Atrial fibrillation ablation improves late survival after concomitant cardiac surgery

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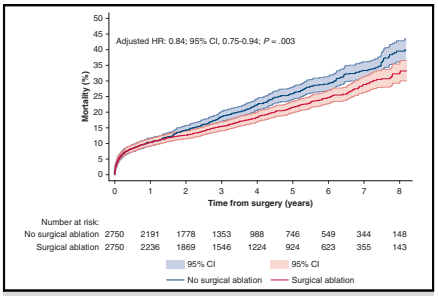
ABSTRACT

Objective: Preoperative atrial fibrillation (AF) increases risk of stroke, heart failure, and all-cause mortality after cardiac surgery. Despite encouraging results and guideline recommendations, surgical ablation (SA) for AF concomitant with other heart surgery remains low. In the current study we aimed to address the long-term mortality after SA concomitant with cardiac surgery.

Methods: This report pertains to the HEart surgery In atrial fibrillation and Supraventricular Tachycardia (HEIST) registry. We identified 20,765 adult patients (62% male) with preoperative AF who underwent conventional sternotomy heart surgery between 2010 and 2021 in 8 tertiary centers in Poland, Netherlands, and Italy. We used Cox proportional hazards models for computations and propensity score matching to minimize differences in baseline characteristics.

Results: Of included patients, 2755 (13.4%) underwent SA for AF. The highest rates of SA were observed for mitral interventions (mitral valve repair or replacement and tricuspid intervention, 25.2%), lowest for isolated coronary artery bypass grafting (6.2%). Patients in the SA group were younger (mean age 64.5 ± 9.0 years vs 68.7 ± 16.0 years; $P < .001$) and lower risk (mean European System for Cardiac Operative Risk Evaluation [EuroSCORE] II, 4.1 vs 5.7; $P < .001$). During the 11-year study period, there was a mortality reduction associated with SA (hazard ratio, 0.57; 95% CI, 0.52-0.62; $P < .001$). After propensity matching, 2750 pairs with similar baseline characteristics were identified. SA was associated with 16% mortality decline (hazard ratio, 0.84; 95% CI, 0.75-0.94; $P = .003$).

Conclusions: In this multicenter, retrospective, propensity matched study, SA concomitant with other cardiac surgery was associated with improved long-term survival regardless of baseline surgical risk. (J Thorac Cardiovasc Surg 2022;■:1-13)



HR, Hazard ratio; *CI*, confidence interval.

CENTRAL MESSAGE

In this multicenter, propensity-matched study surgical ablation concomitant with other cardiac surgery was associated with significantly reduced long-term mortality, regardless of baseline surgical risk.

PERSPECTIVE

Despite guidelines endorsement of the additional use of SA for atrial fibrillation with mitral or CABG surgery, its prevalence across the spectrum of cardiac surgeries is low. We observed a mortality reduction associated with additional use of SA with other general cardiac surgery procedures. Future studies could pave a way to expanding the recommendation for concomitant SA.

See Commentary on page XXX.

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Abbreviations and Acronyms

AF	= atrial fibrillation
AKI	= acute kidney injury
AVR	= aortic valve replacement
AVR/r	= aortic valve replacement/repair
CABG	= coronary artery bypass grafting
CM	= Cox-maze
EuroSCORE	= European System for Cardiac Operative Risk Evaluation
HR	= hazard ratio
LoS	= length of stay
MI	= myocardial infarction
MV	= mitral valve
MVR/r	= mitral valve replacement/repair
PPM	= permanent pacemaker implantation
PS	= propensity score
PSM	= propensity score matching
RR	= risk ratio
SA	= surgical ablation
SMD	= standardized mean difference
TVR/r	= tricuspid valve replacement/repair

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Cardiac surgery remains among the most commonly performed surgical procedures, with more than 300,000 coronary artery bypass grafting (CABG) and valve operations performed annually in the United States.[1] At least as many as 5% of the patients admitted for cardiac surgery present with underlying atrial fibrillation (AF)[2-4] with increasing rates depending on the presence of valvular dysfunction and extent of the cardiac disease.[2] AF itself is also a marker of high-risk patients and a predictor of postoperative complications; among others, a higher adjusted 30-day mortality rate and greater morbidity rates including those for stroke, renal failure, prolonged ventilation, reoperation, and deep sternal wound complications have been reported. Patients with preoperative AF also experience a higher adjusted long-term risk of all-cause death and of a cumulative risk of stroke and systemic embolism compared with those without AF.[5,6]

One way to treat AF and attempt to restore sinus rhythm during concurrent cardiac surgery procedure is surgical ablation (SA). Despite encouraging results and, indeed, unequivocal previous guideline recommendations related to SA[2,7] pointing to its early safety and efficacy in restoring sinus rhythm, SA is, however, seldom performed because of prolonging operative times and vague evidence regarding long-term outcome.[3,8] Recent reports, albeit nonrandomized,[9-14] have again sparked the discussion on long-term results after SA in different cardiac surgery settings with promising outcomes. These, in turn, have led to amending the most recent European guidelines with regard to performing concomitant SA at the time of mitral valve and coronary procedures.[15]

In the current report, we divided patients who underwent cardiac surgery with preoperative AF into 2 groups: cardiac surgery with concomitant SA or cardiac surgery alone. The primary outcome was all-cause long-term mortality.

METHODS

Study Population and Clinical Variables

Because of the retrospective nature of the study and anonymization of the patient data, the ethics committee approval together with patient written consent were waived. Our investigation was a part of the HEart Surgery In atrial fibrillation and Supraventricular tachycardia (HEIST) Registry (NCT04860882). We included all consecutive adult AF patients (age >18 years), who underwent any cardiac surgery procedure and were diagnosed with concomitant AF at 8 tertiary centers in Poland, Netherlands, and Italy between January 2012 and December 2021. Patients were excluded if any of the following conditions applied: (1) underwent transcatheter and/or hybrid procedures, (2) nonsternotomy surgical access, and (3) complete set of European System for Cardiac Operative Risk Evaluation (EuroSCORE) II components not available.[16]

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For patients who underwent surgery, we considered and reported 3 categories of variables as potentially influencing the primary end point: (1) demographic and preoperative conditions: age, sex, EuroSCORE II and its single components, (2) extent of coronary artery disease and/or valvular and/or aortic disease, and (3) surgical variables: urgency, operative technique (eg, on-pump vs off-pump for CABG surgery). The primary end point was mortality at follow-up after cardiac surgery alone versus cardiac surgery with concomitant SA. Secondary outcomes included early mortality (<48 hours and 30-day rates), in-hospital complications, and intensive care unit and hospital length of stay (LoS).

Statistical Analyses

Registry records with >5% of missing data were not considered; in those with <5%, missing data were input using artificial neural networks. Risk ratios (RRs) were used primarily for 30-day/in-hospital outcomes. The ensuing statistical models were used to define the point estimates of the hazard ratios (HRs) and the 95% CIs of the effect size. They were also used to evaluate the performance of SA with respect to cardiac surgery, first for the univariable Cox proportional hazards model, taking into account all sets of variables categorized by: (1) baseline demographic characteristics, (2) extent of disease, and (3) surgical characteristics. Next, a multivariable model was built; inconsistency between univariable and multivariable models was assessed using the Cochran–Mantel–Haenszel test. The multivariable model was then tested for multicollinearity using variance inflation factor.

To account for differences in baseline characteristics a nonparsimonious propensity score (PS) matching (PSM) model was created.[17] The Cox stratified regression model was used to acquire variables for the PSM. Probit regression coefficients along with standard errors were calculated for all covariates. Table E1 lists all variables used in PSM. One-to-one matching on PS was performed without replacement (caliper, 0.2). Standardized mean differences (SMDs) and variance ratios were calculated to assess the balance in covariates postmatch. The overall long-term mortality rate was assessed with Kaplan–Meier curves fitted before (unadjusted model) and after PSM. A Cox proportional hazard model was used to test the association between ablation and long-term mortality. "Phtest" on the basis of Schoenfeld residuals was then used to assess the proportional hazards assumption.

As a further sensitivity analysis to assess the mortality after concomitant SA, patients were stratified according to defined subgroups stratified according to baseline risk. In addition, a separate, independent PSM was performed to exactly match the patients according to the type of surgical procedure in addition to PSM. Appendix E1 shows the details of the additional PSM model. STATA MP version 13.0 software (StataCorp) and the packages "robust," "optmatch," "matchIt," "psmatch2," and "CRTgeeDR" in R Core Team 2013 were used for computations.

RESULTS

Patients Baseline Characteristics

During the course of the study 20,765 patients with AF who underwent heart surgery were identified. At baseline, 62% were men (n = 12,881), aged 68.2 ± 15.3 years, at an average of 5.48 ± 8.28% EuroSCORE II operative risk. Of those, 2755 (13.3%) underwent concomitant SA (Figure 1). Isolated CABG (5439), followed by isolated aortic valve replacement (AVR)/repair (AVR/r; n = 2885), mitral valve (MV) replacement/repair (MVR/r) and tricuspid valve replacement/repair (TVR/r; n = 2434), and isolated MVR/r (n = 2137) were the most commonly performed procedures (Figure 2). Baseline and operative characteristics as well as clinical outcomes of the

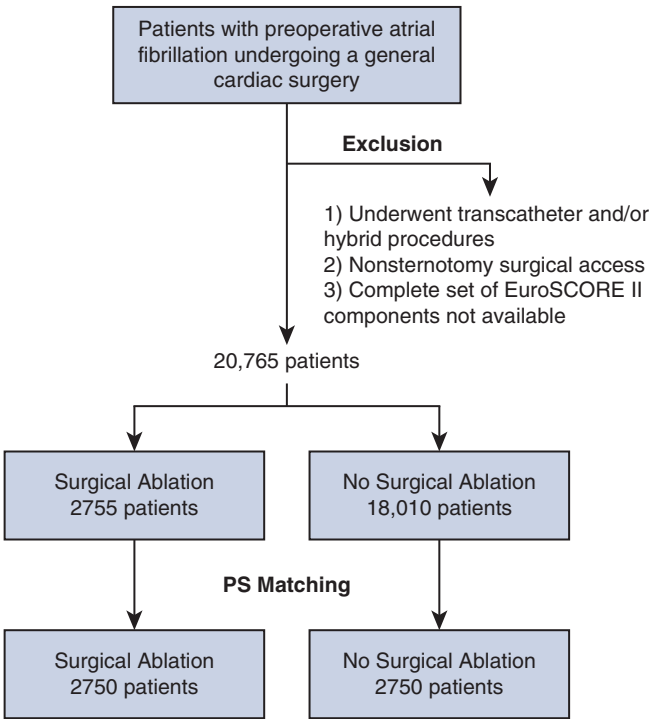

FIGURE 1. Patient flow diagram. *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *PS*, propensity score.

