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Cross-clamp location and perioperative outcomes after open infrarenal abdominal aortic aneurysm repair: A Vascular Quality Initiative® review

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Abstract

Objectives: By analyzing national Vascular Quality Initiative (VQI) data for patients undergoing open infrarenal abdominal aortic aneurysms (AAA) repair, we sought to better characterize the effects of different suprarenal clamping positions on postoperative outcomes.
Methods: We performed a retrospective analysis of a prospectively collected national VQI database for all open infrarenal AAA repairs performed between 2003 and 2017. Patients were initially divided into proximal (above 1 renal, above 2 renals, and supraceliac) and infrarenal clamp groups. Patients were then subdivided into those who underwent surgery between 2003–2010 and those who had surgery between 2011–2017. Univariate followed by multivariate analyses were done to compare the baseline characteristics, preoperative, intraoperative, and postoperative outcomes between the two groups.
Results: During the study period, 9068 open AAA repairs were recorded in the VQI; of these, 5043 met the inclusion criteria. Aortic clamp level was infrarenal in 59% ($N = 2975$), above 1 renal in 15% ($N = 735$), above both renals in 21% ($N = 1053$), and supraceliac in 5% ($N = 280$). The average age was 69 years, and males comprised 73% ($N = 3701$) of the cohort. The overall 30-day mortality for the entire study group was 2.7%. On univariate analysis, patients who underwent proximal clamping had significantly higher 30-day mortality than those undergoing infrarenal clamping (3.7 vs 2.0%, $p < 0.001$). After adjusting for preoperative and intraoperative variables, this difference became nonsignificant. On multivariate analysis, clamping above both renals or the celiac artery was associated with an increased occurrence of postoperative myocardial infarction (odds ratio = 1.44, $p = 0.037$ and odds ratio = 1.78, $p = 0.023$, respectively). All proximal clamp positions were associated with a significant increase in the incidence of AKI and renal failure requiring dialysis. There was no significant difference when looking at overall survival times comparing the suprarenal and infrarenal clamp position groups ($p = 0.1$). Patients who underwent surgery in the latter half of the study period had longer intraoperative renal ischemia time, increased in estimated blood loss, and longer total procedure time.
Conclusions: Suprarenal clamping, at any level, was associated with an increased risk of AKI and renal replacement therapy. Clamping above both renal and celiac arteries was associated with increased cardiac morbidity. Perioperative and long-term mortality was unaffected by clamp level. Patients operating in the latter half of the study had increased estimated blood loss, renal ischemia time, and operative time, which may reflect decreased training in open AAA repair. During open AAA repair, the proximal clamp site should be chosen based on anatomic considerations and not a perceived perioperative mortality benefit. Proximal aortic clamping should always be performed at the safest, distal-most level to reduce cardiac morbidity and the risk of postoperative dialysis.

Keywords

Abdominal aortic aneurysm, open repair, cross-clamp position, perioperative mortality

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Introduction

In the United States today, most infrarenal (IR) abdominal aortic aneurysms (AAA) are repaired using endovascular techniques.[1,2] Open surgical repair (OSR), however, is preferable in patients who do not meet the anatomic requirements for endovascular aneurysm repair.[2] In addition, there are some who advocate that OSR be considered in every unruptured AAA patient meeting the requirement for surgical repair, unless concomitant abdominal pathology exists, such as a hostile abdomen, a stoma or a horseshoe kidney, or significant anesthetic risks exist.[3] During OSR of an IR AAA, proximal aortic control can be obtained at different levels depending on local anatomic factors. The aorta may be clamped at the IR level, above one or both renal arteries, above the superior mesenteric artery, but below the celiac axis origin, or at the supraceliac (SC) level. Each clamp level is associated with a unique risk-benefit profile.[3] For IR AAA repair, the clamp is preferably placed below the lowest renal artery[2]; however, more proximal aortic clamping is preferred in certain situations, such as in the presence of significant aortic wall calcification or atherosclerotic debris within the non-aneurysmal, IR aortic segment.[4,5] Proximal abdominal aortic segments usually harbor less atherosclerotic disease than more distal clamp sites.[6] In addition, placing the clamp above the renal arteries is justified when manipulation or retraction of a large aneurysmal sac is anticipated.[7–10] Despite these advantages, proximal aortic clamping is associated with obligatory renal and visceral ischemia associated with an increased risk of acute kidney injury (AKI) and overall complication rates.[2,11] In a single institution review, we have previously reported that a SC clamp site increased morbidity but not mortality.[12] The current study represents a retrospective review of a large national database to determine current patterns and outcomes of different aortic clamp levels during OSR of IR AAA.

