Preoperative prediction of mortality within 1 year after elective thoracic endovascular aortic aneurysm repair

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Objective: Thoracic endovascular aortic repair (TEVAR) is known to have a survival benefit over open repair in patients with descending thoracic aneurysms and has become a mainstay of therapy. Because death before 1 year after TEVAR likely indicates an ineffective therapy, we have created a predictive model for death within 1 year using factors available in the preoperative setting.

Methods: A registry of 526 TEVARs performed at the University of Florida between September 2000 and November 2010 was queried for patients with degenerative descending thoracic aneurysm as their primary pathology. Procedures with emergent or urgent indications were excluded. Preoperatively available variables, such as baseline comorbidities, anatomic-, and procedure-specific planning details, were recorded. Univariate predictors of death were analyzed with multivariable Cox proportional hazards to identify independent predictors of 30-day (death within 30 days) and 1-year mortality (death within 1 year) after TEVAR.

Results: A total of 224 patients were identified and evaluated. The 30-day mortality rate was 3% (n = 7) and the 1-year mortality rate was 15% (n = 33). Multivariable predictors of 1-year mortality (hazard ratios [95% confidence interval]) included: age >70 years (5.8 [2.1-16.0]; P = .001), adjunctive intraoperative procedures (eg, brachiocephalic or visceral stents, or both, concomitant arch debranching procedures; 4.5 [1.9-10.8]; P = .001), peripheral arterial disease (3.0 [1.4-6.7]; P = .006), coronary artery disease (2.4 [1.1-4.9]; P = .02), and chronic obstructive pulmonary disease (1.9 [1.0-3.9]; P = .06). A diagnosis of hyperlipidemia was protective (0.4 [0.2-0.7]; P = .006). When patients were grouped into those with one, two, three, or four or more of these risk factors, the predicted 1-year mortality was 1%, 3%, 10%, 27%, and 54%, respectively.

Conclusions: Factors are available in the preoperative setting that are predictive of death within 1 year after TEVAR and can guide clinical decision making regarding the timing of repair. Patients with multiple risk factors, such as age ≥70 years, coronary artery disease, chronic obstructive pulmonary disease, and a need for an extensive procedure involving adjunctive therapies, have a high predicted mortality within 1 year and may be best served by waiting for a larger aneurysm size to justify the risk of intervention. (J Vasc Surg 2012;56:1266-73.)

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One of the greatest challenges that any surgeon must face is performing high-risk interventions for prophylactic indications, and this is certainly true in the management of aneurysmal disease of the thoracic aorta. With the U.S. Food and Drug Administration’s approval of thoracic endovascular aortic repair (TEVAR) for descending thoracic aneurysms (DTAs) in 2005, a rapid adoption of this technology has led to TEVAR becoming a mainstay of treatment.1-4 TEVAR quickly supplemented open surgical reconstruction by expanding the patient population for which repair is considered.2 The finding that TEVAR has augmented the total number of repairs instead of supplanting open surgical reconstruction is in some ways explained by the favorable short-term and midterm outcomes of TEVAR in “high-risk” or “no-option” patients.5,6

Multiple studies have demonstrated the perioperative benefit of TEVAR over open surgical treatment4,7,8 and the longer-term survival benefit is generally placed in the context of 5-year survival. Although perioperative or 30-day mortality rates may demonstrate the safety of TEVAR, they do not define late benefit. Similarly, 5-year survival is often related to other comorbidities, such as cardiac disease, malignancy, or cerebrovascular occlusive disease, rather than to a benefit of TEVAR itself. Clinical decision making and patient counseling regarding the timing of intervention tend to focus on the 1-year rupture and dissection risk, against which the risk of intervention and the patient’s anticipated life expectancy are weighed. Most surgeons would agree that death <1 year after a prophylactic intervention defines an ineffective or unnecessary treatment. This concept was previously described by Beck et al9 for open and endovascular (EVAR) repair of infrarenal abdominal aortic aneurysms (AAAs). Although open AAA...
repair had multiple risk predictors for death within 1 year after repair, EVAR had few predictors of death.