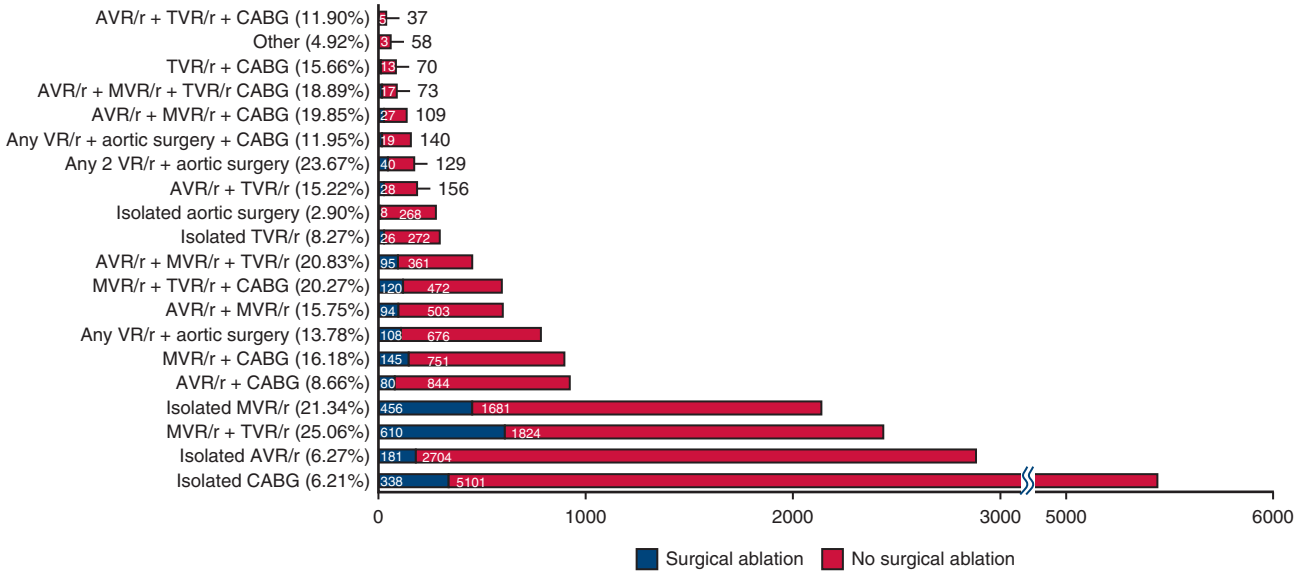

FIGURE 2. Distribution of surgical ablation rates for different types of heart surgery procedures. *AV*, Aortic valve; *R/r*, replacement or repair; *TV*, tricuspid valve; *CABG*, coronary artery bypass grafting; *MV*, mitral valve; *V*, valve.

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unadjusted population are available in Tables E2-E4. The rates of SA varied substantially across surgery types. SA was least performed at the time of isolated aortic surgery (2.90%), nonvalve and non-CABG surgery nonaortic (4.92%), and isolated CABG (6.21%). On the contrary, MVR/r + TVR/r (25.06%), multivalvular with aortic surgery (23.67%), and isolated MVR/r (21.34%) had the highest SA rates. Other variables that were associated with SA performance were identified in uni- and multivariable analyses and are available on Table E5. Mitral ($P < .001$) and tricuspid ($P < .001$) valve procedures as well as elective patient status ($P < .001$) were associated with SA, whereas comorbidities (chronic kidney disease, diabetes, previous myocardial infarction [MI], endocarditis, and aortic surgery) showed a negative correlation ($P < .001$). At 10 years, SA was associated with 43% reduced mortality compared with no SA in an unadjusted analysis (Figure E1).

PSM

One-to-one PSM resulted in 2750 pairs assigned to SA and no ablation groups. Quality of the matching with histogram distribution of PS along with PS estimates are available in Figure E2 and Table E1, respectively. SMDs between PS-matching variables in SA and no SA subgroups was assessed visually (Figure E3); values and variance ratios of respective SMDs are further available in Table E1. Table 1 shows the baseline characteristics of PS-matched patients. There were no marked differences among the patients except for continuous variables age ($P < .001$), EuroSCORE II ($P < .001$), and left ventricular ejection fraction ($P = .012$). There were 3262 (59.6%) male participants; 26.3% with diabetes, and 50.9% were smokers. Nearly one-third underwent previous percutaneous coronary intervention; 13.2% had suffered MI in the past 90 days before surgery. Operative characteristics are further available in Table 2. Most patients were elective (78.1%); 2.2% underwent redo surgery. In patients who underwent extracorporeal circulation heart surgery, SA increased the length of cardiopulmonary bypass and aortic crossclamp times by an average of 19 and 13 minutes, respectively, compared with no SA. In the SA group, 955 patients (35%) underwent pulmonary vein isolation, a further 1695 patients (62%) received a box lesion set, and in 100 patients (4%) a Cox-maze (CM) IV lesion set was performed. Table 3 shows periprocedural complications; there were no major differences between SA and no SA except for an observed propensity for lower rates of early (<48 hours) mortality (0.8% vs 1.4%; RR, 0.59 [95% CI, 0.35-0.98]) and lower rates of permanent pacemaker implantation (PPM; 1.3% vs 2.1%; RR, 0.63 [95% CI, 0.42-0.94]) associated with SA, which were offset by higher rates of respiratory failure (9.5% vs 7.3%). Median hospital LoS and intensive care unit LoS were 12 days versus 10 days ($P < .001$) and 45.1 hours and 44.9 hours ($P = .193$), respectively.

Long-Term Mortality and Risk Dependencies

In the PS-matched model, performing concomitant SA was associated with 16% reduced mortality at long-term follow-up: HR, 0.84; (95% CI, 0.75-0.94); $P = .003$ (Figure 3, *A*). Proportional hazard assumption was not violated ($P = .236$) as also graphically assessed (Figure E4). Since mortality curves started to diverge only after some time, a mortality landmark analysis at 2 years was performed (Figure 3, *B*). When patients were stratified according to baseline procedural risk, we observed a

TABLE 1. Baseline characteristics

Variable	Total (N = 5500)	Surgical ablation (n = 2750)	No surgical ablation (n = 2750)	SMD	*P* value
Age, y	66 (61-71)	66 (60-71)	67 (61-72)	0.192	<.001
Male sex	3262 (59.3)	1624 (59.0)	1638 (59.6)	0.011	.701
EuroSCORE II	2.50 (1.42-4.50)	2.74 (1.56-4.81)	2.33 (1.30-4.17)	0.110	<.001
<1	801 (14.6)	332 (12.1)	469 (17.1)	0.143	<.001
1-2	1343 (24.4)	633 (23.0)	710 (25.8)	0.065	.016
2-3	1073 (19.5)	516 (18.8)	557 (20.3)	0.030	.163
3-4	660 (12.0)	372 (13.5)	288 (10.5)	0.094	<.001
4-5	427 (7.8)	247 (9.0)	180 (6.5)	0.091	.001
5-10	848 (15.4)	458 (16.7)	390 (14.2)	0.060	.011
>10	348 (6.3)	192 (7.0)	156 (5.7)	0.055	.041
Diabetes	1448 (26.3)	748 (27.2)	700 (25.5)	0.039	.150
Oral hypoglycemic drugs	761 (13.8)	377 (13.8)	384 (14.0)	0.008	.815
Insulin with or without oral hypoglycemic drugs	441 (8.0)	228 (8.3)	213 (7.8)	0.020	.487
Smoking	2799 (50.9)	1394 (50.7)	1405 (51.1)	0.008	.767
Hypertension	4275 (77.7)	2125 (77.2)	2150 (78.2)	0.022	.418
Hyperlipidemia	2701 (49.1)	1353 (49.2)	1348 (49.0)	0.004	.914
BMI	28.3 (25.5-31.2)	28.3 (25.5-31.3)	28.1 (25.6-31.1)	0.028	.554
Pulmonary hypertension	1350 (24.5)	677 (24.6)	673 (24.5)	0.001	.925
Severe (PA systolic >55 mm Hg)	280 (5.1)	137 (5.0)	143 (5.2)	0.100	.759
Renal impairment	2767 (50.3)	1361 (49.5)	1406 (51.1)	0.033	.225
Dialysis (regardless of CC)	21 (0.4)	10 (0.4)	11 (0.4)	0.006	.999
Peripheral artery disease	882 (16.0)	457 (16.6)	425 (15.5)	0.032	.255
Cerebrovascular disease	316 (5.8)	155 (5.6)	161 (5.9)	0.009	.729
History of stroke	141 (2.6)	62 (2.3)	79 (2.9)	0.039	.148
History of TIA	168 (3.1)	87 (3.2)	81 (2.9)	0.013	.695
Carotid intervention	23 (0.4)	13 (0.5)	10 (0.4)	0.017	.677
Chronic lung disease	441 (8.0)	202 (7.3)	239 (8.7)	0.042	.074
Asthma	276 (5.0)	133 (4.8)	143 (5.2)	0.017	.538
LVEF, %*	50 (45-60)	52 (45-60)	50 (45-60)	0.072	.012
CAD	1590 (28.9)	814 (29.6)	776 (28.2)	0.030	.271
Previous MI	729 (13.2)	376 (13.7)	353 (12.8)	0.025	.382
Previous PCI	1725 (31.4)	849 (30.9)	876 (31.9)	0.021	.433
NYHA classification					
0	383 (7.0)	204 (7.5)	178 (6.5)	0.030	.168
I	525 (9.6)	278 (10.1)	247 (9.0)	0.030	.169
II	2309 (42.0)	1128 (41.0)	1181 (42.9)	0.039	.148
III	2105 (38.3)	1038 (37.7)	1067 (38.8)	0.022	.421
IV	179 (3.3)	102 (3.7)	77 (2.8)	0.050	.078

