Article published online: 2023-08-24

Atrial Fibrillation after Descending Aorta Repair: Occurrence, Risk Factors, and Impact on Outcomes

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Aorta (Stamford) 2023;11:116–124.

Abstract

Background As risks of repairing the descending thoracic and thoracoabdominal aorta diminish, common complications that may prolong hospital stay, or actually increase risk, require attention. One such complication is postoperative atrial fibrillation (AF). Therefore, we characterized prevalence of, risk factors for, and effects of postoperative atrial fibrillation (PoAF) after descending and thoracoabdominal aorta repair.

Methods From January 2000 to January 2011, 696 patients underwent open descending or thoracoabdominal aorta repair at Cleveland Clinic. Operations approached via median sternotomy ($n = 178$) and patients treated preoperatively for arrhythmias (32 amiodarone, 9 paced) or in AF on preoperative electrocardiogram ($n = 14$) were excluded, leaving 463. Logistic regression analysis identified risk factors for PoAF. Temporal relation of PoAF with postoperative morbidities was determined, and outcomes following PoAF were compared between propensity-matched pairs.

Results New-onset PoAF occurred in 101 patients (22%) at a median 68 hours of post-incision. Risk factors included older age ($p = 0.002$) and history of remote AF ($p = 0.0004$) but not operative details, such as pericardiotomy for cardiac cannulation. Hypoperfusion and neurologic complications tended to precede PoAF, whereas sepsis, respiratory failure, and dialysis followed. Among 94 propensity-matched patient pairs, those developing PoAF were more likely to experience hypoperfusion ($p = 0.006$), respiratory failure ($p = 0.009$), dialysis ($p = 0.04$), paralysis ($p < 0.0001$), longer intensive care unit stay (median 7 vs. 5 d, $p = 0.02$), and longer postoperative hospital stay (median 15 vs. 13 d, $p = 0.004$). However, hospital death was similar (6/94 PoAF [6.4%] vs. 7/94 no PoAF [7.4%], $p = 0.8$).

Conclusion PoAF after descending thoracic aorta surgery is relatively common and a part of a constellation of other serious complications prolonging postoperative recovery. While PoAF was associated with adverse events, it did not impact postoperative cost and mortality. Descending thoracic aorta surgery is by itself comorbid enough, which is likely why PoAF does not have a more significant effect on postoperative recovery and cost.

Keywords
- aortic operation
- atrial fibrillation
- atrial flutter
- surgery
- complications

received
December 7, 2022
accepted after revision
May 26, 2023

DOI https://doi.org/10.1055/s-0043-1770960.
ISSN 2325-4637.

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

Introduction

Atrial fibrillation (AF) is a common complication of cardiac surgery and other thoracic operations, including esophageal and lung resection, which is associated with longer postoperative stay, higher cost, and increased morbidity and mortality.[1–6] Postoperative atrial fibrillation (PoAF) has also been described in the setting of aortic arch surgery, with an occurrence of up to 53%,[7–10] and 10% after repair of the abdominal aorta.[11,12] As risks of descending and thoracoabdominal aorta repair diminish, common complications, such as those that are often thought of as a "nuisance" but consume resources and are associated with adverse events, require attention. Therefore, the focus of this study was to characterize PoAF after open surgical repair of descending thoracic and thoracoabdominal aortic aneurysms and dissections via left thoracotomy.

To accomplish this, we first investigated the timing of occurrence of PoAF and identified risk factors for its development. We then evaluated the temporal relationship of PoAF to other postoperative complications. Finally, we assessed the difference in outcomes between patients who developed PoAF and those who did not, including evaluating the economic impact of PoAF.

