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Frailty Increases the Risk of 30-day Mortality and Morbidity after Elective Abdominal Aortic Aneurysm Repair Independent of Age and Comorbidities

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Frailty Increases the Risk of 30-day Mortality and Morbidity after Elective Abdominal Aortic Aneurysm Repair Independent of Age and Comorbidities

By

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M.D.
University of Cincinnati College of Medicine
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An abstract of
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Frailty Increases the Risk of 30-day Mortality and Morbidity after Elective Abdominal Aortic Aneurysm Repair Independent of Age and Comorbidities

By Sung In Kim

Background: Frailty, defined as a biologic syndrome of increased vulnerability to stressors, has been linked to adverse outcomes after surgery. We evaluated the effect of frailty on 30-day mortality, morbidity, and failure to rescue (FTR) in patients undergoing elective abdominal aortic aneurysm (AAA) repair.

Methods: Patients undergoing elective endovascular AAA repair (EVAR) or open AAA repair (OAR) were identified in the National Surgical Quality Improvement Program database for the years 2005 to 2012. Frailty was assessed using the modified frailty index (mFI) derived from the Canadian Study of Health and Aging (CSHA), which was categorized into tertiles (low, middle, and high). The primary outcome was 30-day mortality. In addition, post-operative morbidity and the contribution of FTR on mortality were evaluated. The effect of frailty on outcomes was assessed by multivariate regression analysis, which was adjusted for age, American Society of Anesthesiology (ASA) class, and co-morbidities.

Results: Of 23,207 patients, 339 (1.5% overall; 1.0% EVAR and 3.0% OAR) died ≤ 30 days of repair. One or more complications occurred in 2,567 patients (11.2% overall; 7.8% EVAR and 22.1% OAR). Odds ratios (ORs) for mortality adjusted for age, ASA class, and other comorbidities in the group with the highest v. lowest frailty tertiles were 1.9 [95% confidence interval (CI), 1.2-3.0] and OAR (OR, 1.8; 95% CI, 1.5-2.1). There was also a higher FTR rate when post-operative complications occurred, with 1.7-fold higher odds of mortality (95% CI, 1.2-2.5) in the highest tertile of frailty compared with the lowest.

Conclusions: Higher mFI, independent of other risk factors, is associated with higher mortality and morbidity in patients undergoing elective EVAR and OAR. The mortality in frail patients is further driven by FTR from post-operative complications. Frailty evaluation may serve as a useful adjunct for pre-operative risk assessment.

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BACKGROUND

With continued growth of the aging population and rapid advances in minimally invasive surgical techniques, surgeons are asked to perform elective surgical procedures in elderly patients with increasing frequency. Currently, 33% of all operative procedures are performed in individuals ≥ 65 years[1]. The trend is especially pronounced in vascular surgery, in which approximately 60% of surgeries are performed in patients ≥ 65 years[1].

Abdominal aortic aneurysms (AAA) are found in up to 8% of men >65 years, and are fatal when they rupture (>80% mortality)[2]. Elective repair is routinely recommended for aneurysms ≥ 5.5 cm in diameter, or aneurysms growing at a rate > 1 cm per year, as they are associated with approximately 20-fold higher risk of rupture compared to smaller and more slowly growing aneurysms[2,3]. Currently, there are two methods of AAA repair: open (OAR) and endovascular (EVAR). Less invasive EVAR is associated with decreased post-operative recovery time, as well as reduced 30-day mortality, and is therefore more often recommended for elderly patients with co-morbidities[2-4]. Factors such as unsuitable anatomy and pre-existing renal insufficiency, however, exclude a subset of patient populations from EVAR. Moreover, despite its short-term mortality benefits, EVAR is associated with higher risk of complications and re-operation[3,4]. Longer-term analysis of randomized trials have so far failed to show overall mortality difference beyond the first two post-operative years[2-4].

Pre-operative evaluation of elderly patients presents myriad challenges, in part due to the presence of multiple co-morbidities and functional impairments in patients that often complicate peri- and post-operative recovery. In such patients, it becomes difficult to weigh the benefits from elective procedures against risks associated with general anesthesia and the physiologic stress of surgery. Furthermore, there are few standardized and easily reproducible tools to predict post-operative outcomes based on pre-operative risk factors. Currently available tools are either limited by subjectivity-based scoring systems or are based on retrospectively collected data points of age and comorbidities, among others[5,6].

