Does ablation of atrial fibrillation at the time of septal myectomy improve survival of patients with obstructive hypertrophic cardiomyopathy?

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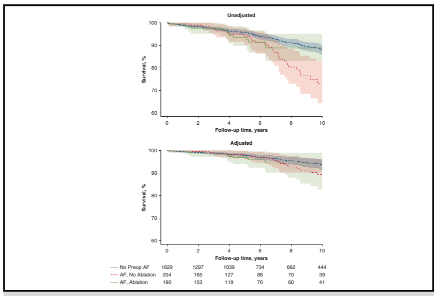
ABSTRACT

Objective: To evaluate the outcomes after septal myectomy in patients with obstructive hypertrophic cardiomyopathy according to atrial fibrillation and surgical ablation of atrial fibrillation.

Methods: We reviewed patients with obstructive hypertrophic cardiomyopathy who underwent septal myectomy at the Mayo Clinic from 2001 to 2016. History of atrial fibrillation was obtained from patient histories and electrocardiograms. All-cause mortality was the primary end point.

Results: A total of 2023 patients underwent septal myectomy, of whom 394 (19.5%) had at least 1 episode of atrial fibrillation preoperatively. Among patients with atrial fibrillation, 76 (19.3%) had only 1 known episode, 278 (70.6%) had recurrent paroxysmal atrial fibrillation, and 40 (10.2%) had persistent atrial fibrillation. Surgical ablation was performed in 190 patients at the time of septal myectomy, including 148 with pulmonary vein isolation and 42 with the classic maze procedure. Among all patients, operative mortality was 0.4%, and there were no early deaths in patients undergoing surgical ablation. Over a median follow-up of 5.6 years, patients with preoperative atrial fibrillation had increased mortality (hazard ratio, 1.36; 95% confidence interval, 0.97-1.91; $P = .070$) after multivariable adjustment for comorbidities. When considering the impact of atrial fibrillation with or without surgical treatment, the adjusted hazard ratio for mortality in patients undergoing ablation compared with no ablation was 0.93 (95% confidence interval, 0.52-1.69; $P = .824$).

Conclusions: Atrial fibrillation is present preoperatively in one-fifth of patients with obstructive hypertrophic cardiomyopathy undergoing myectomy and showed a trend toward higher all-cause mortality. Survival of patients undergoing septal myectomy with preoperative atrial fibrillation was similar between those who did and did not receive concomitant surgical ablation. (J Thorac Cardiovasc Surg 2021;161:997-1006)



Impact of surgical ablation of AF on the survival of patients with HOCM undergoing septal myectomy.

CENTRAL MESSAGE

Preoperative AF showed modestly reduced survival among patients with obstructive HCM undergoing septal myectomy. Concomitant surgical ablation of AF appears to be associated with improved survival.

PERSPECTIVE

AF should be treated at the time of septal myectomy in patients with obstructive HCM. Future studies may focus on the long-term freedom from AF recurrence after surgical ablation and surgical and postoperative strategies to prevent recurrent AF.

See Commentaries on pages 1007 and 1008.

Atrial fibrillation (AF) is a common arrhythmia in patients with hypertrophic cardiomyopathy (HCM) and has been reported to have a prevalence of approximately 20%.[1,2] In patients with HCM, AF has been associated with reduced exercise capacity and thromboembolic events.[3-5] However, the impact of AF on the survival of patients with HCM is controversial. In a study of more than 3000 patients, Siontis and colleagues[1] found a strong association of AF and overall mortality with annual mortality rates of 6.9% and 4.4% in the AF and non-AF groups, respectively; this

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Abbreviations and Acronyms

- AF = atrial fibrillation
- CI = confidence interval
- HCM = hypertrophic cardiomyopathy
- HR = hazard ratio
- IQR = interquartile range
- LA = left atrium
- LV = left ventricle
- OR = odds ratio
- PVI = pulmonary vein isolation

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association was independent of age and sex (hazard ratio [HR], 1.49; $P < .001$).[1] In contrast, Rowin and colleagues[2] reported that AF in patients with HCM is an important risk factor for stroke but is an uncommon primary cause of death. The question of whether AF affects survival is important to surgeons because it may influence the decision to perform a concomitant surgical ablation.