Materials and methods

Patients

All patients undergoing OSR of an IR AAA in the Vascular Quality Initiative (VQI) between 1 January 2003 and 31 December 2017 were reviewed. Symptomatic or ruptured aneurysms were excluded. Patients who had prior aneurysm repair, open conversion from endovascular aneurysm repair, concomitant renal bypass, or no data on cross-clamp position were also excluded from the analysis. Patients were grouped according to aortic clamp positions as reported by the VQI database (IR, above 1 renal artery, above both renal arteries, and SC). For the purposes of this study, proximal clamping denotes placement of the aortic clamp at any level above IR. Supramesenteric (above the superior mesenteric artery but below the celiac artery) was not a reported choice in the VQI database and hence could not be studied independently. Patients who underwent IR clamping and had cold renal perfusion or renal ischemia time > 20 min were excluded from the study.

The present study was reviewed and approved by the Institutional Review Board of the Henry Ford Hospital and conducted in accordance with the Health Insurance Portability and Accountability Act and the prevailing ethical principles governing research.

Variables collected

Sociodemographic variables collected included gender, age, tobacco use, and race/ethnicity (African American, white, and other). Past medical history included coronary artery disease, hypertension, diabetes, congestive heart failure, chronic obstructive pulmonary disease, prior bypass, prior carotid intervention, and prior peripheral vascular intervention. Preoperative variables included preoperative use of antiplatelets, anticoagulants, antihypertensive medications, and preoperative anemia (defined as hemoglobin < 13 g/dl in men and < 12 g/dl in women). Intraoperative variables included operative time, exposure approach, and estimated blood loss (EBL). Postoperative variables included intensive care unit stay, respiratory complications (pneumonia or ventilator use), leg ischemia (in-situ thrombosis or embolism), bowel ischemia, wound complication, return to the operating room, and postoperative stroke.

End points

The primary endpoint was 30-day mortality after IR AAA repair. Secondary endpoints included perioperative morbidity, length of stay (LOS), and overall survival. AKI was defined by the VQI as an increase in creatinine > 0.5 mg/dL from baseline; postoperative dialysis was defined as dialysis requirement within the first 30 postoperative days. The incidence of postoperative myocardial infarction (MI) (based on increased troponin and/or EKG changes) was documented.

Statistical analysis

Patients were initially divided into proximal (above 1 renal, above 2 renals, and SC) and IR clamp groups (Tables 1 and 2). An analysis comparing all four clamping positions was done and reported in supplementary Table 1. Patients were then subdivided into those who underwent surgery between 2003–2010 and those that had surgery between 2011–2017. Continuous variables were presented as means and standard deviation or medians and interquartile range, while categorical variables were described with frequency and percentages. Analysis of variance, Kruskal-Wallis, or chi-square tests were used as appropriate to compare the

Table 1. Baseline demographics stratified by cross-clamp level.

Baseline characteristics	Cross-clamp position		
	Infrarenal, N = 2975 (59%)	Proximal[a], N = 2068 (41%)	p-value
Age, years, mean (SD)	68.85 (8.61)	70.05 (7.82)	< 0.001
Female, N (%)	718 (24.1)	624 (30.2)	< 0.001
Race, N (%)			0.194
African American	95 (3.2)	80 (3.9)	
Other	149 (5.0)	87 (4.2)	
White	2731 (91.8)	1901 (91.9)	
Body mass index, kg/m^2, mean (SD)	27.42 (5.45)	27.19 (5.37)	0.138
Preoperative smoking, N (%)			< 0.001
None	285 (9.6)	138 (6.7)	
Prior	1470 (49.5)	976 (47.2)	
Current	1217 (40.9)	954 (46.1)	
Hypertension, N (%)	2430 (81.7)	1762 (85.2)	0.001
Diabetes, N (%)	459 (15.4)	343 (16.6)	0.283
Prior coronary artery disease, N (%)	773 (26.0)	562 (27.2)	0.371
Prior coronary artery bypass graft, N (%)	274 (15.3)	232 (15.3)	0.982
Prior PCI, N (%)	318 (17.8)	324 (21.3)	0.013
Prior congestive heart failure, N (%)	187 (6.3)	168 (8.1)	0.014
COPD, N (%)	923 (31.1)	701 (33.9)	0.035
ESRD (on dialysis/transplant), N (%)	16 (0.5)	14 (0.7)	0.656
Preoperative creatinine, mg/dl, mean (SD)	1.08 (0.46)	1.10 (0.48)	0.091
ASA class, N (%)			< 0.001
1	13 (0.6)	11 (0.6)	
2	133 (5.8)	95 (5.1)	
3	1543 (67.4)	1133 (60.8)	
4,5	599 (26.2)	625 (33.5)	
Anemia, N (%)	567 (24.0)	504 (26.6)	0.055
Prior bypass, N (%)	115 (3.9)	74 (3.6)	0.651
Prior carotid intervention, N (%)	102 (5.7)	96 (6.3)	0.515
Prior PVI, N (%)	153 (5.1)	120 (5.8)	0.339
Prior amputation, N (%)	20 (0.7)	9 (0.4)	0.345
Preoperative aspirin, N (%)	2000 (67.3)	1387 (67.1)	0.943
Preoperative P2Y12 inhibitor, N (%)	198 (6.7)	171 (8.3)	0.035
Preoperative statin, N (%)	2064 (69.4)	1483 (71.7)	0.083
Preoperative beta-blockers, N (%)	2007 (67.5)	1354 (65.5)	0.149
Preoperative ACE-I/ARB, N (%)	809 (45.3)	727 (47.8)	0.171
Preoperative anticoagulant, N (%)	17 (0.6)	13 (0.6)	0.941
Ejection fraction, N (%)			0.669
≤ 50%	336 (11.3)	246 (11.9)	
> 50%	1859 (62.6)	1296 (62.9)	
Unknown/Not done	776 (26.1)	520 (25.2)	
Maximum AAA diameter, mm, mean (SD)	57.80 (13.44)	60.01 (16.63)	< 0.001