Most of the pre-operative risk stratification for aortic aneurysm and other vascular patients focuses on cardiac risk but does not take pre-operative functional status and/or physiologic reserve into account. Frailty, defined as decrement in emotional, functional, and physiologic reserve, has been shown to be associated with a reduced ability to recover from the insults of a major stressor such as surgery[7]. Frailty has been recently shown to be an independent risk factor for adverse post-surgical outcomes in patients undergoing major surgical procedures, including general surgical, colorectal, oncologic, cardiac, and urologic procedures[7-10].

Frailty is distinct from presence of comorbidities because the domains of frailty encompass physical, mental, and social factors. In a seminal study, Makary et al[11] prospectively used the CHS/Fried FI in patient aged ≥ 65 years and showed that frailty (1) independently predicts post-operative complications, length of stay, and discharge to a skilled or assisted-living facility and (2) enhances conventional risk models, such as the American Society of Anesthesiologists (ASA) classification system.

Multiple studies in the last few years have supported the effect of frailty on increased death and complications in various surgical populations[7-10, 12-15]. The studies are heterogenous; some used prospective methods to assess frailty[5-8,15] and others used registry or retrospective methods[9,11-14]. There is no consensus on the definition and measurement criteria for frailty, even in the geriatric literature[2,16]. Different methods for frailty assessment have been proposed, including computed tomography-guided core muscle size measurements[6,17], nutritional and morphometric measures[15], composite scores of deficit accumulation[10,12,14] , and tests of gait speed, hand grip strength, and balance[7,8,11] as well as a combination of geriatric assessment tools[18].

Our study used the mFI, derived from the CSHA FI and validated using the National Surgery Quality Improvement Program (NSQIP) database by Adams et al[10], Karam et al[12], and Velanovich et al[14]. We chose specifically to study patients undergoing elective AAA, as they often represent older patients with multiple co-morbidities and increased peri-operative mortality risk. Because EVAR has already shown to be associated with lower peri-operative mortality risk[3,4], we chose to look at EVAR and OAR separately. By looking at EVAR and OAR separately, we also sought to minimize potential bias introduced by pre-selection.

In this study, we evaluated the effect of frailty on 30-day mortality and morbidity in patients undergoing elective abdominal aortic aneurysm (AAA) repair. To measure frailty, we used the modified frailty index (mFI). The mFI is based on a deficit accumulation model of frailty and is derived from the CSHA. We hypothesized that peri-operative morbidity, mortality, and failure to rescue (FTR) from major complications are higher in patients with higher degrees of pre-operative frailty, even when controlled for other risk factors of mortality and morbidity. Furthermore, we hypothesized that frailty increases mortality and morbidity risk even in patients undergoing EVAR, despite its minimally invasive nature and shorter operative time.

METHODS

Database

We reviewed existing data within the ACS-NSQIP from 2005 to 2012. The database contains prospectively collected clinical and surgical information for all major inpatient and outpatient surgical procedures performed at > 200 participating hospitals in the United States and Canada. A comprehensive list of preoperative comorbidities, functional status, laboratory values, intraoperative variables, and 30-day postoperative outcomes are available through the database. Patients aged < 16 years were not included in the NSQIP database. In addition, patients aged > 89 were coded as 90+ to protect patient confidentiality.

The ACS-NSQIP training, data collection, and auditing process is highly reliable and has strong inter-rater reliability[14]. The database is deidentified and does not contain any protected health information. The Emory Institutional Review Board waived Institutional Review Board approval and need for patient informed consent given the lack of protected health information and deidentified nature of the database.

Study population

Current Procedural Terminology (CPT) codes (American Medical Association, Chicago, IL) and International Classification of Diseases-Ninth Revision diagnosis codes (AAA without mention of rupture) were used to identify 24,531 patients undergoing endovascular AAA repair (EVAR) and open AAA repair (OAR) from 2005 to 2012. To include only elective repairs, we applied the following exclusion criteria: emergency status, critical patients with ventilator dependence, acute kidney failure, sepsis or septic shock, and transfer from another acute care hospital or from another emergency department. The final study cohort included 23,027 patients. Of these, 5,485

(23.8%) had one or more missing values for the mFI variables (see *mFI* below) and were excluded from the logistic regression model.

Study variables

Our primary outcome was 30-day mortality. Secondary outcomes included occurrence of:

1. Clavien-Dindo class IV complications[15], defined as life-threatening complications or those requiring intensive care management, including postoperative septic shock, myocardial infarction, cardiac arrest, pulmonary embolism, acute renal insufficiency requiring dialysis, ventilation > 48 hours, unplanned intubation, central nervous system complications (coma or stroke), graft failure;
2. Less severe complications, including urinary tract infection, pneumonia, deep vein thrombosis or thrombophlebitis, and surgical site infection, and
3. FTR, defined as likelihood of death from complications occurring in-hospital.