Materials and Methods

Patients

From January 2000 to January 2011, 696 patients underwent open descending or thoracoabdominal aorta repair. Those who were approached via median sternotomy ($n = 178$) were excluded. Of the 518 patients who underwent left thoracotomy, 55 were excluded for preoperative treated arrhythmias (32 taking amiodarone, 9 being paced) or AF on preoperative electrocardiogram (14 patients), leaving 463 patients in the study group. Of these, disease extended to the descending aorta in 124 (27%) and to the thoracoabdominal aorta in 339 (73%; ►**Table 1**). Average age was 61 ± 13 years, and 287 (62%) were men. Forty-six (10%) had a history of remote AF; 319 (69%) were on beta blockers and 208 (45%) on angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers.

Data

Clinical and outcomes data were extracted from the Heart and Vascular Institute's Cardiovascular Information Registry. Additional study data, including details about antiarrhythmic medications, aortic morphology, and operative repair, were abstracted by medical records review into a REDCap electronic data capture tool hosted at Cleveland Clinic.[13] Use of the Cardiovascular Information Registry and additional data collection were approved by the Cleveland Clinic Institutional Review Board, with patient consent waived.

Surgical Details

Indications for operation were predominantly aneurysmal disease ($n = 233$, 50%) and chronic dissection ($n = 204$, 44%; ►**Table 2**). Extent of repair was descending aorta in 181 patients (39%) and thoracoabdominal in 282 (61%). A pericardiotomy was performed for cardiopulmonary bypass cannulation 180 patients (39%).

Endpoints

Postoperative Atrial Fibrillation

PoAF was defined as new-onset AF sustained for at least 5 minutes and documented by 12-lead electrocardiography, physician progress notes, or nursing notes.

Timing of Postoperative Atrial Fibrillation

Interval from time of surgical incision to PoAF was calculated for each patient.

Other Adverse Events

Postoperative complications assessed were sepsis, hypoperfusion requiring vasoconstriction or inotropic support, respiratory failure (defined as return to the intensive care unit [ICU] for respiratory support or need for reintubation, with and without tracheostomy), renal failure (with and without dialysis), and neurologic event (stroke and paralysis/paraplegia).

Cost

The economic impact of PoAF was determined by comparing the direct technical cost of postoperative hospitalization between patients who developed PoAF and those who did not.

Statistical Analysis

Nonparametric estimates of time-related occurrence of PoAF were generated using the Kaplan–Meier method and instantaneous risk by parametric temporal decomposition.[14] Patients were censored at hospital discharge or death in-hospital.

Risk Factors for Postoperative Atrial Fibrillation

Multivariable logistic regression analysis was used with bootstrap bagging variable selection to identify reliable risk factors for PoAF.[15] Briefly, 1,000 data sets were generated by random sampling with replacement, each was analyzed by automated stepwise selection, with an entry criterion of $p \leq 0.10$ and retention criterion of $p \leq 0.05$, and variables or clusters of highly correlated variables that entered into 50% or more of the 1,000 models were chosen for the final model. The analysis strategy involved three distinct models: (1) preoperative variables only, (2) intraoperative variables only, and (3) preoperative plus intraoperative variables (see ►**Appendix 1** for list of variables considered, available in the online version); only the latter is reported in detail.

Balancing Score for Comparison of Outcomes

Because characteristics of patients (►**Table 1**) and their operation (►**Table 2**) differed between patients with and without PoAF, and adverse outcomes were not numerous, we used a balancing score for "natural experiments" (a form of propensity score, but not for comparison of treatments). For this, the parsimonious logistic regression model of preoperative and intraoperative factors described under "Risk factors for postoperative atrial fibrillation" was augmented with the most reliable variables from clinically relevant groups to

Table 1 Patient characteristics stratified by development of postoperative atrial fibrillation

