Invited Commentary

Increased Survival Secondary to Decreased Perioperative Complications in Open Aortic Aneurysm Repair Using Epidural Anesthesia

The Long and the Short of It

Gale L. Tang, MD

Epidural analgesia is widely recognized to be a very effective method of postoperative pain control. Various benefits in terms of postoperative recovery after both major abdominal procedures and open abdominal aortic aneurysm repair have been attributed to the use of postoperative epidural analgesia.[1]

Related article

In the study by Bardia et al[2] in this issue of *JAMA Surgery*, the authors focus instead on the effect of intraoperative adjunctive epidural anesthesia (EA) use by analyzing the Vascular Study Group of New England data registry for patients undergoing elective, open abdominal aortic aneurysm repair. They demonstrated a decrease in postoperative bowel ischemia, need for dialysis, respiratory complications, and short-term reoperation in the EA-general anesthesia (GA) group from the GA-alone group, which translated into a decrease in long-term mortality at 5 years by Kaplan-Meier survival analysis.

The effect of perioperative morbidity leading to an increase in long-term mortality has previously been demonstrated[3] by authors analyzing the Veterans Administration National Surgical Quality Improvement Program database as well as in a more recent meta-analysis.[4] The present study further supports the notion that decreasing immediate postoperative complications results in improvement in long-term patient outcomes. It remains an open question whether EA was truly responsible for the decreased immediate postoperative complications because it is not possible to control for surgeon-related and hospital volume-related factors when using registry data alone. The potential mechanism by which thoracic EA might lead to decreased serious postoperative bowel ischemia is unclear. Its effect on splanchnic blood flow is controversial, as discussed in a recent review by Siniscalchi et al,[5] but decreased sympathetic and immune stimulation may play a role.[6]

From a global perspective, open aortic surgery is on the decline and endovascular aortic repair is expanding with new devices and technology extending into the pararenal and perivisceral arenas. This shift will make randomized trials studying the effectiveness of EA-GA difficult since fewer open procedures are done. Therefore, it seems wise to use any adjuncts at our disposal to reduce postoperative complications as long as the costs and risks are low.

ARTICLE INFORMATION

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REFERENCES

1. Nishimori M, Low JH, Zheng H, Ballantyne JC. Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery. *Cochrane Database Syst Rev*. 2012;(7):CD005059.

2. Bardia A, Sood A, Mahmood F, et al. Combined epidural-general anesthesia vs general anesthesia alone for elective abdominal aortic aneurysm repair [published online September 7, 2016]. *JAMA Surg*. doi:10.1001/jamasurg.2016.2733.

3. Khuri SF, Henderson WG, DePalma RG, Mosca C, Healey NA, Kumbhani DJ; Participants in the VA National Surgical Quality Improvement Program. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Ann Surg*. 2005;242(3):326-341.

4. Pucher PH, Aggarwal R, Qurashi M, Darzi A. Meta-analysis of the effect of postoperative in-hospital morbidity on long-term patient survival. *Br J Surg*. 2014;101(12):1499-1508.

5. Siniscalchi A, Gamberini L, Laici C, Bardi T, Faenza S. Thoracic epidural anesthesia: effects on splanchnic circulation and implications in anesthesia and intensive care. *World J Crit Care Med*. 2015;4(1):89-104.

6. Chen WK, Ren L, Wei Y, Zhu DX, Miao CH, Xu JM. General anesthesia combined with epidural anesthesia ameliorates the effect of fast-track surgery by mitigating immunosuppression and facilitating intestinal functional recovery in colon cancer patients. *Int J Colorectal Dis*. 2015;30(4):475-481.

JAMA Surgery | Original Investigation

Combined Epidural-General Anesthesia vs General Anesthesia Alone for Elective Abdominal Aortic Aneurysm Repair

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IMPORTANCE Epidural analgesia (EA) is used as an adjunct procedure for postoperative pain control during elective abdominal aortic aneurysm (AAA) surgery. In addition to analgesia, modulatory effects of EA on spinal sympathetic outflow result in improved organ perfusion with reduced complications. Reductions in postoperative complications lead to shorter convalescence and possibly improved 30-day survival. However, the effect of EA on long-term survival when used as an adjunct to general anesthesia (GA) during elective AAA surgery is unknown.

OBJECTIVE To evaluate the association between combined EA-GA vs GA alone and long-term survival and postoperative complications in patients undergoing elective, open AAA repair.

DESIGN, SETTING, AND PARTICIPANTS A retrospective analysis of prospectively collected data was performed. Patients undergoing elective AAA repair between January 1, 2003, and December 31, 2011, were identified within the Vascular Society Group of New England (VSGNE) database. Kaplan-Meier curves were used to estimate survival. Cox proportional hazards regression models and multivariable logistic regression models assessed the independent association of EA-GA use with postoperative mortality and morbidity, respectively. Data analysis was conducted from March 15, 2015, to September 2, 2015.

INTERVENTIONS Combined EA-GA.

MAIN OUTCOMES AND MEASURES The primary outcome measure was all-cause mortality. Secondary end points included postoperative bowel ischemia, respiratory complications, myocardial infarction, dialysis requirement, wound complications, and need for surgical reintervention within 30 days of surgery.