Although one might be tempted to assume that the 1-year outcomes after TEVAR would mirror those of EVAR, DTA patients frequently have more advanced comorbidities than their counterparts with infrarenal AAAs and are known to have poorer long-term survival than AAA patients.\textsuperscript{10,19} In addition, the 1-year mortality rate after TEVAR for intact aneurysms ranges from 10% to 18%,\textsuperscript{11,12} which is considerably higher than the 4% to 12% reported after EVAR.\textsuperscript{13,14}

With the idea that death within 1 year after TEVAR performed in the elective setting indicates an ineffective or unnecessary therapy, the purpose of this study was to create a predictive model for mortality within 1 year after TEVAR using preoperatively available risk factors. Such a prediction model can help guide clinical decision making by identifying patients who would benefit most from intervention as well those patients with shorter life expectancy who might be better served with medical management or waiting for a larger aneurysm diameter (ie, rupture risk) to justify repair.

METHODS

Approval for this study was obtained from the Institutional Review Board at the University of Florida College of Medicine.

Patients and database. A dedicated, prospectively maintained endovascular aortic registry is kept at the University of Florida containing all patients who have undergone EVAR and TEVAR. This database contains >50 patient- and procedure-specific variables that are entered by the operating surgeon for each patient at the time of operation. The database undergoes scheduled quality-control audits by study coordinators working within the division. In addition, data within the registry are routinely updated and augmented by complete review of the medical record. Any additional data required for this analysis were obtained by data abstraction from the patient’s electronic medical record.

Additional covariates that were aggregated included preoperative American Society of Anesthesiologists (ASA) Physical Status Classification system score\textsuperscript{15,16} as well as antiplatelet, anticoagulant, and β-blocker use. Also recorded were procedural characteristics such as landing zone, need for procedural adjuncts, spinal drain use, postoperative complications, endoleak, and need for reintervention. Aneurysm diameters were measured using centerline measurements obtained from a three-dimensional reconstruction performed with a TeraRecon Aquarius Workstation (TeraRecon Inc, Foster City, Calif). Patient deaths were confirmed using the Social Security Death Index.

The database was queried for patients with degenerative DTA as their primary pathology. Procedures completed for dissection and urgent or emergency indications were excluded. The analysis excluded patients categorized in the database as having thoracoabdominal aneurysms or patients undergoing visceral debranching; however, patients requiring brachiocephalic debranching (eg, carotid-to-subclavian bypass) or adjunctive stenting to provide proximal or distal landing zones were included.

Risk model design. The primary outcome was 1-year mortality (defined as death within 1 year of TEVAR) and the secondary outcome was 30-day mortality (similarly defined as death within 30 days of TEVAR). Only follow-up data within 1 year of repair were used in the development of the model to predict the primary outcome. Survival was estimated using life-table analysis.

A univariate Cox proportional hazard model was used to identify preoperative risk factors associated with time to death within 1 year after TEVAR. The analysis incorporated follow-up data from time of surgery up to 1 year after TEVAR. Preoperative risk factors found on univariate analysis to have a value of \( P < .2 \) were included in the multivariable model, which was developed using stepwise backward Cox regression. Log-likelihoods were compared with and without inclusion of each predictor in the multivariable model and only included in the final model if the likelihood-ratio test \( P \) value was <.1.

Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for postoperative death within 1 year of TEVAR were estimated from the multivariable model. Cox-Snell residuals were used to predict 1-year mortality (or death occurring within 1 year of repair) based on each patient’s profile of preoperative risk factors. All statistical analysis was performed using Stata 11 software (StataCorp, College Station, Tex).

Definitions. Comorbidities were defined and recorded as follows:

- Coronary artery disease (CAD): any history of myocardial infarction, angina, coronary intervention, or electrocardiograph changes consistent with prior myocardial infarction;
- Cerebrovascular occlusive disease (CVOD): any history of transient ischemic attack, stroke, or prior carotid endarterectomy or stent;
- Congestive heart failure: medical record history, New York Heart Association functional class ≥II, or preoperative evaluation;
- Chronic obstructive pulmonary disease (COPD): medical record history or preoperative pulmonary function testing consistent with the diagnosis;
- Diabetes mellitus: medical record history, requiring insulin or noninsulin drugs;
- Chronic renal insufficiency: creatinine ≥1.8 mg/dL;
- End-stage renal disease: on dialysis;
- Peripheral arterial disease (PAD): ankle-brachial index <0.9, medical record history, prior peripheral endovascular intervention or open infrainguinal reconstruction;
- Hypertension: medical record history, on antihypertensive medications or preoperative blood pressure ≥140/90 mm Hg;
- Dyslipidemia: medical record history, on cholesterol-lowering medications;
- History of aortic surgery.
RESULTS

Between September 2000 and November 2010, 526 TEVARs were performed at the University of Florida. On the basis of the inclusion and exclusion criteria outlined above, 224 patients were identified and further analyzed. Patient demographics are outlined in Table I. Median follow-up for the 224 patients was 27.6 months (range, 0-121; interquartile range, 9.6-48.8 months). Among patients who did not die within 1 year of TEVAR, 82% had >1 year of follow-up.

