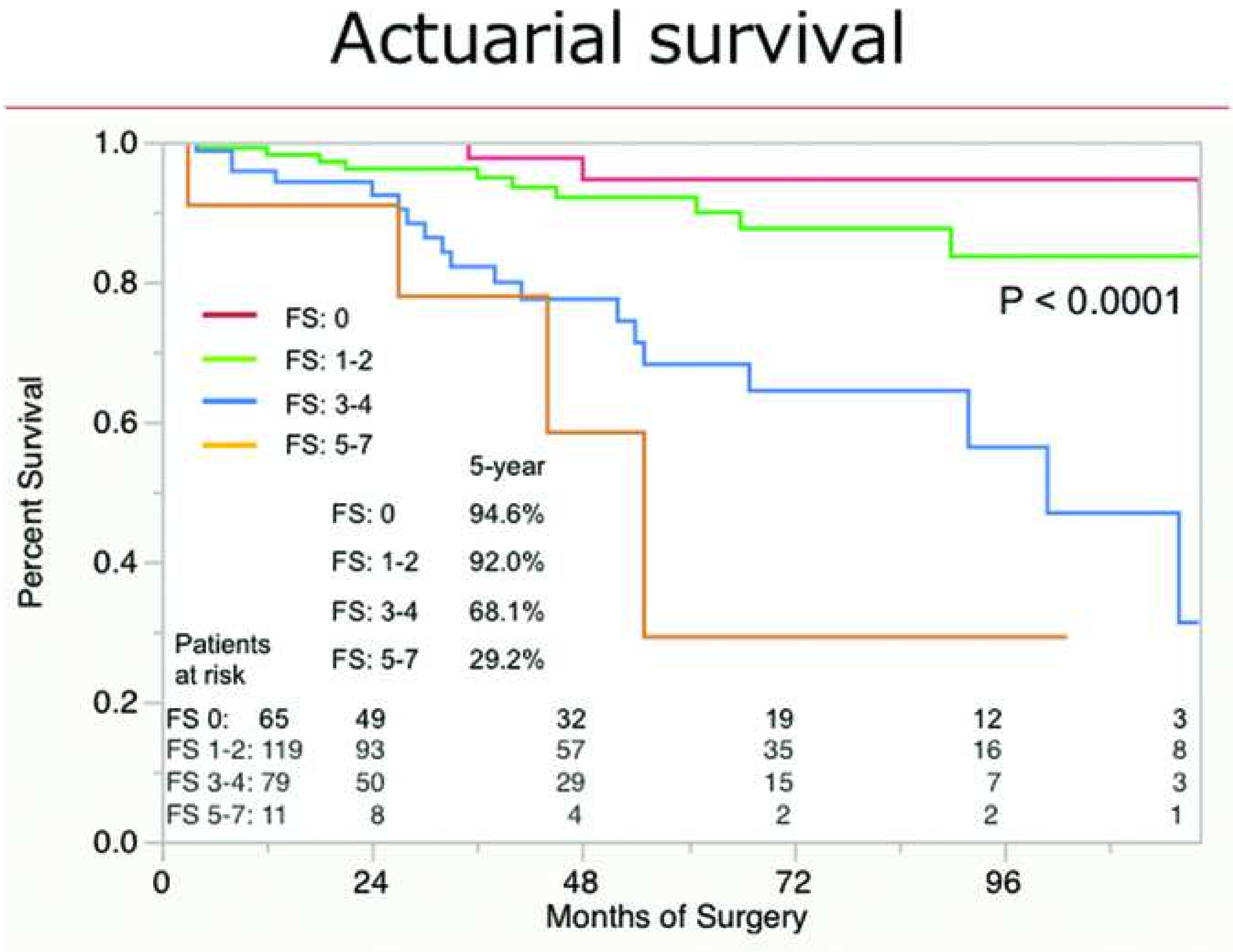
Click here to access/download;Figure;18-00241-fig1.tif




Actuarial survival
1.0
0.8
0.6
0.4
0.2
0.0
Percent Survival
frail
Control age and gender-matched general population to frail group
5-year
frail 57.7%
Control 83.0%
Patients at risk
frail:101 57 32 16 8 3
0
24
48
72
96
120
Months of Surgery


Actuarial survival
1.0
0.8
0.6
0.4
0.2
0.0
Percent Survival
frail (hospital survivors)
Control age and gender-matched general population to frail group
5-year
frail 64.0%
Control 83.0%
Patients at risk
frail:90 57 32 16 8 3
0 24 48 72 96 120
Months of Surgery

FINAL-FIG4


Actuarial survival
Percent Survival
1.0
0.8
0.6
0.4
0.2
0.0
FS: 0
FS: 1-2
FS: 3-4
FS: 5-7
P < 0.0001
5-year
FS: 0 94.6%
FS: 1-2 92.0%
FS: 3-4 68.1%
FS: 5-7 29.2%
Patients at risk
FS 0: 65 49 32 19 12 3
FS 1-2: 119 93 57 35 16 8
FS 3-4: 79 50 29 15 7 3
FS 5-7: 11 8 4 2 2 1
0
24
48
72
96
Months of Surgery