RESULTS A total of 1540 patients underwent elective AAA repair during the study period. Of these, 410 patients (26.6%) were women and the median (interquartile range) age was 71 (64-76) years; 980 individuals (63.6%) received EA-GA. Patients in the 2 groups were comparable in terms of age, comorbidities, and suprarenal clamp location. At 5 years, the Kaplan-Meier–estimated overall survival rates were 74% (95% CI, 72%-76%) and 65% (95% CI, 62%-68%) in the EA-GA and GA-alone groups, respectively ($P < .01$). In adjusted analyses, EA-GA use was associated with significantly lower hazards of mortality compared with GA alone (hazard ratio, 0.73; 95% CI, 0.57-0.92; $P = .01$). Patients receiving EA-GA also had lower odds of 30-day surgical reintervention (odds ratio [OR], 0.65; 95% CI, 0.44-0.94; $P = .02$) as well as postoperative bowel ischemia (OR, 0.54; 95% CI, 0.31-0.94; $P = .03$), pulmonary complications (OR, 0.62; 95% CI, 0.41-0.95; $P = .03$), and dialysis requirements (OR, 0.44; 95% CI, 0.23-0.88; $P = .02$). No significant differences were noted for the odds of wound (OR, 0.88; 95% CI, 0.38-1.44; $P = .51$) and cardiac (OR, 1.08; 95% CI, 0.59-1.78; $P = .82$) complications.

CONCLUSIONS AND RELEVANCE Combined EA-GA was associated with improved survival and significantly lower HRs and ORs for mortality and morbidity in patients undergoing elective AAA repair. The survival benefit may be attributable to reduced immediate postoperative adverse events. Based on these findings, EA-GA should be strongly considered in suitable patients.

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Invited Commentary
Supplemental content

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Open abdominal aortic aneurysm (AAA) repairs are associated with high morbidity and mortality with reported[1-4] rates varying from 12% to 26% and 4% to 6%, respectively.

Epidural analgesia (EA) is a key adjuvant therapy for effective postoperative pain control after AAA surgery.[5] Neuraxial anesthesia in general and EA in particular causes modulation of spinal sympathetic outflow with resultant vasodilatation and consequent increased visceral perfusion and reduced afterload.[6,7] Drawing on these physiologic actions, the effect of EA on reduction of postoperative cardiac, pulmonary, renal, and neurologic complications has been investigated. Although there is accumulating evidence in favor of EA use combined with general anesthesia (EA-GA) during AAA surgery,[8-10] studies showing conflicting findings exist[11,12]; thus, the certainty of the benefits of EA use remains debated.

Bowel ischemia after AAA surgery is a devastating complication with mortality rates approaching 50%.[13,14] Appreciation of the role of EA in increasing splanchnic blood flow is important in this context.[7] Whether this beneficial effect of increased splanchnic flow with EA extrapolates clinically to a reduction in postoperative bowel ischemia is not known. Establishing an association between EA and a reduction in postoperative bowel ischemia after AAA surgery could make a case for outcome benefits of EA, and such early postoperative benefits may ultimately translate into long-term survival advantage as well. To our knowledge, the effect of EA-GA use on bowel ischemia, surgical reintervention for bowel ischemia, and long-term patient survival has not been explored.

On the basis of these considerations, we sought to evaluate the effect of EA-GA use vs GA alone on long-term patient survival and perioperative morbidity, including bowel ischemia and surgical reintervention for bowel ischemia in patients undergoing elective AAA repair. We hypothesized that, owing to sympathetic blockade and blunting of surgical-stress response, EA might exert a beneficial effect on patient recovery[15] by improving outcomes after surgery; these short-term benefits may ultimately translate into a long-term survival advantage. To test our hypothesis, we relied on a large, prospectively maintained, multi-institutional vascular data registry: the Vascular Study Group of New England (VSGNE) data registry.

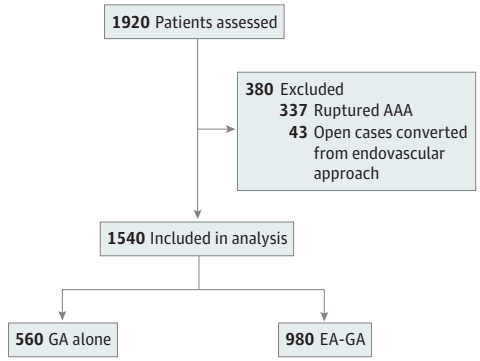
Key Points

Question Is combined epidural anesthesia (EA) and general anesthesia (GA) use compared with GA alone associated with improved long-term survival and fewer postoperative complications in patients undergoing elective, open abdominal aortic aneurysm repair?

Findings In this retrospective analysis of prospectively collected data comprising 1540 patients, combined EA-GA use was associated with a significantly lower hazard of mortality compared with GA alone This mortality benefit could probably be attributable to reduced immediate postoperative adverse events, such as lower odds of 30-day surgical reintervention, bowel ischemia, respiratory complications, and dialysis requirement postoperatively.

Meaning Combined EA-GA should be strongly considered in suitable patients undergoing elective, open abdominal aortic aneurysm repair.

Figure 1. Criteria for Patient Inclusion



Patients who underwent elective, open abdominal aortic aneurysm (AAA) surgery from 2003 to 2011 were assessed using the Vascular Society Group of New England database. EA indicates epidural anesthesia; GA, general anesthesia.

