Outcomes after concomitant arch replacement at the time of aortic root surgery

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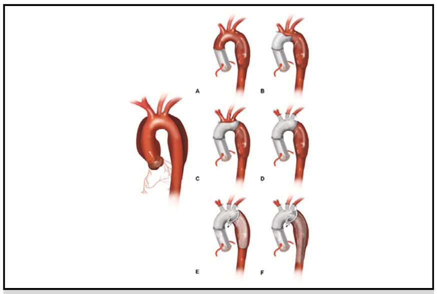
ABSTRACT

Background: Contemporary series of aortic arch replacement at the time of aortic root surgery are limited in number of patients and mostly address hemiarch replacement. We describe outcomes after aortic root and concomitant arch replacement, including total arch replacement.

Methods: This single-institution retrospective review studied 1196 consecutive patients from May 2004 to September 2020 who underwent first-time aortic root replacement. Patients undergoing surgery for endocarditis were excluded (n = 68, 5.7%). Patients undergoing concomitant root and arch replacement were propensity matched with patients undergoing isolated root surgery based on indication, clinical and operative characteristics, demographics, medical history including connective tissue disorders, and urgency. Multivariable Cox proportional hazards and logistic regression modeling were used to assess the primary outcome of all-cause mortality and the secondary outcomes of prolonged ventilator use, postoperative blood transfusion, and debilitating stroke, adjusted for patient and operative characteristics.

Results: Among the 1128 patients who underwent aortic root intervention during the study period, 471 (41.8%) underwent concomitant aortic arch replacement. Most underwent hemiarch replacement (n = 411, 87.4%); 59 patients (12.6%) underwent total arch replacement (with elephant trunk: n = 23, 4.9%; without elephant trunk: n = 36, 7.7%). The mean follow-up time was 4.6 years postprocedure. Operative mortality was 2.2%, and total mortality over the entire study period was 9.2%. Propensity matching generated 348 matches (295 concomitant hemiarch, 53 concomitant total arch). Concomitant hemiarch (hazard ratio, 1.00; 95% confidence interval, 0.54-1.86, $P = .99$) and total arch replacement (hazard ratio, 1.60, 95% confidence interval, 0.72-3.57, $P = .24$) were not significantly associated with increased mortality. Rates of stroke were not significantly different among each group: isolated root (n = 11/348, 3.7%), root + hemiarch (n = 17/295, 5.8%), and root + total arch (n = 3/53, 5.7%) replacement ($P = .50$), nor was the adjusted risk of stroke. Both concomitant arch interventions were associated with prolonged ventilator use and use of postoperative blood transfusions.

Conclusions: Hemiarch and total arch replacement are safe to perform at the time of aortic root intervention, with no significant differences in survival or stroke rates, but increased ventilator and blood product use. (JTCVS Open 2023;13:1-8)



Various aortic root and arch replacement strategies employed in this study are shown.

CENTRAL MESSAGE

Concomitant aortic root and arch replacement is safe and offers comparable survival to aortic root replacement alone while addressing more extensive aortic pathology.

PERSPECTIVE

Replacing the aortic arch at the time of aortic root replacement is controversial; the addition of a period of circulatory arrest may incur additional operative risk. We show that across a diverse range of pathology, and repair strategies, concomitant aortic root and arch repair is safe. Our work supports more extensive aortic replacement through the arch at the time of the index operation.