TEVAR mortality. The overall 30-day and 1-year mortality rates were 3% (n = 7) and 15% (n = 33), respectively (Fig 1). Univariate predictors of 1-year mortality, defined as death within 1 year of repair, included age >70 years (P = .005), CAD (P = .04), congestive heart failure (P = .009), PAD (P = .004), CVOD (P = .07), COPD (P = .07), aneurysm diameter (P = .07), the need for adjunctive procedures (P = .004), and hyperlipidemia (P = .2).

By multivariable analysis, factors independently associated with 1-year mortality included age >70 years (HR, 5.8; 95% CI, 2.1-16.0; P = .001), adjunctive intraoperative procedures (eg, brachiophecalic or visceral stents, concomitant arch debranching procedures; HR, 4.5; 95% CI, 1.9-10.8; P = .001), PAD (HR, 3.0; 95% CI, 1.4-6.7; P = .006), CAD (HR, 2.4; 95% CI, 1.1-4.9; P = .02), and COPD (HR, 1.9; 95% CI, 1.0-3.9; P = .06). A diagnosis of hyperlipidemia was protective (HR, 0.4; 95% CI, 0.2-0.7; P = .006; Table II).

Patients were categorized by the number of preoperative risk factors present in any combination. Patients with four or more risk factors were grouped because few patients had four or five risk factors and no patient had all six. The observed 30-day and 1-year mortality after TEVAR is shown in Fig 2. Patients with one risk factor had 0% mortality rate at 30 days with elective TEVAR and a 1.5% mortality rate within 1 year. In sharp contrast, patients with four or more risk factors had 19% mortality at 30 days and 50% mortality within 1 year. Of note, 67% of the observed deaths at 1 year after TEVAR occurred after the perioperative period (Fig 3).

Prediction of death within 1 year and model validation. In the multivariable model, predicted 1-year mortality ranged from 0.9% with no risk factors up to 54.2% with four or more risk factors. When stratified by zero to one (n = 78; 35%), two (n = 81; 36%), three (n = 48; 22%), or four or more risk factors (n = 16; 7%), the predicted 1-year mortality was 3%, 10%, 27%, and 54%, respectively (Fig 4). Discrimination of the model was assessed with calculation of the C index, or probability that predictions and outcomes are concordant, which ranges from 0.5 (no discrimination) to 1.0 (perfect discrimination). The C index of the multivariable model for mortality within 1 year of TEVAR was satisfactory at 0.77. Calibr-
operative variables associated with death included age
tate clinical decision making and patient counseling. Peri-
be assessed preoperatively to develop a risk score to facili-
study is the first to identify independent variables that can
or unnecessary. Patient discussions regarding risk of an
rection is too short to gain benefit from a prophylactic
ast expectancy when they select appropriate candidates for DTA
repair. Most surgeons agree that if a patient’s life expec-
tancy is 70 years, requirement for an intraprocedural adjunct, PAD,
DIA, and COPD, with a diagnosis of hyperlipid-
emia being protective. The model we have developed to
predict death within 1 year based on these covariates cor-
relates well with observed 1-year mortality rates in our
sample. Patients with multiple risk factors (4+) have a very
high predicted mortality before 1 year (54%), but those
with zero risk factors have only 1% predicted 1-year mor-

that aneurysms of the DTA be repaired at \( \geq 6.0 \text{ cm} \). Most
would consider that elective treatment is an ineffective or
unnecessary intervention when death occurs within 1
year. This study demonstrates that some patients have a
much higher risk of death within 1 year of repair and that
perhaps diameter of repair should be a moving target
with relation to a patient’s risk of death within 1 year
after TEVAR.