Impact of Frailty on Outcomes in Acute Type A Aortic Dissection

Toshihito Gomibuchi, MD, Tatsuichiro Seto, MD, Masaki Komatsu, MD, Haruki Tanaka, MD, Hajime Ichimura, MD, Takateru Yamamoto, MD, Noburo Ohashi, MD, Yuko Wada, MD, Kenji Okada, MD

Department of Cardiovascular Surgery, Shinshu University School of Medicine, Matsumoto, Japan

Corresponding author: Kenji Okada

Department of Cardiovascular Surgery, Shinshu University School of Medicine,

Asahi 3-1-1, Matsumoto, Nagano, 390-8621, Japan

Phone: 0263-37-2657

Fax: 0263-37-2721

E-Mail: keokada@shinshu-u.ac.jp

Meeting presentation: Scientific Posters of the Society of Thoracic Surgeons 54th Annual Meeting, Fort Lauderdale, Florida, January 27–31, 2018.

Word count:

Abstract: 250

Text (including figures, tables and references): ~~4491~~4432

Abstract

Background: Although frailty is used to predict morbidity and mortality, its effect on the outcomes of acute type A aortic dissection (ATAAD) has not been examined. Thus, the objective was to evaluate the role of frailty in predicting postoperative morbidity and mortality in ATAAD.

Methods: A retrospective analysis of a prospectively maintained database was undertaken for all patients (310) undergoing aortic surgery between May 2004 and March 2017. Frailty was evaluated using an index consisting of age >70 years, body mass index <18.5 kg/m^2, serum creatinine >1.2 mg/dL, anemia, history of stroke, hypoalbuminemia, and the psoas muscle area index. One point was given for each criterion met for a frailty score between 0 to 7. Frailty was defined as a score of ≥3.

Results: Of all patients, 106 (34.2%) were defined as frail. In-hospital mortality rates of frail versus non-frail patients were not significantly different (10.4% vs. 8.3%, respectively; P = 0.54). Incidences of postoperative major morbidities without re-exploration for bleeding were also not statistically different. Five-year survival rates were significantly worse for frail patients (57.7% vs. 85.1%; P = 0.0001). A frailty score of ≥ 3 was associated with late mortality and long-term outcomes were clearly stratified by frailty score.

Conclusions: Frailty, as defined using a 7-component frailty index, can serve as an independent predictor of the risk of late mortality in patients undergoing an ATAAD. Such frailty markers, all of which are easily assessed preoperatively, may provide valuable information for patient counseling and risk stratification before aortic surgery.

Key words: acute type A aortic dissection, frailty, rehabilitation

Introduction

Acute type A aortic dissection (ATAAD) is a life-threatening cardiovascular event that requires immediate surgical repair (1). In the field of aortic surgery, treatment methods such as surgical techniques, perioperative care, and sealing grafts have improved dramatically over the past decade. Consequently, improved outcomes in hospital mortality from this disease are well described in the recent literature (2). The aging population is rapidly increasing in many countries. However, with increasing life expectancy of the population comes a rise in the incidence of cardiovascular disease, including ATAAD (3). Frailty, defined as a state of increased vulnerability to stressors caused by a deterioration across multiple physiologic systems, is an emerging concept in clinical medicine. Most extensively investigated in community-dwelling geriatric populations, frail patients have been shown to be predisposed to increased falls, hospitalization, institutionalization, and mortality (4-6). Although frailty has been examined as a predictor of morbidity and mortality, its effect on ATAAD outcomes has not been studied. Therefore, the objective of the present study was to evaluate the role of frailty in predicting postoperative morbidity and mortality in patients undergoing aortic surgery.

Patients and Methods

The Shinshu University School of Medicine Institutional Ethics Committee approved this study (Permission No. 3989-2018). The need for individual patient consent was waived. From May 2004 to March 2017, 310 consecutive patients underwent an emergency open operation for ATAAD at our institution. Medical records were reviewed for preoperative risk factors, operative records, intraoperative events, and postoperative courses.

Frailty Definition

To classify frailty, a score was created that consisted of seven components previously identified in published data as objective indicators of frailty. The components were: 1) age >70 years (6), 2) body mass index <18.5 kg/m2 (7), 3) serum creatinine >1.2 mg/dL (8), 4) anemia (<12.0 g/dL for women, <13.0 g/dL for men) (9), 5) hypoalbuminemia (<3.5 g/dL) (10), 6) a history of stroke (11), and 7) the psoas muscle area index (12). One point was given for each criterion met to determine a frailty score of between 0 and 7. Frailty was defined as a score of ≥3. Risk models for hospital mortality and long-term survival were calculated using multivariable regression modeling.