Methods

Data Source

The VSGNE is a consortium of clinicians, hospital administrators, and research personnel that strives to continuously improve the quality, safety, effectiveness, and cost of caring for patients with vascular disease.[16,17] Briefly, the VSGNE records outcomes after vascular surgery to allow benchmarking among centers for quality assurance and improvement activities. The registry undergoes rigorous auditing at regular intervals for data quality.[18] The study was approved by the Beth Israel Deaconess Medical Center institutional review board. The study was done as a part of our ongoing vascular surgery performance initiative. The data were deidentified and we had no access to any patient identifiers. Informed consent was not required by the institutional review board.

Study Population

The study population consisted of patients 18 years or older who underwent elective, open AAA repair between January 1, 2003, and December 31, 2011. Patients presenting with ruptured AAAs and/or surgical procedures intended as endovascular aortic aneurysm repairs but converted to an open setting were excluded (**Figure 1**). We did not include emergent or ruptured AAA cases since epidural placement is often not considered owing to the emergent nature of the case rather than physician preference. Similarly, endovascular aortic aneurysm repairs seldom undergo an epidural placement preoperatively because of the minimally invasive nature of the intervention. Our final sample consisted of 1540 patients.

Covariates

For each patient, age at the time of surgery, sex, body mass index (BMI [calculated as weight in kilograms divided by height

in meters squared]), smoking status, serum creatinine level, and preoperative medication use, including aspirin, clopidogrel bisulfate, statins, and β-blockers, were recorded. History of hypertension, diabetes, congestive heart failure, chronic obstructive pulmonary disease, coronary artery disease, and coronary revascularization (coronary artery bypass grafting or percutaneous coronary intervention) was noted. Operative variables noted included American Society of Anesthesiologists (ASA) physical status classification (https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system), suprarenal aortic cross-clamp time, cross-clamp location (stratified into the infrarenal artery, unilateral renal artery, bilateral renal artery, or above the celiac trunk clamping), and surgical approach (transperitoneal vs retroperitoneal). The standard ASA score ranges from 1 to 6. Class 5 of the ASA indicates patients who are moribund and ASA 6 indicates those who are brain dead. Both ASA 5 and 6 met the exclusion criteria in our study since we included elective surgeries. Hence, our scale ranged from ASA 1 to 4. Age, BMI, serum creatinine level, operative time, and cross-clamp time were coded in a continuous fashion; the remaining variables were coded in a categorical fashion.

End Points

The primary outcome was all-cause mortality; the VSGNE Quality Initiative routinely collects data on every patient between 1 and 21 months after surgery to ensure data collection for a minimum of 1 year.[16] Data on survival beyond this period were obtained from the Social Security Death Index database (http://www.ntis.gov/products/ssa-dmf/#); the mortality data are updated at regular intervals by the data managers of the VSGNE. Secondary outcomes included (1) 30-day postoperative bowel ischemia, defined as colonoscopic/laparotomy evidence of ischemia, bloody stools in a patient who died prior to colonoscopy or laparotomy (surgically managed bowel ischemia), or presumptive diagnosis with conservative treatment (medically managed bowel ischemia); (2) myocardial infarction, defined as isolated troponin level elevation, electrocardiographic change, or clinical evidence of myocardial infarction; (3) pulmonary complications, including postoperative pneumonia or prolonged (>48 hours) mechanical ventilation; (4) need for dialysis; (5) wound complications, including surgical site infections and dehiscence; and (6) surgical reintervention, defined as return to the operating room after AAA repair within 30 days of the initial intervention. Multiple imputations (Markov chain Monte Carlo method; 10 iterations) were used to account for missing data in 2 variables: BMI (79 [5.1%]) and ASA physical status (77 [5%]).

Statistical Analysis

Categorical variables were described using frequencies and proportions. Medians and interquartile ranges (IQRs) as well as means and SDs were used for continuously coded variables. The χ^2 and unpaired, 2-tailed *t* test or Mann-Whitney test were used to compare proportions and means or medians, respectively. Patients were stratified according to anesthesia type (EA-GA vs GA alone), and rates of postoperative complications and need for reintervention were compared between the 2 groups. For survival analysis, Kaplan-Meier estimates were generated, and the log-rank test was used to determine significance.

For adjusted analyses, parsimonious multivariable logistic regression and Cox proportional hazards regression models were used to analyze associations between the anesthesia type and complications/adverse events and mortality, respectively. Models were adjusted for age, sex, BMI, smoking status, medications, comorbidities, renal function, ASA physical status, suprarenal cross clamp time and cross clamp location, operative time, and surgical approach. For each model, only variables significant on univariable analysis were included in the multivariable model; this process was repeated for each model. We did not assess for collinearity among the variables, which represents a potential limitation of the analysis. Temporal trends in EA-GA utilization were analyzed using a linear regression method—the annual estimated percent of change method—as previously described.[19] All statistical tests were performed using R, version 3.0.2 (R Foundation), with a 2-sided significance level set at $P < .05$; goodness-of-fit tests were performed using Stata, version 14 (StataCorp LP). Data analysis was conducted from March 15, 2015, and to September 2, 2015.

Results

Baseline Characteristics

Table 1 summarizes the baseline characteristics, stratified by anesthesia type. The study cohort comprised 1540 patients, and 980 of these individuals (63.6%) received combined EA-GA. Overall, most patients were men (73.4%) with no significant difference between the 2 study groups ($P = .12$). The median age in both groups was 71 years ($P = .16$). Patients in the 2 groups had similar comorbidities and clamp locations. However, they differed with respect to β-blocker use (GA, 75.4% vs EA-GA, 89.1%; $P = .001$), ASA physical status (ASA class 4: GA, 32.1% vs EA-GA, 27.9%; $P = .02$), operative time (median for GA, 210 [IQR, 154-270] minutes vs EA-GA, 188 [IQR, 150-243] minutes; $P < .001$), suprarenal cross-clamp times (median for GA, 20 [IQR, 4-30] minutes vs EA-GA, 24 [IQR, 19-31] minutes; $P < .01$), and BMI (median for GA, 27.1 [IQR, 23.6-31.1] vs EA-GA, 26.5 [IQR, 23.4-29.8]; $P < .01$).