AAA: abdominal aortic aneurysm, ACE-I/ARB: angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers, ASA: American Society of Anesthesiologists Physical Status Classification, COPD: chronic obstructive pulmonary disease, ESRD: end-stage renal disease, PCI: percutaneous coronary intervention, PVI: peripheral vascular intervention, SD: standard deviation.
[a]Proximal = aortic clamping above one/both renal arteries or supraceliac.

baseline demographics, comorbidities, preoperative variables, intraoperative parameters, and postoperative outcomes stratified by cross-clamp positions. Multivariate generalized linear regression models were performed to examine the association between cross-clamp positions and both primary and secondary outcomes. Linear regression model and incidence rate ratios were calculated for the LOS. Kaplan-Meier curves and Cox regression models were used for survival analysis. Variables with missing rate of > 5% were excluded from the analysis. An “unknown” category was created for other categorical variables with missing values to account for missingness. Any variable with a p-value < 0.1 or thought to be related to the outcome of interest was included in the multivariate analyses. A $p < .05$ was considered statistically significant. All analyses were done using R 4.02.2 (R Foundation for statistical Computing, Vienna, Austria).

Model that predicts 30-day mortality

A supervised machine learning classification model was developed to identify predictors for 30-day mortality. The predictors are clinical attributes based on baseline demographics, preoperative, and intraoperative variables. The objective was to maximize the model's accuracy, sensitivity, and specificity. Feature selection techniques were utilized to identify the top five predictors of 30-day mortality. Feature selection is a process of selecting clinical attributes that have the highest contribution to the mortality class. Based on the application and the type of dataset, chi-square test was used, and the top five clinical attributes that scored highest on the chi-square test were reported. Random forest machine learning classifier was used and showed a strong classification power with an accuracy of 98.5% in predicting whether a patient would die at 30 days, after imputing data from the five predictors. The receiver operating characteristics curve was used to study the area under the curve, which reflects the model's performance.

Results

During the study period, 9068 open IR AAA cases were entered into the VQI registry. After applying the exclusion criteria, 5043 elective IR AAA repairs were left in the dataset, which comprised our study cohort.

Demographics

The mean patient age was 69 years, with males constituting the majority of the sample (73%, N = 3701). There were several statistically significant differences in baseline characteristics between the two groups (Table 1). Females tended to require more proximal clamping than males. Patients undergoing proximal clamping were older, had higher American Society of Anesthesiologists Physical Status Classification scores, and larger aneurysm sizes than IR clamping patients.

Operative variables

Fifty-nine percent of patients underwent IR clamping, 15% had clamping above 1 renal artery, 21% above both renals, and 5% above the celiac. Patients who underwent proximal non-IR clamping had significantly longer renal/visceral ischemia times (26.6 vs 0.2 min, $p < .001$), as well as total procedure time (246 vs 228 min, $p < .001$). Proximal clamping was associated with a higher EBL, and more frequent use of a retroperitoneal approach (Table 2). Concomitant infrainguinal bypass was more frequently performed in the IR group (2.5%) than in the proximal group (1.7%) (p = .45).

Postoperative variables

Compared to the IR group, patients with proximal clamping stayed longer in the intensive care unit (median = 3.0 [2.0–5.0] vs 2.0 [1.0–4.0] days, $p < .001$) and in the hospital (median = 7.0 [6.0–10.0] vs 6.0 [5.0–8.0] days, $p < .001$). Proximal clamping was also associated with higher rates of postoperative cardiac events (MI and congestive heart failure), respiratory, and renal complications (Table 2).

Cardiac morbidity. On multivariate analysis, clamping above both renals or the celiac artery was associated with an increased occurrence of postoperative MI (odds ratio [OR] = 1.44, p = .037 and OR = 1.78, p = .023, respectively). There was no statistically significant increase in the incidence of MI with clamping above 1 renal artery (Table 3).

Length of stay (LOS). When compared to IR clamping, there was an increase in LOS when clamping above the celiac artery (incidence rate ratios of 1.13, $p < .001$). There was no increase in LOS with suprarenal clamping (Table 3).