Characteristic	PoAF ($n = 101$) No. (%) or mean ± SD)	No PoAF ($n = 362$) No. (%) or mean ± SD)	*p*
Demographics:			
Age (y)	65 ± 10	60 ± 14	**0.004**
Sex			0.9
Male	62 (61)	225 (62)	
Female	39 (39)	137 (38)	
Body mass index (kg/m^2)	26 ± 4.5	27 ± 5.1	0.5
Disease of the aorta:			
Prior aorta surgery	40 (40)	170 (47)	0.19
Extent of disease:			0.8
Descending thoracic aorta	26 (26)	98 (27)	
Thoracoabdominal aorta	75 (74)	263 (73)	
Arch involvement	6 (5.9)	14 (3.9)	0.4
Maximum aortic diameter (cm)	6.2 ± 1.2	6.3 ± 1.4	>0.9
Other cardiovascular comorbidities:			
Remote atrial fibrillation[a]	20 (20)	26 (7.2)	**0.0002**
Ejection fraction (%)	54 ± 7.6	55 ± 5.9	0.8
Left atrial diameter (cm)	4.1 ± 0.83	4.0 ± 0.80	0.2
Hypertension	94 (93)	315 (88)	0.12
Prior myocardial infarction	28 (28)	61 (17)	**0.01**
Prior stroke	10 (10)	60 (17)	0.10
Heart failure	10 (10)	32 (8.9)	0.8
Prior cardiac operation	52 (51)	209 (58)	0.3
NYHA functional class:			>0.9
I	57 (67)	181 (62)	
II	20 (24)	93 (32)	
III / IV	8 (9.4)	19 (6.5)	
Noncardiac comorbidities:			
Diabetes mellitus:			
Insulin dependent	2 (2.0)	3 (0.84)	0.3
Noninsulin dependent	7 (7.0)	25 (7.0)	>0.9
Renal disease requiring dialysis:	9 (9.0)	19 (5.3)	0.18
Creatinine (mg/dL)	1.2 ± 1.0	1.1 ± 0.67	0.4
COPD	34 (34)	117 (33)	0.8
Medications:			
ACE inhibitors/ARBs	52 (51)	156 (43)	0.15
Beta blocker	69 (68)	250 (69)	0.8

Abbreviations: ACE/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; PoAF, postoperative atrial fibrillation; SD, standard deviation.
[a]Paroxysmal or persistent atrial fibrillation, but not present on preoperative electrocardiogram.

form a semisaturated model (►**Appendix 1**, available in the online version). A balancing score was calculated for each patient by solving the saturated model for the probability of PoAF.[16,17] Using only the balancing score, PoAF cases were matched to no-PoAF cases using greedy matching techniques. PoAF cases with balancing scores that deviated more than 0.1 from no-PoAF cases were considered unmatched. This yielded 94 well-matched pairs of patients, 93% of possible matches (►**Supplementary Fig. S1**, available in the online version).

Table 2 Operative details stratified by development of postoperative atrial fibrillation

Detail	PoAF ($n = 101$) No. (%) or mean ± SD	No PoAF ($n = 362$) No. (%) or mean ± SD	*p*
Indication:			0.2
Aneurysm	47 (47)	186 (51)	
Acute dissection	3 (3.0)	10 (2.8)	
Chronic dissection	49 (48)	155 (43)	
Coarctation	0 (0)	5 (1.4)	
Aortic fistula and pseudoaneurysm	1 (1.0)	3 (0.83)	
Traumatic transection	0 (0)	2 (0.6)	
Infected graft with aneurysm rupture	1 (1.0)	1 (0.28)	
Emergency operation	4 (4.0)	14 (3.9)	>0.9
Intraoperative details:			
Extent of repair:			0.6
Descending thoracic	37 (37)	143 (40)	
Thoracoabdominal	64 (63)	218 (60)	
Pericardiotomy for cannulation	40 (40)	140 (39)	0.9
CPB time (min)	115 ± 59	99 ± 56	**0.001**
Circulatory arrest	24 (24)	59 (16)	0.09
Circulatory arrest time (min)	31 ± 22	27 ± 28	0.08
Cerebrospinal fluid drain	55 (54)	222 (62)	0.19

Abbreviations: CPB, cardiopulmonary bypass; PoAF, postoperative atrial fibrillation; SD, standard deviation.