Transcatheter ablation for AF in patients with HCM is reported to have a higher risk of relapse compared with that in patients without HCM.[6-8] In contrast, patients undergoing surgical ablation at the time of septal myectomy have demonstrated good results in regard to rhythm control with 80% of patients being free of AF 2 to 5 years postoperatively.[9,10] Enthusiasm for concomitant AF ablation in patients with obstructive HCM should be balanced against possible risks, as one study reported an operative mortality of 6% in patients undergoing the combined procedures.[9] Furthermore, mitral valve regurgitation is an additional risk factor for the development of AF. After myectomy, mitral valve regurgitation is significantly improved and studies have demonstrated left atrial (LA) reverse remodeling,[11,12] which may reduce the late risk of arrhythmia. The need for surgical ablation and its benefit on subsequent survival have not been well studied.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of the Mayo Clinic. We reviewed 2023 patients with obstructive HCM who underwent septal myectomy at the Mayo Clinic from 2001 to 2016 (Figure E1). The primary operation in all patients was transaortic septal myectomy. Clinical information, including history and preoperative examination, was reviewed to determine if the patients had a history of AF. Classification of AF was made according to the latest American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines.[13] Continuous AF sustained more than 7 days was classified as persistent AF. AF terminating spontaneously or with intervention within 7 days of onset was defined as paroxysmal AF. Surgical notes were reviewed to document any ablative procedures performed for AF. Patients were also analyzed after stratification based on concomitant procedures during myectomy other than AF ablation and exclusion of the left atrial appendage. Newly developed or recurrent AF episodes lasting more than 1 hour within 30 days after myectomy were considered to be early postoperative AF, a definition consistent with the Society of Thoracic Surgeons database. This database definition was used for analysis that differs from the definition of early recurrence of AF by the Heart Rhythm Society. Early mortality was all-cause death within 30 days after operation.

Morphologic parameters were obtained from preoperative transthoracic echocardiography. Because the techniques for calculation of LA volume have changed over time, a correction factor was applied to some of the LA volume index values using the corresponding reference ranges. Whereas 81% of these measurements were based on the same technique (reference range, 16-28 mL/m^2) and unchanged for analysis, the remaining values (composed of 5 techniques) were adjusted to approximate a reference range centered at 22 mL/m^2. Septal thickness was obtained at end diastole.

TABLE 1. Baseline characteristics of patients undergoing septal myectomy for obstructive hypertrophic cardiomyopathy

Parameters	N	% Missing	Value
Age	2023	0%	56.1 (45.3-65.6)
Male	2023	0%	1138 (56.3%)
BSA (m^2)	2014	0.4%	2.02 (1.83-2.19)
BMI (kg/m^2)	2014	0.4%	30.3 (26.8-34.5)
Septal thickness (mm)	1966	2.8%	18 (14-21)
LV mass index (g/m^2)	1931	4.5%	146.8 (120.0-181.5)
LA volume index (mL/m^2)	1928	4.7%	48 (38-60)
History of AF	2023	0%	394 (19.5%)
Persistent AF			40 (10.2%)
Recurrent paroxysmal AF			278 (70.6%)
Single episode of paroxysmal AF			76 (19.3%)
Prior ablation of AF			32 (8.1%)
Concomitant ablation of AF (/AF patients)			190 (48.2%)
LAA ligation or amputation (/AF patients)			147 (37.3%)
Other concomitant procedures	2023	0%	509 (25.2%)
MV repair			130 (25.5%)
MV replacement			40 (7.9%)
CABG			172 (33.8%)
Crossclamp time (min)	2013	0.5%	25 (15-38)
CPB time (min)	2013	0.5%	34 (23-50)
AF in postoperative 30 d	2023	0%	542 (26.8%)

Values are reported as n (%) for discrete variables and median (IQR) for continuous variables. *BSA*, Body surface area; *BMI*, body mass index; *LV*, left ventricle; *LA*, left atrium; *AF*, atrial fibrillation; *LAA*, left atrial appendage; *MV*, mitral valve; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass.