Renal function. All proximal clamp positions were associated with a significant increase in the incidence of AKI and renal failure requiring dialysis on multivariate analysis when compared to IR clamping (Table 4).

Year-dependent morbidity and mortality change. A total of 1199 patients underwent surgery between 2003 and 2010, while 3844 had surgery between 2011 and 2017. Patients who underwent surgery in the latter half had higher American Society of Anesthesiologists class, longer intraoperative renal ischemia time, increased EBL, and longer total procedure time (Supplementary Table 2). They also had longer intensive care unit stay (median = 3.0 [2.0–4.0] vs 2.0 [1.0–4.0] days, $p < .001$) and higher rate of postoperative AKI (8.6 vs 13.8%, $p < .001$). They had lower rate of postoperative MI (4.4 vs 6.3%, p = .011). No significant difference was seen in terms of 30-day mortality, leg or bowel ischemia, and wound or respiratory complications (Table 5).

Thirty-day mortality. Overall 30-day mortality for the entire study group was 2.7%. On univariate analysis, patients who

Table 2. Univariate comparison of intra- and postoperative outcomes stratified by infrarenal and proximal clamp positions.

	Cross-clamp position		
	Infrarenal *N* = 2975 (59%)	Proximal[a], *N* = 2068 (41%)	*p*-value
Intraoperative variables			
Renal visceral ischemia time, mins, mean (SD)	0.24 (1.89)	26.58 (20.98)	< 0.001
Exposure, *N* (%)			< 0.001
Anterior	2503 (84.1)	1329 (64.2)	
Retroperitoneal	472 (15.9)	739 (35.8)	
Inferior mesenteric artery completion, *N* (%)			0.125
Occluded	1075 (37.3)	768 (38.9)	
Ligated	1545 (53.6)	1005 (50.9)	
Re-implanted	262 (9.1)	203 (10.3)	
EBL, ml, mean (SD)	1495 (1455)	1785 (1654)	< 0.001
Cold renal perfusion, *N* (%)	0 (0.0)	193 (9.4)	< 0.001
Total procedure time, minutes, mean (SD)	228.01 (94.95)	246.12 (94.74)	< 0.001
Concomitant infrainguinal bypass, *N* (%)	75 (2.5)	34 (1.6)	0.045
Postoperative variables			
ICU stay, days, median [IQR]	2.00 [1.00, 4.00]	3.00 [2.00, 5.00]	< 0.001
Postoperative LOS, days, median [IQR]	6.00 [5.00, 8.00]	7.00 [6.00, 10.00]	< 0.001
Postoperative MI, *N* (%)	128 (4.3)	116 (5.6)	0.04
Postoperative dysrhythmia, *N* (%)	336 (11.3)	266 (12.9)	0.102
Postoperative CHF, *N* (%)	97 (3.3)	96 (4.6)	0.015
Postoperative stroke, *N* (%)	15 (0.7)	15 (0.8)	0.771
Postoperative leg ischemia, *N* (%)	60 (2.0)	53 (2.6)	0.235
Bowel ischemia, *N* (%)	85 (2.9)	84 (4.1)	0.024
Wound complication, *N* (%)	88 (3.0)	58 (2.8)	0.813
Respiratory complications, *N* (%)	253 (8.5)	263 (12.7)	< 0.001
Postoperative renal complications, *N* (%)			< 0.001
None	2673 (90.2)	1626 (78.7)	
Postoperative creatinine increased > 0.5 mg/dL, *N* (%)	256 (8.6)	374 (18.1)	
Requiring dialysis, *N* (%)	35 (1.2)	65 (3.1)	
Return to operating room, *N* (%)	191 (6.4)	156 (7.5)	0.139
30-day mortality, *N* (%)	59 (2.0)	77 (3.7)	< 0.001
Overall mortality, *N* (%)	472 (15.9)	280 (13.5)	0.025

Note: CHF: congestive heart failure, EBL: estimated blood loss, ICU: intensive care unit, IQR: interquartile range, LOS: length of stay, MI: myocardial infarction, mins: minutes, SD: standard deviation.
[a]Proximal = aortic clamping above one/both renal arteries or supraceliac.

Table 3. Multivariate analysis for postoperative myocardial infarction (MI) and linear regression model for length of stay (LOS).

	Postoperative MI multivariate analysis			Postoperative LOS multivariate analysis		
Predictors	Odds ratios	CI	*p*	Incidence rate ratios	CI	*p*
Infrarenal (reference)						
Above 1 renal	0.99	0.63–1.51	0.971	0.98	0.95–1.01	0.247
Above 2 renals	1.44	1.02–2.01	**0.037**	1.02	0.99–1.05	0.165
Supraceliac	1.78	1.06–2.89	**0.023**	1.13	1.08–1.18	**< 0.001***

LOS: length of stay.
*Bold indicates statistical significance ($p < .05$).

underwent proximal clamping had significantly higher 30-day mortality than those undergoing IR clamping (3.7 vs 2.0%, $p < .001$) (Table 2). After adjusting for preoperative variables, above 1 renal and SC clamping were significantly associated with increased odds of 30-day mortality as compared to the IR group (OR = 1.7, $p = .02$ and OR = 2.0,

Table 4. Multivariate analysis for postoperative AKI and postoperative renal failure requiring dialysis.