Frailty was assessed using the mFI (described subsequently). Transfer from a chronic care facility and significant weight loss ≤ 6 months preceding the repair were not part of the mFI but were used as additional measures of frailty in the multivariate regression analysis.

The mFI

To quantitatively measure frailty, we used the 11-point mFI derived from the CSHA FI[2,3] and validated in the NSQIP database[1,3]. Table 1 reports corresponding NSQIP variables for the CSHA FI. The mFI is calculated by adding 1 point for the presence of each variables and dividing the sum by 11. Frailty was used as a scale to compare morbidity and mortality with increasing frailty in EVAR and OAR. There were < 40 patients with mFI ≥ 0.55, which were combined with patients with an mFI of 0.45 to make sample sizes more comparable across indices for Figs 1 and 2. Frailty was then categorized into tertiles (low, middle, and high) for comparative analysis across groups in univariate and multivariate regression analysis.

Statistical analysis

Continuous variables are expressed as means ± standard deviations or as medians with interquartile ranges if they were not normally distributed. Means were compared using unpaired t-tests or analysis of variance. Discrete variables are expressed as counts and percentages, and χ^2 or Fisher exact tests were used to compare proportions. Because the NSQIP database records all patients aged > 90 years of age as "90+," age calculations were performed using 90 as the presumed age for all patients in this age group.

Univariate and multivariate logistic regression analyses were performed to obtain unadjusted and adjusted odds ratios (ORs) for 30-day mortality and morbidity. To control for the increased risk of mortality and morbidity due to advanced age or significant comorbidities, we adjusted for age and ASA Physical Status Classification in the multivariate regression model. Other preoperative variables, including comorbidities and laboratory parameters, were included in the model for 30-day mortality if they demonstrated statistical significance in the univariate regression analysis and did not contain > 10% missing observations. Of these, variables were excluded from the final model if they were associated with $p > 0.10$ in the multivariate model.

Model assumptions were evaluated using the variance inflation factors associated with each variable to check for multicollinearity. The overall model fit was obtained using the C statistic and the Hosmer-Lemeshow goodness-of-fit test. The final multivariate models were built for all AAA repairs and then separately for patients undergoing EVAR and OAR to detect effect modification by the method of repair. Complete case analysis was performed for missing observations, with the assumption that missingness was at random and independent of outcome, given that data were collected in a prospective manner. Furthermore, mortality outcome did not differ significantly between patients with (1.3%) and without (1.5%) missing variables. Fisher exact test was performed to evaluate for relationships between co-variates and patterns of missingness, and did not reveal significant associations.

For the FTR analysis, mortality in patients experiencing one or more complications was examined. The 30-day risks and ORs of mortality in the higher-frailty second or third mFI tertiles compared with the lowest tertile were calculated for patients with postoperative complications. Because preoperative frailty and occurrence of postoperative complications both affect mortality and FTR, we additionally obtained the relative excess risk due to interaction to evaluate this interaction on the additive scale16. The baseline comparative group for this analysis was the cohort of nonfrail patients with no postoperative complications. The statistical analysis was done using SAS 9.2 software (SAS Institute Inc, Cary, NC).

RESULTS

Baseline characteristics

Of 23,027 total patients, 17,668 (76.7%) underwent EVAR. Mean age was 73.4 ± 8.6 years. The mFI was 0.18 ± 0.1 (range 0-0.73), with 7,750 patients (42.7%) within the lowest mFI tertile (values 0-0.09), 6,241 (34.3%) in the middle tertile (0.18), and 4,178 (23.0%) in the highest tertile (0.27-0.73). The distributions of mFI did not differ significantly between patients undergoing EVAR and OAR ($p = 0.710$).

Table 2 reports baseline characteristics for all patients undergoing AAA repair and patient characteristics stratified by type of repair. Patients with OAR were more likely to be younger, female, and have had ≥ 10% weight loss in the last 6 months (all $p < 0.05$), whereas EVAR patients were more likely to have diabetes and peripheral arterial disease and to have undergone prior coronary interventions or surgery. Interestingly, the prevalence of chronic obstructive pulmonary disease (COPD), functional dependence, and residence in a chronic care facility were not very different in the two groups.