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Although diseases of the aorta, namely Stanford type A aortic dissections, and aneurysmal growth of the aorta often involve the aortic root and the aortic arch, major societal guidelines do not discuss strategies to address concomitant root and arch pathology.[1,2] There is still debate regarding whether addressing both root and arch pathology simultaneously is associated with increased morbidity and mortality compared with isolated arch or root surgery.[3,4]

Abbreviations and Acronyms

ARR = aortic root replacement
CI = confidence interval
ET = elephant trunk
HR = hazard ratio
OR = odds ratio
pRBC = packed red blood cells
RCP = retrograde cerebral perfusion
SACP = selective antegrade cerebral perfusion
SMD = standard mean difference

The purpose of this study is to investigate outcomes after aortic root replacement (ARR) with concomitant aortic arch replacement, including hemiarch and total arch replacements with or without elephant trunk (ET). Addition of aortic arch replacement, via hemiarch, total arch, or total arch with ET necessitates a period of hypothermic circulatory arrest, which is associated with additional neurologic and bleeding risk.[5] We hypothesize that addition of aortic arch replacement at the time of ARR may be safe when performed at experienced centers.

METHODS

Patients

This is a single-institution retrospective review of all patients who underwent first-time ARR at a tertiary academic medical center between May 1, 2004, and September 31, 2020. Patients were further categorized by whether they underwent isolated ARR versus root replacement with concomitant aortic arch replacement. The patients undergoing aortic arch intervention were then stratified by hemiarch replacement, total arch replacement, and total arch replacement with ET. Indication, urgency of the operation, and clinical/demographic factors were reviewed. Patients undergoing root replacement for endocarditis were excluded.

Operative Approach

Patients underwent root replacement via mechanical or bioprosthetic composite valve graft, valve-sparing ARR, homograft replacement, or pulmonary autograft replacement (Ross procedure) (Figure 1). Arch replacements were performed under hypothermic circulatory arrest, with either selective antegrade cerebral perfusion, retrograde cerebral perfusion, or both. Cooling temperatures ranged from 16 °C to 38.8 °C. Total arch replacements were performed either with branched grafts with direct anastomoses to the each of the arch vessels or an island/peninsula technique wherein an island/peninsula of aorta containing the ostia of the arch vessels was sewn directly to the graft. Soft ETs were performed with Hemashield Platinum Double Woven Velour grafts (Maquet), and frozen ETs were performed with GORE TAG Conformable Stent Grafts (W. L. Gore & Associates, Inc).

Outcomes

This study compares mortality among patients who underwent isolated ARR, ARR with hemiarch replacement, and ARR with total arch replacement with or without ET over a mean follow-up of 3.6 years (95% confidence interval [CI], 3.3-4.0 years). Thirty-day mortality, postoperative blood transfusion during the index hospitalization, prolonged ventilator dependence, defined as ventilator use for equal to or greater than 24 hours postoperatively, and rates of clinically significant stroke and transient ischemic attack were also analyzed as secondary outcomes. Clinically significant stroke was defined as stroke with lasting neurologic deficits that persisted to at least the first clinic visit, or to 30 days after diagnosis, or stroke that caused mortality. Transient ischemic attack is defined as new onset neurologic deficit with resolution within 24 hours of onset.

Statistical Analysis

Descriptive statistics were performed on the entire cohort. The Shapiro–Francia normality test was performed and confirmed a normal distribution in the data. Bivariable analyses were conducted using *t*-tests or Wilcoxon rank-sum for continuous variables and χ^2 Fisher exact test for categorical variables as appropriate. Unadjusted Kaplan–Meier curves were used to analyze survival over the study period, stratified by isolated ARR, versus ARR plus hemiarch replacement, versus ARR plus total arch replacement with or without ET. The log-rank test statistic was used to compare survival estimates among the 3 groups. Standard mean differences (SMDs) are used to represent residual imbalances after propensity score matching, with values of 0.25 or less considered minimal residual imbalance.[6,7]

Propensity score matching was used to match patients who underwent isolated ARR to patients who underwent ARR + aortic arch replacement, using a one-to-one, nearest-neighbor matching method with a caliper of 0.2. Characteristics used to match patients were indication, age, presence of connective tissue disease, diabetes, previous sternotomy for non-ARR/aortic arch surgery, hypertension, and body mass index.