	Postoperative AKI multivariate analysis			Renal failure requiring dialysis multivariate analysis		
Predictors	**Odds ratios**	CI	*p*	**Odds ratios**	CI	*p*
Infrarenal (reference)						
Above 1 renal	1.96	1.57–2.44	**< 0.001**	1.99	1.97–2.00	**< 0.001***
Above 2 renals	2.23	1.85–2.69	**< 0.001**	3.11	3.07–3.15	**< 0.001**
Supraceliac	2.34	2.11–2.58	**< 0.001**	3.65	3.61–3.69	**< 0.001**

AKI: acute kidney injury.
*Bold indicates statistical significance ($p < .05$).

Table 5. Postoperative morbidity and mortality stratified by the two halves of the 14-year study period.

Variables	2003–2010, *N* = 1199 (23.8%)	2011–2017, *N* = 3844 (76.2%)	*p*-value
ICU stay, median [IQR]	2.00 [1.00, 4.00]	3.00 [2.00, 4.00]	**< 0.001***
Postoperative LOS, median [IQR]	7.00 [5.00, 8.00]	7.00 [5.00, 9.00]	0.175
Postoperative MI, *N* (%)	75 (6.3)	169 (4.4)	**0.011**
Postoperative dysrhythmia, *N* (%)	155 (12.9)	447 (11.6)	0.247
Postoperative CHF, *N* (%)	52 (4.3)	141 (3.7)	0.338
Respiratory complications, *N* (%)	132 (11.0)	384 (10.0)	0.34
Postoperative renal complications, *N* (%)			**< 0.001**
None	1064 (89.5)	3235 (84.2)	
Postoperative creatinine increased > 0.5 mg/dL, *N* (%)	102 (8.6)	528 (13.8)	
Requiring dialysis	23 (1.9)	77 (2.0)	
Postoperative leg ischemia, *N* (%)	20 (1.7)	93 (2.4)	0.156
Bowel ischemia, *N* (%)	37 (3.1)	132 (3.4)	0.625
Wound complication, *N* (%)	42 (3.5)	104 (2.7)	0.179
Return to operating room, *N* (%)	70 (5.9)	277 (7.2)	0.119
Postoperative stroke, *N* (%)	2 (1.9)	28 (0.7)	0.41
30-day mortality, *N* (%)	24 (2.0)	112 (2.9)	0.11
Overall mortality, *N* (%)	430 (35.9)	322 (8.4)	**< 0.001**

CHF: congestive heart failure, ICU: intensive care unit, IQR: interquartile range, LOS: length of stay, MI: myocardial infarction.
*Bold indicates statistical significance ($p < .05$).

$p = .04$, respectively). However, after including intraoperative variables (renal ischemia time, EBL, total procedure time, and concomitant infrainguinal bypass) in the multivariate analysis, this difference became nonsignificant (Table 6).

Female gender (OR = 1.96, p = .001), current smoking (OR = 2.82, p = .039), history of chronic obstructive pulmonary disease (OR = 1.74, p = .006) or prior carotid intervention (OR = 2.74, p = .002), and the performance of a concomitant infrainguinal bypass (OR = 2.7, p = .034) were associated with increased 30-day mortality (Table 6).

Overall survival. The overall mortality with a median follow-up time of 46 months was 15%. On univariate analysis, patients who underwent proximal clamping had significantly higher overall mortality than those undergoing IR clamping (13.5 vs 15.9%, p = .025) (Table 2). However, this association became nonsignificant on multivariate analysis with/without the inclusion of intraoperative variables (Table 7). Factors that were associated with decreased long-term survival included current smoking, history of coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, or anemia; higher preoperative creatinine; and history of a prior carotid procedure. Patients taking aspirin or statin were noted to have improved overall survival (hazard ratio = 0.81, p = .019 and hazard ratio = 0.82, p = .019, respectively). There was no significant difference when looking at the Kaplan-Meier curves comparing the survival time of the two clamp position groups (p = .05) (Figure 1).

Predictors of 30-day mortality. The top five clinical attributes that scored highest on the chi-square test were age, body mass index, preoperative creatinine level, intraoperative estimated blood loss, and total procedure time. The random forest model showed an accuracy of 98.5% for predicting 30-day mortality after imputing data from these five predictors. The area under the

Table 6. Multivariate analysis for 30-day mortality.