Thirty-day mortality

Death ≤ 30 days occurred in 339 patients (1.5%), with a nearly 3-fold increased risk of death among patients who underwent OAR (3.0%) compared with the less invasive EVAR (1.0%). For both operations, there was a statistically significant trend ($p < 0.001$) of increasing mortality with increasing mFI (Fig 1). The 30-day mortality in the highest category of frailty (mFI range 0.45-0.73) was 9% for OAR and 4% for EVAR. For purposes of comparison in regression analysis, we categorized frailty into tertiles (three groups). The unadjusted ORs comparing mortality in the highest to lowest frailty tertile were 3.3 [95% confidence interval (CI) 2.1, 5.0] for OAR and 2.6 (95% CI 1.7, 3.9) for EVAR (Table 3).

Thirty-day morbidity

Similar to mortality, a statistically significant trend ($p < 0.001$) was noted in the occurrence of any complications with increasing degree of frailty in the EVAR and OAR groups (Fig 2). There was a steep increase in risk of any complications from an mFI of 0.36 to an mFI of ≥ 0.45, with almost a 10-fold increase in EVAR (2.4% to 20.1%) and OAR (4.8% to 47.3%) complications. One or more Clavien-Dindo class IV complications occurred in 1,310 (5.7%). The ORs of occurrence of these class IV complications in the highest frailty groups were 2.6 (95% CI 2.2, 3.2) times higher in OAR and 2.3 (95% CI 1.9, 2.8) times higher in EVAR (Table 3) compared with the lowest frailty group. Less severe complications (e.g., urinary tract infection, pneumonia, superficial/deep surgical site infections, and deep venous thrombus/thrombophlebitis) occurred in 1,501 patients (6.5%) and more frequently among frail patients, with ORs of 2.3 (95% CI 1.8, 2.8) for OAR and 1.9 (95% CI 1.6, 2.3) for EVAR.

Multivariate regression

Table 4 reports the results from the multivariate regression analysis. Although significantly associated with death in the univariate analyses, the covariates of current smoking status, preoperative dialysis, hemiplegia, paraplegia, preoperative wound infection, bleeding disorder, recent transfusion, and chemoradiation were excluded from the final model (based on the criteria in the Methods section). After adjusting for other clinical and demographic factors, patients in the highest tertile of frailty had 2.3 (95% CI 1.4, 3.7) and 1.9 (95% CI 1.2, 3.0) times increased odds for death in the OAR and EVAR groups, respectively, compared with the non-frail or lowest tertile of frailty. Admission from a chronic care facility (OR 4.4, 95% CI 1.9, 10.4) and significant weight loss (OR 5.0, 95% CI 2.4, 10.3) were also significantly associated with death after EVAR, but not OAR. The models were robust and fit the observed data well as tested using the C statistic and Hosmer-Lemeshow test (Table 4).

Table 5 reports the adjusted ORs obtained from separate multivariate analyses for 30-day morbidity. Compared with the least frail patients, the most frail patients were 1.7 (95% CI 1.3, 2.1) and 1.8 (95% CI 1.5, 2.1) times more likely to experience severe (Clavien-Dindo class IV) complications after EVAR and OAR, respectively. Frail patients were also 1.5 times (95% CI 1.2, 1.9) more likely to undergo re-operation after OAR. Contrastingly, frailty was not a significant predictor of reoperation after EVAR ($p > 0.05$). The three most common re-intervention subgroups were lower extremity exploration for ischemia, lower extremity incision and drainage procedures for seroma/hematoma or infection, and exploratory laparotomy.

Failure to rescue

FTR is a significant driver of in-hospital mortality[19], especially in aortic aneurysm repair[20,21]. The term describes a phenomenon in which patients experience higher likelihood of death from complications occurring in the hospital. In the absence of complications, the overall risk of death is low, at 0.37% (OAR 0.67%, EVAR 0.29%), whereas in the presence of complications, the risk of death (FTR) is substantially higher, at 10.3% (OAR 11.1%, EVAR 9.6%). Because frailty also affects mortality, we looked at the effect modification of frailty on the risk of FTR for both types of repair. Table 6 reports the increasing risk of FTR as frailty increases for both OAR and EVAR. Comparison of risk ORs for mortality among patients with post-repair complications revealed that compared with the least frail, the most frail patients were almost twice more likely to die after EVAR (OR 1.8, 95% CI 1.1, 3.0) and after OAR (OR 1.7, 95% CI 1.0, 2.8) when one or more complications occurred ≤ 30 days after the aneurysm repair (Table 6). The relative excess risk due to interaction was 16.1 ($p = 0.01$), suggesting that the combination of frailty and complications increase the risk odds of mortality beyond what is expected in the absence of additive interaction.