Among propensity-matched patients, multivariable Cox proportional hazards modeling was used to analyze postoperative survival, and multivariable logistic regression modeling was used to analyze association with postoperative stroke, blood transfusions, and prolonged ventilator dependence. The covariates for the multivariable models were initially chosen based on clinical reasoning and biologic plausibility and then optimized based on variate *P* values and the Akaike and Bayesian information criteria, which are iterative methods for selecting the most parsimonious multivariable model and limit confounding.[8] The final multivariable models adjust for race, age, sex, body mass index, history of connective tissue disease, indication for operation, hypertension, hyperlipidemia, type 2 diabetes, preoperative ejection fraction, scheduled versus emergency status, and previous sternotomy for nonaortic root/arch surgery. Multiple imputation using regression techniques was performed on variables with less than or equal to 1% missing data.

Analyses were performed using statistical software (STATA 16.0, IC; StataCorp). The study was approved by the Stanford University School of Medicine Institutional Review Board (#50520; approved September 14, 2021).

RESULTS

Patient Characteristics

Of 1196 patients who underwent first-time ARR during the study period, 471 (41.8%) underwent concomitant aortic arch replacement. Within this cohort, most underwent hemiarch replacement (n = 411, 87.4%), followed by total arch replacement without ET (n = 37, 7.8%), total arch replacement with soft ET (n = 15, 3.2%), and total arch with frozen ET (n = 7, 1.5%). Baseline demographics stratified by extent of operation are included in Table 1. Most patients were White (n = 800, 70.9%), followed by Asian (n = 153, 13.6%), "other" (which included mixed race, or undisclosed race) (n = 124, 11%), African American (n = 49, 4.3%), and Native American (n = 2, 0.2%). The most common indication for surgery (root vs root + arch) was aortic aneurysm (n = 820, 72.7%), followed by