TABLE 2. Baseline characteristics of patients stratified by atrial fibrillation and ablation

Parameters	No AF (n = 1629)	AF, with ablation (n = 190)	AF, no ablation (n = 204)
Age (y)	55.3 (44.4-65.2)	57.0 (49.5-65.2)	60.5 (49.7-69.0)
Male	896 (55.0%)	127 (66.8%)	115 (56.4%)
Septal thickness (mm)	18 (14-21)	18 (15-22)	18 (15-21)
LA volume index (mL/m^2)	45.0 (36.8-56.0)	60.0 (47.0-76.0)	53.0 (41.0-66.0)
Classification of AF			
Single paroxysmal AF	-	12 (6.3%)	64 (31.4%)
Recurrent paroxysmal AF	-	146 (76.8%)	132 (64.7%)
Persistent AF	-	32 (16.8%)	8 (3.9%)
Prior ablation	-	19 (10.0%)	13 (6.4%)
Concomitant procedure	400 (24.6%)	51 (26.8%)	58 (28.4%)
MV operation	131 (8.0%)	23 (12.1%)	17 (8.3%)
Crossclamp time (min)	24.0 (15.0-36.0)	35.0 (20.0-48.0)	24.0 (15.0-39.0)
CPB time (min)	33.0 (23.0-47.0)	47.5 (35.0-72.0)	33.0 (23.0-50.0)
Postoperative AF	454 (27.9%)	41 (21.6%)	47 (23.0%)

Values are reported as n (%) for discrete variables and median (IQR) for continuous variables. *AF*, Atrial fibrillation; *LA*, left atrium; *MV*, mitral valve; *CPB*, cardiopulmonary bypass.

Vital status was determined using LexisNexis Accurint (New York City, NY), which links data from a number of sources including the Social Security Death Master File and state death records. If death from any cause was identified in these records, the reported death date was used. Otherwise, patients were considered to be alive and were censored 2 weeks before the date their vital status was searched. In the present study, all-cause mortality was analyzed as the primary outcome. The planned primary comparison was the survival difference between patients with and without preoperative AF. Further subgroup analysis was conducted to determine the impact of ablation procedure on survival, difference between Cox-maze operation and pulmonary vein isolation (PVI), and impact of early postoperative AF on long-term survival.

Continuous variables are reported as median (interquartile range [IQR]), and discrete variables are reported as number (%) in descriptive analyses stratified by AF groups. Corresponding statistical tests for assessing the unadjusted association between baseline characteristics and AF group were based on Kruskal–Wallis tests and Pearson chi-square tests. For the comparison of LA volume index between AF groups, the raw measurements were analyzed using a stratified proportional odds logistic model to adjust for variation across techniques. The model estimates the relative difference (odds ratio) between AF groups separately within each stratum to derive an overall effect by pooling estimates over the 6 techniques. Unadjusted survival curves for preoperative AF groups were analyzed with Kaplan–Meier estimates. To construct risk-adjusted survival curves, multivariable Cox proportional hazard (PH) models were fitted by stratifying on AF group, thereby avoiding assumption of PH for this effect, and by adjusting for relevant baseline covariates (Tables E1 and E2). Formal testing to assess differences in unadjusted and adjusted survival curves was done using univariable and multivariable Cox PH regression, with AF group as the primary independent variable. For all regression analyses, multiple imputation was used to predict infrequently missing covariates (no variable was missing more than 5%) from the other baseline variables and survival outcome. We used the R function aregImpute in the Hmisc package, with additive regression and predictive mean matching, to generate 10 imputed datasets on which the Cox survival models were fitted. Final analysis results were pooled by averaging these regression estimates and using bootstrapping to correct the standard errors for uncertainty. Assumptions of PH from the fitted models were verified globally for the set of predictors as well as individually for the AF grouping variable using Schoenfeld residual plots and tests. Statistical analyses were performed with SAS (version 9.4; SAS Institute Inc, Cary, NC) and the rms, Hmisc, and survminer packages in R (version 3.6; R Foundation, Vienna, Austria). No correction for multiple comparisons was made when analyzing differences in more than 2 groups.