DISCUSSION

Our study shows that contemporary national surgical results for aneurysm repair in elective patients have considerable variation on morbidity and mortality based on frailty, and that frailty is an independent predictor of perioperative outcomes. Furthermore, frailty drives FTR in patients who experience post-operative complications. The effect of frailty is not restricted to just open AAA repair but also significantly increases death and complications in the minimally invasive approach of EVAR.

Our study showed and overall mortality of 1% in the EVAR group and 3.0% in the OAR group, very similar to the DREAM and OVER trials[22,23]. In the highest category of frailty, however, the 30-day mortality was 4% for EVAR and 9% for OAR (Fig 1), which is substantially higher than any randomized trial to date. Moreover, major morbidity in the OVER trial was only 4% at 1 year in both groups[22], whereas in our study, the patients in the highest category of frailty had a 20% risk of major complications in the EVAR group and 47% in the OAR group (Fig 2) in the 30-day period.

The large disparity in the post-operative risk of death and complications for frail patients compared with non-frail patients is important to recognize and inform decision making and obtaining consent before AAA repair. The randomized controlled trials had stringent inclusion criteria, which included patients who were eligible for both OAR and EVAR. As shown in our study, AAA repair is being widely used across the nation in patients who are vulnerable to complications and further FTR, including those with multiple comorbidities, ASA class 4 to 5, functional dependence, and residence in chronic care facilities, among others.

Another significant finding of our study is that frailty predicts risk of post-operative morbidity and mortality independently of age and has a more significant effect size. Sixteen percent of the population was aged < 65 years. Although older age is an important risk factor for adverse outcomes after surgery, frailty may be present in a younger population group that would be missed if frailty assessment is restricted to the geriatric population. Using a cutoff of mFI > 0.2 as a definition of frailty resulted in a prevalence of 20% frailty in the population aged < 65 years and 24% for those ≥ 65 years.

The strong association of frailty with post-operative death and complications had similar ORs for the EVAR and OAR groups (Tables 4 and 5), suggesting that the risk on a multiplicative scale for increasing frailty is independent of the type of the type of repair chosen. Revenig et al[24] recently showed a similar phenomenon of increased complications in frail patients (OR 5.9, p = 0.025) undergoing minimally invasive general surgical, urologic, and oncologic procedures. They cautioned that the advent of minimally invasive techniques has potentially led surgeons to increasingly use these techniques in frail patients, thinking that the techniques would be well tolerated in situations where the patient might not be a candidate for traditional open techniques. In our study, the most frail in the EVAR group had a 4% mortality risk, 20% risk of any complications, and an 11% risk of FTR in the event of any complication.

Redefining pre-operative risk stratification has received a lot of attention in the recent surgical literature[25]. There is an increased emphasis to look beyond the traditional factors, such as age, ASA class, and organ-specific (cardiac/pulmonary) risk assessment to a more patient-centered approach that can individualize risk stratification for surgical patients without being cumbersome. Frailty may be one such tool that can be added to the standard pre-operative risk assessment and guide pre-operative counseling for treatment approaches and optimizing anesthetic and operative choices, as well as anticipating post-operative morbidity and aggressively pursuing rescue from complications to prevent death.

Our study was limited by retrospective analysis of a national database, which does not contain other variables of interest for frailty analyses such as gait speed or grip strength. The mFI therefore relies on a model of accumulating deficits, including medical comorbidities and functional status. Despite these limitations, we chose to utilize the mFI, as it has been validated in the NSQIP database. Moreover, we also demonstrated that admission from chronic care facilities and significant weight loss were significant predictors of death in the multivariate regression model; as these variables serve as adjunct indicators of frailty, we felt that significance of these functional variables further strengthened the link between frailty and post-operative mortality.

Another limitation of our study was the inability to extensively explore the interplay of frailty and FTR. There is a definite association, as well as an additive effect, of frailty and complications contributing to death. However, the presence of frailty may possibly be associated with a reluctance to attempt rescue; using the variables available in the NSQIP database, we were unable to answer this question and therefore cannot establish causality between frailty and FTR. Other constraints of the NSQIP database include use of a record review rather than prospective data collection by nurse abstractors and a limitation of follow-up to 30 days from the operation. Also, participation in the NSQIP database is voluntary and may not be a true representation of national estimates. Despite these limitations, the NSQIP database provided a large representative sample size for our study during a 7-year period, with significant trends seen in AAA morbidity and mortality based on frailty.

SUMMARY

Higher mFI, independent of other risk factors (e.g., older age, higher ASA classification, presence of medical co-morbidities), is associated with higher mortality and morbidity in patients undergoing elective EVAR and OAR for AAA. The mortality in frail patients is further driven by FTR from post-operative complications.

