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Predictors of perioperative morbidity and mortality in open abdominal aortic aneurysm repair

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ABSTRACT

Introduction: The major advantage of endovascular abdominal aortic aneurysm repair (EVAR) over open repair (OAR) is improved perioperative morbidity and mortality. Long term results of the two modalities are comparable. We sought to quantify factors predicting perioperative morbidity and mortality in patients undergoing OAR.

Methods: Consecutive non-ruptured OAR were analyzed for patient demographic factors, perioperative variables including blood pressure, temperature, and glucose control, intraoperative factors, and complications including wound, pulmonary, renal and cardiac, and 30-day mortality. Uni- and multivariate analysis was performed to determine predictors of morbidity and mortality.

Results: 240 elective open AAA repairs over 10 consecutive years were performed. 46% required suprarenal clamping. At least one complication occurred in 47% and 30-day mortality was 5.4%. By multivariate analysis, independent predictors of morbidity (any complication) were suprarenal clamping (OR 1.8, 95% CI 1.1−3.2, $p = 0.029$), operative time (OR 1.005, 95% CI 1.002−1.008, $p = 0.002$), and low postoperative temperature (OR 1.6, 95% CI 1.1−2.3, $p = 0.025$). Multivariate predictors of 30 day mortality included advanced age (OR 1.2, 95% CI 1.1−1.3, $p = 0.002$) and operative time (OR 1.007, 95% CI 1.001−1.013, $p = 0.024$). Glucose control did not predict morbidity or mortality.

Conclusions: Control of postoperative temperature is a potentially modifiable factor that may reduce morbidity in patients undergoing open AAA repair, thereby minimizing the early advantage of EVAR.

Introduction

The repair of abdominal aortic aneurysms (AAA) has undergone a transformation since the widespread adoption and dissemination of endovascular repair (EVAR). While initially offered primarily to high risk individuals not felt to be suitable for open AAA repair (OAR), EVAR has greatly surpassed OAR in frequency and is generally considered the primary repair option in anatomically suitable candidates. While initially confined to the infrarenal aortic segment, emerging technology, including fenestrated and branched EVAR, have further decreased the need for open repair, such that it is increasingly rare that an endovascular solution cannot be found.

Initial skepticism about EVAR centered on questions of durability. As opposed to OAR, where the AAA is completely repaired, EVAR is a method of AAA exclusion with variable amounts of sac shrinkage and the potential for persistent sac perfusion via endoleaks with sac expansion. Accordingly, secondary interventions are often pursued to treat endoleaks and sac expansion. While the early postoperative advantages of EVAR over OAR with respect to perioperative morbidity and mortality are unquestioned, and overall long term device durability and freedom from aneurysm related mortality are favorable, there remains evidence that over time the advantages of EVAR over OAR diminish, particularly with respect to need for secondary interventions.[1–4] Furthermore, in an era of health care cost containment, EVAR incurs ongoing cost due to the need for lifelong surveillance, in comparison with relatively infrequent surveillance needs for OAR beyond the perioperative period.

Therefore, while clearly in decline, there is and most likely will be an ongoing need for OAR, even if in a more limited scope. For those undergoing OAR, the problem of increased perioperative morbidity and mortality remains an important issue. The ability to improve these outcomes would potentially mitigate the initial advantage of EVAR over OAR. While many demographic risk factors that lead to morbidity and mortality are beyond the control of the

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surgeon, some variables are potentially modifiable, particularly as they pertain to the intra- and postoperative care of patients. The goal of the present study was to characterize risk factors associated with perioperative morbidity and mortality in a cohort of patients undergoing OAR, and to identify potentially modifiable risk factors.

Materials and methods

Consecutive patients undergoing OAR of nonruptured infrarenal, juxtarenal, or perirenal AAA over a 10 year period were identified from a prospectively maintained operative database (Microsoft Excel, Richmond, WA). Ruptured AAA were excluded. Patient data was accrued from the operative database and the patients' electronic medical records (Epic, Verona, WI). Choice of operation was at the discretion of the surgeon based on preoperative computerized tomography (CT) imaging. In general, open repair was preferred in patients who did not meet the Instruction for Use (IFU) of standard commercial endovascular devices, including proximal neck length <15 mm length, inappropriate neck characteristics (calcification, thrombus, angulation), or inappropriate iliac anatomy for access or distal sealing. The data predate use of fenestrated and branched devices.

Similarly, operative approach was at the discretion of the surgeon. For most cases involving suprarenal clamping, and for all where supramesenteric clamping is needed, a retroperitoneal approach was preferred. A transperitoneal approach was only used if the aneurysm could be repaired without dividing the left renal vein, a maneuver that is avoided by the authors.

