The relation between physical fitness, frailty and all-cause mortality after elective endovascular abdominal aortic aneurysm repair

Lassima M. Reijnen, MSc,[a] Daphne Van der Veen, MSc,[a] Michiel C. Warlé, MD PhD,[b] Suzanne Holewijn, PhD,[a] Jan-Willem Lardenoije, MD PhD,[a] *and* Michel M. P. J. Reijnen, MD PhD,[a,c] *Arnhem, Nijmegen, and Enschede, The Netherlands*

ABSTRACT

Background: Accurate determination of probable surgical outcomes is fundamental in decision-making regarding appropriate abdominal aortic aneurysm treatment. These outcomes depend, among other factors, on patient-related factors such as physical fitness. The primary aim of this study was to evaluate the correlation between physical fitness, measured by the metabolic equivalent of task (MET) score and the five-factor Modified Frailty Index (MFI-5), and all-cause mortality.

Methods: Four hundred twenty-nine patients undergoing elective endovascular treatment of an infrarenal aortic aneurysm (EVAR) from January 2011 to September 2018 were identified in an existing local abdominal aortic aneurysm database. Physical fitness was measured by the MFI-5 and the METs as registered during preoperative screening. The primary end point was 1-year all-cause mortality and secondary end points included 5-year all-cause mortality, freedom from aneurysm-related mortality and aneurysm-related reinterventions. Correlations were analyzed using Spearman's rho and survival was analyzed using Kaplan-Meier analyses. The effect of physical fitness on mortality was assessed by binary logistics regression analyses.

Results: There was a positive correlation between the MFI-5 and 1-year all-cause mortality (Rho $= 0.163$; $P = .001$), but not between the METs and 1-year all-cause mortality (Rho $= -0.083$; $P = .124$). A significant correlation between both MFI-5 and METs and 5-year all-cause mortality was observed (Rho $= 0.255$; $P < .001$ and Rho $= -0.154$; $P = .004$). When stratified by the MFI-5, the 1- and 5-year follow-up survival rates were 95.1% and 85.9%, respectively, in the group with the lowest MFI-5 and 74.5% and 33.1% in the group with the highest MFI-5 score ($P = .007$ and $P < .001$). When stratified by METs categories for 1-year follow-up, no significant differences in survival between the groups were observed ($P = .090$). The 5-year follow-up survival rate was 39.4% in the lowest METs category and 76.3% in the highest METs category ($P = .039$). Logistic regression analysis, assessing the impact of age, sex, METs, and the MFI-5 on the risk of all-cause mortality, showed that only age and the MFI-5 made a significant contribution.

Conclusions: There is a significant positive association between the MFI-5 and both the 1- and 5-year all-cause mortality rates after EVAR; METs only correlated with the 5-year all-cause mortality. Only age and the MFI-5 contributed to predicting overall survival after EVAR; therefore, it could be recommended to add the MFI-5 for guidance in preoperative counselling. (J Vasc Surg 2021;■:1-10.)

Keywords: Aortic aneurysm; Frailty; Physical fitness; Elective surgical procedures

An abdominal aortic aneurysm (AAA) is a potential lethal cardiovascular disease because of its high morbidity and mortality risk in case of rupture.[1] Originally, AAA treatment consisted of open surgical repair, but nowadays the preferred approach for treatment is endovascular repair (EVAR).[2,3] Previous research has shown a benefit of EVAR over open repair regarding 30-day mortality, although this advantage is lost on long-term follow-up.[4,5]

Decision-making regarding appropriate AAA treatment remains complex. Fundamental to this process is an accurate determination of probable clinical outcomes. These outcomes depend on a variety of factors, among which are factors relating to the patients' health, including physical activity and frailty. Frailty is a multidimensional syndrome of decreased reserve and resistance to stressors resulting from cumulative declines and causing vulnerability to adverse outcomes.[6,7] Frailty has

From the Department of Vascular Surgery, Rijnstate, Arnhem[a]; the Department of Vascular Surgery, Radboudumc, Nijmegen[b]; and the Multi-Modality Medical Imaging group, TechMed Centre, University of Twente, Enschede.[c]

Supported by the Rijnstate "Vriendenfonds." This fund did not have any involvement in the research.

Author conflict of interest: none.

Additional material for this article may be found online at www.jvascsurg.org.

Correspondence: Michel M. P. J. Reijnen, MD PhD, Department of Vascular Surgery, Rijnstate, Wagnerlaan 55 PO Box 9555, 6800 TA, Arnhem, The Netherlands (e-mail: mmpj.reijnen@gmail.com).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2021.04.039

been shown as an independent risk factor for predicting postsurgical outcomes in patients, such as 30-day mortality in elective AAA treatment.[8,9]

One of the various frailty indexes is the five-factor Modified Frailty Index (MFI-5).[10] It is based on the 70-item scale developed by the Canada Study of Health and Aging and the Modified Frailty Index (MFI).[11-13] These indexes are based on a measuring of deficit accumulation identifying functional and physiologic decline and have been validated as predictors of mortality and postoperative complications in the vascular surgery population using the American College of Surgeons National Surgical Quality Improvement Program database.[10,11,14,15]

Physical activity can be measured using the metabolic equivalent of task (MET) by scaling how much energy a specific physical effort will take related to the required energy at rest.[16] Different kinds of physical activities have been described and assigned intensity levels in METs in a compendium by Ainsworth et al.[17] The association between all-cause mortality and physical activity is related to the total energy expenditure as well as the intensity at which physical activity might be performed.[18,19] Guidelines have recommended to use METs as reference thresholds of absolute intensities using the following classification: light, less than 3.0 METs; moderate, 3.0 to 5.9 METs; and vigorous 6.0 or more METs.[19]

The primary aim of the current study was to evaluate the relation between physical fitness and all-cause mortality in patients undergoing elective endovascular AAA repair. To assess physical fitness, the METs as registered during the preoperative screening and the MFI-5 were used. The hypothesis was that mortality is lower in physical fit patients (high METs and low MFI-5).

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective cohort study
- **Key Findings:** Elective endovascular aneurysm repair (EVAR) was conducted in 429 patients. There was a significant association between baseline five-factor Modified Frailty Index (MFI-5) and 1- and 5-year all-cause mortality ($P = .001$; $P < .001$). There was a significant association between baseline metabolic equivalent of task and 5-year all-cause mortality ($P = .004$).
- **Take Home Message:** Scoring systems, like the metabolic equivalent of tasks and particularly the MFI-5, can be used for the prediction of survival after endovascular aneurysm repair and thus used for guidance in preoperative counselling.