The minimally invasive nature of TEVAR has provided
lower perioperative morbidity and mortality compared with
an open operation, and the number of patients
deemed eligible for repair has expanded greatly without
strong evidence for longer-term benefit. Despite the
perioperative advantage of TEVAR, the all-cause mortality
within 1 year for the elective endovascular management of
DTA has been documented to range from 10% to
18%\(^3,11,12\), which is consistent with our results (Fig 1).
With relatively low 30-day major morbidity and mortality,
the sobering 1-year mortality outcomes after TEVAR fur-
ther emphasizes the need to understand what patient pop-
ulations will be best served with prophylactic intervention.

As endovascular therapies continue to be offered to
high-risk patients and the risk-to-benefit ratio becomes less
dramatic, a call for comparative effectiveness research and
development of regional quality improvement registries has
been made to address this issue.\(^{19}\) To this end, improved
decision-making algorithms and patient-centered out-
comes (eg, life expectancy, functional recovery, and major
adverse events) need to become the focus of studies high-
lighting the potential efficacy of endovascular therapy in the
thoracic aorta. Previous reports have documented univari-
ate predictors for short-term mortality after TEVAR\(^{20}\) but
are limited by small sample size and low event rates.

This analysis identifies independent risk factors associ-
ated with death within 1 year after TEVAR. These include
age \( \geq 70 \) years, adjunctive intraoperative procedures, PAD,
CVOD, CAD, and COPD, with a diagnosis of hyperlipid-
emia being protective. The model we have developed to
predict death within 1 year based on these covariates cor-
relates well with observed 1-year mortality rates in our
sample. Patients with multiple risk factors (4+) have a very
high predicted mortality before 1 year (54%), but those
with zero risk factors have only 1% predicted 1-year mor-

An important point in this analysis is that most deaths
did not occur in the perioperative period (Fig 2). This
emphasizes the importance and utility of looking at other
outcome measures, such as 1-year mortality, to determine
procedural efficacy. Nowygrod et al\(^{23}\) highlighted the ef-
effect of endovascular technologies on complication and
mortality profiles for a number of index peripheral vascular
operations but cautioned that endovascular interventions are
not always safer than their open counterparts, particu-
larly when compared over longer follow-up intervals. These
observations detail the ongoing need for critical reassess-
ment of evolving technologies and the requirement for risk
stratification to guide clinical decision making.
Using mortality within 1 year as an end point provides a useful counterpoint to the frequently cited annual rupture or dissection risk of thoracic aortic aneurysms when discussing timing of repair. Although aneurysm diameter is a somewhat imprecise variable for rupture risk prediction, as highlighted in the infrarenal aorta, an accepted estimate for rupture and dissection risk in DTA patients with an aneurysm size of 6 to 6.5 cm is 10% to 14% per year. Although current practice guidelines recommend repair in patients with aneurysms ≥6.0 cm,18 our study highlights specific populations of patients whose 1-year mortality rate is much greater than 10% to 14% if they undergo repair. Interestingly, our data suggest that surgeons at our institution are already taking these factors into consideration—offering low-risk patients repair at a mean diameter of 5.5 cm and the highest-risk patients repair at an average diameter of 7.0 cm (Fig 5). This indicates that we are probably waiting longer to offer elective repair to sicker patients or are using a higher threshold for risk of rupture or dissection before offering repair. When estimated annual rupture and dissection risk is compared with predicted mortality risk within 1 year for each risk factor grouping, it appears that patients with multiple risk factors should perhaps have larger-diameter aneurysms before repair to justify risk and benefit of the operation (Fig 6).

Another interesting finding within our analysis was the effect of hyperlipidemia on patient mortality. For the entire patient cohort, 49% of the patients were taking a statin drug; however, for those patients with a diagnosis of hyperlipidemia, the use of statins (79%) correlated well with the rate of hyperlipidemia diagnosis (P < .0005). This suggests that the finding of hyperlipidemia as being protective may
be a surrogate for statin use. A number of other reports have documented the pleiotropic benefits of statin therapy in the treatment of pathology localized to the extracranial carotid, coronary, infrarenal aortic, and lower extremity arterial beds.24-28 This was an unexpected finding in this study, and interpreting the results would be presumptive owing to the nature of the diagnosis of hyperlipidemia determined from medical record review and not a biochemical diagnosis, along with many other confounding issues with statin therapy. The statin variable was not prospectively recorded, and data for this variable were missing in 21% of the patients, so it was not incorporated into the predictive model. Further studies will be needed to determine if statins or hyperlipidemia confer survival benefit in DTA patients.