Data are presented as n (%) or median (interquartile range) except where otherwise noted. *SMD*, Standardized mean difference; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *BMI*, body mass index; *PA*, pulmonary artery; *CC*, creatinine clearance; *TIA*, transient ischemic attack; *LVEF*, left ventricular ejection fraction; *CAD*, coronary artery disease; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *NYHA*, New York Heart Association. *Missing data.

relationship between performance rates of SA and increasing EuroSCORE II threshold values (coefficient, 0.024; $P < .001$; Figure 4, *A*) in frequency weighted regression (ie, patients with higher EuroSCORE II were more likely to receive SA). The mortality reduction associated with SA was maintained across baseline risk strata without any significant trend (Figure 4, *B*).

Additionally, a separate, exact PSM model was built to match the patients within the surgery type groups (Appendix E1) "isolated CABG," "isolated AVR/r," "isolated MVR/r," and "MVR/r + TVR/r" groups were chosen as the most commonly performed procedures (Figure 5). Greater differences in long-term mortality were seen for SA and no SA in isolated MVR/r and MVR/r + TVR/r

TABLE 2. Operative characteristics after PS matching

Variable	Total (N = 5500)	Surgical ablation (n = 2750)	No surgical ablation (n = 2750)	SMDs	*P* value
Procedural characteristics					
Redo surgery	123 (2.2)	62 (2.3)	61 (2.2)	0.002	.999
IABP	9 (0.2)	3 (0.1)	6 (0.2)	0.027	.343
I.V. inotropes	77 (1.4)	31 (1.1)	46 (1.7)	0.046	.087
Preoperative mechanical ventilation	20 (0.4)	6 (0.2)	14 (0.5)	0.040	.078
Urgency					
Elective	4298 (78.1)	2171 (78.9)	2127 (77.3)	0.055	.615
Surgery					
CPB time, minutes	123 (93-162)	132 (102-171)	113 (86-152)	0.343	<.001
Crossclamp time, minutes	83 (62-111)	90 (69-115)	77 (58-105)	0.290	<.001
CABG	1539 (28.0)	770 (28.0)	769 (28.0)	0.001	.999
Mitral valve	3210 (58.4)	1605 (58.4)	1605 (58.4)	0.002	.999
Aortic valve	1227 (22.4)	615 (22.4)	612 (22.3)	0.001	.948
Tricuspid valve	1889 (34.4)	944 (34.4)	945 (34.4)	0.001	.999
Two valves	1824 (33.2)	912 (33.2)	912 (33.2)	0.001	.999
Three valves	247 (4.5)	123 (4.5)	124 (4.5)	0.002	.999
Aortic surgery	284 (5.2)	129 (4.7)	155 (5.6)	0.043	.114
Concomitant LAAO	1446 (26.3)	734 (26.7)	712 (25.9)	0.018	.520

Data are presented as n (%) or median (interquartile range) except where otherwise noted. *SMDs*, Standardized mean differences; *IABP*, intra-aortic balloon pump; *I.V.*, intravenous; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass graft; *LAAO*, left atrial appendage occlusion.

subgroups (log rank $P = .079$ and $P = .103$, respectively) as opposed to isolated CABG and isolated AVR/r procedures.

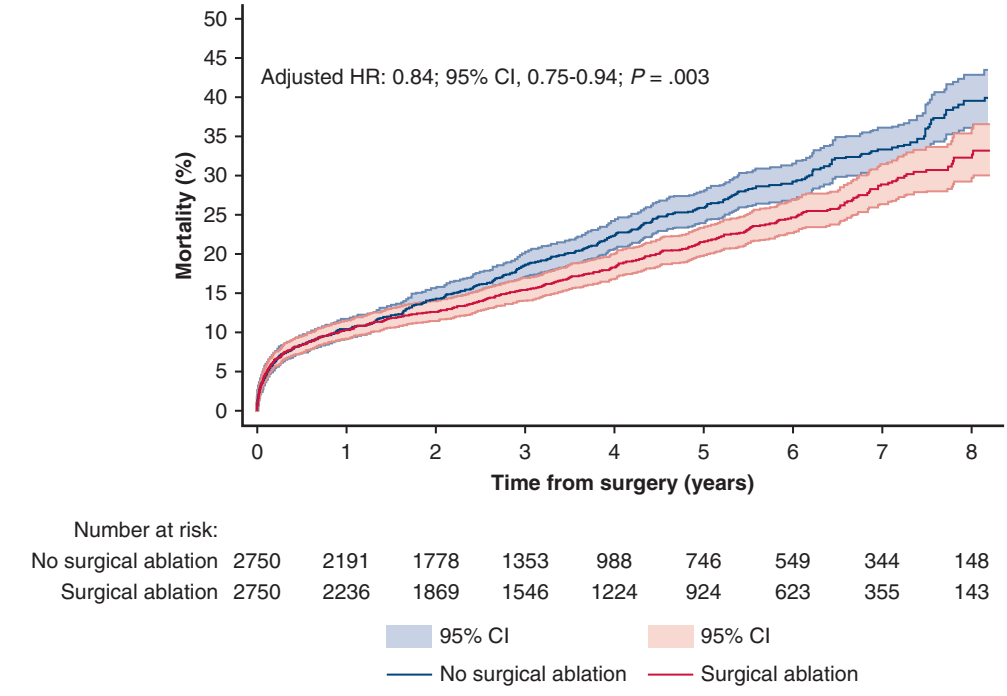
DISCUSSION

The current registry analysis provides new insights into performing SA at the time of other cardiac surgery procedures in patients with underlying AF. The main findings are: (1) there is a considerable discrepancy regarding SA frequencies depending on the type of surgical procedure, (2) SA is performed more willingly in patients at higher risk thresholds (although we acknowledge that the additional use of SA increases EuroSCORE II by itself), (3) while not compromising early safety, SA is associated with reduced long-term mortality, regardless of the initial risk profile as indicated by EuroSCORE II (Figure 6).

TABLE 3. In-hospital outcomes after PS matching

Variable	Surgical ablation (n = 2750), n (%)	No surgical ablation (n = 2750), n (%)	Relative risk (IQR)	*P* value
Early postoperative mortality (48 h)	23 (0.8)	39 (1.4)	0.59 (0.35-0.98)	.044
30-Day mortality	130 (4.7)	128 (4.7)	1.02 (0.80-1.29)	.899
Cardiac tamponade and/or rethoracotomy for bleeding	298 (10.8)	298 (10.8)	1.00 (0.80-1.16)	.999
Periprocedural MI	11 (0.4)	7 (0.3)	1.57 (0.61-4.05)	.349
Respiratory failure	261 (9.5)	202 (7.3)	1.29 (1.08-1.54)	.004
Prolonged ICU stay (return or >72 h)	809 (29.4)	758 (27.6)	1.07 (0.98-1.16)	.128
Neurologic complications	73 (2.7)	77 (2.8)	0.95 (0.69-1.30)	.741
Multiorgan failure	88 (3.2)	73 (2.7)	1.21 (0.89-1.64)	.231
Gastrointestinal complications	41 (1.5)	37 (1.3)	1.11 (0.72-1.72)	.648
Acute kidney failure and/or dialysis	129 (4.7)	120 (4.4)	1.08 (0.84-1.37)	.560
Superficial sternal wound infection	39 (1.4)	40 (1.5)	0.98 (0.63-1.51)	.910
Deep sternal wound infection	24 (0.9)	17 (0.6)	1.41 (0.76-2.62)	.275
Mediastinitis	13 (0.5)	11 (0.4)	1.18 (0.53-2.63)	.683
PPM	37 (1.3)	59 (2.1)	0.63 (0.42-0.94)	.025

IQR, Interquartile range; *MI*, myocardial infarction; *ICU*, intensive care unit; *PPM*, permanent pacemaker.