METHODS

All patients electively treated for an infrarenal AAA by endovascular means between January 2011 and September 2018 were identified in an existing local AAA database and analyzed retrospectively. The study was conducted according to the principles of all applicable Dutch laws, Algemene Verordening Gegevensbescherming (AVG), Wet op de geneeskundige behandelingsovereenkomst (WGBO), and codes of conduct. A waiver from the medical ethical committee was obtained and approval from the Local Feasibility Committee (LHC). Informed consent was waived by the institutional review board.

Files were screened for demographic characteristics, vascular characteristics, preoperative comorbidities, medication, procedural data, hospitalization data, follow-up data, laboratory values, adverse events including mortality data are all available through the database. Additionally, the MFI-5 and MET scores were obtained from the medical chart.

Follow-up included outpatient clinic visits at 30 days; 6, 12, 18, and 24 months; and annually thereafter unless events required closer examination. Follow-up consisted of clinical examination, laboratory values, contrast-enhanced computed tomography scanning and/or duplex ultrasound imaging.

For data collection and management, the Research Manager software was used which is fully validated and includes an audit trail ("the Research Manager", Deventer, the Netherlands). All patients received a study number by which all data has been coded. The principal investigator, trained doctor, or doctor in training had access to the coded source data, if necessary.

Study population. Patients were included if electively treated for infrarenal AAA with endovascular repair and if the MET score was registered during preoperative screening and/or the MFI-5 score could be calculated. Exclusion reasons were objection to the use of their medical records for research, both MFI-5 and MET scores missing, complex endovascular repair, including iliac branched devices, fenestrated and branched endografts and chimney procedures, emergent repair or revision surgery after previous abdominal aortic repair.

End points and definitions. The primary end point was 1-year all-cause mortality defined as any death occurring within 12 months with a 6-month window after the original procedure for not every patient had their 1-year follow-up at 12 months, regardless of the cause of death. Secondary end points included the 5-year all-cause mortality, defined as any death occurring within 66 months after the original procedure, regardless of cause; the AAA-related mortality, defined as death resulting from rupture, endograft infection, or thrombosis; and AAA-related reinterventions, defined as reinterventions aiming at maintaining AAA exclusion or distal perfusion.

The MFI-5 was used to quantitatively measure frailty. Five variables assessed in the MFI-5 were derived from the medical chart and matched to preoperative variables (Table I). The presence of one of each of the following five items gave a patient one point: functional status (functional health status before surgery either partially dependent, defined as use of a walking cane or walker, weekly assistance of persons or high Katz activities of daily living, or totally dependent, defined as wheelchair bound, daily assistance of persons, or low Katz activities of daily living); diabetes mellitus (controlled by diet, oral agents, or insulin); history of chronic obstructive pulmonary disease; congestive heart failure within 30 days before surgery; and hypertension requiring medication. Functional status was a standard question in the nurses' questionnaire asked at the moment of hospitalization, the other four items were standard assessed in the preoperative screening conducted by an anesthesiologist. Total points for each patient divided by 5 (total available points) gave the patient's MFI-5 score (range, 0.0-1.0). Increasing MFI-5 score implies an increase in frailty and a decrease in physical fitness.

METs as registered during the preoperative screening, conducted by anesthesiologists in accord with current guidelines for preoperative cardiovascular assessment. METs are based on a subjective estimation of minimum activities or degree of exercise tolerance a patient was able to perform and were used as a scale to compare morbidity and mortality (Table II).[20] In case METs were not registered, remarks of activity were noted. If applicable, those activities were linked to MET score definitions (Table II) or METs using the 2011 Compendium of Physical Activities.[17] If not, a comment about being able to walk more than 100 meters or the ability to perform normal domestic work whether or not in combination with exercise tolerance good/condition excellent/very fit/normal and self-sufficient scored MET 4. Exercise tolerance moderate/condition fair/limited and self-sufficient or otherwise in combination with the comment stairs+ scored MET 3. Two researchers independently compared and evaluated the METs, remarks of activities or degree of exercise tolerance. In case of other remarks, consensus was achieved by consulting an independent researcher. After all METs were rated, the scores were independently compared and evaluated by two researchers. Results were discussed and a final METs was allocated. METs were categorized as recommended by the guidelines[19]: light, less than 3 METs; moderate, 3 to 6 METs; and vigorous, 6 or more METs. Increasing METs implies an increase in capability to perform physical activities and an increase in physical fitness.

Statistical analysis. Normality was determined based on visual inspection of the normality graphs and tested using the Kolgomorov method. Continuous variables (numeric) were expressed as mean ± standard deviations or as median with interquartile ranges if not normally distributed. Discrete variables (categorical) were expressed as number followed by percentage.

Cumulative rates of overall survival, freedom from aneurysm-related mortality and freedom from AAA-related reinterventions were analyzed using Kaplan-Meier analyses and included censoring for patients lost to follow-up. Kaplan-Meier analyses were compared by MFI-5 and METs categories using log-rank test. Associations between survival, MFI-5 and METs categories were tested with the χ^2 test using Yates' correction for continuity or the Pearson χ^2. Effect size was tested using phi coefficient or Cramer's V. Two-sided *P* values of less than .05 were considered significant.

Correlations were analyzed using the Spearman's rho between all-cause mortality and physical fitness measured by MFI-5 and METs.

Binary logistic regression analyses were performed to obtain adjusted odds ratios (ORs) for survival. To control for the increased risk of all-cause mortality, the model was adjusted for age, sex, METs and MFI-5. Model assumptions were evaluated using tolerance and the variance inflation factors associated with each variable to check for multicollinearity. The model fit was obtained using the Omnibus tests of model coefficients and the Hosmer-Lemeshow goodness of fit test. Additional subgroup analyses were performed by METs categories. Statistical analyses were performed using IBM SPSS Statistics (SPSS version 25.0 for windows, IBM Corporation, Armonk, NY).