Temporal Relationship of Postoperative Atrial Fibrillation to Outcomes

To answer the question of whether preceding postoperative complications may be associated with occurrence of PoAF or whether they were coincident with or followed PoAF with greater frequency than if PoAF had not occurred, the interval between other complications and PoAF was determined by intensive medical records review. Complications occurring 12 hours before onset of PoAF were categorized as preceding PoAF; those occurring within 12 hours of PoAF, either before or after, were considered coincident with PoAF; and those developing more than 12 hours after onset of PoAF were categorized as following PoAF. If a patient experienced more than one complication of the same type, the complication occurring first after surgery was used to calculate the interval from PoAF

Costs

Postoperative cost data were available for the subgroup of operations performed from January 1, 2003 to January 1, 2011. For each balancing score-matched pair, ratio of cost for the patient who developed PoAF to the patient who did not was calculated. Bootstrapping was used to estimate the confidence distribution of median cost ratio

Results

Occurrence and Timing of Postoperative Atrial Fibrillation

A total of 101 patients (22%) developed PoAF after open thoracoabdominal aorta repair. Median time to PoAF was 68 hours (15th and 85th percentiles, 39 and 159 h; ►**Fig. 1**). The instantaneous risk of PoAF peaked at 44 hours.

Risk Factors for Postoperative Atrial Fibrillation

Preoperative factors associated with PoAF were older age and history of remote AF (►**Table 3**, ►**Fig. 2**). Once these factors were accounted for, no intraoperative factor, including use of cardiopulmonary bypass or pericardiotomy for cardiac cannulation, was associated with PoAF. Date of operation was not associated with either an increase or a decrease in PoAF (►**Supplementary Fig. S2**, available in the online version).

Temporal Relationship of Postoperative Atrial Fibrillation to Other Complications

Of the 101 patients who developed PoAF, 47 required inotropic support or vasoconstriction for hypoperfusion (►**Table 4**). Hypoperfusion tended to precede PoAF, occurring at a median interval of 41 hours earlier. Neurologic complications also tended to precede PoAF rather than follow. Thus, 6 patients developed both stroke and PoAF, with stroke occurring at a median interval of 42 hours before PoAF; 11 patients developed both paralysis and PoAF, with paralysis occurring at a median interval of 45 hours before PoAF (►**Fig. 3**).

Unlike hypoperfusion and neurologic complications, sepsis, respiratory failure, and dialysis tended to follow PoAF. Sepsis occurred in 9 of the 101 patients who developed PoAF, at a median interval of 7 days after onset of PoAF. Respiratory failure was common in patients who developed