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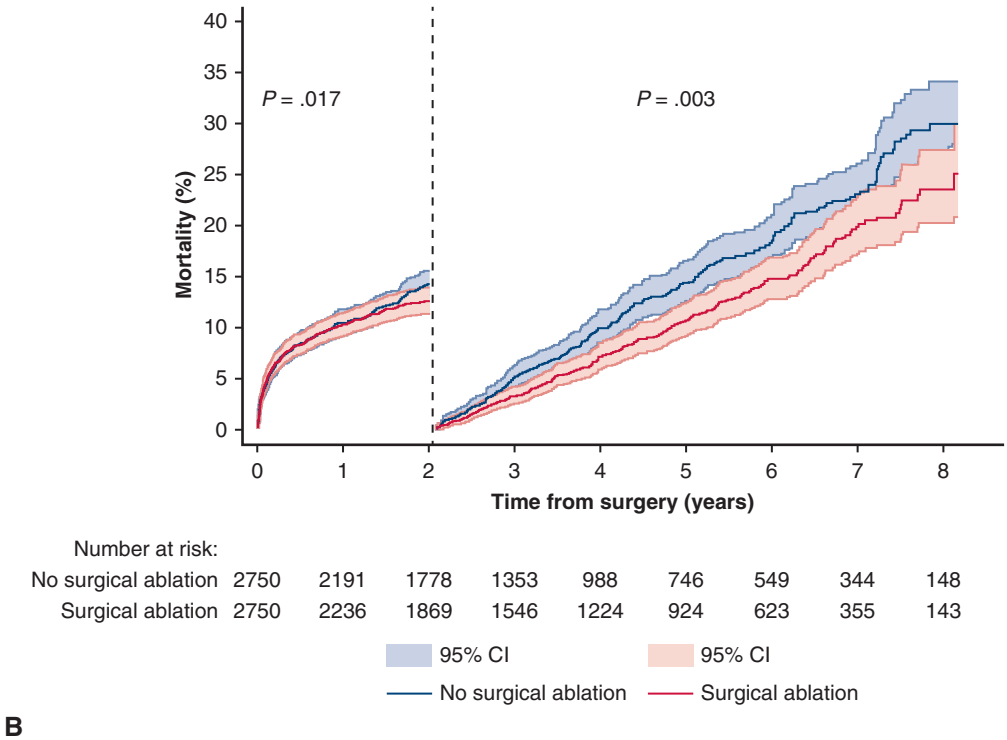

B

FIGURE 3. A, PS-matched survival analysis. Surgical ablation versus no surgical ablation. Cox proportional hazard ratio (*HR*) with 95% CIs. B, Mortality landmark analysis. Log rank *P* values. *CI*, Confidence interval.

Surgical Ablation Performance

The current analysis represents one of the world's biggest data set designed to assess long-term outcomes after cardiac surgery in patients with underlying AF. Certainly though, the predominance of SAs performed within the registry time frames and volume leaves a great deal to be desired. In contrast to the biggest available pieces of evidence in which concomitant SA frequencies reached 48.3% and

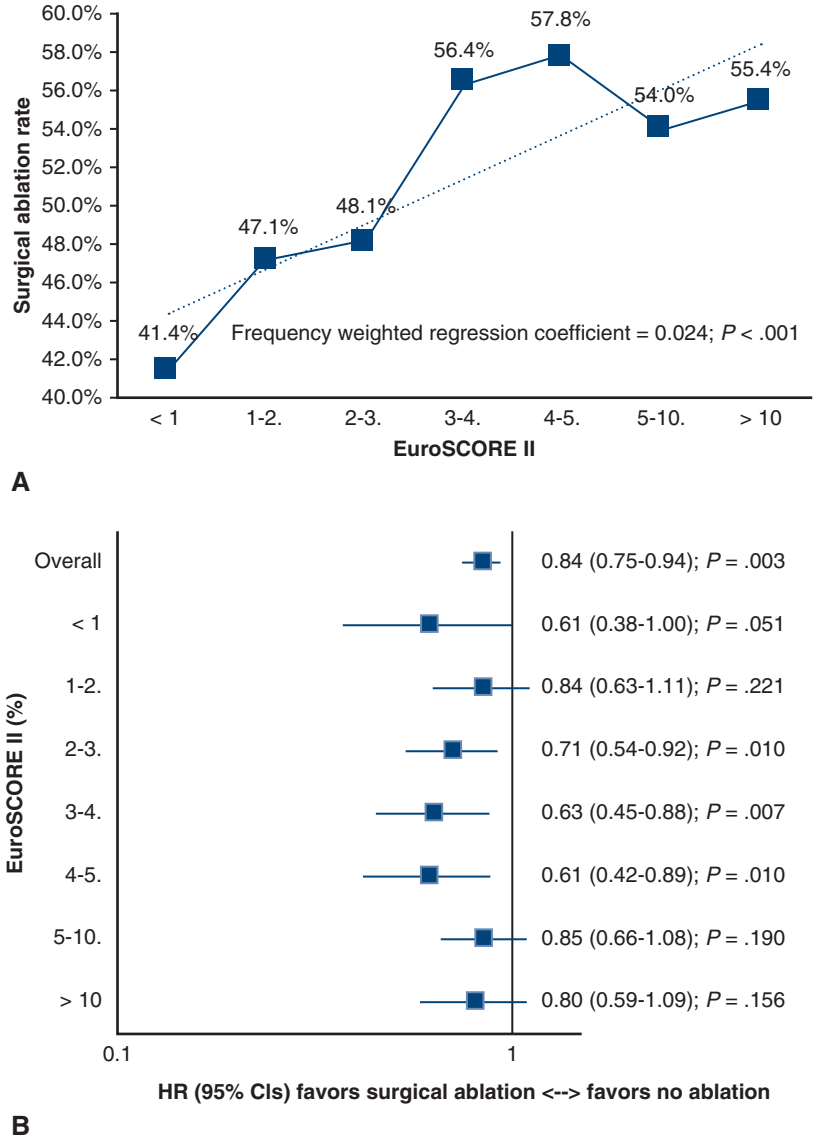

FIGURE 4. Frequency weighted regression: surgical ablation rate versus EuroSCORE II (A); subgroup analysis: propensity score-matched Cox proportional hazard ratio (*HR*) with 95% CI for the comparison of surgical ablation versus no surgical ablation across EuroSCORE II thresholds (B). *EuroSCORE*, European System for Cardiac Operative Risk Evaluation. *CI*, Confidence interval.

35.4% in the Society of Thoracic Surgeons Adult Cardiac Surgery Database[2] and Society of Thoracic Surgeons Medicare-linked database of CABG patients,[5] respectively, in the current analysis 2775 ablations performed reached a modest 13.4% rate. Badhwar and colleagues[2] reported mitral operations having the highest rate of SA (68.4%), followed by AVR (39.3%) and CABG (32.8%). In the current study, we found the variability of the distribution of ablation performance rates according to surgery type. Surgical ablation was more often performed with the increasing complexity of the cardiac procedure; MV with tricuspid valve intervention had the highest rate (25.06%) and isolated aortic surgery had lowest (2.9%). We observed a low predominance of SA during isolated CABG (6.21%) which was previously noted and explained in the report by Malaisrie and colleagues,[5] who showed that among 361,138 patients who underwent isolated CABG, 37,220 (10.3%) had preoperative AF; yet, in only 13,161 (35.4%) SA was performed. There remains a paucity of data on concomitant ablation prevalence from European centers. Previous reports from the Polish National Registry of Cardiac Surgery Procedures (KROK),[14] showed a disturbing 4.4% SA rate in isolated and 7.9% in combined CABG patients with underlying AF. There might be several reasons for a low adoption rate of SA. The complexity of CM III and IV lesion sets, along with a low emphasis on SA during standard cardiac surgeon training,[14,18,19] the higher reported incidence of PPM,[2] increased crossclamp

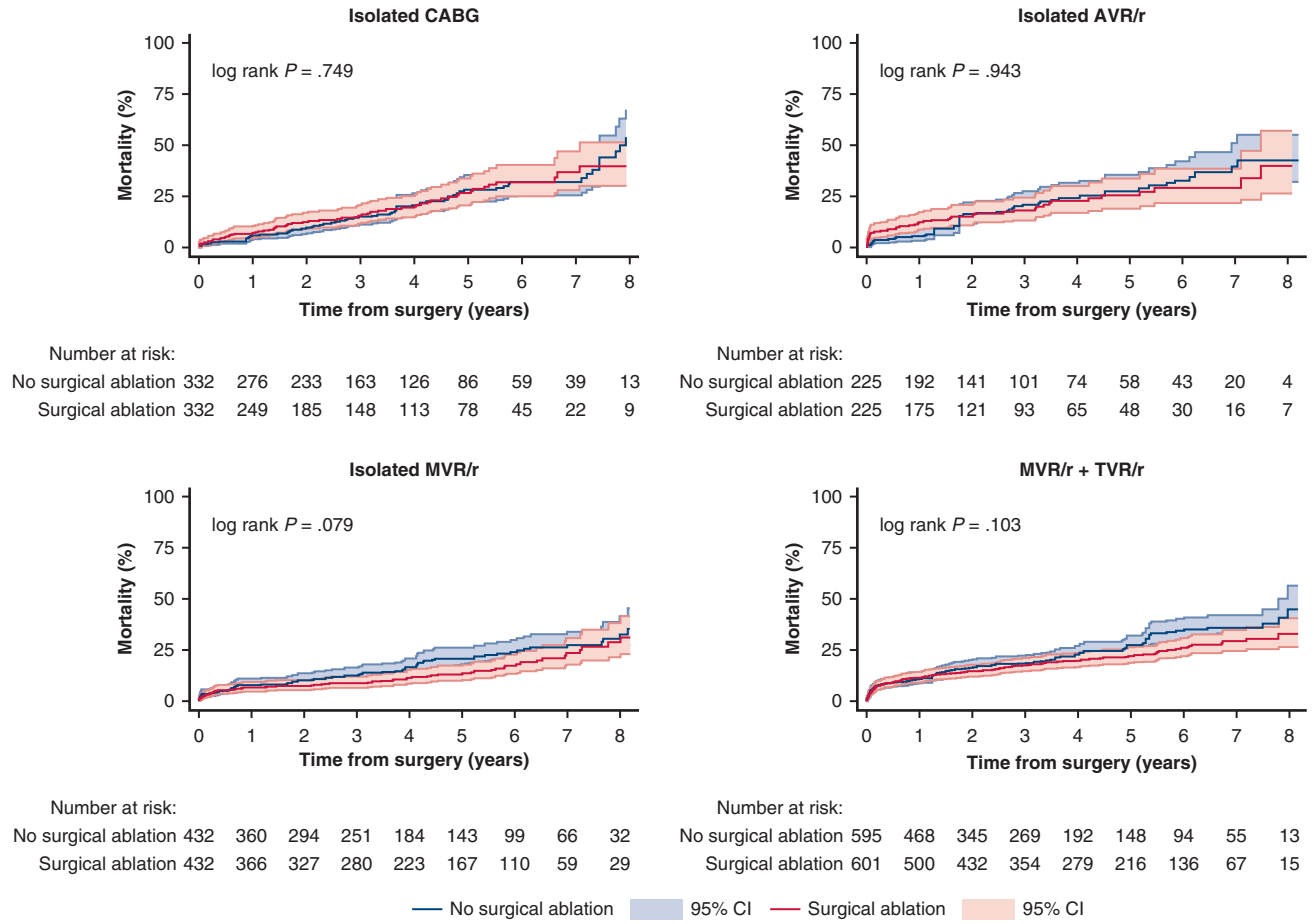

FIGURE 5. Subgroup analysis stratified according to the type of surgical procedure. Surgical ablation versus no surgical ablation. *CABG*, Coronary artery bypass grafting; *AVR/r*, aortic valve replacement/repair; *MVR/r*, mitral valve replacement/repair; *TVR/r*, tricuspid valve replacement/repair; *CI*, Confidence interval.