Data included patient demographics, comorbidities and intra- and postoperative variables regarding the surgical procedure and postoperative care, including operative time, proximal clamp site, blood loss and transfusions, intraoperative blood pressure, intra- and postoperative core body temperature, and postoperative glucose control. Outcomes evaluated included perioperative (within 30 days of surgery) morbidity and mortality. Morbidity was defined as a composite endpoint consisting of any perioperative complication (cardiac, pulmonary, gastrointestinal, renal, wound, or bleeding complications). Cardiac complications included both myocardial infarction (EKG changes or troponinemia) and new arrhythmia. Pulmonary complications were defined as pneumonia or prolonged (>3 days) ventilation. Gastrointestinal complications included any gastrointestinal bleeding or ischemia. Renal complications included renal insufficiency (rise in serum creatinine >0.5 mg/dL from baseline) or renal failure requiring dialysis. Bleeding complications included operative site bleeding requiring return to the operating room. Wound complications included any wound breakdown requiring operative intervention or infection requiring antibiotic therapy. Perioperative mortality included any death within 30 days of surgery or during the index hospitalization.

Continuous data are reported as means ± standard deviation for normally distributed data, and median with range for nonparametric data. Categorical data are reported as percentage. Univariate analysis was performed using student's *t*-test for normally distributed continuous data, Mann-Whitney *U* test for nonparametric data, and Fisher's exact or Chi-square test for categorical data. Stepwise multivariate logistic regression analysis was performed to determine independent risk factors for morbidity and mortality. Univariate variables with statistical significance <0.10 were included in the multivariate models. Statistical analysis was performed using SPSS version 25. This study was approved by the Institutional Review Board at Oregon Health & Science University. Due to the retrospective nature of the study and use of deidentified data, informed consent was waived.

Results

309 OAR were performed during the ten year study period. 69 ruptured AAA were excluded leaving 240 cases for analysis. Patient demographic data are listed in Table 1.

Intraoperative factors are listed in Table 2. Suprarenal clamping was utilized in 46% of patients with retroperitoneal exposure in 69%, reflecting a high percentage of juxtarenal aneurysms.

Postoperative complications are listed in Table 3. 113 patients (47%) met the primary composite endpoint of having at least one complication. The most common complications were pulmonary (20%), which was most often prolonged ventilator time, renal insufficiency (15%), and cardiac complications (arrhythmia 11%, myocardial infarction 10%). Almost all complications were transient and had resolved at the time of hospital discharge. 30 day mortality was 5.4%.

Univariate analysis was performed to determine variables associated with perioperative morbidity and mortality. This was divided into preoperative variables (Table 1), intraoperative variables (Table 2), and postoperative variables (Table 4). Preoperative demographic variables (Table 1) associated with morbidity included female sex ($p = 0.026$), and history of cerebrovascular disease ($p = 0.006$). Increased age ($p = 0.004$) was associated with mortality. Intraoperative variables (Table 2) associated with morbidity included larger aneurysms ($p = 0.04$), need for suprarenal clamping ($p = 0.001$), prolonged operative time ($p < 0.001$), increased blood loss ($p = 0.005$) and need for blood transfusions ($p < 0.001$). Prolonged operative time ($p = 0.006$), blood loss

Table 1
Patient demographics of the overall group and cohorts with and without morbidity and mortality.

Factor	Overall (n = 240)	Complications (n = 113)	No complications (n = 127)	Significance	Death (n = 13)	No death (n = 227)	Significance
Age	69.3 ± 8.7	70.5 ± 7.8	68.2 ± 9.3	0.759	75.9 ± 7.5	68.9 ± 8.6	0.004
Sex (%male)	191 (80%)	83 (74%)	108 (85%)	0.026	11 (85%)	179 (79%)	0.619
Body Mass Index	27.5 ± 5.3	27.5 ± 5.5	27.5 ± 5.0	0.421	25.3 ± 4.7	27.6 ± 5.3	0.115
Coronary artery disease	125 (52%)	47 (42%)	68 (54%)	0.064	7 (54%)	118 (52%)	0.896
Diabetes mellitus	34 (14%)	17 (15%)	17 (13%)	0.713	1 (8%)	33 (15%)	0.491
Current smoker	120 (50%)	52 (43%)	68 (54%)	0.244	3 (23%)	117 (52%)	0.084
Ever smoker	210 (88%)	97 (86%)	113 (89%)	0.463	11 (85%)	199 (88%)	0.669
Cerebrovascular disease	65 (27%)	40 (35%)	25 (20%)	0.006	4 (31%)	61 (27%)	0.753
Renal insufficiency (serum creatinine>1.5)	40 (17%)	23 (20%)	17 (13%)	0.148	2 (15%)	38 (17%)	0.899
Hypercholesterolemia	140 (58%)	63 (56%)	77 (61%)	0.444	6 (46%)	134 (59%)	0.396
Chronic obstructive pulmonary disease	82 (34%)	43 (38%)	39 (31%)	0.231	6 (46%)	76 (34%)	0.376
Prior vascular surgery	10 (4%)	3 (3%)	7 (6%)	0.342	1 (8%)	9 (4%)	0.433

Table 2
Operative data of the overall group and cohorts with and without morbidity and mortality.