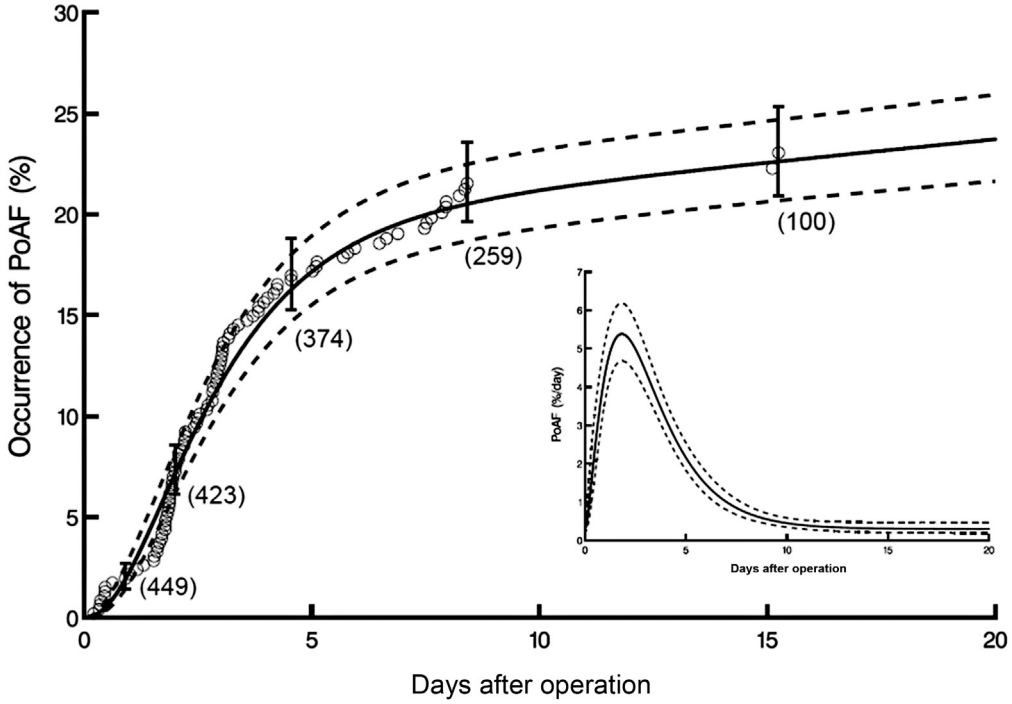

Fig. 1 Occurrence and incidence of postoperative atrial fibrillation (PoAF). Kaplan–Meier estimates are represented by a symbol at each event, vertical lines are 68% confidence limits equivalent to ± 1 standard error, and solid line within dashed confidence band is the parametric estimate. Inset shows instantaneous risk of PoAF.

Table 3 Incremental risk factors for postoperative atrial fibrillation

Risk factor	Coefficient ± SE	*p*	Reliability (%)[a]
Preoperative:			
Older age	0.031 ± 0.0099	**0.002**	49
History of atrial fibrillation	1.2 ± 0.33	**0.0004**	65
Intraoperative:			
Cardiopulmonary bypass used	0.84 ± 0.40	**0.03**	55
Preoperative and intraoperative combined:			
Older age	0.031 ± 0.0099	**0.002**	50
History of atrial fibrillation	1.2 ± 0.33	**0.0004**	64

Abbreviation: SE, standard error.
[a]Percent of times variable appeared in 1,000 bootstrap models.

PoAF, occurring in 37 of 101 (25 required tracheostomy). Respiratory failure occurred more than 12 hours after PoAF in 25 of 37 cases, with a median interval of 3.6 days. PoAF also generally preceded dialysis-dependent renal failure. Twenty-nine patients who developed PoAF also developed renal failure, with 17 requiring dialysis. Of these 17, 10 developed PoAF at least 12 hours before being placed on dialysis. Median interval between PoAF and dialysis-dependent renal failure was 2 days.

Association of Postoperative Atrial Fibrillation with Early Outcomes

Among 94 balancing score-matched pairs, those who developed PoAF were more likely to have experienced hypoperfusion ($p = 0.006$), respiratory failure ($p = 0.009$), tracheostomy ($p = 0.007$), dialysis ($p = 0.04$), and paralysis ($p < 0.0001$) at any time postoperatively (►**Table 5**). In addition, they had a longer ICU stay (median 7 vs. 5 d, $p = 0.02$; ►**Supplementary Fig. S3A**, available in thr online version) and longer postoperative hospital stay (median 15 vs. 13 d, $p = 0.004$; ►**Supplementary Fig. S3B**, available in the online version). Occurrence of sepsis and stroke was similar, as was hospital mortality (6/94 PoAF [6.4%] vs. 7/94 no PoAF [7.4%], $p = 0.8$).

Economic Impact

Among the 94 balancing score-matched patients, 67 who developed PoAF and 75 who did not have cost data available. Median cost ratio was 1.0 (15th and 85th percentiles, 0.90 and 1.3), indicating that cost of postoperative hospitalization was not significantly higher among patients who developed PoAF.