RESULTS

Baseline Characteristics

As shown in Table 1, the median age of the 2023 study patients was 56.1 years (IQR, 45.3-65.6) and 1138 (56.3%) of them were male. A history of AF was recorded in 394 patients (19.5%); of these, the arrhythmia was persistent in 40 patients (10.2%) and paroxysmal in 354 patients (89.8%). More specifically, 76 patients (19.3%) with paroxysmal AF had only 1 known episode of AF before septal myectomy. Before the operation, a total of 32 patients (8.1%) with AF had prior transcatheter or surgical ablation of the arrhythmia, including 27 patients (7.6%) with paroxysmal AF and 5 patients (12.5%) with persistent AF.

Compared with patients without preoperative AF, patients with AF were older (58.5 [49.5-67.3] years vs 55.3 [44.4-65.2] years, $P < .001$), were more likely to be male (61.4% vs 55.0%, $P = .021$), and had higher values of LA volume index ($P < .001$) (Table E3). In particular, there was a 3-fold increased odds of higher LA volume index for patients with AF (odds ratio [OR], 3.09; 95% confidence interval [CI], 2.51-3.79; $P < .001$). An increased LA index was also associated with classification of AF. Compared with patients with a single episode of AF preoperatively, the odds of higher LA volume index did not differ significantly for patients with recurrent paroxysmal episodes (OR, 1.44; 95% CI, 0.90-2.29; $P = .126$), but was markedly increased for patients with persistent AF (OR, 9.46; 95% CI, 4.55-19.69; $P < .001$).

Surgical Ablation

At the time of septal myectomy, 190 patients underwent surgical ablation of AF, and 147 patients had concomitant ligation or amputation of the left atrial appendage. There were significantly increased odds of higher LA volume index for both AF subgroups with ablation (OR, 4.48; 95% CI, 3.39-5.91; $P < .001$) and without ablation (OR, 2.16; 95% CI, 1.64-2.83; $P < .001$) relative to the group with no AF, as well as increased odds of higher LA volume index for patients with AF with ablation compared with no ablation (OR, 2.07; 95% CI, 1.44-2.99; $P < .001$). Also, compared with those with AF but no ablation, patients who had surgical AF ablation were more likely to have persistent AF (16.8% vs 3.9%) and less likely to have single paroxysmal AF (6.3% vs 31.4%; overall $P < .001$) (Table 2).

There were 8 (0.4%) deaths early (<30 days) after myectomy. Only 1 of them had AF preoperatively, and this patient did not undergo surgical ablation. Early postoperative AF occurred in 542 patients (26.8%), including 454 patients without preexisting AF. Four of the 8 patients who died early experienced postoperative AF.

Among patients with only 1 episode of AF, ablation at the time of myectomy was performed in 12 (15.8%); in those with recurrent paroxysmal AF, ablation was performed in 146 (52.5%). Among patients with persistent AF, ablation was performed in 32 (80.8%). Ablation procedures included bilateral PVI in 148 patients (13 patients with persistent AF) and cut-and-sew maze procedures in 42 patients (19 patients with persistent AF) (Table E3). Although patients undergoing the standard maze procedure more often had persistent AF (45.2% vs 8.8%, $P < .001$), they also showed a trend toward lower rates of early AF recurrence (11.9% vs 24.3%, $P = .084$).