The Barthel Index is a popular instrument for assessing the activities of daily living (ADL) (13). The total score ~~is~~ranges from 100~~, with ≤20 indicating ~~ (totally ~~dependent, ≤40 indicating severe impairment, ≥60 indicating highly ~~independent~~, and ≥85 indicating independent~~ patient) to 0 (completely dependent patient) with lower scores representing greater nursing dependency (14).

Definition of Clinical Presentation

Cardiogenic shock was defined as having a preoperative systolic blood pressure less than 80 mmHg or having a need for intravenous inotropic agents. Malperfusion syndromes were defined as signs or symptoms due to disrupted blood flow to end-organ systems such as the central nervous system (CNS), or to the coronary, visceral, or extremities' circulatory systems. CNS disorders caused by malperfusion syndrome were classified as transient or persistent according to the duration of the clinical presentation. Postoperative *de novo* neurologic dysfunction was considered permanent if it persisted at a patient's discharge and was a result of an intraoperative procedure. Transient dysfunction was defined as a temporary loss of orientation, slurred speech, agitation, or poor responses to commands. Neurologic dysfunction caused by preoperative brain malperfusion, deep shock status, cardiopulmonary resuscitation (CPR), requiring preoperative or postoperative supported percutaneous cardiopulmonary support (PCPS), and postoperative atrial fibrillation was excluded from *de novo* neurologic dysfunction. Preoperative independence in ADL was defined as a patient's ability to perform basic activities as follows: light housework, eating, toileting, and walking.

Surgical Protocol

The principal aim of our surgical strategy for treating ATAAD was to excise the primary entry tear. If the primary entry tear was oriented toward the ascending aorta, we performed a ATAAD repair using a hemiarch replacement (HAR) or partial arch replacement (PAR) with an intimal tear exclusion to reduce in-hospital mortality and morbidity in patients older than 70 years. We applied a total arch replacement

(TAR) when a HAR or PAR could not exclude the intimal tear. Arterial cannulation sites were determined according to the patient's status, preoperative organ malperfusion, and the preference of the surgeon; however, the femoral artery with the right axial artery was the most frequent choice. A venous cannula was inserted into the right atrium to the superior and inferior vena cava; cardiopulmonary bypass was then established and systemic cooling was initiated. After systemic body hypothermia induced minimal tympanic temperatures below 23°C, and minimal rectal temperatures below 30°C, the ascending aorta was opened, and antegrade selective cerebral perfusion was initiated. A gelatin-impregnated quadfurcated Dacron graft (Gelweave from Vascutek Ltd, Terumo Corporation, Inchinnan, Scotland; or J Graft Shield Neo from Japan Lifeline Co., Ltd., Tokyo, Japan) or Triplex (Terumo Corporation, Tokyo, Japan) was used. After completion of the distal anastomosis of the prosthetic graft, lower body circulation was reinstituted through a branch graft, and the tympanic/rectal temperature was rewarmed early. The proximal anastomosis of the graft was completed, followed by coronary reperfusion. Finally, the aortic arch vessels were reconstructed (15).

Follow-up

Follow-up information on survival, general health status, need for aortic reoperation, rupture, and causes of death were obtained from patients' medical records at our outpatient clinic or by telephoning patients or their relatives.

Statistical Analysis

Data were processed using JMP 12.0 software (SAS Institute Inc, Cary, NC, USA). Continuous values are expressed as the mean ± standard deviation (SD). Data were analyzed by the $\chi 2$ test or Fisher's exact test for categorical variables. Logistic regression analysis was performed to identify the risk factors for hospital mortality. Clinically relevant variables with $P < 0.05$ on univariable analysis were incorporated into multivariable models. Survival was assessed by the Kaplan–Meier method. A Cox proportional hazard analysis, into which all preoperative variables in patient profiles were incorporated, was used to determine the risk factors for late mortality. Differences were considered statistically significant at $P < 0.05$.

Results

Preoperative Patient Characteristics

Of the study patients, 106 (34.2%) were defined as frail (frailty score ≥3). Thirty-six (34.0%) patients of the frail group and 11 (5.4%) patients of the nonfrail group were octogenarians. Age ($P < 0.0001$), cerebrovascular disease ($P < 0.0001$), shock status ($P < 0.0001$), cardiopulmonary resuscitation ($P = 0.0005$), cardiac tamponade ($P < 0.0001$), transient CNS malperfusion ($P = 0.03$) and coma ($P = 0.05$) were significantly more prevalent in the frail group than in the younger group. Body weight ($P < 0.0001$), body mass index ($P = 0.0002$), serum albumin levels ($P < 0.0001$), hemoglobin ($P < 0.0001$), and estimated glomerular filtration rate (eGFR; $P < 0.0001$) were significantly lower in the frail group. Both the EuroSCORE II and JapanSCORE were significantly higher in the frail group ($P < 0.0001$ for both; Table 1).