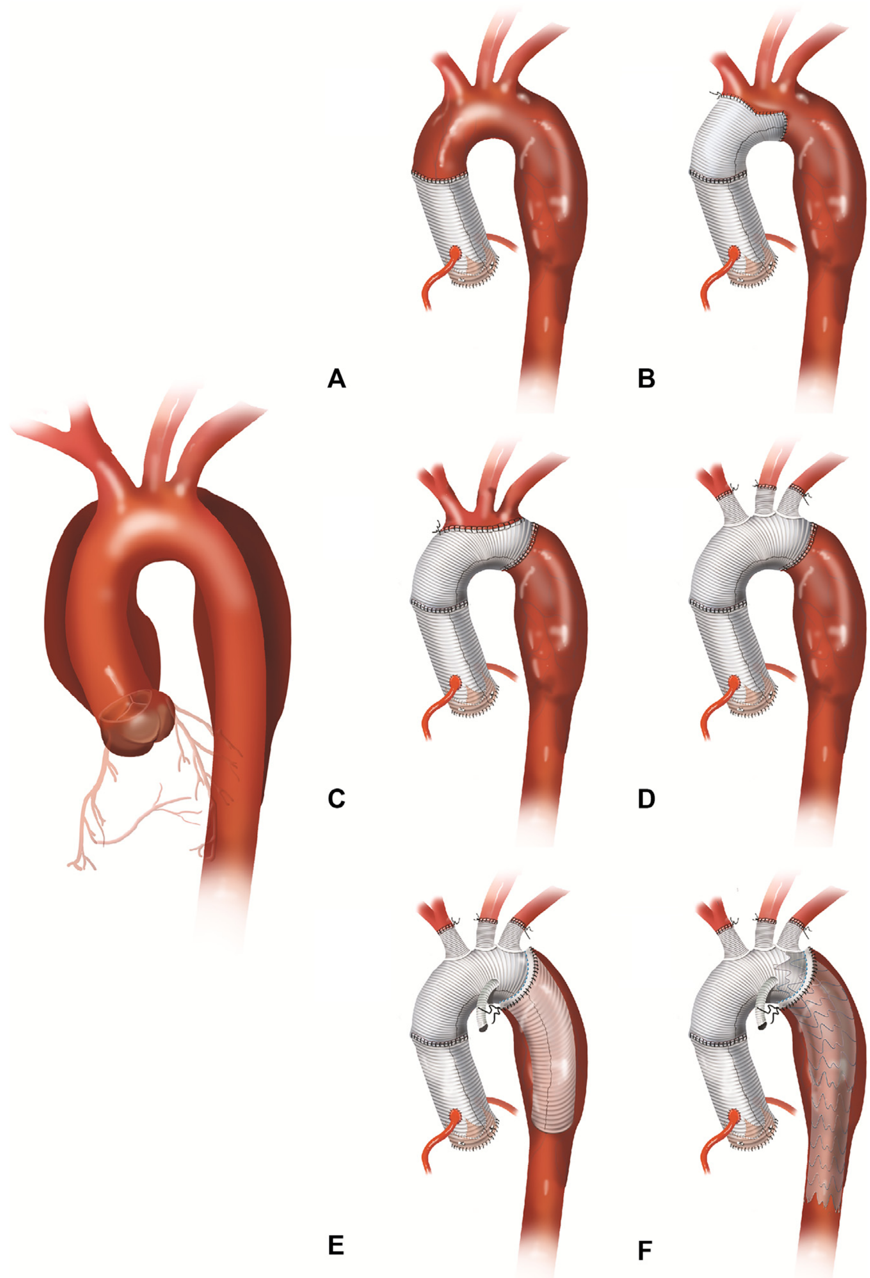

FIGURE 1. Root replacement with or without arch replacement. Demonstration of the various repair strategies used in this patient population; for illustration purposes, a valve-sparing root replacement (A) is shown paired with hemiarch (B), total arch (branched graft [C] and island [D] technique), and total arch with soft (E) and frozen elephant trunk (F).

Stanford type A aortic dissection (n = 212, 18.7%). Of the type A aortic dissections, 15 (7.2%) were chronic dissections. Arch surgery was indicated when the aneurysm or dissection propagated into the aortic arch or beyond. Addition of an ET was indicated when significant descending aortic pathology was present at the time of root and arch intervention.

Perfusion

Mean temperatures for patients undergoing ARR alone were 29.8 ± 3.4 °C; for ARR + hemiarch: 24.8 ± 3.1 °C ; and for patients undergoing ARR + total arch: 22.5 ± 3.5 °C. Among patients undergoing ARR + hemiarch, 87% of patients underwent selective antegrade cerebral perfusion (SACP), 12.4% underwent retrograde cerebral perfusion

TABLE 1. Patient demographics

	Root	Root + hemiarch	Root + total arch	Standard difference
Age, y	50.9 ± 17.0	57 ± 13	56.9 ± 13.3	0.38
Male	507 (77.2%)	319 (77.8%)	41 (69.5%)	0.02
BMI, kg/m^2	26.9 ± 6.0	27.7 ± 5.5	27.1 ± 5.7	0.18
Connective tissue disease	82 (12.6%)	14 (3.5%)	7 (11.8%)	0.13
Type 2 diabetes	59 (9.0%)	31 (7.6%)	2 (3.4%)	0.07
Redo sternotomy	90 (13.7%)	51 (12.4%)	26 (44.1%)	0.07
Hypertension	415 (63.2%)	296 (72.4%)	45 (76.3)	0.21
Crossclamp times, min	182.7 ± 65.0	195 ± 51.9	255.0 ± 60.9	0.34
Cerebral perfusion strategy				
Selective antegrade		300 (87.0)	49 (87.5)	
Retrograde		43 (12.4)	1 (1.8)	
Combined antegrade and retrograde		2 (0.6)	6 (10.7)	
Cooling temp, °C	29.9 ± 3.8	24.8 ± 3.1	22.5 ± 3.4	1.6

BMI, Body mass index.