PUBLIC HEALTH IMPLICATIONS

The goal of elective AAA repair is to prevent fatal rupture and prolong life in patients whose rupture risk is high, compared with operative risk. Because AAA generally develops in patients ≥ 65 years, often with multiple co-morbidities, it is difficult to predict the mortality benefit offered by elective surgery. Despite the advances in minimally invasive surgery and comparative reduction in peri-operative recovery time (compared to more invasive open surgeries), frail patients face increased and previously unrecognized risks of post-operative mortality and morbidity. Shared decision making between physicians and patients becomes especially important in this context, for which benefits need to be carefully weighed against the potential harms of undergoing a physiologically stressful procedure.

Clinical tools that offer quantifiable measures of risk have been used in other contexts, such as the widely used CHA2DS2-VASc score, which predicts ischemic stroke risk in patients with atrial fibrillation[26]. CHA2DS2-VASc score helps determine the need for chronic anticoagulation, which increases the risk of catastrophic bleeding and requires close monitoring of drug level. It is our goal that the mFI will similarly aid physicians with pre-operative risk stratification by (1) providing a measurable and unified scoring system to define frailty, and (2) accurately assess the benefits and harms associated with elective repair (when compared to AAA rupture risk).

FUTURE DIRECTIONS

Further studies are needed to explore the best measures of frailty that are easy to administer in a clinic setting and resource-effective for routine use in pre-operative evaluation. The mFI has been validated using the NSQIP database, but external validation in a prospective cohort study is needed for widespread clinical applicability.

Different methods for frailty assessment have been proposed in other studies, including computed tomography-guided muscle size measurements[6,17], nutritional and morphometric measures[15], composite scores of deficit accumulation[10,12,14], and tests of gait speed, hand grip strength, and balance[7,8,11], as well as a combination of geriatric assessment tools[18]. Addition of these measures to the mFI to build a more comprehensive scoring system may help increase the predictive power and yield a more accurate tool for pre-operative risk assessment.

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TABLES

Table 1. Derivation of the NSQIP modified frailty index from the Canadian Study of Health and Aging (CSHA) frailty index

	CHSA Frailty Index	NSQIP Modified Frailty Index
Functional and cognitive impairment	Problems with dressing Problems with bathing Problems with personal grooming Problems with cooking Problems with going out alone	Pre-operative functional health status – partially or totally dependent
	Clouding or delirium History relevant to cognitive impairment or loss Family history relevant to cognitive impairment	Impaired sensorium
Medical co-morbidities	History of diabetes mellitus	Diabetes mellitus – noninsulin or insulin
	Chronic lung disease	History of severe chronic obstructive pulmonary disease
	Acute airway disease	Current pneumonia
	Congestive heart failure	Congestive heart failure within 30 days before surgery
	Myocardial infarction	History of myocardial infarction within past 6 months before surgery
	Cardiac disease	Previous percutaneous coronary intervention or cardiac surgery History of angina within1 month before surgery
	Arterial hypertension	Hypertension requiring medication
	Cerebrovascular problems	History of transient ischemic attack
	History of stroke	Cerebrovascular accident or stroke with neurologic deficit
	Decreased peripheral pulses	History of revascularization or amputation for peripheral vascular disease Rest pain or gangrene

Table 2. Baseline characteristics of patients undergoing elective abdominal aortic aneurysm (AAA) repair stratified by endovascular AAA repair (EVAR) and open AAA repair (OAR)

Variable[a]	All patients (n = 23,027)	EVAR (n = 17,668)	OAR (n = 5,359)	P value
Age, years	73.4 ± 8.6	74.1 ± 8.5	71.0 ± 8.6	< 0.001
Female gender	4,553 (19.8)	3,160 (17.9)	1,393 (26.0)	< 0.001
ASA[b] classification				< 0.001
No or mild disturbance	1,528 (6.6)	1,219 (6.9)	309 (5.8)	
Severe disturbance	16,723 (72.7)	13,026 (73.8)	3,697 (69.1)	
Life threatening or moribund	4,756 (20.7)	3,411 (19.3)	1,345 (25.1)	
Chronic obstructive pulmonary disease	4,420 (19.2)	3,393 (19.2)	1,027 (19.2)	0.968
Myocardial infarction ≤ 6 months	180 (1.0)	127 (0.9)	53 (1.2)	0.141
Previous percutaneous coronary intervention, cardiac surgery, or angina	6,871 (37.8)	5,286 (38.6)	1,585 (35.3)	< 0.001
Diabetes mellitus requiring medication	3,445 (15.0)	2,761 (15.6)	684 (12.8)	< 0.001
Hypertension requiring medication	18,570 (80.6)	14,145 (80.1)	4,425 (82.6)	< 0.001
Previous revascularization, amputation, rest pain, or gangrene	1,124 (6.2)	317 (7.1)	807 (5.9)	0.006
Functional dependence	703 (3.1)	550 (3.1)	153 (2.9)	0.342
Transferred from a chronic care facility	157 (0.7)	121 (0.7)	36 (0.7)	0.170
Impaired sensorium	27 (0.2)	21 (0.2)	6 (0.1)	1.000
Weight loss > 10% body weight ≤ 6 months	278 (1.2)	195 (1.1)	83 (1.6)	0.012