RESULTS

Baseline patient and AAA characteristics are depicted in Table III. Four hundred twenty-nine vascular surgery patients were identified who underwent elective endovascular AAA repair within the study period and from whom MFI-5 and/or METs were registered (Supplementary Fig, online only). Males compromised 85.1% of the patients, and the median age was 74.0 years (interquartile range, 67.0-78.5). Totally dependent/partially dependent functional status was applicable for 19.8% of the patients and 48% of the patients had American Society of Anesthesiologists class higher than 3. MFI-5 was 0 in 15.4% of the patients, 0.2 in 43.1%, 0.4 in 27.7%, 0.6 in 9.8%, and 0.8 in 3.7%. METs were classified in three categories: light, moderate, and vigorous. The majority (59.9%) was classified as moderate. In 42 patients (9.8%), MET 3 was assigned according to the 2011 Compendium of Physical Activities[17] or derived from the MET definitions (Table II). In 31 patients (7.2%), MET 4 was allocated according to the 2011 Compendium of Physical Activities[17] or derived from the MET definitions (Table II). In 17 patients (4.0%) who were allocated MET 3 and 69 patients (16.1%) who were allocated MET 4, it was not possible to assign a MET score according to the 2011 Compendium of Physical Activities[17] or to derive it from the MET definitions (Table II) and the MET score was assigned based solely on the comment about exercise tolerance. Functional status was missing in one

Table I. Derivation of the five-factor Modified Frailty Index score (*MFI-5*)

Variables	MFI-5	AAA database
Functional and cognitive impairment	Independent functional status before surgery	Self-sufficient/independent Use of tools Assistance of persons Katz ADL
Medical comorbidities	History of diabetes	None Diabetes mellitus type II, controlled by diet or oral agents Diabetes mellitus type II, insulin-controlled Diabetes mellitus type I Unknown
	COPD	History of COPD
	Congestive heart failure (within 30 days before surgery)	History of heart failure
	Hypertension requiring medication	None (cutoff point, diastolic pressure usually lower than 90 mm Hg) Controlled (cutoff point, diastolic pressure usually lower than 90 mm Hg) with single drug Controlled with two drugs Requires more than 2 drugs or is uncontrolled Unknown

AAA, Abdominal aortic aneurysm; *ADL*, activities of daily living; *COPD*, chronic obstructive pulmonary disease.

Table II. Metabolic equivalent of task score (*MET*)

MET score	Definition
1	Due to condition unable to walk independent
2	Is able to walk independent indoor
3	Is able to perform light domestic work or walk down a stair
4	Is able to walk short distances (minimum 100 meters) or perform normal domestic work
5	Is able to walk long distances or cycle
6	Is able to perform demanding domestic work or take care of the garden
7	Is able to walk up hills or run short distances
>8	Is able to exercise

patient, which led to a missing MFI-5 score. In 85 patients (19.8%), comments about their ability to perform physical activities or degree of exercise tolerance were lacking, which led to missing MET scores.

Survival. The overall survival rate at the 1-year follow-up was 90.6%. At the 5-year follow-up, the cumulative survival rate was 66.4% and cumulative freedom of AAA-related mortality rate was 97.1% (Fig 1).

Through 1 year of follow-up, 39 patients (9.1%) died; 4 (0.9%) were AAA related. Of these AAA-related deaths, one patient died due to an anterior AAA rupture immediately after endovascular repair after which a median laparotomy complicated by a massive myocardial infarction with unsuccessful resuscitation. One patient died due to an AAA rupture 5 days after endovascular repair, another died due to bowel ischemia, and the last patient died due to sepsis caused by an infected endograft 3 months after the index procedure. During follow-up to 9 years, 134 patients (31.2%) died; 9 (2.1%) were AAA related, including the above mentioned patients. In those 134 patients who died, MET scores were missing in 30 patients (7.0%); and in all 134 patients MFI-5 scores were known.

When stratified by MFI-5, the survival rates at the 1- and 5-year follow-ups were 95.1% and 85.9%, respectively, in the group with the lowest MFI-5, indicating a good level of physical fitness (Fig 2, *A*). With an increasing MFI-5, a decrease in survival rates was observed at the 1- and 5-year follow-ups ($P = .007$ and $P < .001$). In the group with the highest MFI-5 score, the survival rates were 74.5% and 33.1%, respectively, at the 1- and 5-year follow-ups. There were significant associations between the MFI-5 score and survival at 1-year follow up ($\chi^2 = 14.256$; $P = .007$) and 5-year follow-up ($\chi^2 = 32.120$; $P < .001$). Cramer's V showed significant effect sizes (0.183 and 0.274, respectively).

When stratified by METs categories, no significant differences in survival between groups were observed at the 1-year follow-up ($P = .090$), although there was a trend for worse survival in the light METs category (Fig 2, *B*). There was a significant association between the METs categories and 5-year survival ($\chi^2 = 7.017$; $P = .030$). Cramer's V showed a significant effect size (0.143). The 5-year survival rate was 39.4% in the lowest METs category. With increasing METs category, an increase in survival rate was found ($P = .039$), with the highest METs category having a survival rate of 76.3%.

Correlation. The correlation between the MFI-5 score and 1-year all-cause mortality showed a significant

Table III. Baseline characteristics

Patient characteristics	Median (IQR)[a]
Age, years	74.0 (67.0-78.5)
Male sex	365 (85.1)
Body mass index, kg/m^2	26.5 (24.1-29.1)
Systolic blood pressure, mm Hg	142.0 (128.0-154.0)
Diastolic blood pressure, mm Hg	80.0 (73.0-88.0)
Current smoker	147 (34.2)
History of smoking	53 (50.6)
Functional dependence	85 (19.8)
MFI-5 score	
0	66 (15.4)
0.2	185 (43.1)
0.4	119 (27.7)
0.6	42 (9.8)
0.8	16 (3.7)
MET score	
1	8 (1.9)
2	23 (5.4)
3	68 (15.9)
4	125 (29.1)
5	64 (14.9)
6	33 (7.7)
7	7 (1.6)
8	16 (3.7)
ASA classification	
1	1 (0.2)
2	219 (51.0)
3	185 (43.1)
4	21 (4.9)
Cardiac disorder	
Arrhythmia	66 (15.4)
Congestive heart failure	34 (7.9)
Coronary artery disease	43 (10.0)
Myocardial infarction	101 (23.5)
Coronary artery bypass grafting	57 (13.3)
Percutaneous coronary intervention	76 (17.7)
Diabetes mellitus requiring medication	87 (20.3)
Hypertension requiring medication	321 (74.8)
Chronic obstructive pulmonary disease	89 (20.7)
Hyperlipidemia requiring medication	302 (70.4)
Anticoagulant therapy	360 (83.9)
Aneurysm morphology	
Infrarenal aortic neck diameter, mm	24.0 (21.0-26.0)
AAA maximum diameter, mm	57.0 (53.0-63.0)
Infrarenal aortic neck length, mm	25.4 (17.0-35.0)
Angle between AAA and neck	39.9 (27.0-53.5)
Endograft type	
Endovascular aneurysm repair	
Medtronic Endurant	186 (43.4)
Gore Excluder	86 (20.0)
Endologix AFX	22 (5.1)
Endologix Powerlink	2 (0.5)
Endurant EVO	7 (1.6)
Endologix Ovation	2 (0.5)
Cook Zenith	4 (0.9)
Endologix Nellix	120 (28.0)