Kaplan-Meier Survival Analysis

Median follow-up in the GA and EA-GA cohorts was 2.9 and 3.7 years, respectively; all patients had a minimum of 4.5 months of follow-up, with a maximum follow-up of 102 months. At 5 years, the Kaplan-Meier–estimated overall survival rates were 65% (95% CI, 62%-68%) and 74% (95% CI, 72%-76%) in the GA and EA-GA groups, respectively (log-rank, $P < .01$) (**Figure 2**A).

Univariable Postoperative Outcomes

In univariable analyses, bowel ischemia rates were 4.5% and 2.3% for the GA and EA-GA groups, respectively ($P = .03$). Postoperative dialysis rates were 3.8% and 1.7% in the GA and EA-GA groups, respectively ($P = .01$) (eTable 1 in the Supple-

Table 1. Demographics and Intraoperative Variables

Baseline Characteristics	Total (N = 1540)	GA (n = 560)	EA-GA (n = 980)	Effect Estimate (95% CI)[a]	*P* Value
Age, median (IQR), y	71 (64 to 76)	71 (64 to 77)	71 (65 to 76)	0.40 (−0.46 to 1.26)	.16
Women, No. (%)	410 (26.6)	162 (28.9)	248 (25.3)	0.83 (0.66 to 1.05)	.12
BMI, median (IQR)	26.8 (23.5 to 30.2)	27.1 (23.6 to 31.1)	26.5 (23.4 to 29.8)	0.80 (0.22 to 1.38)	<.01
Comorbidities, No. (%)					
Hypertension	1276 (82.9)	459 (82)	817 (83.4)	1.10 (0.84 to 1.45)	.48
Diabetes	221 (14.4)	92 (16.4)	219 (22.3)	0.78 (0.59 to 1.01)	.08
Coronary artery disease	500 (32.5)	169 (30.2)	331 (33.8)	1.18 (0.94 to 1.48)	.14
Coronary revascularization[b]	450 (29.2)	148 (26.4)	302 (30.8)	1.24 (0.98 to 1.56)	.07
CHF	98 (6.4)	39 (7)	59 (6)	0.85 (0.56 to 1.29)	.46
COPD	546 (35.5)	213 (38)	333 (34)	0.84 (0.68 to 1.05)	.10
Serum creatinine, median (IQR), mg/dL	1 (0.9 to 1.3)	1 (0.8 to 1.2)	1 (0.9 to 1.3)	−0.02 (−0.06 to 0.02)	.09
CKD stage, No. (%)[c]					
1	558 (36.2)	197 (35.2)	361 (36.8)	1.37 (0.64 to 2.96)	.26
2	543 (35.3)	185 (33)	358 (36.5)	1.45 (0.67 to 3.13)	
3	234 (15.2)	96 (17.1)	138 (14.1)	1.08 (0.49 to 2.38)	
4	135 (8.8)	50 (8.9)	85 (8.7)	1.28 (0.56 to 2.91)	
5	42 (2.7)	20 (3.6)	22 (2.2)	0.83 (0.32 to 2.16)	
6	28 (1.8)	12 (2.1)	16 (1.6)	1 [Reference]	
Smoking, No. (%)	1422 (92.3)	521 (93)	901 (92)	0.88 (0.59 to 1.31)	.51
Drugs, No. (%)					
Statins	998 (64.8)	356 (63.6)	642 (65.5)	1.09 (0.88 to 1.36)	.47
β-Blockers	1295 (84.1)	422 (75.4)	873 (89.1)	2.67 (2.02 to 3.52)	.001
Aspirin and/or clopidogrel bisulfate	1124 (73)	395 (70.5)	729 (74.4)	1.21 (0.96 to 1.53)	.10
ASA class, No. (%)[d]					
1-3	1087 (70.6)	380 (67.9)	707 (72.1)	1.22 (0.98 to 1.53)	.02
4	453 (29.4)	180 (32.1)	273 (27.9)	1 [Reference]	
Operative time, median (IQR), min	193 (152 to 255)	210 (154 to 270)	188 (150 to 243)	16.30 (7.42 to 25.19)	<.001
Suprarenal cross-clamp time, median (IQR), min[e]	23 (15 to 30)	20 (4 to 30)	24 (19 to 31)	−6.92 (−15.1 to −2.01)	<.01
Proximal clamp location, No. (%)[f]					
Infrarenal artery	1091 (70.8)	391 (70.1)	700 (71.4)	1.14 (0.75 to 1.72)	.58
Unilateral renal artery	155 (10.1)	52 (9.3)	103 (10.5)	1.26 (0.75 to 2.11)	
Bilateral renal artery	188 (12.2)	75 (13.4)	113 (11.5)	0.96 (0.59 to 1.57)	
Above celiac trunk	103 (6.7)	40 (7.2)	63 (6.4)	1 [Reference]	
Surgical approach, No. (%)[g]	1216 (79)	449 (80.2)	767 (78.3)	0.89 (0.69 to 1.15)	.39

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; EA, epidural anesthesia; GA, general anesthesia; IQR, interquartile range.