time,[20] the fact that SA at the time of other procedures might have not been reimbursed in certain European countries previously,[14] and lack of evidence on survival benefit from randomized controlled trials.[21] We performed uni- and multivariable analyses to identify predictors of concomitant SA performance during routine cardiac surgery. Mitral and tricuspid valve procedures as well as elective patient status were independently associated with higher SA rates, whereas comorbidities (chronic kidney disease, diabetes, previous MI, endocarditis) and aortic surgery were negative predictors. Studies to investigate barriers to SA concomitant with other cardiac surgery are warranted. With a recent eruption of data regarding the safety of SA in different clinical scenarios[14,20,21] that led to a change of the guideline recommendations[15] we should expect more favorable trends in SA application.

Surgical Ablation and Operative Risk

One important finding of the current analysis is that SA did not compromise early patient safety. Importantly, SA in addition with cardiac procedures yielded mortality reductions long-term regardless of baseline surgical risk. In the current study, as opposed to numerous previous reports, we did not observe increased rates of PPM with SA[22] and acute kidney injury (AKI) observed shortly after surgery as also reported previously in patients who underwent SA concomitant with CABG.[20] Conversely, 48-hour mortality was lower (RR, 0.59 [95% CI, 0.35-0.98], $P = .044$) in ablated patients and 30-day mortality unchanged. Indeed, Ad and colleagues[23] showed that adding a full CM procedure did not affect the operative morbidity or mortality of CABG or AVR procedures whereas Al-Atassi and colleagues[24] showed that concomitant AF ablation did not increase the surgical risk in patients who underwent isolated CABG, AVR, or combined CABG and AVR. Other previous reports, in addition, showed a lower incidence of stroke, multiorgan failure, and mortality in MV[13] and CABG patients,[14] whereas AKI and PPM rates were unchanged. Higher performance rates of ablation in patients at higher risk, as observed in the current study, deserve a commentary because of the general reluctance to perform SA in excessive risk subjects.[19] In 2012 Ad

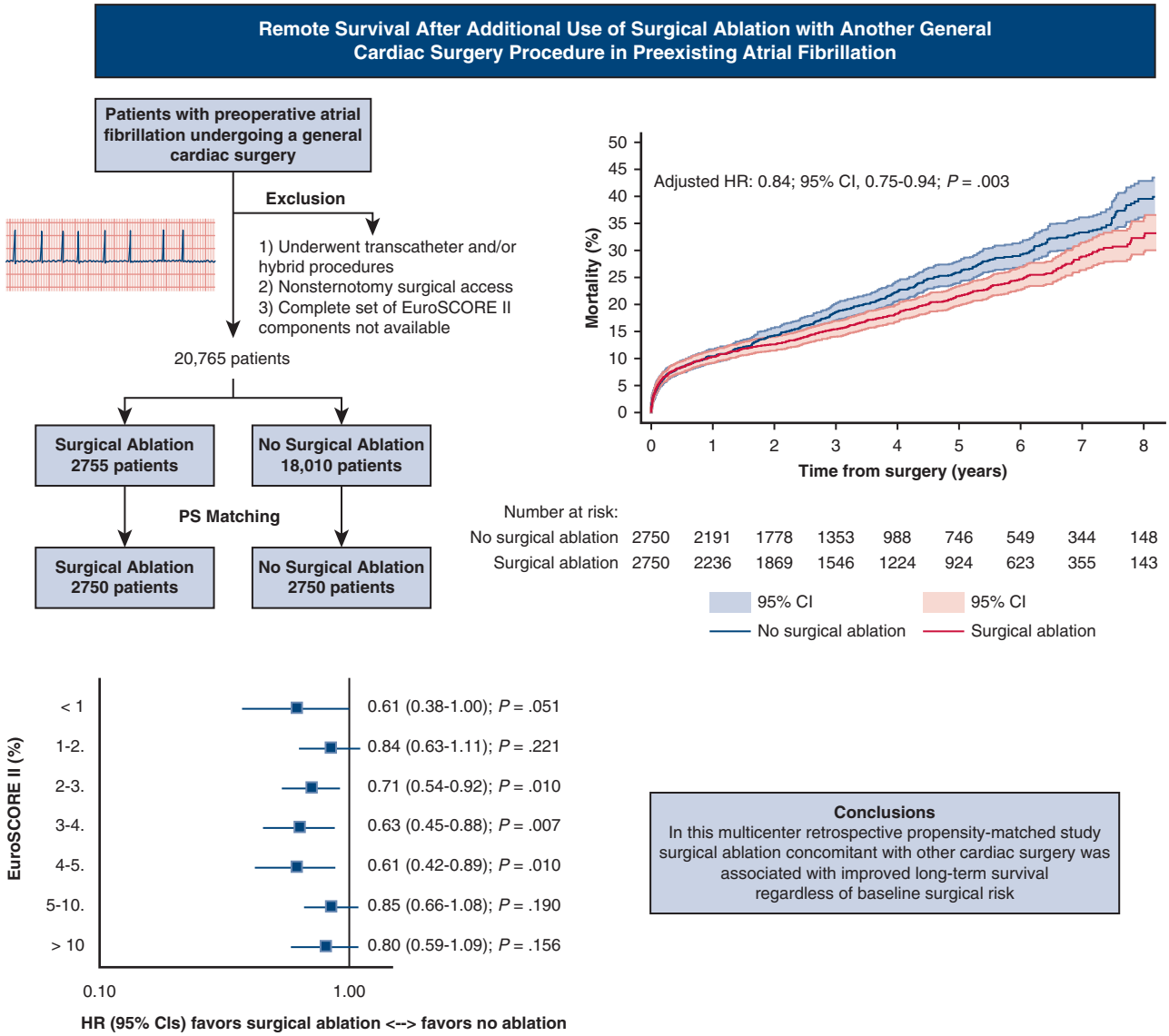

FIGURE 6. Graphical depiction of the study's methods, results, and implications. *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *HR*, hazard ratio; *CI*, Confidence interval; *PS*, propensity score.

and colleagues[25] analyzed >1700 cardiac surgery patients deemed high risk (additive EuroSCORE >6) and reported that the SA procedure did not add operative risk to patients considered high risk, and potentially improved long-term outcome for the subgroup of patients who had their AF ablated. The perioperative outcomes were similar among groups, including length of stay, permanent stroke, renal failure, 30-day readmission rate, and operative (<30 days) mortality.

Long-Term Efficacy and Safety

In our study SA in addition to another general cardiac surgery was associated with a >15% long-term mortality reduction in a PS-matched population. Beneficial effects were maintained across the baseline risk spectrum. Sensitivity analysis, which matched patients exactly on the type of procedure, showed the differences in late mortality was mostly present in mitral and tricuspid valve surgeries with no trend observed in isolated AVR/r or CABG. The effect of adding SA to aortic valve surgery is not well studied, however, 1 study of CABG or AVR showed lower a mortality rate in the SA group.[26] Previous recommendations for SA concomitant with other cardiac surgeries had been made on the basis of multiple studies, including randomized controlled trials.[21,27] These studies showed operative safety and improved return to sinus rhythm. Even when pooled together in a meta-analysis,[28] the effect on patient-important outcomes, including mortality and stroke was not affected by SA. One of the first reports to address long-term safety of concomitant SA was

again one by Ad and colleagues,[29] who reported that freedom from an embolic stroke at 7 years was 96.6% (0.4 strokes per 100 patient-years) with most patients off anticoagulation medication after SA concomitant with mitral valve procedures. In another report, no differences were found in long-term freedom from stroke (96.1% vs 96.6%), for mitral and nonmitral surgeries when SA was performed.[30] One study by Bakir and colleagues[31] directed at non-only mitral valve procedures showed improved late, 7-year survival associated with sinus rhythm maintenance after SA, at the cost of higher rates of AKI shortly after the surgery. However, all SAs were CM IV sets of lesions that prolonged, nearly by 70 minutes, the cardiopulmonary bypass duration which together with excessive N-terminal-prohormone brain natriuretic peptide release from the atria could have led to the increased propensity of AKI in this group.