AAA, Abdominal aortic aneurysm; *ASA*, American Society of Anesthesiologists Physical Status Classification; *IQR*, interquartile range; *MFI-5*, five-factor Modified Frailty Index; *MET*, metabolic equivalent of task.
[a]All results are tested for normality with Kolmogorov-Smirnov <0.05. Continuous variables are expressed as median with interquartile ranges. Discrete variables are expressed as number (%).

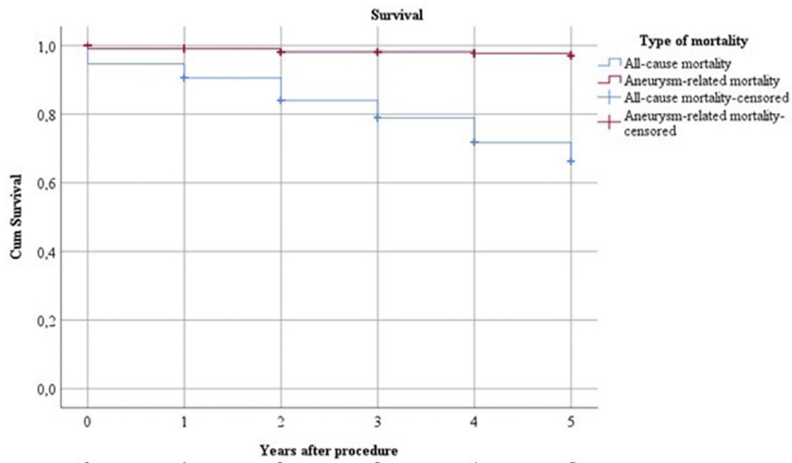
positive correlation (Rho = 0.163; *P* = .001), whereas no correlation between the METs and 1-year all-cause mortality was observed (Rho = −0.083; *P* = .124) (Supplementary Table I, online only). The correlation between both MFI-5 and METs and 5-year all-cause mortality showed significant correlations (Rho = 0.255; *P* < .001 and Rho = −0.154; *P* = .004).

There was a negative correlation between MFI-5 and METs (Rho = −0.308; 95% confidence interval [CI], −0.4 to −2.09; *P* < .001). The higher the MFI-5, the lower the METs.

The correlation between both MFI-5 (Rho = 0.063; *P* = .195) and METs (Rho = −0.062; *P* = .253) and AAA-size showed no significant correlation.

Binary logistic regression analysis. Direct logistic regression was performed to assess the impact of age, sex, METs and MFI-5 on the likelihood of survival after elective endovascular AAA-repair. The full model containing all predictors was statistically significant (χ^2 [13, n = 343] = 50.086; *P* < .001; Supplementary Table II, online only). The model as a whole explained between 19.3% of the variance in survival and correctly classified 73.8% of cases. Only age and MFI-5 made a statistically significant contribution to the model. Age recorded an OR of 0.934 (95% CI, 0.900-0.969; *P* < .001). An MFI-5 score of 0.2 did not reach a statistically significant OR. However, an MFI-5 score of 0.4 recorded an OR of 0.362 (95% CI, 0.133-0.984; *P* = .046). The OR of an MFI-5 score of 0.6 was 0.103 (95% CI, 0.031-0.342; *P* < .001). The OR of an MFI-5 score of 0.8 was 0.180 (95% CI, 0.040-0.815; *P* = .026). This finding indicates that elderly patients and patients with higher MFI-5 scores are less likely to survive after elective endovascular AAA repair while controlling for other factors in the model. In this model, sex and METs do not seem to contribute to predicting survival after elective endovascular AAA repair.

When stratified by METs categories, a statistically significant contribution of age and MFI-5 was observed in the



Years after procedure	0	1	2	3	4	5
All-cause mortality						
No. at Risk	406	355	294	249	201	147
Survival (%)	94.6	90.6	84.0	78.9	71.8	66.4
Standard Error	0.011	0.014	0.019	0.022	0.025	0.027
Aneurysm-related mortality						
No. at Risk	425	317	314	221	220	158
Survival (%)	99.1	99.1	98.1	98.1	97.7	97.1
Standard Error	0.005	0.005	0.007	0.007	0.008	0.010

Fig 1. Overall cumulative freedom from all-cause mortality and aneurysm-related mortality.

moderate METs category. The vigorous METs category did not reach statistical significance although a trend was observed for only MFI-5 to contribute to the model whereas in the light METs category none of the predictors made a statistically significant contribution.

Freedom from reinterventions. Within the study follow-up, a first reintervention was necessary in 82 patients and a second reintervention was required in 24 of them, with a mean time to reintervention of 2.5 ± 0.22 years and 2.8 ± 0.33 years, respectively. A third reintervention was necessary in six patients, and one patient had a total of four reinterventions in 7 years. At the 1- and 5-year follow-ups, the freedom from reintervention rate was 92.7% and 73.7%, respectively. The reinterventions were not related to the type of endograft used.

When stratified by MFI-5, both at the 1- and 5-year follow-ups, no difference was observed in freedom from reintervention rate although there was a trend for less reinterventions for worse MFI-5 (Fig 3, *A*).

When stratified by METs categories, at the 1-year follow-up, the freedom from reintervention rate was 96.8% in the group with the lowest METs category (Fig 3, *B*). With increasing METs category a decrease in freedom from reintervention rate was found ($P = .033$), with the highest METs category having a freedom from reintervention rate of 84.6%. There was a significant association between freedom from reintervention and METs categories ($\chi^2 = 6.411$; $P = .041$). Cramer's V showed a significant effect size (0.137). At the 5-year follow-up, no significant differences in freedom from reintervention rate between groups were observed ($P = .167$), although there was a trend for lower freedom from reintervention rate with increasing METs category.