[a]ASA, American Society of Anesthesiologists Physical Status Classification

[b]Continuous variables are expressed as mean ± standard deviation, and categorical variables are reported in total number of observations with associated percentage.

Table 3. Unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) for middle and high tertiles of frailty (low modified frailty index [mFI] is the reference group) on death, Clavien-Dindo class IV complications, and other complications, obtained from univariate regression analysis

Outcome	mFI tertile	All repairs[a] (n = 18,169)	EVAR[a] (n = 13,675)	OAR[a] (n = 4,494)
Death	Low	1	1	1
	Middle	1.6 (1.2-2.2)	1.7 (1.1-2.5)	1.6 (1.0-2.6)
	High	2.8 (2.1-3.8)	2.6 (1.7-3.9)	3.3 (2.1-5.0)
Clavien-Dindo class IV complications[b]	Low	1	1	1
	Middle	1.5 (1.3-1.7)	1.4 (1.1-1.7)	1.6 (1.3-2.0)
	High	2.4 (2.0-2.7)	2.3 (1.9-2.8)	2.6 (2.2-3.2)
Other complications[c]	Low	1	1	1
	Middle	1.4 (1.2-1.6)	1.3 (1.0-1.5)	1.5 (1.2-1.9)
	High	2.0 (1.7-.2.3)	1.9 (1.6-2.3)	2.3 (1.8-2.8)

[a]All results are statistically significant at $p < 0.05$.

[b]Includes post-operative septic shock, myocardial infarction, cardiac arrest, pulmonary embolism, acute renal insufficiency requiring dialysis, ventilation > 48 hours, unplanned intubation, central nervous system complications (coma or stroke), and graft failure

[c]Includes post-operative urinary tract infection, superficial/deep surgical site infection, pneumonia, and deep venous thrombosis/thrombophlebitis

Table 4. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) obtained from the multivariate logistic regression analysis for 30-day mortality.

Predictor variable	All repairs[a] (n = 17,542)	EVAR[b] (n = 13,184)	OAR[c] (n = 4,358)
mFI			
Low	1	1	1
Middle	1.4 (1.0, 1.9)	1.4 (0.9, 2.2)	1.4 (0.9, 2.2)
High	2.0 (1.5, 2.8)	1.9 (1.2, 3.0)	2.3 (1.4, 3.7)
ASA class	1.6 (1.3, 2.1)	1.6 (1.1, 2.2)	1.4 (1.0, 2.0)
Age	1.1 (1.0, 1.1)	1.1 (1.0, 1.1)	1.1 (1.1, 1.1)
Female gender	1.5 (1.1, 2.0)	1.2 (0.8, 1.9)	1.3 (0.9, 2.0)
Admission from a chronic care facility	2.3 (1.0, 4.9)	4.4 (1.9, 10.4)	0.3 (0.0, 2.4)
Recent, unintended weight loss >10% body weight	3.1 (1.7, 5.8)	5.0 (2.4, 10.3)	1.3 (0.4, 4.4)
Serum creatinine	1.3 (1.2, 1.4)	1.3 (1.2, 1.5)	1.2 (0.9, 1.4)

ASA, American Society of Anesthesiologists Physical Status Classification; EVAR, endovascular abdominal aortic aneurysm repair; mFI, modified frailty index; OAR, open abdominal aortic aneurysm repair.

[a]c = 0.73, p = 0.08. The c-statistic represents the areas under the receiver operating curve; p-value was obtained from the Hosmer-Lemeshow test, where $p > 0.05$ signifies that the model fits the observed data well.