With the advancements of technology and improvements in ablation sources, the efficacy of complex lesion sets, as in CM III or CM IV, can be maintained with shorter operative times.[32] In our study, only a small percentage of patients underwent a CM IV pattern ablation. It remains to be declared if mortality reduction in the SA patients could further increase with higher adoption of CM IV or other complex ablation lesion sets. However, there are reports available pointing to no difference in SA efficacy observed in patients having undergone biatrial compared with uniatrial lesion SA.[33] Although several concepts, such as restricting the lesion sets to pulmonary vein isolation alone in higher-risk patients, deserve further investigation, the value of SA for long-term outcome, regardless of its extent during the index procedure, is extraordinary also outside the field of mitral valve surgery.[34]

Limitation

Certain limitations inherent to the analysis of a retrospective registry need to be acknowledged. First, the registry did not collect, at the time of conception, the data regarding long-term outcomes other than all-cause mortality (eg, long-term stroke, rehospitalization for heart failure, repeat revascularization, redo surgery and other procedures, eg, catheter ablation or percutaneous coronary intervention); these could further enhance the registry and might have influenced the remote outcome. Second, the number of PPM implantations might be underestimated, because reimbursement policy favors PPM implantation after an index hospitalization for borderline indications; together with the fact that the exact timing of PPM implantation was not available in the registry, PPM implantation in the current analysis should be regarded as one occurring during index hospitalization. Lower rates of PPM observed in the SA group require further investigation, although one recent analysis showed SA was not prognostic of PPM after valve and arrhythmia surgery.[35] Third, certain detailed baseline and operative data such as AF type and duration, ablation energy source, ablation duration, and additional ablation lines are not recorded. Fourth, the subgroup analysis on the EuroSCORE II thresholds and mortality HRs should be regarded as exploratory because the choice of thresholds is arbitrary and additional matching within thresholds themselves for baseline risk factors ineffective. Additionally, the registry does not include information on anticoagulation drugs, drug adherence, and follow-up examinations including echocardiography. Finally, although PSM accounted for all of the variables included in the EuroSCORE II and other surgically relevant characteristics, minimizing selection bias in an attempt to even baseline patients' characteristics, unmeasured biases, and confounders might remain, making the association between SA and mortality reduction valid only to the extent an analysis of a nonrandomized controlled trials study allows.

CONCLUSIONS

In this multicenter, retrospective, PS-matched study, SA concomitant with other cardiac surgery was associated with a significantly improved long-term survival. This benefit was observed regardless of baseline surgical risk.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://www.aats.org/resources/1307.

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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Key Words: surgical ablation, arrhythmia, adult cardiac surgery, long-term survival, registry

Discussion

Presenter: Dr Michal Pasierski

Dr Jennifer Walker *(Boston, Mass)*. I have one important question that came to my mind when I was reviewing the paper. I think we listened to the first talk this afternoon about the efficacy of the Cox-Maze and the importance of doing a complete lesion set, but only 4% of your patients had a complete lesion set and 97% of them had some form of that. Is there a way that you differentiated your survival in the paper based on the lesion set that you chose for the patients? Is that something that will affect what you plan to do going forward or how does that relate?

Dr Michal Pasierski *(Warsaw, Poland)*. That's a good point. Yes, that's something that we tend to do, although, as noted, the absolute number of the Cox-Maze procedure was rather low. Therefore, I'm not sure whether we can power an analysis for mortality. However, yes, that's an important issue, and in the future we definitely would like to study the differences between the different methods of surgical ablation.

Dr Steven Bolling *(Ann Arbor, Mich)*. Dr Pasierski, this is a nice study. It's good or bad to see that our European colleagues are just as bad at treating atrial fibrillation?

Dr Pasierski. Worse.

Dr Bolling. Worse, okay, as we are. Is there a program, vis-a-vis our presentation next from our state registry at Michigan, to improve this level of treatment in Europe?

Dr Pasierski. I don't want to speak for the whole of Europe, but as far as I know, there are none, at least not in Poland. But yes, it's an important point, and I think that's where we should aim for in the future.

Dr Niv Ad *(Takoma Park, Md)*. I enjoyed your presentation. Maybe an unfair question to you, but I think it's important to mention it here. Do you know how many surgeons participated in the entire cohort?

Dr Pasierski. In the entire study?

Dr Ad. Yes.

Dr Pasierski. I'm not sure.

Dr Ad. I'll get to the point. In your propensity match, did you also match the surgeons?

Dr Pasierski. No, we did not.

Dr Ad. Yes, because I believe that atrial fibrillation surgery improves survival. I have no doubt. I mean, I've done thousands of them, and there's no question about it. That's what I see all the time. But the problem we are running into here is actually selection bias because the more experienced surgeons and the better surgeons are probably those who performed surgical ablation, and this may impact the results. So, we have to be careful, and this is why we have in this day and age to push the issue forward to get some more prospective data that are going to control for all those confounders. I think it's an important point.

Dr Pasierski. Thank you. Yes, I agree.

APPENDIX E1. SUPPLEMENTARY METHODS

PSM model for the sensitivity analysis taking into account the exact matching to the type of surgical procedure.