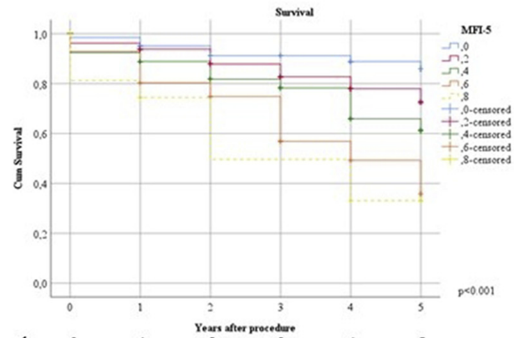
DISCUSSION

In the present study, we have shown that there is a significant positive correlation between the MFI-5 score and survival at the 1- and 5-year follow-ups. In addition, there is a significant negative association between the METs categories and 5-year survival.

In assessing the impact of age, sex, METs, and MFI-5 on the risk of all-cause mortality after EVAR, using logistic regression analysis, only age and MFI-5 made a significant contribution to the model; sex and METs did not contribute. This finding could partly be explained by the fact that the female subgroup was relatively small, so that statistics with regard to sex are not meaningful. For the same reason, we chose to not conduct further sex analysis as this should be examined in a larger cohort. Also, of the 134 patients who had died during follow-up, only 103 were included in the logistic analysis, as both METs and MFI-5 needed to be registered. For 30 patients, METs was missing so this may have led to an underestimation of the contribution of METs to this model.

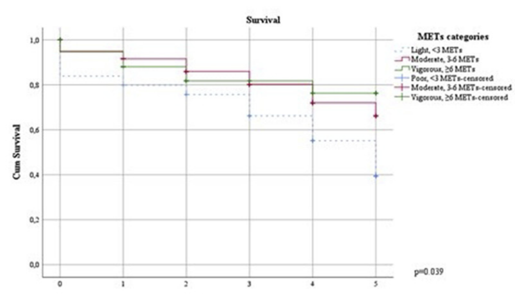
Previous research has shown that prehabilitation with preoperative physical activity before colorectal cancer or

A



MFI-5 (N=428)							
0 (N=66)	Years after procedure	0	1	2	3	4	5
	No. At Risk	65	57	46	39	38	29
	Survival (%)	98.5	95.1	91.2	91.2	88.8	85.9
	Standard Error	0.015	0.027	0.038	0.038	0.044	0.051
0.2 (N=185)	Years after procedure	0	1	2	3	4	5
	No. At Risk	178	154	133	114	97	67
	Survival (%)	96.2	93.8	87.8	82.8	77.9	72.5
	Standard Error	0.014	0.018	0.026	0.031	0.035	0.040
0.4 (N=119)	Years after procedure	0	1	2	3	4	5
	No. At Risk	110	100	81	66	48	39
	Survival (%)	92.4	88.9	81.8	78.3	65.9	61.2
	Standard Error	0.024	0.029	0.037	0.041	0.051	0.054
0.6 (N=42)	Years after procedure	0	1	2	3	4	5
	No. At Risk	39	32	27	19	13	8
	Survival (%)	92.9	80.3	74.8	56.8	49.2	35.8
	Standard Error	0.040	0.062	0.069	0.083	0.087	0.092
0.8 (N=16)	Years after procedure	0	1	2	3	4	5
	No. At Risk	13	11	6	6	4	2
	Survival (%)	81.3	74.5	49.7	49.7	33.1	33.1
	Standard Error	0.098	0.110	0.138	0.138	0.133	0.133

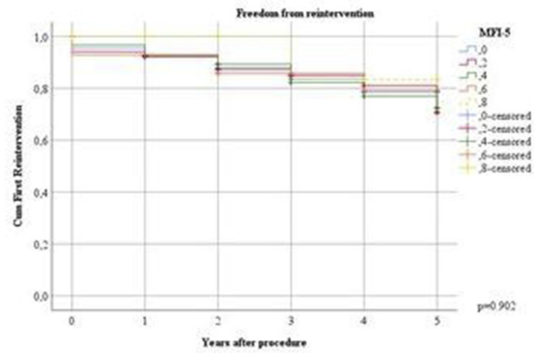
B



METs category (N=344)							
Light (N=31)	Years after procedure	0	1	2	3	4	5
	No. At Risk	26	20	18	14	10	5
	Survival (%)	83.9	79.9	75.7	66.2	55.2	39.4
	Standard Error	0.066	0.074	0.081	0.095	0.106	0.121
Moderate (N=257)	Years after procedure	0	1	2	3	4	5
	No. At Risk	244	217	183	155	123	90
	Survival (%)	94.9	91.6	85.9	80.2	72.0	66.2
	Standard Error	0.014	0.018	0.023	0.027	0.032	0.035
Vigorous (N=56)	Years after procedure	0	1	2	3	4	5
	No. At Risk	53	40	26	15	14	9
	Survival (%)	94.6	88.0	81.8	81.8	76.3	76.3
	Standard Error	0.030	0.046	0.061	0.061	0.077	0.077

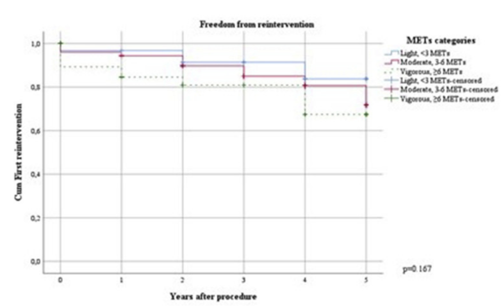
Fig 2. A, One- and 5-year freedom from all-cause mortality, stratified by the five-factor Modified Frailty Index score (*MFI-5*). **B,** One- and 5-year freedom from all-cause mortality, stratified by metabolic equivalent of task categories (*METs*).