Intraoperative Data

Table E1 shows intraoperative data. Operation and cardiopulmonary bypass times were significantly shorter in the frail group because the mode of surgery was mostly limited to the replacement of the hemiarch aorta in 70 patients (66.0%) of the frail group, but was applied to 73 patients (35.8%) of the younger, nonfrail group ($P < 0.0001$).

Early Outcomes

Mortality and morbidities rates are shown in Table 2. Overall, hospital mortality in the frail group was 10.4% (11/106); causes of death were low cardiac output syndrome (three patients), sepsis (three patients), multiple-organ failure (two patients), stroke (one patient), rupture of abdominal aortic aneurysms (one patient), and re-dissection of aorta (one patient). The hospital mortality rate in the nonfrail group was 8.3% (17/204); causes of death were low cardiac output syndrome (three patients), stroke (six patients), multiple-organ failure (four patients), sepsis (one patient), re-dissection of aorta (one patient), acute myocardial infraction (one patient), and cardiac tamponade (one patient). A difference in the in-hospital mortality of frail versus nonfrail patients was not noted ($P = 0.54$). Statistical differences in the incidences of postoperative major morbidities without re-exploration for bleeding was not observed between the two groups. The postoperative Barthel Index was significantly lower in the frail group, with 46 patients (43.4%) transferred to a rehabilitation hospital.

Table E2 shows univariable and multivariable analyses of hospital mortality. Preoperative shock (*P* = 0.002), cardiopulmonary resuscitation (*P* = 0.0001), overall malperfusion (*P* = 0.0008), coronary malperfusion (*P* = 0.004), visceral malperfusion (*P* < 0.0001), extremities malperfusion (*P* = 0.03), coma (*P* = 0.01), concomitant procedure (*P* < 0.0001), and long duration of cardiopulmonary bypass (≥4 hours, *P* = 0.04) were identified as risk factors for postoperative hospital mortality by univariable analysis~~.~~ ~~Visceral malperfusion~~, whereas surgical procedure and age were not. Preoperative shock (odds ratio [OR], ~~26.86~~3.07; *P* = 0.~~001~~01), and concomitant procedure (OR, ~~3.38~~5.66; *P* ~~=~~≤ 0.~~02~~001) were determined to be risk factors for postoperative hospital mortality by multivariable analysis, whereas having a frailty score ≥3 was not.

Late Outcomes

Follow-up was completed in 95.2% of patients, with the mean follow-up period being 44.4 ± 36.7 (range, 1–148, median 38) months. The number of overall late deaths was 38 (frail group, n = 23; nonfrail group, n = 15~~) in response to cerebral vascular disease (n = 6), pneumonia (n = 5), malignancy (n = 4), senility (n = 2), unknown cause (n = 2), sepsis (n = 1), graft infection (n = 1), rupture of aortic aneurysms (n=1), and re-dissection of aorta (n = 1) in the frail group, and cerebral vascular disease (n = 3), pneumonia (n = 2), malignancy (n = 2), senility (n = 2), unknown cause (n = 2), graft infection (n = 1), sepsis (n = 1),~~

~~heart failure (n = 1), and myelodysplastic syndromes (n = 1) in the nonfrail group.~~). Figure 1 shows overall long-term survival assessed by the Kaplan–Meier method. Survival rates at 1, 5 and 10 years after surgery were 85.8%, 57.7% and 27.8% in the frail group, respectively, and 90.4%, 85.1% and 72.9% in the nonfrail group, respectively, with a significant difference noted between the groups (P = 0.0001). The 5-year survival rates in age- and sex-matched general populations in comparison to the frail group were 83.0% (Figures 2, 3). Figure 4 shows that long-term survival was worse across the higher categories of the frailty score. Cox proportional hazard analysis (Table 3) showed that a frailty score ≥3 (hazard ratio [HR], ~~3.34; P = 0.009), male (HR, 5.09~~4.71; P < 0.0001), male (HR, 3.57; P = 0.0005), preoperative ADL independence (HR, ~~18.64~~14.39; P = 0.002), and ~~hemoglobin~~overall malperfusion (HR, ~~0.70~~2.23; P = 0.~~004~~02) were significant risk factors for long-term mortality according to multivariable analysis