(RCP), and 0.6% underwent a combined approach. Among those undergoing ARR + total arch, 87.5% underwent SACP, 1.8% underwent RCP, and 10.7% underwent a combined strategy. Overall, patients who underwent SACP were cooled to a mean temperature of 24.6 ± 3.1 °C; those who underwent RCP were cooled to 24.9 ± 3.6 °C. Patients who underwent SACP primarily underwent axillary cannulation (49.3%), followed by innominate cannulation (43.8%).

Operative Outcomes

Thirty-day mortality for the entire patient cohort was 2.62% (95% CI, 2.60%-2.64%), and long-term survival over the study period was 92.8% (95% CI, 89.4%-92.9%). Figure 2 demonstrates the unadjusted Kaplan–Meier survival plot stratified by extent of arch replacement (none, hemiarch, and total arch), with log-rank testing showing no significant difference in survival among the 3 approaches ($P > .05$).

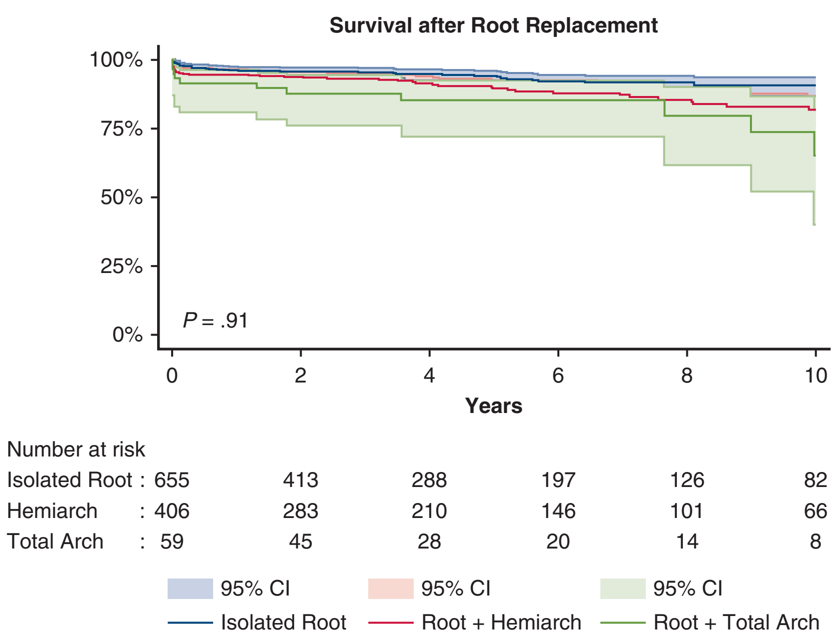

FIGURE 2. Survival after root replacement stratified by concomitant arch intervention. *CI*, Confidence interval.

Stroke rates were comparable among the 3 patient cohorts, with no statistically significant difference in rates of incidence. For ARR alone, the stroke rate was 3.7%, for ARR + hemiarch, 5.8%, and for ARR + total arch ± ET, 5.7%, $P > .05$. Rates of transient ischemic attack were comparable as well. For ARR alone, the rate of transient ischemic attack was 2.4%, for ARR + hemiarch, 2.0%, and for ARR + total arch ± ET, 3.4%, $P = .74$. Among total arch replacements, 93.2% were zone 3 replacements, and 6.8% were zone 2 replacements.

Rates of prolonged ventilator dependency varied based on extent of arch replacement; 34.5% of patients undergoing isolated ARR had prolonged ventilator dependency, whereas 44.9% of those undergoing concomitant hemiarch replacement, and 59.3% of those undergoing total arch replacement had prolonged ventilator dependency ($P < .01$).