SI conversion factor: To convert serum creatinine to micromoles per liter, multiply by 88.4.

[a] Effect estimates are presented as mean differences for continuous variables (age, BMI, serum creatinine level, operative time, and cross-clamp time) and odds ratios for categorical variables (all other factors).

[b] Includes patients with a history of coronary artery bypass grafting or percutaneous coronary intervention.

[c] Estimated glomerular filtration rate for stage 1, 90 mL/min or more; stage 2, 60-89 mL/min; stage 3, 45-59 mL/min; stage 4, 30 to 44 mL/min; stage 5, 15 to 29 mL/min; and stage 6, less than 15 mL/min. Stages were determined using the Modified Diet in Renal Disease equation.[20]

[d] The ASA scale is described in the Methods section.

[e] Included only unilateral renal, bilateral renal, and above-celiac trunk clamping.

[f] Data on 3 patients were missing.

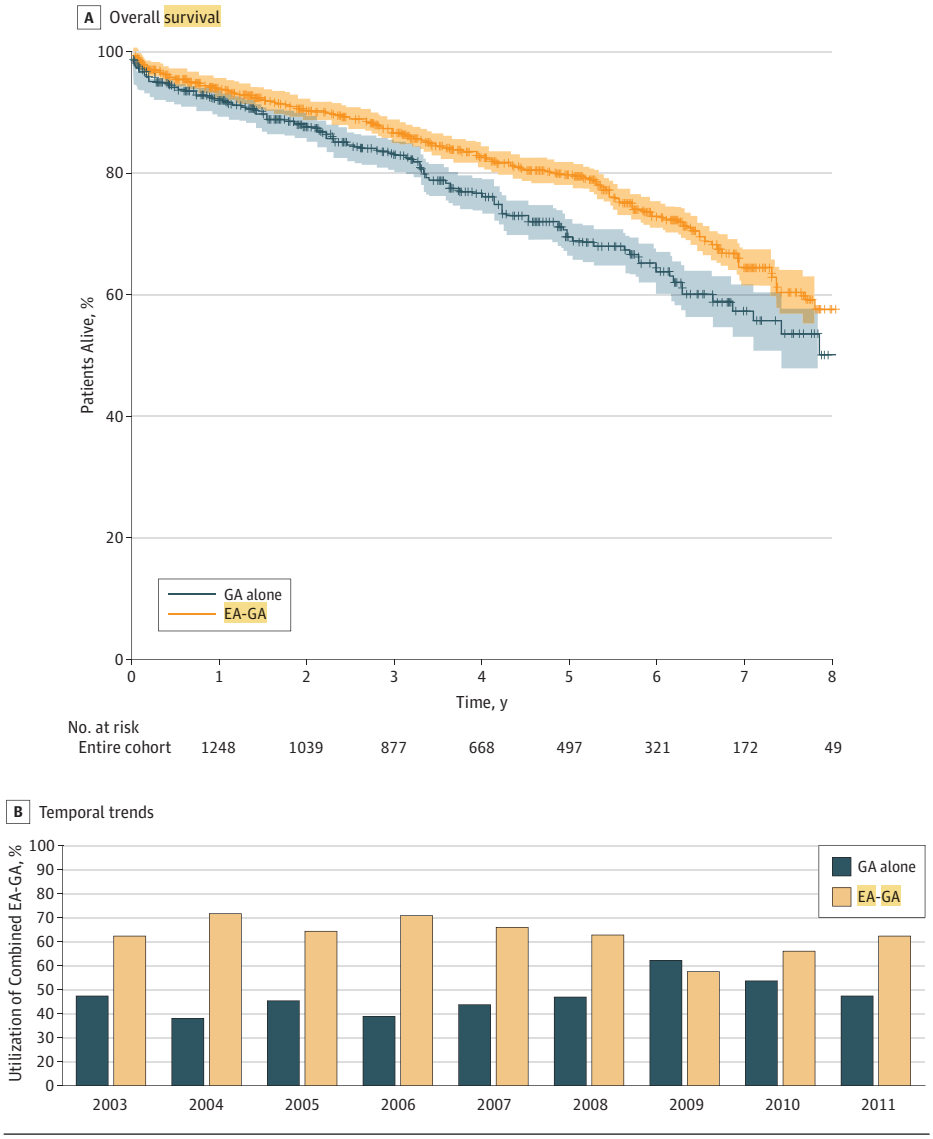
[g] Could be transperitoneal or retroperitoneal; here, the percentages are reported for the transperitoneal approach.

ment). There was a signal toward lower pulmonary complications in patients in the EA-GA group, but it did not achieve statistical significance (GA, 14.7% vs EA-GA, 11.4%; *P* = .06). No significant differences were noted in the rates of wound and cardiac complications. Finally, patients undergoing EA-GA had significantly lower rates of 30-day reintervention (GA, 8.8%; vs EA-GA, 5.6%; *P* = .01). No significant differences were noted in 30-day mortality (*P* = .37).