Comment

Life expectancy is steadily increasing in many countries and with it comes a higher incidence of cardiovascular diseases, including ATAAD (16). Surgical outcomes for ATAAD have been improving in Japan (2) as well as the rest of the world (17), with several studies reporting on good results from the surgical repair of ATAAD in elderly patients (3, 18). Bachet reported (19) that age did not provide an objective criterion of any individual’s health condition in elderly patients with acute aortic dissection. In this regard, in addition to the usual surgical scores, indices of frailty developed mostly by geriatricians would be of some interest and could better identify those individuals actually at major perioperative risk ~~for acute aortic dissection~~. The concept of frailty, which is a term widely used to denote a multidimensional syndrome of the loss of reserves such as energy, physical ability, and cognition, as well as increased vulnerability, has recently been established (20). Lee and colleagues (6) reported the first study of frailty in cardiac surgery patients, with frailty a risk for postoperative complications and an independent predictor of in-hospital mortality, institutional discharge, and reduced midterm survival. Fried et al reported cycle of frailty that frailty is consistent with the several clinical markers and represent an adverse, potentially downward spiral of energetics (21). Ganapathi et al defined frailty using a frailty index consisting six components (age, body mass index, anemia, history of stroke, hypoalbuminemia, and total psoas volume). They showed these frailty were associated with discharge to a destination other than home and poorer 30-day and/or in-hospital and 1-year survival after proximal aortic replacement surgery (5). However, these frailty index consisting six components do not contain renal dysfunction. Walker SR et al reported an association of frailty and physical function in patients with non-dialysis CKD (8). Therefore, we classified frailty consisted of seven components previously identified in published data as objective indicators of frailty. Frailty screening improves risk assessments in cardiac surgery patients.

Preoperative clinical severity, such as shock status, ~~CPA~~CPR, or malperfusion syndrome, deeply affect morbidity and mortality after surgical treatment of ATAAD (~~21~~22). Patients of the frail group were older and more likely to be female. They were also more likely to have comorbid disease, including a more frequent history of previous stroke, and chronic renal insufficiency. Frail patients were likely to have severe preoperative status, such as shock, cardiopulmonary resuscitation, and transient CNS malperfusion. However, we found that the in-hospital mortality rate was 10.4% for the frail group while the in-hospital mortality or complication rate without re-exploration for bleeding did not differ from those of the nonfrail group. The reason there was no difference in the results might be that we performed a ATAAD repair using a HAR or PAR in frail patients. We previously performed ATAAD repair using HAR or PAR with intimal tear exclusion to reduce rates of in-hospital mortality and morbidity in patients older than 70 years. We found that HAR and PAR with entry tear exclusion reduced deaths associated with ATAAD in elderly patients, without increasing the risk of reoperation and aortic-related death (~~22~~23). Owing to this, emergent surgery for frail patients with ATAAD showed acceptable mortality.

The Barthel Index at discharge was significantly lower for the frail group. Our study showed that the postoperative ADL for frail patients had deteriorated, meaning that frail patients generally took a lot of time for rehabilitation. Therefore, of the frail patients, 43.4% were transferred to a rehabilitation hospital in response to the increased time needed to recover well after surgery.~~ All patients without a permanent neurologic deficit were discharged home, while all bedridden patients had a permanent neurologic deficit or paraplegia. ~~

The five-year survival rate for the frail group, who were discharged from hospital after treatment for ATAAD, was 57.7% in our study. The frail group had a significantly lower survival rate than the nonfrail group (P = 0.0001). The five-year survival rates of a general population that was age- and sex-matched to the frail group were 83.0% in both cases. Cox proportional hazard analysis determined that having a frailty score ≥3 was a risk factor for late mortality according to univariable and multivariable analysis. These findings suggested that patients who were frail have poor long-term outcomes. Furthermore, the long-term outcomes after ATAAD were clearly stratified by frailty score. We think that the adverse prognosis for patients with frail affected the frail itself rather than the postoperative influence. Participation in self-selected exercise activities is independently associated with delaying the onset and the progression of frailty (24). Therefore, regular exercise might be examined as a potential factor in frailty prevention for postoperative patients.

In-hospital mortality of the octogenarian and younger groups were 6.3% and 9.5%, respectively (*P* = 0.49). 5-year survival rates in the octogenarian and younger groups were 52.2% and 80.2%, respectively (*P* = 0.08). 46.8% of octogenarian patients were transferred to a rehabilitation hospital in responds to the increased time for octogenarian patients to recover well after surgery. Emergency surgery for octogenarians with ATAAD showed acceptable mortality. The option of surgical management for ATAAD in octogenarians should not be disregarded solely due to the advanced age of the patients.

We are a policy to perform surgery in any patients. In an emergency clinical setting, aggressive surgical treatment may be a reasonable option for frail patients. However, We are at a loss as to whether to perform surgery on a very high frailty patient such as bedridden. Consult the patient's family, but the family also become confused. Hata and colleagues (~~23~~25) described how about 20% of their octogenarian patients with ATAAD who underwent surgery became bedridden forcing families to take responsibility for patients who experienced unconsciousness, had dementia, or became bedridden. Consequently, for patients with a severe frailty, there may often be a hesitation about whether to perform surgery. While JapanSCORE and EuroSCORE II are useful for predicting hospital mortality, they are not related to late outcomes. On the other hand, Frailty score is useful for predicting late outcomes. For this reason, frailty markers may provide valuable information when counseling patients and in late mortality risk stratification before surgery.