The use of blood products postoperatively also varied based on extent of arch replacement; 40.9% of patients who underwent isolated ARR required a postoperative blood transfusion, compared with 62.8% of those undergoing concomitant hemiarch replacement and 80.7% of those undergoing concomitant total arch replacement ($P < .01$). However, among patients who did receive postoperative blood products, the number of units of packed red blood cells (pRBCs) did not vary significantly based on extent of arch replacement: patients who underwent isolated ARR received an average of 4.4 ± 8.1 units of pRBCs, whereas patients who underwent ARR + hemiarch received an average of 4.9 ± 9.5 units of pRBCs, and who underwent ARR + total arch received an average of 5.1 ± 6.2 units of pRBCs ($P = .72$).

Among patients undergoing ARR + total arch ± ET, the rate of permanent paraplegia was 5.1%. Eight patients (13.6%) needed downstream intervention for worsening thoracoabdominal aortic pathology, with 4 (50%) undergoing open thoracoabdominal aortic replacement, and 4 (50%) undergoing thoracic endovascular aortic repair. The rate of vocal cord injury necessitating injection laryngoplasty was 18.8%.

On univariable analysis, emergency status was associated with increased risk of mortality among patients undergoing ARR + hemiarch replacement (hazard ratio [HR], 2.6; 95% CI, 1.6-4.5, $P < .01$).

Propensity Matching

Propensity matching generated 349 matches between patients who underwent isolated ARR and ARR patients who underwent concomitant arch replacement (296 hemiarch matches, and 53 total arch matches), and 21 of 23 (91%) patients who underwent total arch replacement with frozen ET were included in the matched cohort. Baseline characteristics after propensity matching are shown in Table 2.

Multivariable Modeling

Results of multivariable modeling performed on the propensity-matched cohort of patients are shown in Table 3. When stratified by extent of arch replacement performed, compared with isolated ARR, there were no significant differences in mortality risk (ARR + hemiarch HR, 1.00; 95% CI, 0.54-1.85, $P = .99$; ARR + total arch HR, 1.60; 95% CI, 0.73-3.57, $P = .24$). Similarly, risk of postoperative permanent stroke was comparable among each group: (ARR + hemiarch odds ratio [OR], 1.70; 95% CI, 0.73-3.97, $P = .22$; ARR + total arch OR, 2.02; 95% CI, 0.51-8.08, $P = .32$). Both the risk of prolonged ventilator dependency (ARR + hemiarch OR, 1.51; 95% CI,

TABLE 2. Patient characteristics after propensity matching

	Root	Root + hemiarch	Root + total arch	Standard difference
Age, y	57.9 ± 13.9	56 ± 14	56.3 ± 13.1	0.14
Male	274 (78.9%)	233 (78.9%)	37 (69.8%)	0.03
BMI, kg/m^2	27.9 ± 5.9	27.6 ± 5.2	26.8 ± 5.8	0.06
Connective tissue disease	24 (6.8%)	12 (4.1%)	7 (13.2%)	0.06
Type 2 diabetes	31 (8.8%)	19 (6.5%)	2 (3.8%)	0.11
Redo sternotomy	63 (17.7%)	42 (14.2%)	25 (47.2%)	<0.04
Hypertension	259 (74%)	206 (69.8%)	39 (73.6)	0.08
Crossclamp times, min	171.6 ± 62	200.9 ± 51.7	256.5 ± 59.3	0.63
Cerebral perfusion strategy				
Selective antegrade		212 (86.2)	43 (86.0)	
Retrograde		33 (13.4)	1 (2)	
Combined antegrade and retrograde		1 (0.4)	6 (12)	
Cooling temp, °C	30.0 ± 4.3	24.9 ± 3.1	22.7 ± 3.6	1.56

BMI, Body mass index.