Multivariable Adjusted Hazards and Odds

In adjusted analyses (**Table 2**), patients who received EA-GA had significantly lower hazards of mortality compared with patients undergoing GA alone (hazard ratio [HR], 0.73; 95% CI, 0.57-0.92; *P* = .01). Similarly, patients in the EA-GA group had significantly lower odds of surgical reintervention (odds ratio [OR], 0.65; 95% CI, 0.44-0.94; *P* = .02). These patients also had lower odds of bowel ischemia (OR, 0.54; 95% CI, 0.31-0.94;

Figure 2. Survival and Use of Combination Epidural and General Anesthesia (EA-GA) for Abdominal Aortic Aneurysm (AAA) Surgery



A, Survival after AAA surgery stratified according to EA use. Kaplan-Meier estimates with 95% Hall-Wellner CI bands; patients who received EA-GA had lower all-cause mortality (26%; 95% CI, 24% to 28%) compared with those who received GA alone (35%; 95% CI, 32% to 38%) at 5 years (log-rank $P < .01$). B, No change in EA-GA utilization rates was observed for elective, open AAA surgery during the 9-year study period. Annual estimated percentage change, −2.4% (95% CI, −5.1% to 0.4%; $P = .13$).

$P = .03$), respiratory complications (OR, 0.62; 95% CI, 0.41-0.95; $P = .03$), and dialysis requirement postoperatively (OR, 0.44; 95% CI, 0.23-0.88; $P = .02$); furthermore, the odds for bowel ischemia requiring surgical treatment were substantially decreased (OR, 0.21; 95% CI, 0.07-0.53; $P < .001$) (Table 2). No significant differences were noted for the odds of wound complications (OR, 0.88; 95% CI, 0.38-1.44; $P = .51$) and myocardial infarction (OR, 1.08; 95% CI, 0.59-1.78; $P = .82$). These findings held true after propensity score adjustment for mortality as well (eTable 2 in the Supplement provides details on propensity-adjusted analysis).

Thirty-Day Interval Complications and Association With Hazards of Mortality

To examine whether the improvement noted in long-term overall survival in patients undergoing combined EA-GA was associated with improvement in their short-term postoperative outcomes, we constructed Cox proportional hazards regression models accounting for 30-day interval complications. These models were adjusted for ischemic bowel, pulmonary, renal, and cardiac complications in addition to the anesthesia type and other preoperative and intraoperative factors detailed in the Methods section (**Table 3**). Four separate models were constructed; models 1 to 3 accounted for individual complications with which EA-GA demonstrated significant association (pulmonary complications, need for dialysis, and bowel ischemia; Table 2). Model 4 accounted for all 3 complications. In models 1 to 3, a residual independent beneficial association of EA-GA use with survival was noted, whereas once all 3 complications were accounted for, EA-GA use became a nonsignificant indicator of survival outcome (HR, 0.82; 95% CI, 0.62-1.06; $P = .08$) (Table 3, model 4). We evaluated for interactions among anesthesia exposure and bowel ischemia, pulmonary complications, and postoperative dialysis in our

Table 2. Multivariable Logistic Regression and Cox Proportional Hazards Regression Models Evaluating the Association of EA-GA Anesthesia With Postoperative Outcomes and Patient Survival[a]

Outcome	EA-GA[b] OR (95% CI)	P Value	GOF[c]
Mortality			
Overall[d]	0.73 (0.57-0.92)	.01	0.23
30 d	0.74 (0.29-1.84)	.51	0.17
Complications			
Bowel ischemia			
Medical management	0.93 (0.48-2.21)	.98	0.14
Surgical management	0.21 (0.07-0.53)	<.001	0.11
Any	0.54 (0.31-0.94)	.03	0.19
Pulmonary	0.62 (0.41-0.95)	.03	<0.01
Postoperative			
Myocardial infarction	1.08 (0.59-1.78)	.82	0.34
Dialysis	0.44 (0.23-0.88)	.02	0.46
Wound complications	0.88 (0.38-1.44)	.51	0.12
Return to operating room	0.65 (0.44-0.94)	.02	0.62

Abbreviations: EA, epidural anesthesia; GA, general anesthesia; GOF, goodness-of-fit; OR, odds ratio.

[a] Multivariable logistic regression used for evaluation of postoperative outcomes; Cox proportional hazards regression analyses used for evaluation of survival. Models were adjusted for age, sex, body mass index, comorbidities, smoking status, renal function, medications, American Society of Anesthesiologists class, clamp location, suprarenal clamp time, operative time, and surgical approach.

[b] Reference category is GA alone.

[c] Hosmer-Lemeshow GOF statistic for logistic-regression models and global GOF statistic for Cox proportional hazards regression model.

[d] Results are reported as hazard ratio (95% CI).

Table 3. Cox Proportional Hazards Models Evaluating the Association of Postoperative Adverse Events With Patient Survival

Indicator[a]	Overall Mortality, HR (95% CI)	P Value
Model 1		
Bowel ischemia		
No	1 [Reference]	<.01
Yes	2.36 (1.48-3.77)	
EA-GA		
GA alone	1 [Reference]	.03
Yes	0.76 (0.60-0.95)	
Model 2		
Pulmonary complications		
No	1 [Reference]	<.01
Yes	2.52 (1.89-3.24)	
EA-GA		
GA alone	1 [Reference]	.03
Yes	0.77 (0.61-0.98)	
Model 3		
Postoperative dialysis		
No	1 [Reference]	<.01
Yes	4.93 (3.03-8.08)	
EA-GA		
GA alone	1 [Reference]	.04
Yes	0.80 (0.63-0.99)	
Model 4		
Bowel ischemia		
No	1 [Reference]	.04
Yes	1.64 (1.03-2.64)	
Pulmonary complications		
No	1 [Reference]	<.01
Yes	2.08 (1.59-2.82)	
Postoperative dialysis		
No	1 [Reference]	<.01
Yes	3.25 (1.99-5.39)	
EA-GA		
GA alone	1 [Reference]	.08
Yes	0.81 (0.62-1.06)	

Abbreviations: EA, epidural anesthesia; GA, general anesthesia; HR, hazard ratio.