A



MFI-5 (N=428)							
0 (N=66)	Years after procedure	0	1	2	3	4	5
	No. At Risk	63	54	43	37	32	19
	First reintervention (%)	95.5	92.0	88.0	83.4	78.5	78.5
	Standard Error	0.026	0.034	0.043	0.051	0.059	0.059
0.2 (N=185)	Years after procedure	0	1	2	3	4	5
	No. At Risk	174	148	126	105	85	55
	First reintervention (%)	94.1	92.2	87.3	84.9	81.1	70.8
	Standard Error	0.017	0.020	0.026	0.029	0.033	0.045
0.4 (N=119)	Years after procedure	0	1	2	3	4	5
	No. At Risk	115	96	77	58	44	32
	First reintervention (%)	96.6	92.8	89.3	82.2	77.0	72.4
	Standard Error	0.017	0.025	0.031	0.042	0.049	0.055
0.6 (N=42)	Years after procedure	0	1	2	3	4	5
	No. At Risk	39	26	24	13	12	5
	First reintervention (%)	92.9	92.9	85.7	85.7	79.1	79.1
	Standard Error	0.040	0.040	0.061	0.061	0.085	0.085
0.8 (N=16)	Years after procedure	0	1	2	3	4	5
	No. At Risk	12	9	6	5	2	2
	First reintervention (%)	100	100	100	83.3	83.3	83.3
	Standard Error				0.152	0.152	0.152

B



METs category (N=344)							
Light (N=31)	Years after procedure	0	1	2	3	4	5
	No. At Risk	30	18	17	12	11	4
	First reintervention (%)	96.8	96.8	91.4	91.4	83.8	83.8
	Standard Error	0.032	0.032	0.060	0.060	0.091	0.091
Moderate (N=257)	Years after procedure	0	1	2	3	4	5
	No. At Risk	247	214	176	143	112	72
	First reintervention (%)	96.1	94.3	89.8	85.0	80.7	71.7
	Standard Error	0.012	0.015	0.020	0.025	0.030	0.039
Vigorous (N=56)	Years after procedure	0	1	2	3	4	5
	No. At Risk	50	36	22	12	10	5
	First reintervention (%)	89.3	84.6	80.9	80.9	67.4	67.4
	Standard Error	0.041	0.051	0.060	0.060	0.101	0.101

Fig 3. A, One- and 5-year freedom from reinterventions, stratified by the five-factor Modified Frailty Index score (*MFI-5*). **B,** One- and 8-year freedom from reinterventions, stratified by metabolic equivalent of task categories (*METs*).

thoracic surgery has positive effects on postoperative outcomes.[21] Physical activity and frailty are methods to assess physical fitness. Nevertheless, there is no consensus on the definition and measurement criteria for frailty and different methods to assess frailty have been used, including methods that focus primarily on assessing comorbidities.[9-11,13-15,22-27] In contrast with comorbidities, it is possible to influence physical fitness preoperatively. Various studies have supported the impact of frailty on increased mortality and other complications after vascular surgery.[8,10,11,14,15,22,24,26,27] Most of these studies used retrospective or registry methods,[10,11,14,15,22] just as the current study, but some used prospective methods to evaluate frailty.[9,24,26,27] Still, it remains unclear if prehabilitation before vascular surgery is associated with a decrease in the incidence of long-term postoperative complications such as all-cause mortality.

In the current study, the MFI-5 was used to measure frailty, based on the Canada Study of Health and Aging and the MFI and validated for the vascular surgery population.[10-13] METs was used to assess physical activity, being a subjective scoring system. Sometimes it was not noted in the case files as a final score, but described as a minimum activity a patient was able to perform, making it less accurate. In these cases, it remained unclear if the patient was able to perform more vigorous activities. This factor may have led to an underestimation of patients' abilities to perform physical activities. In other cases, a description of a patient's exercise tolerance was noted instead of a MET score. Even though different kinds of physical activities have been described and assigned intensity levels in METs by Ainsworth et al, METs remains an estimation of one's ability to perform certain activities as energy expenditure during a certain physical activity differs on the basis of various person related factors (eg, age, sex) and the environmental conditions under which the activity was performed. The grouping of MET scores that were not able to be assigned to the 2011 compendium or derived from the MET definitions in MET 3 and 4 could account for the fact that the MET score was not sensitive enough to be a significant variable for the overall 1-year data.

Previous research suggests that the risk for increasing frailty is independent of the type of repair chosen for AAA repair.[8] The perception that frail patients might better tolerate EVAR than conventional open AAA repair might have led surgeons to increasingly use these techniques, specifically in frail patients.[24] In this study, only elective endovascular AAA repair was examined. All patients had uncomplicated AAA, so the relation between physical fitness and 1-year all-cause mortality might be stronger in complex endovascular techniques such as fenestrated EVAR or open repair or in acute cases. Future studies are needed to explore the strength of the relation between physical fitness, assessed by the MFI-5 and METs and survival in other AAA techniques.

The sober 1- and 5-year survival in the highest MFI-5 group found in this study raises the question if a conservative approach in this population would not be justified since the risk of rupture appears to be lower than the risk of all-cause mortality.[2] It underscores the importance of individualized risk stratification in clinical decision making algorithms. The American Society of Anesthesiologists and MET scores are already part of the standard preoperative screening, as recommended in the guidelines of the European Society of Anesthesiology, even though the association between the American Society of Anesthesiologists score and 1-year mortality after EVAR remains questionable.[20,28] The Society for Vascular Surgery/American Association for Vascular Surgery Medical Comorbidity Grading System, however, also correlates well with both the 1-year all-cause mortality and major adverse events.[28] As the current study clearly has shown a relation with the estimated survival, which seems to outperform the MET score, the MFI-5 could be added to guide preoperative counselling for EVAR. As mentioned, there are many methods to assess frailty and comorbidities and further research to develop a broad, practical risk assessment tool, including comorbidities as well as physical fitness and frailty, is necessary.

A significant correlation was observed between the METs and the reintervention rates at 1 year. Patients that had a better physical fitness had a higher likelihood for reinterventions, although this difference disappeared at 5-year follow-up. This correlation might be partly explained by a potential lower threshold for reinterventions in fitter patients. However, all patients were considered to be fit for EVAR at time of surgery and a similar pattern was not observed for the MFI-5. Therefore, this association remains to be elucidated. Fitness is not the only variable to be considered when predicting freedom from reinterventions. Because our main objective was 1- and 5-year mortality, we did not look at the type of intervention or indication for reintervention when assessing the influence of MFI-5 and METs. Future studies are needed to explore the effect of MFI-5 and METs on reinterventions after AAA repair.

This study was limited by its retrospective nature. A retrospective analysis was conducted, which does not contain variables of interest for certain frailty analysis such as grip strength or gait speed. Also, partly owing to the transition of to electronic patient files a number of MET scores were lost. Besides, METs were not reported in all patients, which might have caused a selection bias. This was mostly the case in patients treated before 2016. Standardized recording of MET scores during the preoperative screening will contribute to an even more accurate derivation of the MET scores. One of the strengths of this study is that there is no limitation in follow-up, as in the National Surgical Quality Improvement Program database that only tracks patients for 30 days,[8,10,11,14,15] and we were able to assess long-term outcomes as well.