TABLE 3. Outcomes after isolated root replacement versus root replacement with concomitant arch replacement

Multivariable Cox proportional hazards and logistic regression modeling of outcomes*		
Survival		
Arch extent	**Hazard ratio (95% CI)**	***P* value**
Isolated root	Ref†	
Root + hemiarch	1.00 (0.54-1.86)	.99
Root + total arch ± elephant trunk	1.60 (0.73-3.57)	.24
Postoperative debilitating stroke		
Arch extent	**Odds ratio (95% CI)**	***P* value**
Isolated root	Ref†	
Root + hemiarch	1.70 (0.73-3.97)	.22
Root + total arch ± elephant trunk	2.02 (0.51-8.08)	.32
Prolonged ventilator use		
Arch extent	**Odds ratio (95% CI)**	***P* value**
Isolated root	Ref†	
Root + hemiarch	1.51 (1.06-2.15)	.02
Root + total arch ± elephant trunk	3.70 (1.94-7.06)	<.01
Postoperative blood transfusion during index hospitalization		
Arch extent	**Odds ratio (95% CI)**	***P* value**
Isolated root	Ref†	
Root + hemiarch	2.08 (1.46-2.96)	<.01
Root + total arch ± elephant trunk	3.70 (1.73-7.89)	<.01

CI, Confidence interval. *Each analysis represents a multivariable regression adjusted for race, age, sex, body mass index, history of connective tissue disease, indication for operation, hypertension, hyperlipidemia, type 2 diabetes, preoperative ejection fraction, scheduled versus emergency status, and previous sternotomy for nonaortic root/arch surgery. †Isolated root replacement was used as the reference group to which concomitant arch replacement was compared.

1.06-2.15, $P = .02$; ARR + total arch OR, 3.70; 95% CI, 1.94-7.06, $P < .01$) and postoperative blood transfusion (ARR + hemiarch OR, 2.08; 95% CI, 1.46-2.96, $P < .01$; ARR + total arch OR, 3.70; 95% CI, 1.73-7.89, $P < .01$) were significantly associated with concomitant arch replacement, with greater risk associated with further extent of aorta replaced.

DISCUSSION

This is single-center series describes outcomes after concomitant arch replacement at the time of ARR. We show that survival and rates of debilitating postoperative stroke are comparable among patients undergoing ARR, with or without hemiarch/total arch replacement. In addition, we include the largest reported group of patients to undergo ARR with total arch replacement and deployment of a frozen ET. The risk of prolonged ventilator dependency and the need for postoperative blood transfusion was greater in patients who underwent concomitant aortic arch replacement with ARR.

Our study builds upon the foundation laid by Malaisrie and colleagues' study[9] of 384 patients who underwent ARR, of whom 177 (46%) underwent concomitant hemiarch replacement. In their 133 propensity-matched pairs, the authors demonstrate comparable survival and stroke rates among patients undergoing isolated ARR and ARR with hemiarch, and they also note the increased blood product use among patients undergoing concomitant hemiarch replacement. Our study extends these findings by studying a diverse population of patients undergoing concomitant root and arch surgery, including those who underwent total arch replacement, in addition to a range of root-replacement strategies including valve-sparing root replacements.

In a similar population of patients undergoing scheduled aortic arch replacement, Keeling and colleagues[4] demonstrate in a multi-institution registry study that 320 patients who underwent concomitant ARR experienced similar mortality and stroke rates. Notably, this cohort excluded emergency surgery and was homogeneous in terms of cerebral protection strategies and cooling temperatures.

Our results differ significantly from the contemporary Canadian Thoracic Aortic Collaborative study of concomitant aortic root repair during index arch repair in 1099 patients showing increased mortality risk with concomitant ARR at the time of aortic arch repair.[3] Although this study population differs from our population in that aortic arch replacement was the index procedure in their cohort and root replacement was the index procedure in our population, Hage and colleagues[3] include aortic dissections, valve-sparing root techniques, and patients undergoing total arch replacement with frozen ET. They demonstrate a greater incidence of stroke in the entire population and suggest that mortality is worse in patients undergoing concomitant ARR and arch replacement, with patients undergoing emergency surgery faring the worse.