Physical performance measures, such as gait speed, have also been used as a standard tool to evaluate the preoperative frailty and disabilities of patients (~~24~~26). However, ATAAD is an emergency event, meaning there is no time to evaluate physical performance. In contrast, such frailty markers are easily assessed preoperatively.

Limitations

The limitations of this investigation included that this was a retrospective study from a single center. In our study, the majority of patients showed preoperative independence in ADL. However, patients with impaired physical activity may not have been transferred to our hospital because of an inoperative condition, and may have been medically treated in another hospital. In addition, the logistic regression analysis for hospital mortality was limited by a small number of events because our surgical approach generally provided satisfactory outcomes. The mean follow-up period was also short (44.4 ± 36.7 months; range, 1–148 months; median, 38 months).

In conclusion, frailty, as defined using a seven-component frailty index, can serve as an independent predictor of late mortality risk in patients undergoing surgery in ATAAD. Such frailty markers, all of which are easily assessed preoperatively, may provide valuable information for patient counseling and risk stratification prior to surgery.

Funding Statement: The authors have nothing to disclose with regard to commercial support.

Conflict of interest: The authors wish to state that they have no conflicts of interest to declare.

References

1. Omura A, Miyahara S, Yamanaka K, Sakamoto T, Matsumori M, Okada K, et al. Early and late outcomes of repaired acute DeBakey type I aortic dissection after graft replacement. The Journal of thoracic and cardiovascular surgery. 2016;151(2):341-8.

2. Committee for Scientific Affairs Affairs The Japanese Association for Thoracic Surgery, Masuda M, Okumura M, Doki Y, Endo S, Hirata Y, et al. Thoracic and cardiovascular surgery in Japan during 2014 : Annual report by The Japanese Association for Thoracic Surgery. General thoracic and cardiovascular surgery. 2016;64(11):665-97.

3. Omura A, Matsuda H, Minami H, Nakai H, Henmi S, Murakami H, et al. Early and Late Outcomes of Operation for Acute Type A Aortic Dissection in Patients Aged 80 Years and Older. Ann Thorac Surg. 2017;103(1):131-8.

4. Chikwe J, Adams DH. Frailty: the missing element in predicting operative mortality. Semin Thorac Cardiovasc Surg. 2010;22(2):109-10.

5. Ganapathi AM, Englum BR, Hanna JM, Schechter MA, Gaca JG, Hurwitz LM, et al. Frailty and risk in proximal aortic surgery. J Thorac Cardiovasc Surg. 2014;147(1):186-91 e1.

6. Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010;121(8):973-8.

7. Challa S, Sharkey JR, Chen M, Phillips CD. Association of resident, facility, and geographic characteristics with chronic undernutrition in a nationally represented sample of older residents in U.S. nursing homes. The journal of nutrition, health & aging. 2007;11(2):179-84.

8. Walker SR, Gill K, Macdonald K, Komenda P, Rigatto C, Sood MM, et al. Association of frailty and physical function in patients with non-dialysis CKD: a systematic review. BMC nephrology. 2013;14:228.

9. Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood. 2006;107(5):1747-50.

10. Watanabe A. Why albumin now? Let's think about albumin measurement methods, the definition of hypoalbuminemia, and microheterogeneity. Nutrition. 2005;21(11-12):1156-7.

11. Farhat JS, Velanovich V, Falvo AJ, Horst HM, Swartz A, Patton JH, Jr., et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. The journal of trauma and acute care surgery. 2012;72(6):1526-30; discussion 30-1.

12. Ikeno Y, Koide Y, Abe N, Matsueda T, Izawa N, Yamazato T, et al. Impact of sarcopenia on the outcomes of elective total arch replacement in the elderlydagger. Eur J Cardiothorac Surg. 2017;51(6):1135-41.

13. Mahoney FI, Barthel DW. FUNCTIONAL EVALUATION: THE BARTHEL INDEX. Maryland state medical journal. 1965;14:61-5.

14. Sumi M, Ariyoshi T, Miura T, Hashimoto W, Hashizume K, Matsukuma S, et al. Are octogenarians in good condition after cardiac valvular surgery? Ann Thorac Cardiovasc Surg. 2014;20(6):1021-5.

14. Quinn TJ, Langhorne P, Stott DJ. Barthel index for stroke trials: development, properties, and application. Stroke. 2011;42(4):1146-51.

15. Okada K, Omura A, Kano H, Sakamoto T, Tanaka A, Inoue T, et al. Recent advancements of total aortic arch replacement. J Thorac Cardiovasc Surg. 2012;144(1):139-45.

16. Olsson C, Thelin S, Stahle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation. 2006;114(24):2611-8.

17. Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A, et al. Presentation, Diagnosis, and Outcomes of Acute Aortic Dissection: 17-Year Trends From the International Registry of Acute Aortic Dissection. J Am Coll Cardiol. 2015;66(4):350-8.