Predictors	Odds ratios	CI	*p*
Cross-clamp position: Infrarenal	Reference		
Above 1 renal	1.70	0.91–3.06	0.086
Above 2 renals	1.39	0.80–2.40	0.238
Supraceliac	1.44	0.63–3.04	0.360
Age	1.08	1.05–1.11	**< 0.001***
Female gender	1.96	1.29–2.94	**0.001**
Renal ischemia time per 30-min increase	1.09	0.77–1.47	0.618
Preoperative smoking: None	Reference		
Prior smoking	1.88	0.79–5.56	0.196
Current smoking	2.82	1.15–8.52	**0.039**
COPD	1.74	1.17–2.58	**0.006**
Preoperative anemia	1.43	0.92–2.20	0.105
Prior carotid intervention	2.74	1.41–5.01	**0.002**
Preoperative ACEi/ARBs	1.78	1.11–2.91	**0.019**
Preoperative ejection fraction: > 50%	Reference		
≤ 50%	0.45	0.28–0.75	**0.002**
Unknown/not done	0.51	0.28–0.93	**0.028**
Concomitant infrainguinal bypass	2.70	0.97–6.27	**0.034**
Preoperative creatinine	1.31	0.95–1.67	0.055

Note: ACEi: angiotensin-converting enzyme inhibitor, ARBs: angiotensin receptor blockers, COPD: chronic obstructive pulmonary disease.
*Bold indicates statistical significance ($p < .05$).

Table 7. Multivariate analysis for overall survival.

Predictors	Hazard ratios	CI	*p*
Cross-clamp position: Infrarenal	Reference		
Above 1 renal	0.96	0.72–1.28	0.772
Above 2 renals	1.02	0.78–1.34	0.862
Supraceliac	1.09	0.76–1.55	0.646
Age	1.07	1.05–1.08	**< 0.001***
Female gender	1.18	0.99–1.40	0.067
Renal ischemia time per 30-min increase	1.04	0.85–1.28	0.670
Preoperative smoking: None	Reference		
Prior	1.34	0.97–1.86	0.079
Current	1.62	1.15–2.29	**0.006**
Chronic obstructive pulmonary disease	1.38	1.17–1.62	**< 0.001**
Coronary artery disease	1.34	1.13–1.60	**0.001**
Congestive heart failure	1.39	1.06–1.81	**0.015**
Preoperative anemia	1.40	1.13–1.74	**0.002**
Prior carotid intervention	1.90	1.26–2.88	**0.002**
Preoperative aspirin	0.81	0.68–0.96	**0.016**
Preoperative statin	0.82	0.69–0.97	**0.019**
Preoperative creatinine	1.29	1.15–1.45	**< 0.001**

*Bold indicates statistical significance ($p < .05$).

receiver operative characteristics curve was .991 (Figure 2).

Discussion

This study retrospectively examined the VQI database to determine the effect of the aortic clamp level on the outcome of patients undergoing open IR AAA repair. Our analysis revealed that after controlling for preoperative and intraoperative variables, the level of aortic cross-clamping in open IR AAA repair was not associated with increased mortality. However, more proximal clamping did correlate with an increase in postoperative renal and cardiac complications as well as LOS. This correlates with our previous

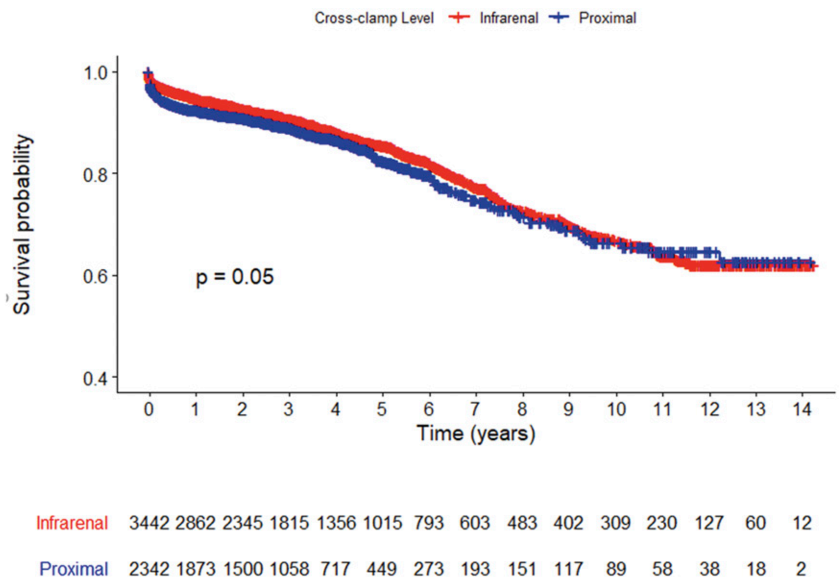

Figure 1. Kaplan-Meier curves comparing overall survival between patients that had infrarenal or proximal cross-clamping.