[a] In addition to the specific indicators listed, models were adjusted for age, sex, body mass index, comorbidities, smoking status, renal function, medications, American Society of Anesthesiologists class, clamp location, suprarenal clamp time, operative time, surgical approach, and postoperative cardiac complications. Global goodness-of-fit statistics: model 1, 0.21; model 2, 0.09; model 3, 0.35; and model 4, 0.44.

regression models, and none of the interaction terms was significant (bowel ischemia, $P = .06$; pulmonary complications, $P = .07$; and postoperative dialysis, $P = .05$).

Trends in Epidural Use

We next analyzed the trends in EA-GA use during the study period. There was no significant change in the utilization of EA-GA during the 9-year study period (annual estimated percentage change, −2.4%; 95% CI, −5.1% to 0.4%; $P = .13$) (Figure 2B).

Discussion

Our study demonstrates 4 findings. First, combined EA-GA use is associated with improvement in long-term survival compared with use of GA alone in patients undergoing elective, open AAA surgery. Second, the findings showed that the odds for any surgical reintervention and postoperative bowel ischemia requiring surgical intervention are significantly reduced in patients receiving EA-GA. Third, we noted that the mortality benefit of EA-GA appears to be driven by reduction in immediate postoperative complications (Table 3, model 4); the reduction in postoperative complications that are significantly associated with EA-GA use, including pulmonary complications, need for dialysis, and bowel ischemia, demonstrate its significance in improving long-term survival (additional analysis noted in the eFigure in the Supplement further supports this finding). Finally, from a quality improvement perspective, we did not note any change in EA utilization during the 9-year study period (January 1, 2003, to December 31, 2011) within the VSGNE (Figure 2B).

As stated above, evidence exists both in favor of and against the use of EA; however, there has been a preponderance of reports demonstrating the beneficial effects of EA on cardiopulmonary, renal, and neurologic outcomes as well as a possible 30-day mortality benefit.[9,10,21] Nevertheless, none of these

studies addressed the effects of EA-GA on long-term patient survival, reintervention risk, and bowel ischemia. Pöpping et al[21] and Wijeysundera et al[10] reported that EA use may have a beneficial effect on 30-day mortality. However, in both of those studies, long-term survival benefits were not evaluated. Those studies also suggested that the benefits of EA use may be procedure specific since the survival benefit was not noted across all surgical procedures. To our knowledge, the present study is the first to suggest that EA use in addition to GA is associated with a significant survival advantage as well as lower odds of reoperation in patients undergoing elective AAA repair. Furthermore, we demonstrate that this survival benefit seems to be driven by improvement in immediate postoperative outcomes.

Ischemic colitis continues to be a grave complication of AAA repair with significant postoperative sequelae.[13,14,22] In this context, postoperative EA is known to preserve bowel perfusion and motility and reduce the incidence of postoperative ileus.[23,24] These favorable effects are implied by the EA-induced sympathetic blockade and preservation of splanchnic circulation.[6,7] However, the effects of EA on specifically reducing postoperative bowel ischemia have not been investigated. Our study addresses this limitation of evidence and demonstrates a clear benefit of EA on postoperative ischemic colitis. This finding is clinically significant and, if confirmed in future trials, EA use could be an important yet easily modifiable factor in preventing bowel ischemia in patients undergoing elective AAA repair.

Furthermore, we corroborate findings from previous level 1 studies and report that pulmonary complications and the need for postoperative dialysis are significantly reduced in patients receiving EA-GA. Studies by Park et al[8] and Nishimori et al[9] reported that EA was associated with faster extubation rates, shorter intensive care unit stays, and superior pulmonary outcomes after major abdominal surgery. We believe that our study represents a timely addition to the growing body of evidence on the benefits of EA in patients undergoing major abdominal surgery. Taken together, findings from the present study and previous studies make a strong case for adoption of EA use during elective AAA repairs and call for efforts to minimize physician preference–driven use of EA.[25]

Finally, from a quality improvement perspective within the VSGNE, we noted that there was no significant change in the practice patterns of EA use during the 9-year study. However, we may not have observed an improvement in practice patterns in our cohort because high-quality evidence regarding the benefits of EA has emerged only within the past 3 to 4 years and our study period ended in 2011. Nonetheless, because one of the primary functions of the VSGNE consortium is to constantly monitor and improve outcomes in patients, these findings call for institutional efforts directed at investigating the patterns of EA use in more contemporary settings and improvement in these practice patterns, if needed, across the VSGNE participant sites.