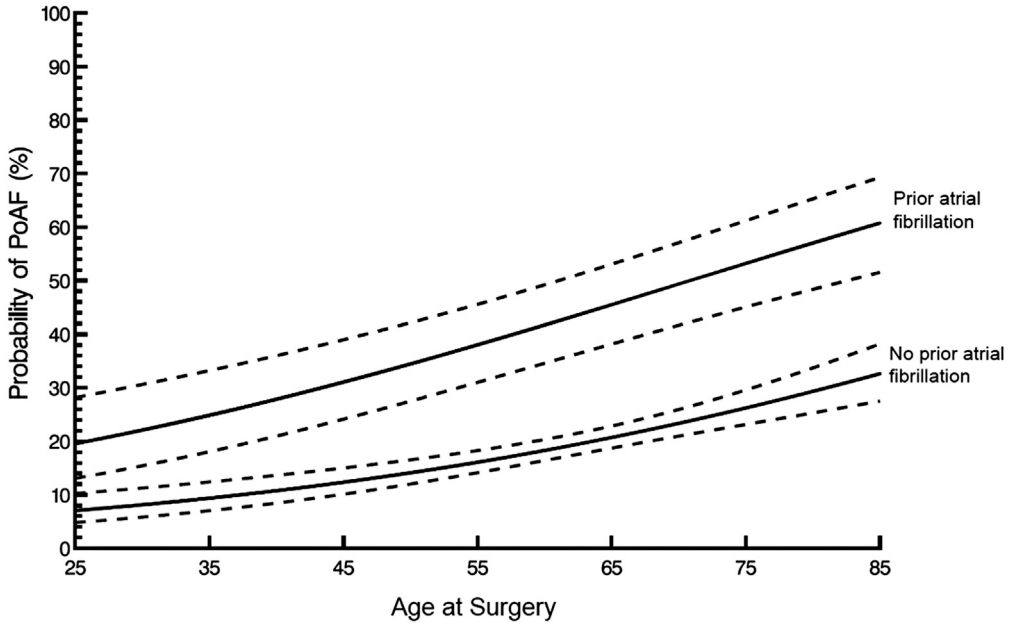

Fig. 2 Nomogram depicting predicted risk of postoperative atrial fibrillation (PoAF) with and without history of atrial fibrillation, although not present on preoperative echocardiogram, by age. Solid lines are parametric risks of PoAF enclosed within dashed 68% confidence bands equivalent to ± 1 standard error. Nomogram is based on the multivariable equation shown in ►**Table 3**.

Table 4 Temporal relationship of postoperative atrial fibrillation to other morbidities

Morbidity	Total	Prior to PoAF	Coincident	After PoAF
Hypoperfusion	47	24	7	6
Stroke	6	4	0	2
Paralysis	11	5	1	2
Sepsis	9	2	0	7
Respiratory failure	37	6	4	25
Tracheostomy	25	2	1	21
Renal failure	29	12	4	12
Dialysis	17	4	3	10

Abbreviation: PoAF, postoperative atrial fibrillation.
Note: Onset of morbidity was unavailable for 3 patients who developed paralysis, 2 who developed respiratory failure, 1 who required tracheostomy, and 1 who developed renal failure.

Discussion

We found that 22% of patients who underwent open thoracoabdominal repair developed PoAF. Median interval from surgery to onset of PoAF was 68 hours, whereas the highest risk was at 44 hours, with age and history of atrial fibrillation as only significant risk factors. PoAF tended to occur 41, 42, and 45 hours after hypoperfusion, stroke, and paralysis, respectively, and 7 days, 3.6 days, and 12 hours before sepsis, respiratory failure, and dialysis, respectively. Those who developed PoAF were more likely to have experienced hypoperfusion, respiratory failure, tracheostomy, dialysis, and paralysis at any time postoperatively. Occurrence of sepsis, stroke, and hospital mortality was similar, as was the cost of postoperative hospitalization, in patient with and without PoAF.