18. Kawahito K, Kimura N, Yamaguchi A, Aizawa K, Misawa Y, Adachi H. Early and Late Surgical Outcomes of Acute Type A Aortic Dissection in Octogenarians. Ann Thorac Surg. 2018;105(1):137-43.

19. Bachet J. Outcomes of limited proximal aortic replacement for type A aortic dissection in octogenarians: What does "age" mean? J Thorac Cardiovasc Surg. 2016;152(2):447.

20. Furukawa H, Tanemoto K. Frailty in cardiothoracic surgery: systematic review of the literature. Gen Thorac Cardiovasc Surg. 2015;63(8):425-33.

2121. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M146-56.

22. Kondoh H, Satoh H, Daimon T, Tauchi Y, Yamamoto J, Abe K, et al. Outcomes of limited proximal aortic replacement for type A aortic dissection in octogenarians. J Thorac Cardiovasc Surg. 2016;152(2):439-46.

2223. Komatsu K, Takano T, Terasaki T, Wada Y, Seto T, Fukui D, et al. Surgical outcomes of acute type A aortic dissection in elderly patients. Ann Thorac Surg. 2014;97(5):1576-81.

2324. Peterson MJ, Giuliani C, Morey MC, Pieper CF, Evenson KR, Mercer V, et al. Physical activity as a preventative factor for frailty: the health, aging, and body composition study. The journals of gerontology Series A, Biological sciences and medical sciences. 2009;64(1):61-8.

25. Hata M, Sezai A, Niino T, Yoda M, Unosawa S, Furukawa N, et al. Should emergency surgical intervention be performed for an octogenarian with type A acute aortic dissection? J Thorac Cardiovasc Surg. 2008;135(5):1042-6.

2426. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. Jama. 2011;305(1):50-8.

Formatted: Font color: Text 1

Table 1. Preoperative status of patients

Variables	Overall n = 310 (%)	Frail n = 106 (%)	Nonfrail n = 204 (%)	*P* value
No. of patients, (%)	310	106 (34.2)	204 (65.8)	
Age, y, mean ± SD	67.5 ± 11.9	76.2 ± 7.9	63.0 ± 11.1	<.0001
Octogenarians	47 (15.2)	36 (34.0)	11 (5.4)	<.0001
Male gender	155 (50.0)	41 (38.7)	114 (55.9)	.006
Body mass index	23.3 ± 3.95	22.1 ± 3.5	23.9 ± 4.1	.0002
Diabetes mellitus	15 (4.8)	8 (7.6)	7 (3.4)	.16
Hypertension	206 (66.5)	79 (74.5)	127 (62.3)	.03
Hemodialysis	10 (3.2)	8 (7.6)	2 (1.0)	.004
Connective tissue disease	11 (3.5)	0	11 (5.4)	.02
Coronary artery disease	15 (4.8)	6 (5.7)	9 (4.4)	.59
Cerebrovascular disease	27 (8.7)	21 (19.8)	6 (2.9)	<.0001
Prior cardiac surgery	12 (3.9)	5 (4.7)	7 (3.4)	.55
Preoperative ADL independence	304 (98.1)	102 (96.2)	202 (99.0)	.19
Preoperative status				
Shock	74 (23.9)	40 (37.7)	34 (16.7)	<.0001
Cardiopulmonary resuscitation	21 (6.8)	15 (14.2)	6 (2.9)	.0005
Cardiac tamponade	69 (22.3)	42 (39.6)	27 (13.2)	<.0001
Organ malperfusion	129 (41.6)	43 (40.6)	86 (42.2)	.81
CNS	71 (22.9)	31 (29.3)	40 (19.6)	.06
Transient	40 (12.9)	20 (18.9)	20 (9.8)	.03
Persistent	24 (7.7)	12 (11.3)	12 (5.9)	.12
Coronary	14 (4.5)	5 (4.7)	9 (4.4)	1.00
Visceral	7 (2.3)	2 (1.9)	5 (2.5)	1.00
Extremities	42 (13.5)	9 (8.5)	33 (16.2)	.08
Coma	11 (3.5)	7 (6.6)	4 (2.0)	.05
Aortic valve insufficiency > III	38 (12.3)	12 (11.3)	26 (12.8)	.86
Albumin (g/dL)	3.6 ± 0.5	3.3 ± 0.5	3.8 ± 0.4	<.0001
Hemoglobin (g/dL)	12.7 ± 1.9	11.3 ± 1.6	13.5 ± 1.6	<.0001
eGFR (mL/min/1.73 m^2)	59.9 ± 23.8	49.4 ± 25.0	65.4 ± 21.3	<.0001
DeBakey classification				
Type I	198 (63.9)	53 (50.0)	145 (71.2)	
Type II	96 (31.0)	49 (46.2)	47 (23.0)	.0002
Type IIIb retrograde	16 (5.2)	4 (3.8)	12 (5.9)	
EuroSCORE II	6.8 ± 6.5	9.3 ± 6.8	5.5 ± 5.8	<.0001
JapanSCORE				

30 days' operative mortality (%)	13.8 ± 10.5	17.8 ± 12.8	11.8 ± 8.3	<.0001
30 days' operative mortality/morbidity (%)	40.4 ± 12.7	46.2 ± 14.3	37.4 ± 10.6	<.0001

SD, standard deviation; ADL, activities of daily living; CNS, central nervous system; eGFR, estimated glomerular filtration rate.