Despite its merits, our study is not devoid of limitations, with the first being those associated with a retrospective review. However, these data were prospectively collected as part of a rigorously maintained, robust data registry with quality control.[16,18] Second, details on aortic pathology, type of graft used, and anesthetic drugs were not available. eTable 3 in the Supplement provides details on epidural practice patterns at the major VSGNE centers; we compiled this table in an effort to mitigate the lack of information on the type of epidural solution, timing of epidural placement, and the duration of use in the VSGNE database. However, data on clamp location, suprarenal cross-clamp time if used, and total operative time were available and adjusted for in our study; these data represent the most important surrogates for AAA extent and severity. Third, information regarding neurologic outcomes was not consistently available; we therefore could not assess the effects of EA-GA use on these outcomes. Fourth, a higher proportion of patients in the EA-GA group received β-blockers and had a lower ASA class. These differences could possibly confound the results even after adjustment. However, we did not note any differences in cardiac outcomes in the 2 groups that would be expected if the survival advantage were driven solely by the effect of β-blockers and ASA class. Fifth, we were not able to account for center and operator level variance and experience, which is an important variable when assessing procedure-based studies and could have confounded our results. Finally, the exact cause of patient mortality in our study population could not be ascertained. However, establishment of a specific cause can sometimes be difficult, if not impossible, to determine in patients with multiple comorbidities. Despite these limitations, we believe our study provides valuable data on the association of EA with long-term patient survival, bowel ischemia, and reintervention risk relying on a large, multi-institutional, contemporary cohort of patients.

Conclusions

The addition of EA to GA in patients undergoing elective AAA repair is associated with a significant long-term survival benefit. This survival benefit is possibly the result of reduced rates of immediate major postoperative complications. Epidural analgesia in addition to GA should be strongly considered in suitable patients undergoing elective AAA repair.

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REFERENCES

1. Schlösser FJ, Vaartjes I, van der Heijden GJ, et al. Mortality after elective abdominal aortic aneurysm repair. *Ann Surg*. 2010;251(1):158-164.

2. Blankensteijn JD. Mortality and morbidity rates after conventional abdominal aortic aneurysm repair. *Semin Interv Cardiol*. 2000;5(1):7-13.

3. Prinssen M, Verhoeven EL, Buth J, et al; Dutch Randomized Endovascular Aneurysm Management (DREAM)Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med*. 2004;351(16):1607-1618.

4. Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *N Engl J Med*. 2015;373(4):328-338.

5. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA*. 2003;290(18):2455-2463.

6. Kapral S, Gollmann G, Bachmann D, et al. The effects of thoracic epidural anesthesia on intraoperative visceral perfusion and metabolism. *Anesth Analg*. 1999;88(2):402-406.

7. Sielenkämper AW, Eicker K, Van Aken H. Thoracic epidural anesthesia increases mucosal perfusion in ileum of rats. *Anesthesiology*. 2000;93(3):844-851.

8. Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: a randomized, controlled Veterans Affairs cooperative study. *Ann Surg*. 2001;234(4):560-569.

9. Nishimori M, Low JH, Zheng H, Ballantyne JC. Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery. *Cochrane Database Syst Rev*. 2012;7(7):CD005059.

10. Wijeysundera DN, Beattie WS, Austin PC, Hux JE, Laupacis A. Epidural anaesthesia and survival after intermediate-to-high risk non-cardiac surgery: a population-based cohort study. *Lancet*. 2008;372(9638):562-569.

11. Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95(5):1054-1067.

12. Rigg JR, Jamrozik K, Myles PS, et al; MASTER Anaethesia Trial Study Group. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. *Lancet*. 2002;359(9314):1276-1282.

13. Becquemin JP, Majewski M, Fermani N, et al. Colon ischemia following abdominal aortic aneurysm repair in the era of endovascular abdominal aortic repair. *J Vasc Surg*. 2008;47(2):258-263.

14. Brewster DC, Franklin DP, Cambria RP, et al. Intestinal ischemia complicating abdominal aortic surgery. *Surgery*. 1991;109(4):447-454.

15. Liu S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia: their role in postoperative outcome. *Anesthesiology*. 1995;82(6):1474-1506.

16. Society for Vascular Services. Vascular Quality Initiative. Improving vascular care. http://www.vascularqualityinitiative.org/. Accessed August 18, 2015.

17. Matyal R, Shakil O, Hess PE, et al. Impact of gender and body surface area on outcome after abdominal aortic aneurysm repair. *Am J Surg*. 2015;209(2):315-323.

18. Cronenwett JL, Likosky DS, Russell MT, et al. A regional registry for quality assurance and improvement: the Vascular Study Group of Northern New England (VSGNNE). *J Vasc Surg*. 2007;46(6):1093-1101.

19. Anderson WF, Camargo MC, Fraumeni JF Jr, Correa P, Rosenberg PS, Rabkin CS. Age-specific trends in incidence of noncardiac gastric cancer in US adults. *JAMA*. 2010;303(17):1723-1728.

20. National Institute of Diabetes and Digestive and Kidney Diseases. MDRD for adults (conventional units). https://www.niddk.nih.gov/health-information/health-communication-programs/nkdep/lab-evaluation/gfr-calculators/adults-conventional-unit/Pages/adults-conventional-unit.aspx. Published April 28, 2015. Accessed August 14, 2016.

21. Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056-1067.

22. Björck M, Bergqvist D, Troëng T. Incidence and clinical presentation of bowel ischaemia after aortoiliac surgery—2930 operations from a population-based registry in Sweden. *Eur J Vasc Endovasc Surg*. 1996;12(2):139-144.

23. Jørgensen H, Wetterslev J, Møiniche S, Dahl JB. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. *Cochrane Database Syst Rev*. 2000;(4):CD001893.

24. Liu SS, Wu CL. Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence. *Anesth Analg*. 2007;104(3):689-702.

25. Subramaniam B, Simon BA. Epidural analgesia—the jury is in. *Ann Surg*. 2014;259(6):1068-1069.