Code

```
.egen surgery=group(isolated CABG isolated
AVR/r isolated MVR/r MVR/rTVR/r)
.logit ablation (varlist sTable1+ isolated CABG
isolated AVR/r isolated MVR/r MVR/rTVR/r)
. predict pscore if e(sample), pr
. gen pscore2=surgery*10+pscore
. bootstrap r(att): psmatch2 ablation,
pscore(pscore2) outcome() neighbor(1) caliper(0.5)
. bootstrap r(att): psmatch2 ablation,
pscore(pscore2) outcome() kernel bw(0.06) caliper(0.5)
. bootstrap r(att): psmatch2 ablation,
pscore(pscore2) outcome() radius caliper(0.5)
. psmatch2 ablation, pscore(pscore2)
outcome() caliper(0.5)
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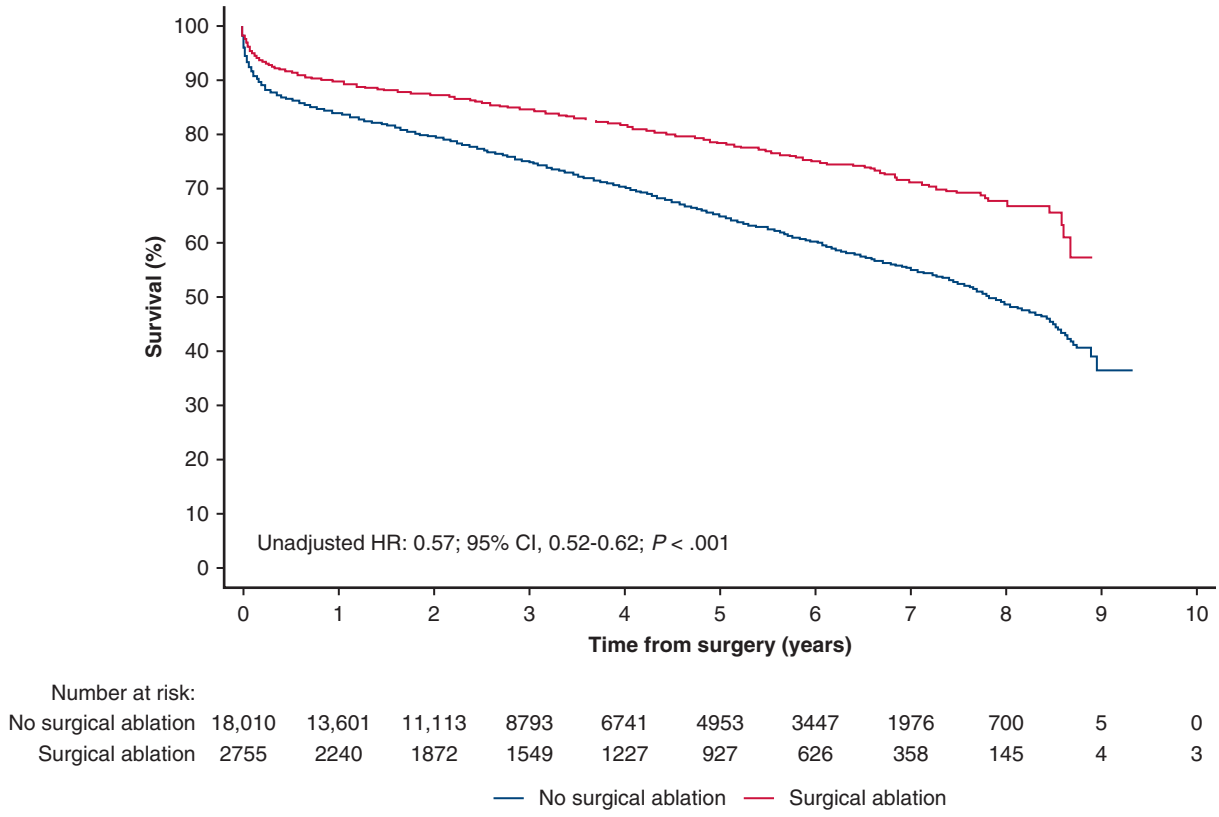

FIGURE E1. Kaplan–Meier survival curves with Cox proportional hazard ratio (*HR*) and 95% CI for the comparison surgical ablation versus no surgical ablation fit before propensity score matching. *CI*, Confidence interval.

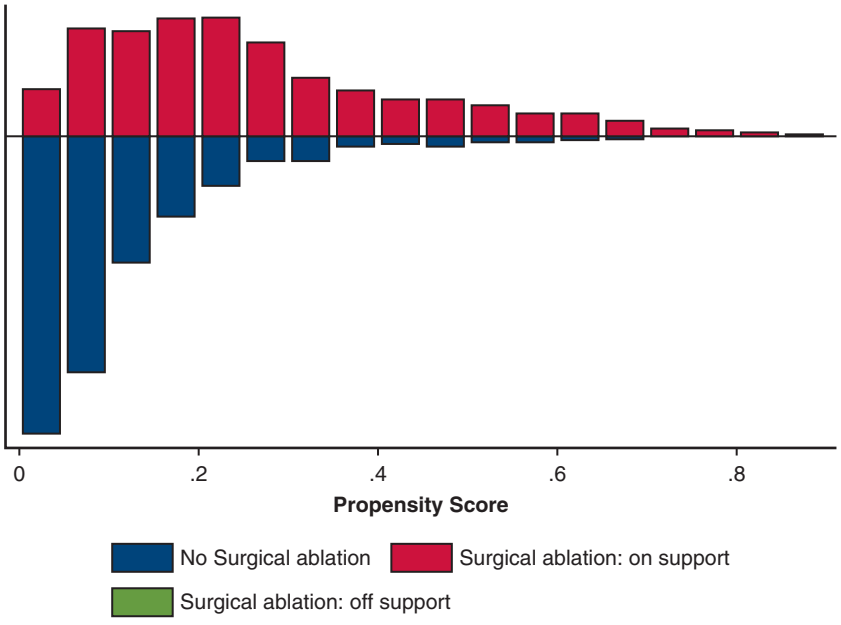

FIGURE E2. Histogram distribution of propensity scores.

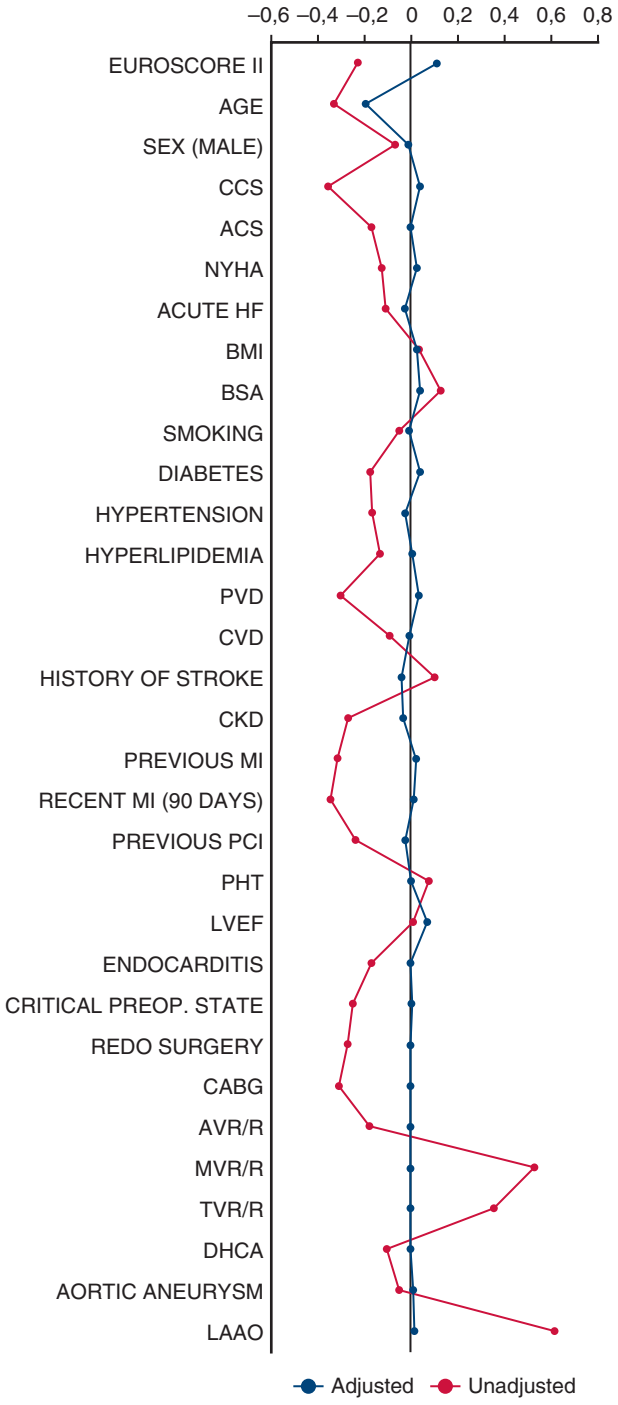

FIGURE E3. Standardized mean difference between propensity score-matching variables in surgical ablation and no surgical ablation subgroups before and after matching. *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *CCS*, Canadian Cardiovascular Society scale; *ACS*, acute coronary syndrome; *NYHA*, New York Heart Association functional classification; *HF*, heart failure; *BMI*, body mass index; *BSA*, body surface area; *PVD*, peripheral vessel disease; *CVD*, cerebrovascular disease; *CKD*, chronic kidney disease; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *PHT*, pulmonary hypertension; *LVEF*, left ventricular ejection fraction; *PREOP*, preoperative; *CABG*, coronary artery bypass grafting; *AVR/R*, aortic valve replacement/repair; *MVR/R*, mitral valve replacement/repair; *TVR/R*, tricuspid valve replacement/repair; *DHCA*, deep hypothermia cardiac arrest; *LAAO*, left atrial appendage occlusion.

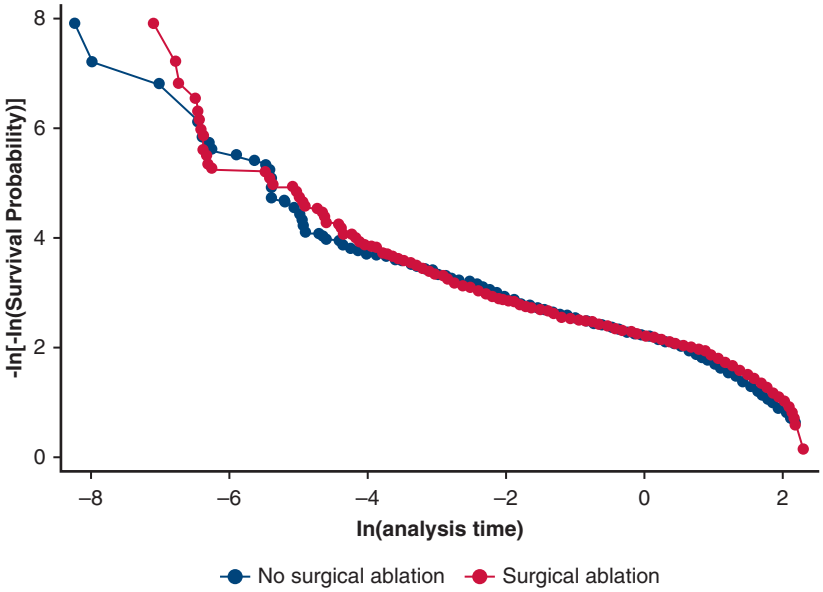

FIGURE E4. Cox model log-log survival probability against analysis time.

TABLE E1. Propensity scores and SMD assessment after matching

Variable	Propensity score				SMD					
	Coefficient (95% CI)	SE	z	*P* value	SA	No SA	Bias, %	*t* test	*P* value	VR
EuroSCORE II	0.025 (0.020-0.031)	0.003	8.73	<.001	4.127	4.327	−2.8	−1.200	.230	1.19
Age	−0.022 (−0.025 to −0.019)	0.002	−14.63	<.001	64.517	64.313	1.6	0.760	.446	1.19
Male sex	−0.152 (−0.223 to −0.081)	0.036	−4.18	<.001	0.594	0.573	4.3	1.560	.119	1.00
ACS	−0.424 (−0.736 to −0.113)	0.159	−2.67	.008	0.003	0.003	0.3	0.240	.808	1.00
NYHA	−0.113 (−0.142 to −0.084)	0.015	−7.54	<.001	2.209	2.247	−4	−1.450	.148	1.11
Acute HF	−0.641 (−1.272 to −0.009)	0.322	−1.99	.047	0.001	0.002	−0.9	−0.820	.414	2.00
BMI	−0.010 (−0.019 to −0.001)	0.004	−2.25	.024	28.588	28.544	0.9	0.340	.735	1.21
BSA	0.566 (0.350-0.782)	0.110	5.13	<.001	1.962	1.956	2.5	0.900	.370	1.20
Smoking	0.019 (−0.033 to 0.071)	0.026	0.72	.47	0.510	0.503	1.4	0.520	.602	1.00
Diabetes	−0.079 (−0.135 to −0.023)	0.028	−2.79	.005	0.273	0.290	−3.8	−1.410	.160	1.04
Hypertension	−0.001 (−0.066 to 0.065)	0.033	−0.01	.991	0.776	0.770	1.5	0.530	.600	1.03
Hyperlipidemia	−0.024 (−0.076 to 0.028)	0.027	−0.92	.358	0.500	0.470	6.1	2.200	.028	1.00
PVD	−0.270 (−0.339 to −0.200)	0.035	−7.63	<.001	0.171	0.176	−1.1	−0.440	.663	1.06
CVD	0.042 (−0.062 to 0.146)	0.053	0.79	.429	0.058	0.065	−2.7	−1.030	.304	0.96
History of stroke	−0.425 (−0.835 to −0.016)	0.209	−2.04	.042	0.003	0.003	0	0.000	1.000	0.79
CKD	−0.153 (−0.208 to −0.098)	0.028	−5.47	<.001	0.497	0.482	3.1	1.100	.272	1.00
Previous MI	−0.138 (−0.211 to −0.064)	0.038	−3.66	<.001	0.138	0.135	0.9	0.360	.719	1.05
Previous PCI	−0.046 (−0.102 to −0.010)	0.029	−1.6	.109	0.286	0.288	−0.4	−0.150	.879	0.98
PHT	−0.086 (−0.149 to −0.023)	0.032	−2.69	.007	0.248	0.275	−6.2	−2.160	.031	1.00
LVEF	−0.000 (−0.000 to 0.000)*	0.000	−0.1	.921	51.394	49.452	0	4.930	<.001	1.83
Endocarditis	−0.902 (−1.139 to −0.666)	0.121	−7.47	<.001	0.008	0.006	1.4	0.820	.410	1.00
Critical preoperative state	−1.053 (−1.315 to −0.792)	0.133	−7.91	<.001	0.008	0.011	−1.6	−1.000	.315	1.05
Redo surgery	−0.797 (−0.930 to −0.664)	0.068	−11.75	<.001	0.023	0.027	−1.9	−0.970	.334	1.02
CABG	−0.113 (−0.181 to −0.045)	0.035	−3.26	.001	0.280	0.249	6.5	2.520	.012	1.00
AVR/r	−0.125 (−0.186 to −0.063)	0.031	−3.99	<.001	0.224	0.215	2	0.760	.445	1.00
MVR/r	0.416 (0.354-0.478)	0.032	13.15	<.001	0.584	0.633	−10.1	−3.640	.000	1.00
TVR/r	0.063 (−0.002 to 0.128)	0.033	1.91	.056	0.344	0.360	−3.6	−1.180	.238	1.00
DHCA	−1.198 (−1.938 to −0.459)	0.377	−3.18	.001	0.001	0.001	−1.2	−1.000	.317	1.00
Aortic aneurysm	−0.107 (−0.225 to 0.011)	0.060	−1.77	.077	0.046	0.039	3.3	1.300	.194	1.04
LAAO	0.915 (0.846-0.985)	0.035	25.85	<.001	0.277	0.246	8.6	2.530	.011	1.02

SMD, Standardized mean difference; *CI*, confidence interval; *SE*, standard error; *SA*, surgical ablation; *VR*, variance ratio; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *ACS*, acute coronary syndrome; *NYHA*, New York Heart Association functional classification; *HF*, heart failure; *BMI*, body mass index; *BSA*, body surface area; *PVD*, peripheral vessel disease; *CVD*, cerebrovascular disease; *CKD*, chronic kidney disease; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *PHT*, pulmonary hypertension; *LVEF*, left ventricular ejection fraction; *CABG*, coronary artery bypass grafting; *AVR/r*, aortic valve replacement/repair; *MVR/r*, mitral valve replacement/repair; *TVR/r*, tricuspid valve replacement/repair; *DHCA*, deep hypothermia cardiac arrest; *LAAO*, left atrial appendage occlusion. *Values are rounded to 2 decimal places from the original: −0.000000137 (−0.00000286 to 0.00000259).

TABLE E2. Baseline characteristics before PS matching