There are several limitations to this study, including the retrospective, single-center nature of the inquiry and the inherent selection bias that exists in this type of analysis. No standardized treatment protocol was implemented during the study interval, so the effect of aneurysm diameter and the constellation of patient comorbidities on individual surgeon decision making cannot be readily defined.

Furthermore, despite a novel description of a preoperative prediction model for death within 1 year after elective TEVAR for DTA, the reported estimation of this model’s discrimination and calibration are inherently optimistic assessments based on the original derivation data set. External validation in a multicenter cohort or registry data set, or both, is mandatory before broader application in routine clinical practice. The data analysis relied on several definitions to document patient comorbidities, and the severity and resulting clinical effect is not readily known from this type of data abstraction.

In addition, no open surgical counterpart was reported during the same interval, so comparisons are not possible. Ultimately, perioperative decision making is individualized to the patient, so use of a predictive model only serves to inform the physician–patient discussion but not to make definitive decisions.

CONCLUSIONS

Death within 1 year of elective TEVAR likely represents an unnecessary or ineffective therapy. It is important to note that most deaths within 1 year of TEVAR do not occur in the perioperative period. Multiple factors available in the preoperative setting are associated with death before 1 year after TEVAR and can be used for preoperative decision making and patient counseling. Patients with any combination of four or more independent predictors of 1-year mortality have a predicted mortality of >50%. Therefore, older and sicker patients may be best served by waiting for a larger aneurysm size to justify the risk of the procedure.

AUTHOR CONTRIBUTIONS

Conception and design: SS, CC, AB
Analysis and interpretation: SS, CC, AB
Data collection: SS
Writing the article: SS, CC, AB
Critical revision of the article: SS, CC, RF, PH, TB, TM, TH, AB
Final approval of the article: SS, CC, RF, PH, TB, TM, TH, AB
Statistical analysis: CC
Obtained funding: Not applicable
Overall responsibility: SS
SS and CC participated equally and share first authorship.
REFERENCES


DISCUSSION

Dr Hazim J. Safi (Houston, Tex). I thank Adam Beck, MD, for sending me this manuscript well in advance. The authors have developed a prediction model for 30-day and 1-year mortality after thoracic endovascular aortic repair (TEVAR). It is an important contribution to our vascular literature. Most surgeons make this assessment implicitly when deciding on how to manage patients with aneurysms. I congratulate the authors for quantifying the relationship between the risk factors and mortality rate. However, I wish that the authors had conducted an analysis to evaluate the effect of known statin use on the hazard ratio. This might provide some assistance in interpreting the otherwise paradoxical findings. I have three questions:

1. Why didn’t the authors use the effective glomerular filtration rate instead of the creatinine level in predicting an adverse outcome?

2. Can the authors elaborate on the incidence of neurological deficit, stroke, paraplegia or paraparesis, and its impact on mortality rate?

3. Can the authors establish the need for adjunct procedures preoperatively?

I thank the authors for their beautifully written manuscript and advances in our understanding of the risk factors that are present in TEVAR.

Dr Adam W. Beck. Thank you, Dr Safi. With regard to your first question regarding using the estimated glomerular filtration rate (eGFR) rather than creatinine, we have preoperative creatinine in our database, so that was the value that we used for the analysis. However, I do agree that eGFR would be a more accurate description of the patients’ renal function. We used a fairly strict definition for renal insufficiency, with a creatinine of 3.0 mg/dL, and perhaps using
eGFR might allow us to find an association with renal function and 1-year mortality.

In terms of the neurological complications of TEVAR and how they affect outcome after surgery, this project was meant to look at preoperative predictors of mortality, so we did not include operative complications in the model. Spinal cord ischemia after TEVAR is an academic interest to our group, and we have looked at the effect that it has on mortality. Our rate of spinal cord ischemia is about 9%, with a permanent deficit in 4%, and having that complication after TEVAR profoundly negatively affects survival.

Regarding whether we can predict the need for adjunctive procedures preoperatively, the answer is yes and no. I think we can predict the majority of the adjunctive procedures, such as carotid subclavian bypass, endo, or open conduits, as well as chimneys performed to create proximal and distal landing zones. However, there were some adjunctive procedures that were performed based on intraoperative decision making.

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