[b]c = 0.73, p = 0.87

[c]c = 0.77, p = 0.65

Table 5. Adjusted odds ratios and 95% confidence intervals comparing highest to lowest tertile of frailty, obtained from the multivariate logistic regression analysis for 30-day morbidity, adjusted for age and American Society of Anesthesiologists Physical Status Classification

Outcome	All repairs[a] (n = 17,542)	EVAR[a] (n = 13,184)	OAR[a] (n = 4,358)
Clavien-Dindo class IV complications	1.7 (1.4, 1.9)	1.7 (1.3, 2.1)	1.8 (1.5, 2.1)
Other complications	1.5 (1.3, 1.7)	1.4 (1.2, 1.7)	1.7 (1.4, 2.1)
Re-operation	1.2 (1.1, 1.4)	1.1 (0.9, 1.3)	1.5 (1.2, 1.9)

EVAR, endovascular abdominal aortic aneurysm repair; OAR, open abdominal aortic aneurysm repair.

[a]All results are statistically significant with $p < 0.05$, except for re-operation after EVAR.

Table 6. Risk of failure to rescue (FTR)[a] across frailty tertiles for open abdominal aortic aneurysm (AAA) repair (OAR) and endovascular AAA repair (EVAR)[b]

		mFI tertile		
Repair	Number	Low	Middle	High
OAR	4,494	8.9	10.2	14.2
Risk of FTR, % OR (95% CI)		1 (ref)	1.2 (0.7-2.0)	1.7 (1.0-2.8)
EVAR	13,675	6.7	12.0	11.3
Risk of FTR, % OR (95% CI)		1 (ref)	1.9 (1.1-3.2)	1.8 (1.1-3.0)
All repairs	18,169	7.7	11.1	12.7
Risk of FTR, % OR (95% CI)		1 (ref)	1.5 (1.0-2.2)	1.7 (1.2-2.5)

CI, confidence interval; mFI, modified frailty index; OR, odds ratio; ref, reference tertile

[a]Death in patients experiencing post-operative complications

[b]ORs (95% CI) for FTR, by frailty tertile (lowest tertile is reference)

FIGURES

Figure 1. Percentage of patients who died ≤ 30 days after elective open aneurysm repair (OAR) and endovascular aneurysm repair (EVAR), stratified by the modified frailty index (mFI). An increasing mFI indicates higher frailty.

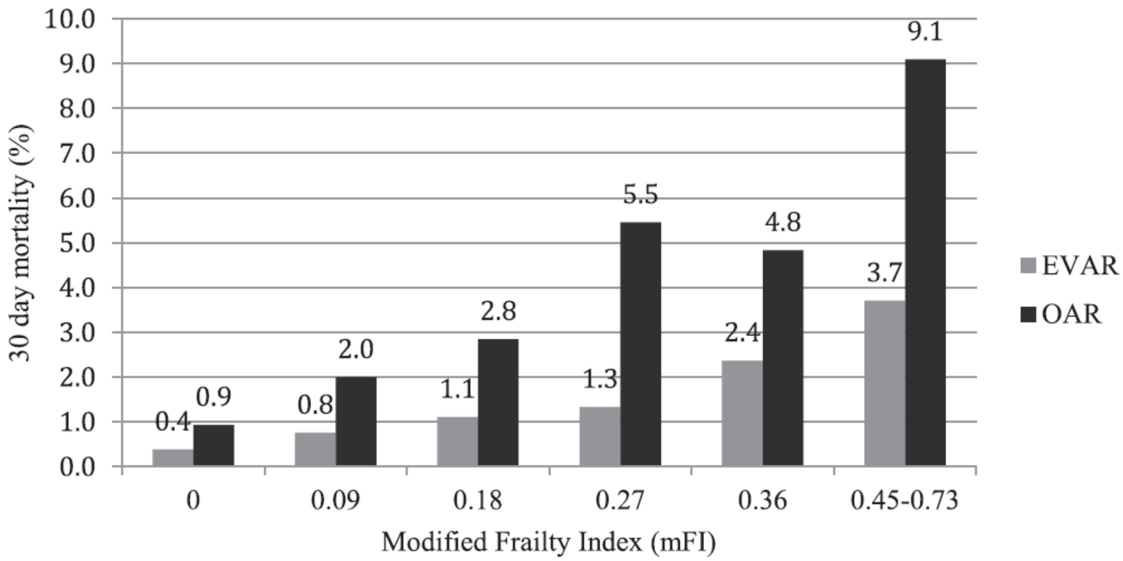

Figure 2. Percentage of patients who experienced major (Clavien-Dindo class IV) post-operative complications ≤ 30 days after elective open aneurysm repair (OAR) and endovascular aneurysm repair (EVAR), stratified by the modified frailty index (mFI). An increasing mFI indicates higher frailty.