Variable	Surgical ablation (n = 2755)	No surgical ablation (n = 18,010)	*P* value
Age, y	66 (60-71)	69 (63-75)	<.001
Male sex	1627 (59.1)	11,254 (62.5)	.001
EuroSCORE II*	2.74 (1.56-4.81)	2.92 (1.59-5.90)	<.001
<1	337 (12.2)	1742 (9.7)	<.001
1-2	633 (23.0)	4470 (24.8)	.037
2-3	516 (18.8)	3010 (16.7)	.010
3-4	372 (13.5)	2042 (11.3)	.001
4-5	247 (9.0)	1352 (7.5)	.004
5-10	458 (16.7)	3096 (17.2)	.342
>10	192 (7.0)	2298 (5.7)	<.001
Diabetes	749 (27.2)	6329 (35.1)	<.001
Oral hypoglycemic drugs	377 (13.8)	2987 (16.6)	<.001
Insulin with or without oral hypoglycemic drugs	228 (8.3)	2262 (12.6)	<.001
Smoking	1396 (50.7)	9590 (53.2)	.012
Hypertension	2128 (77.4)	15,072 (83.8)	<.001
Hyperlipidemia	1354 (49.3)	10,010 (55.8)	<.001
BMI*	28.3 (25.5-31.3)	28.0 (25.1-31.2)	.033
Pulmonary hypertension	677 (24.6)	3857 (21.4)	<.001
Severe (PA systolic >55 mm Hg)	137 (5.0)	934 (5.2)	.677
Renal impairment	1362 (49.5)	11,283 (62.6)	<.001
Dialysis (regardless of CC)	10 (0.4)	207 (1.1)	<.001
Peripheral artery disease	457 (16.6)	425 (15.5)	.255
Cerebrovascular disease	155 (5.6)	1438 (8.0)	<.001
History of stroke	62 (2.3)	818 (4.5)	<.001
History of TIA	87 (3.2)	602 (3.3)	.648
Carotid intervention	13 (0.5)	108 (.6)	.501
Chronic lung disease	202 (7.3)	1926 (10.7)	<.001
Asthma	133 (4.8)	1059 (5.9)	.035
LVEF, %†*	52 (45-60)	50 (40-58)	<.001
CAD	815 (29.6)	7820 (43.4)	<.001
Previous MI	376 (13.7)	4718 (26.2)	<.001
Previous PCI	850 (30.9)	7611 (42.3)	<.001
NYHA classification			
0	207 (7.5)	974 (5.4)	<.001
I	280 (10.1)	1822 (1.1)	.999
II	1128 (41.0)	7198 (39.9)	.297
III	1038 (37.7)	6498 (36.1)	.085
IV	102 (3.7)	1526 (8.5)	<.001

Data are presented as median (interquartile range) or n (%). *EuroSCORE*, European System for Cardiac Operative Risk Evaluation; *BMI*, body mass index; *PA*, pulmonary artery; *CC*, creatinine clearance; *TIA*, transient ischemic attack; *LVEF*, left ventricular ejection fraction; *CAD*, coronary artery disease; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *NYHA*, New York Heart Association. *Please refer to Table E1 for mean values. †Missing data.

TABLE E3. Operative characteristics before PS matching

Variable	Surgical ablation (n = 2755)	No surgical ablation (n = 18,010)	*P* value
Procedural characteristics			
Redo surgery	62 (2.3)	1477 (8.2)	<.001
IABP	3 (0.1)	154 (0.9)	<.001
I.V. inotropes	31 (1.1)	788 (4.4)	<.001
Preoperative mechanical ventilation	6 (0.2)	283 (1.6)	<.001
Endocarditis	22 (0.8)	561 (3.1)	<.001
Urgency			
Elective	2175 (78.9)	11,530 (64.1)	<.001
Surgery			
CPB time, minutes	132 (102-171)	104 (79-141)	<.001
Crossclamp time, minutes	90 (69-115)	70 (50-96)	<.001
CABG	772 (28.0)	7651 (42.5)	<.001
Mitral valve	1606 (58.3)	5899 (32.8)	<.001
Aortic valve	617 (22.4)	5424 (30.1)	<.001
Tricuspid valve	945 (34.3)	3377 (18.8)	.999
Two valves	912 (33.2)	3188 (17.7)	<.001
Three valves	124 (4.5)	481 (2.7)	<.001
Aortic surgery	129 (4.7)	1179 (6.5)	<.001
Concomitant LAAO	734 (26.6)	925 (5.1)	<.001

Data are presented as median (interquartile range) or n (%). *IABP*, Intra-aortic balloon pump; *I.V.*, intravenous; *CPB*, cardiopulmonary bypass; *CABG*, coronary artery bypass grafting; *LAAO*, left atrial appendage occlusion.

TABLE E4. In-hospital outcomes before PS matching

Variable	Surgical ablation (n = 2755), n (%)	No surgical ablation (n = 18,010), n (%)	Relative risk (IQR)	*P* value
Early postoperative mortality (48 h)	23 (0.8)	448 (2.5)	0.34 (0.22-0.51)	<.001
30-Day mortality	130 (4.7)	1528 (8.5)	0.56 (0.47-0.66)	<.001
Cardiac tamponade and/or rethoracotomy for bleeding	298 (10.8)	1870 (10.4)	1.04 (0.93-1.17)	.468
Periprocedural MI	11 (0.4)	104 (0.6)	0.69 (0.37-1.29)	.272
Respiratory failure	261 (9.5)	1485 (8.2)	1.15 (1.01-1.30)	.032
Prolonged ICU stay (return or >72 h)	810 (29.4)	5333 (29.6)	0.99 (0.93-1.06)	.840
Neurologic complications	73 (2.7)	594 (3.3)	0.80 (0.63-1.02)	.072
Multiorgan failure	88 (3.2)	686 (3.8)	0.84 (0.67-1.04)	.117
Gastrointestinal complications	37 (1.3)	310 (1.7)	0.78 (0.56-1.09)	.427
Acute kidney failure and/or dialysis	129 (4.7)	955 (5.3)	0.88 (0.74-1.06)	.182
Superficial sternal wound infection	39 (1.4)	326 (1.8)	0.78 (0.56-1.09)	.161
Deep sternal wound infection	24 (0.9)	160 (0.9)	0.98 (0.64-1.50)	.928
Mediastinitis	13 (0.5)	94 (0.5)	0.90 (0.51-1.61)	.886
PPI	37 (1.3)	231 (1.3)	1.05 (0.74-1.48)	.786

IQR, Interquartile range; *MI*, myocardial infarction; *ICU*, intensive care unit; *PPI*, permanent pacemaker implantation.

TABLE E5. Univariable and multivariable analysis of factors associated with concomitant surgical ablation

Variable	Univariable		Multivariable		Inconsistency	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	*P* value	VIF
Diabetes	0.70 (0.64-0.75)	<.001	0.83 (0.75-0.91)	<.001	.013	1.03
CKD	0.58 (0.53-0.63)	<.001	0.60 (0.55-0.65)	<.001	.580	1.03
Dialysis	0.31 (0.17-0.59)	<.001	0.56 (0.29-1.05)	.071	–	–
NYHA IV	0.42 (0.33-0.52)	<.001	0.53 (0.43-0.66)	<.001	.149	1.14
Previous MI	0.45 (0.40-0.50)	<.001	0.56 (0.50-0.64)	<.001	.011	1.09
Redo	0.26 (0.20-0.34)	<.001	0.26 (0.20-0.34)	<.001	.999	1.03
IE	0.25 (0.16-0.38)	<.001	0.37 (0.24-0.58)	<.001	.214	1.04
Elective status	2.10 (1.92-2.31)	<.001	1.52 (1.37-1.69)	<.001	<.001	1.28
MV	2.87 (2.65-3.12)	<.001	2.29 (2.08-2.54)	<.001	.001	1.48
AV	0.67 (0.61-0.74)	<.001	0.76 (0.61-0.85)	<.001	.307	1.11
TV	2.26 (2.07-2.47)	<.001	1.27 (1.14-1.41)	<.001	<.001	1.40
Aortic surgery	0.71 (0.59-0.85)	<.001	0.92 (0.77-1.13)	.422	–	–
					Mean VIF	1.16

OR, Odds ratio; *CI*, confidence interval; *VIF*, variance inflation factor; *CKD*, chronic kidney disease; *NYHA*, New York Heart Association functional classification; *MI*, myocardial infarction; *IE*, infective endocarditis; *MV*, mitral valve; *AV*, aortic valve; *TV*, tricuspid valve.