	All (n = 240)	Complications (n = 113)	No complications (n = 127)	Significance	Death (n = 13)	No death (n = 227)	Significance
AAA diameter	6.3 ± 1.2	6.5 ± 1.2	6.2 ± 1.3	0.04	7.0 ± 0.9	6.3 ± 1.3	0.06
Exposure:	166 (69%)	79 (70%)	87 (69%)	0.81	6 (46%)	160 (71%)	0.118
Retroperitoneal	74 (31%)	34 (30%)	40 (31%)		7 (54%)	67 (29%)	
Transperitoneal							
Proximal clamp:	129 (54%)	48 (43%)	81 (64%)	0.001	4 (31%)	125 (55%)	0.150
Infrarenal	111 (46%)	65 (57%)	46 (36%)		9 (69%)	102 (45%)	
Suprarenal							
Graft type:	131 (55%)	67 (59%)	64 (50%)	0.167	9 (69%)	122 (54%)	0.392
Bifurcated	109 (45%)	46 (41%)	63 (50%)		4 (31%)	105 (46%)	
Tube							
Operative time (minutes)	358 ± 91	381.7 ± 94.9	336.3 ± 82.6	<0.001	424 ± 98	353 ± 90	0.006
Blood loss (mL)	1952 ± 2172	2362 ± 2684	1579 ± 1483	0.005	4742 ± 5578	1790 ± 1684	<0.001
PRBC (units)	2.1 ± 2.3	2.9 ± 2.7	1.4 ± 1.6	<0.001	5.5 ± 4.4	1.9 ± 2.0	<0.001
Temperature (low)	35.1 ± 0.64	35.1 ± 0.65	35.1 ± 0.62	0.545	35.0 ± 0.7	35.1 ± 0.6	0.480
Temperature (mean)	35.5 ± 0.62	35.5 ± 0.59	35.5 ± 0.65	0.929	35.4 ± 0.8	35.5 ± 0.6	0.430
Systolic Blood Pressure (low)	84.5 ± 10.2	83.2 ± 11.4	85.7 ± 8.8	0.063	79.6 ± 18.6	84.8 ± 9.5	0.075
Systolic Blood Pressure (mean)	117.2 ± 10.9	116.3 ± 10.4	118.1 ± 11.4	0.214	112.2 ± 13.0	117.5 ± 10.7	0.084

Table 3
Perioperative morbidity and mortality.

Complication	Frequency (n = 240)
Any complication	113 (47%)
Pulmonary	47 (20%)
Renal insufficiency	35 (15%)
Arrhythmia	27 (11%)
Myocardial infarction	23 (10%)
Wound	20 (8%)
Gastrointestinal	10 (4%)
Renal failure (dialysis)	9 (4%)
Stroke	2 (1%)
Bleeding	7 (3%)
Lower extremity ischemia	5 (2%)
Death	13 (5%)

($p < 0.001$) and transfusions ($p < 0.001$) were also associated with mortality. There was a trend towards low intraoperative systolic blood pressure associated with both morbidity ($p = 0.063$) and mortality ($p = 0.084$). Patients who experienced complications and death had longer ICU length of stay ($p < 0.001$), longer time on mechanical ventilation ($p < 0.001$), and a longer hospital length of stay ($p \leq 0.001$) (Table 4). Low postoperative temperature was also associated with both morbidity ($p = 0.006$) and mortality ($p = 0.015$).

Multivariate logistic regression analysis was performed to identify factors associated with the composite endpoint of postoperative complication and 30 day mortality. Significant associations for complications included suprarenal clamping (OR 1.8, 95% CI 1.1–3.2, $p = 0.029$), operative time (OR 1.005, 95% CI 1.002–1.008, $p = 0.002$), and low postoperative temperature (OR 1.6, 95% CI 1.1–2.3, $p = 0.025$). Multivariate predictors of 30 day mortality included advanced age (OR 1.2, 95% CI 1.1–1.3, $p = 0.002$) and operative time (OR 1.007, 95% CI 1.001–1.013, $p = 0.024$).