The incidence of descending thoracic and thoracoabdominal aneurysms rose by 52% in men and 28% in women from 1987 to 2002.[18] This increase is attributable to the aging population, increased awareness, and improved imaging modalities. Similarly, advances in surgical techniques and postoperative care have led to improvements in outcomes but have not changed the annual prevalence of PoAF (►**Supplementary Fig. S2**, available in the online version). This is consistent with the finding that patient characteristics, namely older age and history of AF, are the main predictors of PoAF. Notably, sternotomy and pericardiotomy for cannulation are not related to development of PoAF in this population.

New-onset PoAF is a common complication of cardiac and general thoracic surgery, occurring in 20 to 50% of patients. It

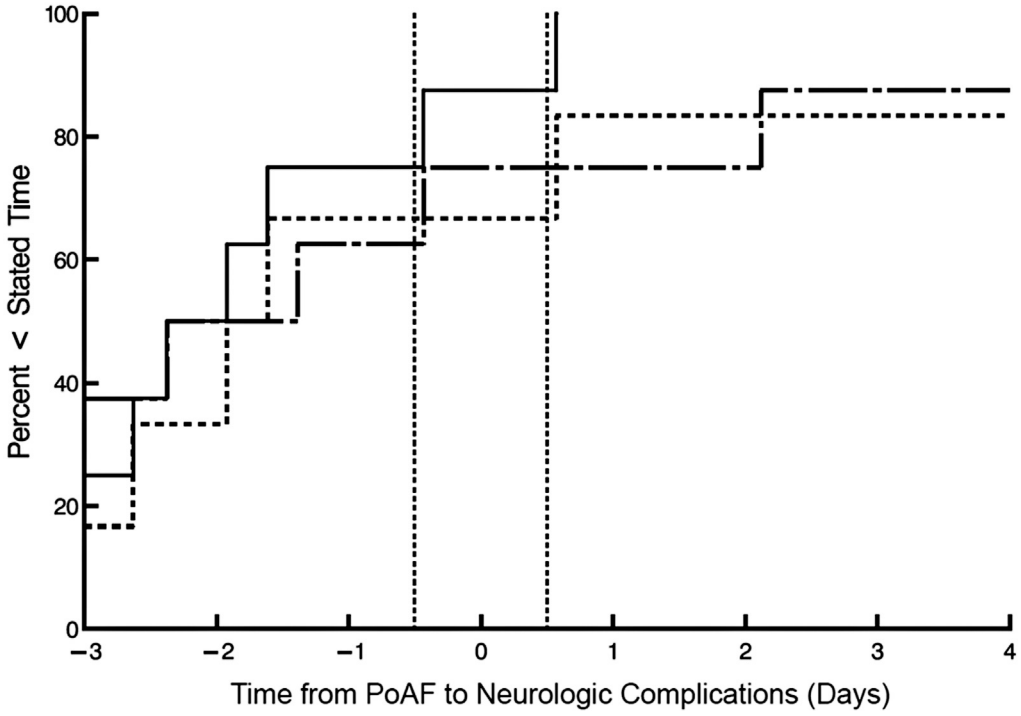

Fig. 3 Time from postoperative atrial fibrillation (PoAF) to any neurologic complication (solid line, $n = 15$), stroke (dotted line, $n = 6$), paralysis (dash–dot–dash line, $n = 11$). The two vertical dashed lines enclose the interval for which we categorized the complication as occurring coincident with PoAF.

Table 5 Operative details stratified by development of postoperative atrial fibrillation

Outcome/length of stay	PoAF ($n = 94$) No. (%) or 15/50/85 percentile	No PoAF ($n = 94$) No. (%) or 15/50/85 percentile	*p*
Outcome:			
Hospital death	6 (6.4)	7 (7.4)	0.8
Sepsis	9 (9.6)	5 (5.3)	0.3
Respiratory failure	34 (36)	18 (19)	**0.009**
Tracheostomy	23 (24)	9 (9.6)	**0.007**
Hypoperfusion	43 (46)	25 (27)	**0.006**
Renal failure requiring dialysis	16 (17)	7 (7.4)	**0.04**
Permanent stroke	6 (6.4)	5 (5.3)	0.8
Paralysis/paraplegia	11 (12)	0 (0)	**<0.0001**
Length of stay:			
Intensive care unit length of stay (d)[a]	3.0/6.9/29	2.9/5.1/17	**0.02**
Operative length of stay (d)[a]	8.3/15/40	7.8/13/24	**0.004**