CONCLUSIONS

There is a significant relation between 1-year all-cause mortality after endovascular treatment of an AAA and the MFI-5. There is a significant relation between 5-year all-cause mortality and both MFI-5 and METs. Only age and MFI-5 contributed to predicting overall survival after EVAR and therefore it could be recommended to add the MFI-5 for guidance in preoperative counselling. Further prospective research is needed to clarify if these scores can be helpful in the decision-making process in patients with an AAA.

AUTHOR CONTRIBUTIONS

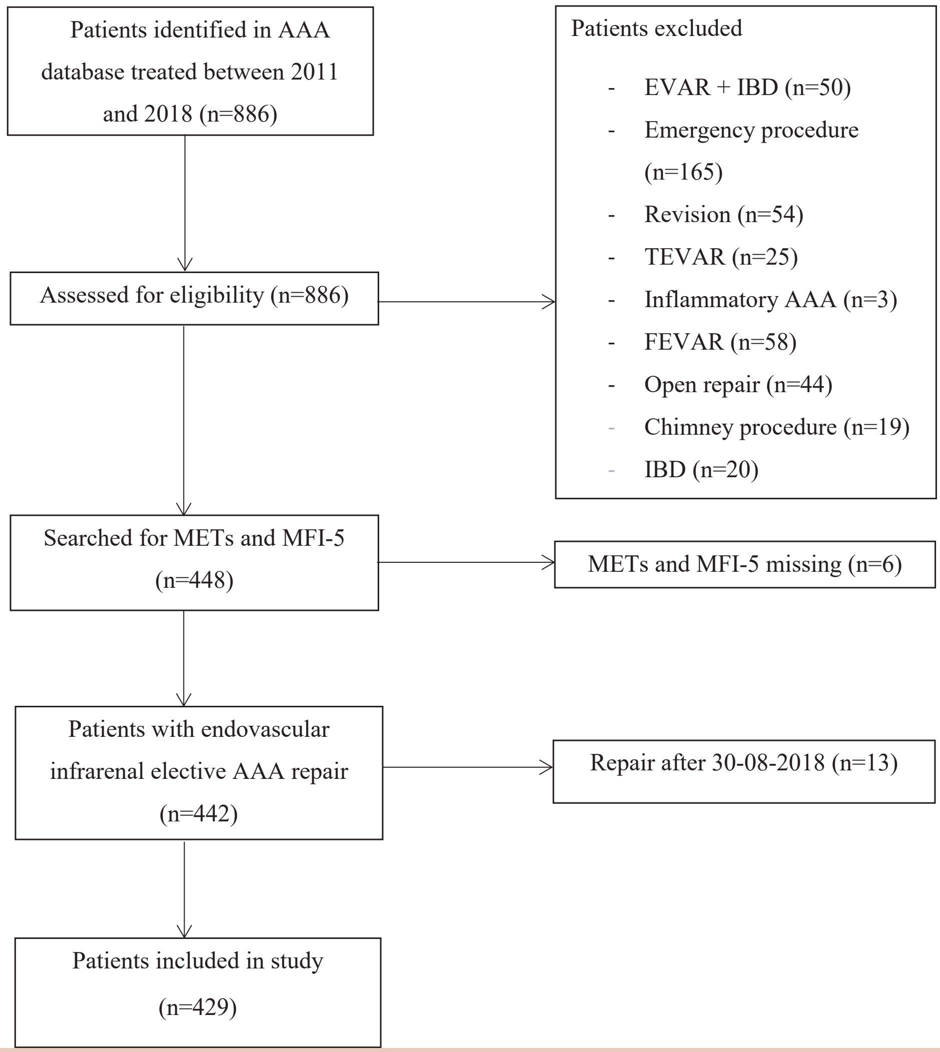
Conception and design: LR, DVdV, MW, SH, JL, MR
Analysis and interpretation: LR, SH
Data collection: LR, DVdV, SH
Writing the article: LR
Critical revision of the article: LR, DVdV, MW, SH, JL, MR
Final approval of the article: LR, DVdV, MW, SH, JL, MR
Statistical analysis: LR, SH
Obtained funding: SH, MR
Overall responsibility: MR