Table 2. Postoperative data

Variables	Overall n = 310 (%)	Frail n = 106 (%)	Nonfrail n = 204 (%)	*P* value
No. of patients, (%)	310	106	204	
Thirty-day mortality	25 (8.1)	11 (10.4)	14 (6.9)	.28
Hospital mortality	28 (9.0)	11 (10.4)	17 (8.3)	.54
New-onset neurologic dysfunction	32 (10.3)	9 (8.5)	23 (11.3)	.56
Temporary neurologic deficit	7 (2.3)	4 (3.8)	3 (1.5)	.24
Permanent neurologic deficit	25 (8.1)	5 (4.7)	20 (9.8)	.13
Renal failure requiring hemofiltration	29 (9.4)	8 (7.6)	21 (10.3)	.54
Re-exploration for bleeding	15 (4.8)	1 (0.9)	14 (6.9)	.02
Tracheostomy	19 (6.1)	8 (7.6)	11 (5.4)	.46
Prolong mechanical ventilation time >48 h	127 (41.0)	44 (41.5)	83 (40.7)	.90
Intensive care unit stay (days)	7.2 ± 8.1	7.8 ± 8.3	6.9 ± 8.0	.35
Hospital stay (days)	36.9 ± 31.0	38.2 ± 32.5	36.3 ± 30.3	.60
Transfer to rehabilitation hospital	94 (30.3)	46 (43.4)	48 (23.5)	.0004
Barthel Index (2010~)	80.3 ± 30.2	70.5 ± 32.7	85.7 ± 27.4	.0006

Table 3. Univariable and multivariable analyses of late mortality (excluding hospital deaths)

	Univariable		Multivariable	
Variables	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Frailty score ≥3	4.21 (2.20–8.27)	<.0001	3.35 (1.36–8.46).0094.71 (2.32–9.75) <.0001	
Male gender	2.04 (1.06–4.13)	.03	5.07 (2.36–11.3.57 (1.71) <.0001–8.00) .0005	
Preoperative transient Neurologic deficit	3.19 (1.51–6.34)	.003	1.44 (0.42–6.21)	.58
Shock	2.14 (1.06–4.14)	.04	1.45 (0.78 (0.2667–2.16) .6598) .34	
Cardiopulmonary resuscitation	4.85 (1.42–12.6)	.02	1.32 (0.30–4.92)	.70
Cardiac tamponade	2.69 (1.36–5.16)	.005	1.51 (0.52–4.47)	.45
Malperfusion (overall)	2.41 (1.26–4.78)	.008	1.22 (0.32–3.77).752.23 (1.15–4.51) .02	
Cerebral	2.36 (1.18–4.54)	.02	1.46 (0.28–7.03)	.64
Kidney	2.83 (1.11–6.27)	.03	2.29 (0.58–9.32)	.23
Preoperative ADL independence	14.36 (3.37–42.18)	.002	18.6214.39 (3.49–81.5301–52.73)	.002
Albumin	0.23 (0.11–0.49)	.0001	0.77 (0.30–2.08)	.60
Hemoglobin	0.66 (0.55–0.80)	<.0001	0.70 (0.55–0.89)	.004
eGFR (mL/min/1.73 m^2)	0.98 (0.97–0.99)	.03	1.01 (0.99–1.02)	.38

HR, Hazard ratio; ADL, activities of daily living; eGFR, estimated glomerular filtration rate; CI, confidence interval.

Figure legends

Figure 1. Survival curves of frail and nonfrail patients after discharge from hospital.

Figure 2. Survival curves of frail patients who were surgically treated compared with age- and sex-matched general populations.

Figure 3. Survival curves of frail patients after discharge from the hospital compared with age- and sex-matched general populations.

Figure 4. Survival curves across stratified frailty scores (FS).

Abbreviations and Acronyms

ATAAD = acute type A aortic dissection

ADL = activities of daily living

CNS = central nervous system

CPR = cardiopulmonary resuscitation

PCPS = percutaneous cardiopulmonary support

HAR = hemiarch replacement

PAR = partial arch replacement

TAR = total arch replacement

SD = standard deviation

eGFR = estimated glomerular filtration rate

OR = odds ratio

HR = hazard ratio