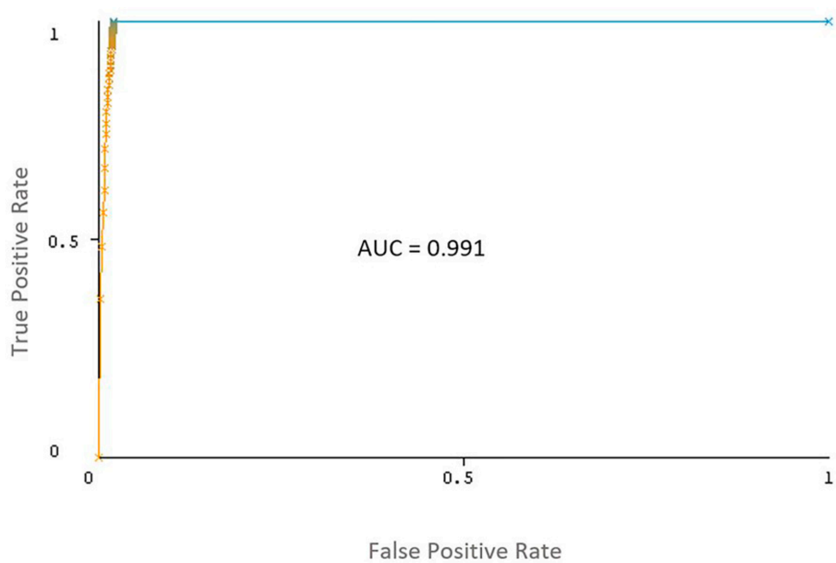

Figure 2. Receiver operating characteristics curve showing the area under the curve (AUC) of the machine learning prediction model of 30-day mortality.

research that suggests that the level of clamping, when adjusted for other intraoperative variables, does not increase mortality.[4,12]

Aortic clamping is associated with a multitude of pathophysiologic responses that contribute to overall mortality. These responses include renal ischemia and cardiac stress, in addition to humoral factors such as acidosis and sympathetic activation.[13–15] Additionally, SC clamping has been associated with a coagulopathy, namely, a fibrinolytic state, which is generated in a time-dependent manner.[16] Systemic coagulopathy has also been associated with visceral ischemia, owing to the increased intestinal permeability and bacterial translocation, or from hepatic ischemia and primary fibrinolysis.[17] The overall 30-day mortality after open IR AAA repair in this review was 2.7%. This value is consistent with contemporary studies that report short-term (30 days) mortality for OSR of IR AAAs of 0.6%–8.2%.[18–25] On univariate analysis, clamping proximal to the renal arteries was associated with a higher mortality. This result held true for the above 1 renal and celiac clamping positions on multivariate analysis that included only preoperative variables but dropped out on multivariate analysis that accounted for intraoperative variables. This suggests that an efficient SR operation with low renal ischemia time and EBL does not have increased 30-day mortality when compared to IR operations. In their study, Chong et al.[11] also failed to find a significant association between clamp level and mortality. El-Sabrout and Reul[26] highlighted a large increase in mortality associated with SR/SC clamping. However, on subgroup analysis, their SR group had more preoperative risk factors and underwent more extensive surgeries. Another study by Varkevisser et al.[27] highlighted an increase in 30-day mortality in patients with SC clamping. However, the variables included on multivariate analysis were selected a priori and did not include intraoperative factors. In addition, important confounding variables, such as renal ischemia time, were not accounted for in the analysis.

The cardiac response to aortic clamping is well-described—as peripheral vascular resistance increases, there is an increase in left ventricular afterload[15,28] with a concomitant decrease in cardiac output.[15,29] These changes are exaggerated in patients with coronary artery disease and can lead to areas of significant oxygen supply/demand mismatch with concomitant wall motion abnormalities and ventricular dysfunction.[17,30,31] The level of aortic clamping has been implicated in the degree of cardiac strain,[32] with more proximal clamp positions causing larger increases in cardiac strain and decreases in cardiac output.[17,33] El-Sabrout and Reul[26] described a doubling (4 vs 2%) in the incidence of cardiac complications in patients with SR/SC aortic clamping compared to IR clamping, with the resulting cardiac complications being more frequently fatal in the SR/SC aortic clamping group (63 vs 40%). However, this study included ruptured aneurysms, which were significantly more frequent in the SR/SC group. The current study examined only elective IR AAAs and documents a significant increase in MI in the SC and above 2 renals groups; clamping above 1 renal artery was not associated with an increase in MI. Our outcome is in agreement with the findings of Roizen et al.[33] who described SC clamping causing greater depression in the cardiac index with increased end systolic and diastolic volumes than more distal clamp positions. In addition, the greater de-clamping hypotension associated with the release of SC control versus IR is well-recognized and a probable contributor to cardiac dysfunction.