Discussion

In this study we identified factors associated with increased risk of perioperative morbidity and mortality following OAR. Perioperative complications were common, occurring in 47% of the patient cohort. 30 day mortality was 5.4%. By multivariate analysis, factors associated with perioperative morbidity included use of a suprarenal clamp, operative time, and low postoperative temperature (<36 °F). Multivariate predictors of postoperative mortality included advanced age and prolonged operative time. While patient demographics and comorbidities are not modifiable, knowledge of increased risk due to specific comorbidities can lead to heightened awareness in postoperative care. With respect to cardiac risk factors, all patients undergo preoperative electro- and echocardiography for risk stratification, with stress testing for those at high risk. In a review of the Vascular Quality Initiative database, routine stress testing has not been shown to reduce major adverse cardiac events or mortality following AAA repair.[5] Additionally, the VA randomized trial did not show significant benefit to coronary revascularization in those undergoing elective major vascular surgery.[6] However, neither of these studies specified the site of proximal cross clamping in OAR. Given the increased cardiac demands with more proximal cross clamping, more extensive preoperative cardiac workup should be considered in this particular group.

The use of suprarenal clamping is likely a reflection of more complicated cases and arises more out of necessity than choice. We have previously reported increased complication rates when suprarenal clamping is needed.[7] This is likely to be an ongoing trend, since straightforward OAR of infrarenal AAAs has essentially disappeared, as these patients are almost always anatomically suitable for EVAR. The adoption of fenestrated EVAR is increasingly replacing the need for OAR for most straightforward juxta- and

Table 4
Postoperative factors of the overall group and cohorts with and without morbidity and mortality.

	All (n = 240)	Complications (n = 113)	No complications (n = 127)	Significance	Death (n = 13)	No death (n = 227)	Significance
ICU length of stay (days)	3 (1–142)	6 (1–142)	2 (1–16)	<0.001	19 (1–142)	3 (1–59)	<0.001
Ventilator days	0 (0–142)	0 (0–142)	0 (0–3)	<0.001	19 (0–142)	0 (0–64)	<0.001
Glucose (low)	111.9 ± 31.3	113.3 ± 33.1	110.6 ± 29.6	0.504	106.4 ± 42.1	112.2 ± 30.6	0.515
Glucose (high)	154.2 ± 31.8	158.1 ± 34.9	150.5 ± 28.4	0.112	161.3 ± 37.7	153.7 ± 31.5	0.466
Glucose (mean)	133.6 ± 27.6	136.4 ± 31.0	131.1 ± 24.0	0.146	136.6 ± 34.4	133.5 ± 27.3	0.689
Temperature (low) (°C)	35.9 ± 0.74	35.7 ± 0.7	36.0 ± 0.7	0.006	35.4 ± 0.8	35.9 ± 0.7	0.015
Temperature (mean) (°C)	37.0 ± 0.50	37.0 ± 0.5	37.0 ± 0.5	0.725	36.8 ± 0.3	37.0 ± 0.5	0.261
Hospital length of stay (days)	7 (0–142)	10 (0–142)	6 (2–29)	<0.001	19 (0–142)	7 (2–81)	0.001

perirenal AAAs as well. The majority of OAR in the current health care environment will likely all have anatomic complexity that will necessitate challenging repairs. To as great a degree as possible, distal clamp placement and minimizing operative times should be emphasized.

Similarly, prolonged operative times may be an inevitable aspect of case complexity. However, prolonged operative times have been noted to be an independent factor predicting perioperative complications in a number of different surgical procedures.[8–10] In a recent meta analysis, complication risk was noted to double with operations lasting more than two hours, with a 14% increase in complication risk with every additional 30 min of operative time.[11] Regardless of case complexity, every effort should be made to minimize operative times.

Increased intraoperative blood loss and packed red blood cell transfusions were noted to be associated with both perioperative morbidity and mortality. Blood loss is most likely a reflection of case complexity and difficulty, and the increased transfusion requirement in these patients is intuitive. However, there is increasing evidence that blood transfusions are an independent risk factor for perioperative morbidity and mortality.[12,13] The reason for this is unclear but it is hypothesized that postoperative transfusions may cause immunosuppressive effects or fluid shifts that lead to myocardial stress, pulmonary edema, or pneumonia or other infections. This has resulted in more restrictive thresholds for transfusions (hemoglobin level of 7–8 g/dL),[14] a practice that we have also adopted.