The study by Hage and colleagues[3] includes 12 centers in Canada, over 16 years, during which a total of 1099 patients underwent concomitant ARR at the time of aortic arch replacement. Assuming an even distribution of cases among the 12 centers, each center may have performed around 91 combined aortic root and arch replacements over the study period, whereas our individual center series included 471 patients who underwent aortic arch replacement over a similar 16-year study period. The comparable survival and stroke rates between isolated root replacement versus concomitant arch replacement in our cohort may be a result of a volume–outcome relationship that has been described previously in cardioaortic surgery, wherein greater individual center volume of specific aortic procedures is associated with improved survival and lower postoperative morbidity.[10-13]

There is a growing emphasis in medicine for the management of complex surgical pathology to regionalize to high-volume centers of excellence, as has been demonstrated for mitral valve surgery,[14,15] heart and lung transplantation,[16,17] and even treatment for aortic dissection by our center.[18] Care for patients undergoing complex aortic root and arch surgery similarly involves experienced, multidisciplinary teams throughout the perioperative and postoperative period. As such, it may be reasonable at facilities equipped with such resources and experience to pursue more extensive repair of thoracic aortic disease in appropriate surgical candidates, as is the philosophy at our institution. When appropriate, this strategy may mitigate the risk of reoperation, avoiding the potential added morbidity of repeat aortic repair.[19]

Even at a high-volume center with comparable risk of stroke and mortality among patients undergoing isolated ARR and ARR with concomitant hemiarch or total arch replacement, it is important to note the morbidity associated with prolonged ventilator use and increased need for postoperative blood transfusion demonstrated in our study. Prolonged ventilator dependency exposes patients to increased risk of ventilator associated pneumonia, and the potential for sepsis and multiorgan failure, as well as limitations to physical rehabilitation after cardiac surgery, all contributing to potentially worse mortality after cardiac surgery.[20,21] In addition, blood transfusions, although extremely common in cardiac surgery, portend increased risk of infection, transfusion reactions, and lung injury.[22,23] Although concomitant arch replacement at the time of ARR was associated with prolonged ventilator dependency and increased need for postoperative blood transfusion, mortality was similar among groups in this study, suggesting that it is safe to proceed with concomitant arch and root replacement while acknowledging and being prepared to manage the potential complications associated with prolonged ventilator dependency and postoperative blood transfusion in these patients.

Limitations

This study faces limitations in its use of single-institution retrospective data; generalizability may be limited, given the specific patient selection factors used at our institution. The patient population included in this study demonstrates a heterogeneous range of primary pathology, from aneurysmal disease to degenerative aortic root disease, with a multitude of repair strategies employed, including both valve-sparing and valve-replacement approaches. Although this may reflect the natural variation in the presentation and management of aortic root and arch pathology, it may introduce confounding into the analysis. In addition, selection bias plays a role in determining candidacy for concomitant aortic root and arch replacement among these patients. Furthermore, socioeconomic factors and insurance status were not studied and may impact outcomes. To address these issues, robust propensity score matching was employed, and multivariable regression modeling was used to limit confounding. In ideal propensity score matching, there would be no residual imbalances, with SMDs <0.10, although SMDs <0.25 are still considered small imbalances. Although residual imbalances after propensity matching likely exist, all variables with SMD >0.10 except cooling temperature and crossclamp time were included in the multivariable model, providing double adjustment for any residual confounding.

CONCLUSIONS

We demonstrate that it is safe to perform concomitant aortic root and arch replacement when indicated, with all groups experiencing similar low mortality and postoperative stroke rates. There is an increased risk of postoperative blood product use and prolonged ventilator dependence in patients undergoing concomitant aortic arch replacement. Center experience and volume may be related to safety and efficacy of concomitant aortic root and arch replacement, and regionalization to high-volume centers may play a role in the treatment of advanced thoracic aortic disease.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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