Abbreviation: PoAF, postoperative atrial fibrillation.
[a]$n = 94$ in PoAF; $n = 93$ in no PoAF.

is associated with increased morbidity and mortality and is a major health and economic burden that often requires additional intervention and longer hospital stay.[1,3–6,8–10,12]

Similar incidence follows our thoracoabdominal cohort, and as other studies found predominant risk factors in our cohort are age and history of AF. Interestingly, we did not find an association of AF with higher postoperative hospital costs, despite being associated with complications like hypoperfusion, respiratory failure, tracheostomy, dialysis, and paralysis, and longer hospital stay. This could possibly be because thoracoabdominal aortic repairs represent one of the most comorbid operations and hospital recovery is long and burdened with management of various medical issues regardless of onset of PoAF. Postoperative pain, respiratory recovery after diaphragmatic takedown and reconstruction, end organ malperfusion and reperfusion, and neurologic

complications are common postoperative issues in this patient population. While treatment for PoAF may significantly prolong hospital stay in cases of isolated primary valve repair, after thoracoabdominal repair it is more likely that PoAF becomes relatively less significant among other postoperative complications. For similar reasons there was no difference in sepsis, stroke, and hospital mortality. We can see some evidence of that in our temporal relationship analysis.

We looked into the temporal characteristics of PoAF and other postoperative complications to assess for potential associations. Interestingly, hypoperfusion, stroke, and paralysis preceded the onset of PoAF. This may imply that the cascade of factors that are byproducts of these kind of hypoperfusion–reperfusion–related complications may play a role in the development of PoAF.[19–21]

Sepsis, respiratory failure, and dialysis, which may involve different pathways in the inflammatory cascade, happened after the onset of PoAF.[22–24] PoAF occurred about 12 hours before the need for dialysis. Assessing the temporal relationship for this complication is difficult, given the potential that electrolyte balance from kidney failure may cause PoAF. However, PoAF can worsen heart function, potentiate hypotension, and increase pressor use causing further deterioration of kidney function and need for dialysis.

Sepsis, respiratory and renal failure are all slower developing complications than the others and are best treated by early recognition and multimodal proactive therapy. The finding that these serious complications were preceded by PoAF suggests that PoAF may serve as an important harbinger of more serious complications.

One should take heed of this warning provided by PoAF in higher-risk patients following thoracoabdominal aortic repair.

Strengths and Limitations

This is a single-institution study that includes only patients undergoing open thoracoabdominal aortic surgeries. Despite the problem of generalizing results from a single institution, this enabled a high level of detail in our analysis but associations between complications were limited by small numbers and we were unable to explore causation. To compensate for selection bias in this nonrandomized observational study, we used propensity scores to match patients with similar demographic and comorbidity profiles.

Conclusion

PoAF after descending thoracic aorta surgery is relatively common and often a part of a constellation of other serious complications prolonging postoperative recovery. While PoAF was associated with adverse events, it did not impact postoperative cost and mortality but it may serve as an important harbinger of more serious slower developing complications like sepsis, respiratory and renal failure.

Funding
This work was supported by an award from the American Heart Association, the Gus P. Karos Registry Fund, and the Kenneth Gee and Paula Shaw, PhD, Chair in Heart Research, held by Dr. Blackstone.

Conflict of Interest
Eric E. Roselli, MD is a consultant for Artivion, Edwards, Gore, Medtronic, Terumo Aortic. The other authors declare no conflict of interest related to this article.

Acknowledgments
None.

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