Renal dysfunction is frequent after open AAA repair. Recognized predictors of postoperative renal failure include preoperative renal dysfunction, the presence of renovascular disease, and the location and duration of aortic clamping.[26,34–38] Even IR aortic clamping has been shown to decrease renal blood flow and clearance, while increasing renal vascular resistance.[39,40] Clamping above the renal arteries is associated with a much larger decrease in renal perfusion related to a direct physical reduction in renal blood flow. Clamping at this level is also associated with oxygen free-radical-induced downregulation of both nitric oxide and prostaglandin GE_2 production, which further impairs renal cortical blood flow.[41] In the study by El-Sabrout and Reul,[26] SR/SC clamping was associated with a fourfold (12.6 vs 3.35%) increase in transient renal dysfunction in patients clamped SR/SC when compared to those clamped IR. These results are mirrored in a study by Sasaki et al.[42] who reported that proximal clamping was associated with an increased incidence of renal dysfunction (28.6% above 1 renal and 50% above 2 renals) when compared to IR clamping (8.4%). In this review of VQI data, all three proximal aortic clamp levels were associated with an increased incidence of AKI when compared to the IR group, in which ORs of 2.0, 2.2, and 2.3 were found for above 1 renal, above 2 renals, and SC clamping, respectively (Table 4). All proximal clamp positions were also associated with increased odds of postoperative kidney failure requiring dialysis when compared to the IR group (Table 4). Similar ORs were obtained when looking at patients who had temporary or permanent dialysis (Supplementary Table 3). These results are in agreement with a study by O'Donnell et al.[37] who reported an OR of 1.4 for postoperative renal dysfunction after clamping above both renals, and an OR of 1.7 after SC clamping.

The increased LOS in the SC group is not unexpected given the increase in complexity of these cases. Not only did these patients have longer operating times, but they also experienced more serious morbidity—cardiac complications and renal failure requiring renal replacement therapy—than the other groups.

The machine learning model showed excellent performance in predicting 30-day mortality of our patient cohort undergoing elective open AAA repair after imputing data from the top five predictors of mortality, which were age, body mass index, preoperative creatinine, intraoperative estimated blood loss, and total procedure time. Previous studies looking at predictors of 30-day mortality after open AAA repair share similar risk factors, such as increased age and higher preoperative creatinine level.[43] Knowledge of these predictors can help in the preoperative risk stratification of patients and optimization of potentially modifiable factors, such as increased weight and creatinine levels. Limiting intraoperative blood loss and procedure time might be key in reducing the chance of dying at 30 days. Further studies are needed to validate this predictive model. In our current study, open surgical procedures for elective AAA repair done in the latter half of the study (2011–2017) had significantly higher postoperative renal and cardiac complications as compared to the initial half (2003–2010), although no statistical significance was reached when looking at perioperative mortality. This may be caused by patients' comorbidities or complexity of the aneurysms that were not accounted for in our dataset. However, we think that this may reflect a trend to decreased training in open operations. This hypothesis is supported by the fact that there was higher renal ischemia time, intraoperative EBL, and total procedure time found in the latter half group. In addition, a recent study by Smith et al.[44] evaluated the temporal trends of surgery trainee open AAA repair volume in accredited vascular surgery training programs and found a 38% decrease in open AAA repair training volume over a 4-year period.

This study has several limitations. First, its retrospective methodology allows determination of only association and not causation. Second, multivariate analysis accounts only for identified variables and a number of unmeasured risk factors may also contribute to confounding. Third, the analyzed data is derived from a national database that does not allow study of the cause of death. Another limitation is the fact that supramesenteric (between the superior mesenteric artery and the celiac) clamping was not studied. Some authorities believe that clamping at this level avoids some of the complications associated with total visceral ischemia induced by SC clamping.[45] This clamp level, however, is rarely used because of the extra exposure required and hence was not a variable choice in the VQI registry. And finally, there was no data to identify the reason for proximal aortic clamping in patients presenting for repair of an IR AAA, and whether clamping position was changed intraoperatively. Difficult anatomy and consequently a more complex procedure undoubtedly drove the choice for proximal clamping, skewing our results.

Conclusions

Utilizing the national VQI database, this study found that patients presenting for elective OSR of an IR AAA who underwent proximal aortic clamping, at any level, were older than those clamped at an IR level; in addition, they had more comorbidities and larger aneurysms size. On multivariate analysis, 30-day mortality was unaffected by clamp level. Clamping above both renal or celiac arteries was associated with an increased risk of postoperative MI. Similarly, clamping the aorta above 1 renal artery or higher was associated with postoperative AKI and renal replacement therapy. Patients operating in the latter half of the study had increased EBL, renal ischemia time, and operative time, which may reflect decreased training in open AAA repair. During open AAA repair, the proximal clamp site should be chosen based on anatomic considerations and not a perceived perioperative mortality benefit. Proximal aortic clamping should always be performed at the safest, distal-most level to reduce cardiac morbidity and the risk of postoperative dialysis.

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Supplemental Material

Supplemental material for this article is available online.

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