REFERENCES

1. Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS, et al. The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Arch Intern Med 2000;160:1425-30.
2. Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. J Vasc Surg 2018;67:2-77.e2.
3. Wanhainen A, Mani K, de Borst GJ. The most important news in the new ESVS 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysm. J Cardiovasc Surg 2019;60:485-9.
4. Blankensteijn JD, de Jong SE, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SM, et al. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. N Engl J Med 2005;352:2398-405.
5. Stather PW, Sidloff D, Dattani N, Choke E, Bown MJ, Sayers RD. Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm. Br J Surg 2013;100:863-72.
6. Abellan van Kan G, Rolland Y, Houles M, Gillette-Guyonnet S, Soto M, Vellas B. The assessment of frailty in older adults. Clin Geriatr Med 2010;26:275-86.
7. Dana F, Capitan D, Ubre M, Hervas A, Risco R, Martinez-Palli G. Physical activity and frailty as indicators of cardiorespiratory reserve and predictors of surgical prognosis: general and digestive surgery population characterization. Rev Esp Anestesiol Reanim 2018;65:5-12.
8. Arya S, Kim SI, Duwayri Y, Brewster LP, Veeraswamy R, Salam A, et al. Frailty increases the risk of 30-day mortality, morbidity, and failure to rescue after elective abdominal aortic aneurysm repair independent of age and comorbidities. J Vasc Surg 2015;61:324-31.
9. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg 2010;210:901-8.
10. Subramaniam S, Aalberg JJ, Soriano RP, Divino CM. New 5-factor modified frailty index using American College of Surgeons NSQIP data. J Am Coll Surg 2018;226:173-81.e8.
11. Karam J, Tsiouris A, Shepard A, Velanovich V, Rubinfeld I. Simplified frailty index to predict adverse outcomes and mortality in vascular surgery patients. Ann Vasc Surg 2013;27:904-8.
12. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. ScientificWorldJournal 2001;1:323-36.
13. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. J Gerontol A Biol Sci Med Sci 2007;62:738-43.
14. Pandit V, Zeeshan M, Nelson PR, Hamidi M, Jhajj S, Lee A, et al. Frailty syndrome in patients with carotid disease: simplifying how we calculate frailty. Ann Vasc Surg 2020;62:159-65.
15. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. J Surg Res 2013;183:104-10.
16. Blond K, Brinklov CF, Ried-Larsen M, Crippa A, Grontved A. Association of high amounts of physical activity with mortality risk: a systematic review and meta-analysis. Br J Sports Med 2020;54:1195-201.
17. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr, Tudor-Locke C, et al. 2011 compendium of physical activities: a second update of codes and MET values. Med Sci Sports Exerc 2011;43:1575-81.
18. Bauman AE. Updating the evidence that physical activity is good for health: an epidemiological review 2000-2003. J Sci Med Sport 2004;7(1 Suppl):6-19.
19. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc 2007;39:1423-34.
20. Kristensen SD, Knuuti J, Saraste A, Anker S, Bøtker HE, Hert SD, et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J 2014;35:2383-431.
21. Onerup A, Angenete E, Bock D, Börjesson M, Fagevik Olsén M, Grybäck Gillheimer E, et al. The effect of pre- and post-operative physical activity on recovery after colorectal cancer surgery (PHYSSURG-C): study protocol for a randomised controlled trial. Trials 2017;18:212.
22. Lee JS, He K, Harbaugh CM, Schaubel DE, Sonnenday CJ, Wang SC, et al. Frailty, core muscle size, and mortality in patients undergoing open abdominal aortic aneurysm repair. J Vasc Surg 2011;53:912-7.
23. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392-7.
24. Revenig LM, Canter DJ, Taylor MD, Tai C, Sweeney JF, Sarmiento JM, et al. Too frail for surgery? Initial results of a large multidisciplinary prospective study examining preoperative variables predictive of poor surgical outcomes. J Am Coll Surg 2013;217:665-70.e1.
25. Robinson TN, Eiseman B, Wallace JI, Church SD, McFann KK, Pfister SM, et al. Redefining geriatric preoperative assessment using frailty, disability and co-morbidity. Ann Surg 2009;250:449-55.
26. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC Jr, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. Am J Surg 2013;206:544-50.
27. Reeve TE 4th, Ur R, Craven TE, Kaan JH, Goldman MP, Edwards MS, et al. Grip strength measurement for frailty assessment in patients with vascular disease and associations with comorbidity, cardiac risk, and sarcopenia. J Vasc Surg 2018;67:1512-20.
28. Dijkstra ML, van Sterkenburg SM, Lardenoye JW, Zeebregts CJ, Reijnen MM. One-year outcomes of endovascular aneurysm repair in high-risk patients using the Endurant stent-graft comparison of the ASA classification and SVS/AAVS medical comorbidity grading system for the prediction of mortality and adverse events. J Endovasc Ther 2016;23:574-82.

Submitted Aug 12, 2020; accepted Apr 16, 2021.

Additional material for this article may be found online at www.jvascsurg.org.



Supplementary Fig (online only). Inclusion flowchart. *AAA,* Abdominal aortic aneurysm; *EVAR,* endovascular aneurysm repair; *IBD,* iliac branched device; *TEVAR,* thoracic endovascular aortic repair; *FEVAR,* fenestrated endovascular aortic repair; *METs,* metabolic equivalent of task score; *MFI-5,* factor-5 modified frailty index.

Supplementary Table I (online only). Spearman's Rho correlation for mortality in follow-up categories and physical fitness measured with the five-factor Modified Frailty Index (*MFI-5*) and metabolic equivalent of task (*MET*)

	All repairs (n = 429)	
All-cause mortality (n = 134)	MFI-5 (n = 428)	METs (n = 344)
30 days (n = 4; 1; 3)	−0.046	0.034
Six months (n = 23; 18; 5)	0.128[a]	−0.102
One year (n = 39; 32; 7)	0.163[a]	−0.083
Two year (n = 62; 53; 9)	0.178[a]	−0.079
Three year (n = 78; 66; 12)	0.212[a]	−0.113[b]
Four year (n = 98; 81; 17)	0.248[a]	−0.133[b]
Five year (n = 110; 91; 19)	0.255[a]	−0.154[a]
Six year (n = 122; 102; 20)	0.294[a]	−0.179[a]
Seven year (n = 131; 109; 22)	0.251[a]	−0.177[a]
Eight year (n = 133; 111; 22)	0.245[a]	−0.171[a]
Nine year (n = 134; 112; 22)	0.253[a]	−0.171[a]

[a]Results are statistically significant at $P = .01$ (2-tailed).
[b]Results are statistically significant at $P = .05$ (2-tailed).

Supplementary Table II (online only). Adjusted odds ratios (*ORs*) and 95% confidence interval (*CI*) obtained from the binary logistic regression analysis for overall survival

									95.0% CI for OR	
Step 1[a]	Variable		B	SE	Wald	df	*P* value	OR	Lower	Upper
	Sex		0.049	0.365	0.018	1	.893	1.050	0.514	2.145
	Age		−0.069	0.019	13.349	1	.000	0.934	0.900	0.969
	MFI-5	0.0			16.410	4	.003			
		0.2	−0.782	0.486	2.586	1	.108	0.458	0.176	1.187
		0.4	−1.016	0.510	3.969	1	.046	0.362	0.133	0.984
		0.6	−2.270	0.611	13.822	1	.000	0.103	0.031	0.342
		0.8	−1.714	0.770	4.952	1	.026	0.180	0.040	0.815
	METs	1	−0.097	1.040	0.009	1	.926	0.908	0.118	6.972
		2	−0.142	0.860	0.027	1	.869	0.868	0.161	4.686
		3	−0.434	0.760	0.327	1	.567	0.648	0.146	2.869
		4	−0.066	0.740	0.008	1	.929	0.936	0.219	3.993
		5	−0.093	0.770	0.015	1	.903	0.911	0.201	4.118
		6	0.565	0.846	0.447	1	.504	1.760	0.336	9.232
		7	0.286	1.296	0.049	1	.826	1.331	0.105	16.884
		>8			3.622	7	.822			
	Constant		6.979	1.487	22.012	1	.000	1073.440		

MFI-5, Five-factor Modified Frailty Index; *METs,* metabolic equivalent of task score; *SE,* standard error.
[a]Variables entered on step 1 are sex, age, METs, and MFI.