Perioperative temperature control is an important adjunct to minimize postoperative surgical complications. Hypothermia is increasingly being recognized as a contributing factor in a number of perioperative complications. The causes of hypothermia are likely multifactorial, including heat loss from open abdominal and retroperitoneal exposure, prolonged operative times, infusion of hypothermic fluids, and low ambient temperatures relative to core body temperature. Several studies have demonstrated the association of hypothermia with systemic sequelae, including coagulopathy, surgical site infections, and cardiovascular complications in high risk patients.[15,16] Both active and passive measures of warming should be used, including the use of warmed intravenous and irrigation fluids, the use of forced air patient warming systems, and maintaining higher ambient temperatures. In this study, postoperative hypothermia was associated with an increased complication rate by multivariate analysis and mortality in univariate analysis, emphasizing the need to carry out these measures beyond the operating room and into the intensive care unit setting. As a result of this study we have instituted more meticulous warming techniques to maintain normothermia in the operating room, ICU and in the transition between these environments.

Interestingly, perioperative glucose control did not affect morbidity or mortality in this study, despite having been identified as a factor influencing perioperative morbidity in prior studies.[17,18] We felt that a possible explanation for this was that our surgical intensivists already have very strict blood glucose protocols and tightly control postoperative glucose levels, so the ranges of glucose levels in our patient cohort was already very narrow and hyperglycemia rare, thereby minimizing discriminatory ability of this measure. We therefore still continue to advocate for close monitoring and controlling of blood glucose levels, despite lack of influence in the outcomes of this study.

Similarly, while smoking was not an independent risk factor for morbidity or mortality, pulmonary complications were the most frequent morbidity, and every effort is made to address the importance of smoking cessation both pre- and postoperatively. We also frequently use epidural analgesia, frequent respiratory therapy in intubated patients, and incentive spirometry and early mobilization in extubated patients to reduce the risk of pulmonary complications.

Renal insufficiency was the second most frequent complication in this series, although the need for dialysis was rare and no patients required permanent hemodialysis. We routinely administer mannitol (50 mg intravenous) intraoperatively prior to aortic clamping. No other renal adjunctive methods were used. Others have advocated the use of intraoperative renal cooling,[19] however, a recent Cochrane analysis did not demonstrate definitive benefit of adjunctive renal protective measures during aortic procedures.[20]

This study has several limitations, mainly due its retrospective nature. While the number of patients meeting the composite morbidity endpoint was adequate for comparison with the cohort without morbidity, the individual morbidity components were too small to perform meaningful subgroup analysis. For example, blood glucose levels have most frequently been associated with wound complications, but there were not enough wound complications in this cohort for meaningful analysis of this. Similarly, the mortality group was small, limiting comparisons and creating the possibility of both type 1 and 2 statistical errors. As noted, it is difficult to separate cause and effect in our analysis, so while we found some statistically significant factors associated with morbidity and mortality, we cannot draw any conclusions about the causes of these outcomes.

Despite these limitations, we feel that the results have important implications for the future of OAR. As this procedure continues to decrease due to further expansion of EVAR including fenestrated and branched technologies, OAR will become an increasingly complex operation, performed by surgeons with decreasing experience. Current projections are that by the year 2020, the average vascular trainee will complete between one to three OAR during their training.[21] (12) The gradual conversion to an integrated vascular residency will create further challenges. Residents completing an integrated vascular residency (0 + 5) graduate with a comparable number of aneurysm procedures to those in the traditional pathway (5 + 2),[22] however, this is spread out over five years instead of two, and does not take into account the open abdominal surgical experience, both vascular and general, accrued by those in the traditional pathway.

It is difficult to imagine how the vascular surgeon of the future will develop and maintain adequate skills to perform these procedures. Even if all elective AAA can ultimately be treated with endovascular techniques, there will be occasional urgent/emergent procedures that will require an open approach. Furthermore, there are multiple reports of open surgery for failed EVAR,[23,24] an operation being performed with increasing frequency in our facility as well. A recent review of the Medicare database that, while there was minimal association between surgical volume and EVAR mortality, both surgeon and hospital volume were strongly associated with OAR mortality.[25] In another study from Canada, OAR volume was not associated with mortality, but was associated with postoperative complications and need for reoperation.[26] OAR will likely become a procedure relegated to high volume aortic centers, and will clearly require a multidisciplinary team of experienced surgeons, anesthesiologists, and intensivists, in addition to nurses and mid-level providers, to optimize results in these increasingly complex procedures.

Conclusions

OAR has been largely replaced with EVAR but remains an operation that can be safely done with acceptable results. While a number of risk factors for perioperative morbidity and mortality are beyond the control of the surgeon, perioperative hypothermia represents a potentially modifiable factor that may mitigate some of the short term risks of OAR.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2018.12.054.

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