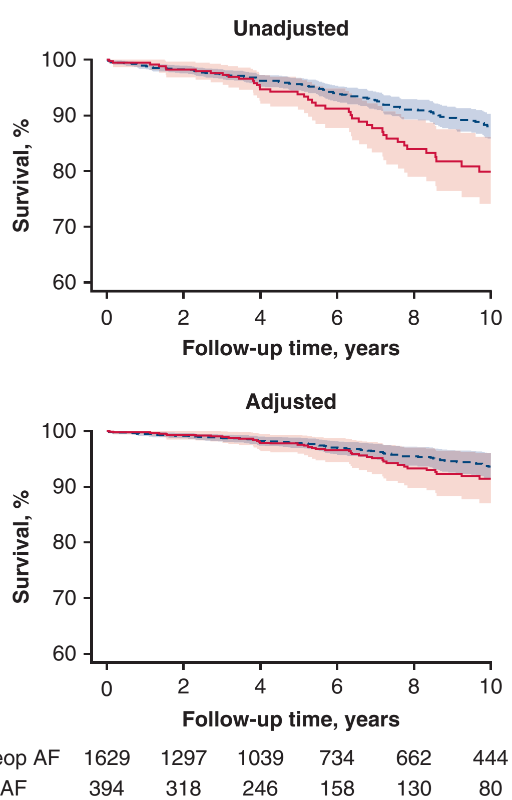


FIGURE 1. Survival of 2023 patients undergoing septal myectomy with and without preoperative AF. Patients with preoperative AF had marginally reduced survival (HR, 1.36; 95% CI, 0.97-1.91; $P = .070$) following septal myectomy after adjustment for comorbidities. *AF*, Atrial fibrillation.

Long-Term Survival

All-cause mortality was evaluated over a median (IQR) follow-up of 5.6 (3.0-10.5) years. To assess survival differences among AF groups adjusting for age, sex, body mass index, septal thickness, left ventricular mass index, posterior wall thickness, New York Heart Association class, surgery year, and concomitant procedures, multivariable Cox models were performed on all available patients using multiple imputation (Tables E1 and E2). As shown in Figure 1, when controlling for these factors, patients with preexisting AF had modestly worse survival (HR, 1.36; 95% CI, 0.97-1.91; $P = .070$). Interestingly, there was little separation of these survival curves through the first 5 years after myectomy. To evaluate survival according to AF and surgical ablation in the total cohort, patients in the AF group were further divided into "AF, with ablation" or "AF, no ablation" groups. Compared with patients without preexisting AF, neither patients who underwent surgical ablation of AF (HR, 1.31; 95% CI, 0.79-2.15; $P = .291$) nor patients with unablated AF (HR, 1.40; 95% CI, 0.94-2.09; $P = .102$) showed statistically significant differences in survival in the risk-adjusted analysis (Figure 2). The adjusted HR for mortality in patients undergoing ablation compared with those patients with preoperative AF who did not have concomitant surgical ablation was 0.93 (95% CI, 0.52-1.69; $P = .824$). There were also no differences in survival between patients with paroxysmal AF and persistent AF ($P = .941$). A subgroup analysis of the 190 patients who underwent ablation showed equivocal effects of procedure type on unadjusted survival (maze vs PVI: HR, 0.37; 95% CI, 0.10-1.33; $P = .127$) (Figure 3, Table E4).

The incidence of new-onset AF in patients without preexisting AF was higher than the early recurrence of preexisting AF (27.9% vs 22.3%, $P = .026$). Early recurrence of AF (n = 88/394) was similar in ablation and nonablation groups (21.6% vs 23.0%, $P = .728$) and was not univariately associated with long-term survival (HR, 0.59; 95% CI, 0.21-1.67; $P = .322$). Subgroup analysis of 1629 patients without preoperative AF showed associations of older age, thinner septa, and greater posterior wall thickness with development of early new-onset AF (Table 3). Moreover, patients with early new-onset AF had a higher degree of atrial enlargement and more mitral valve procedures. After adjusting for baseline

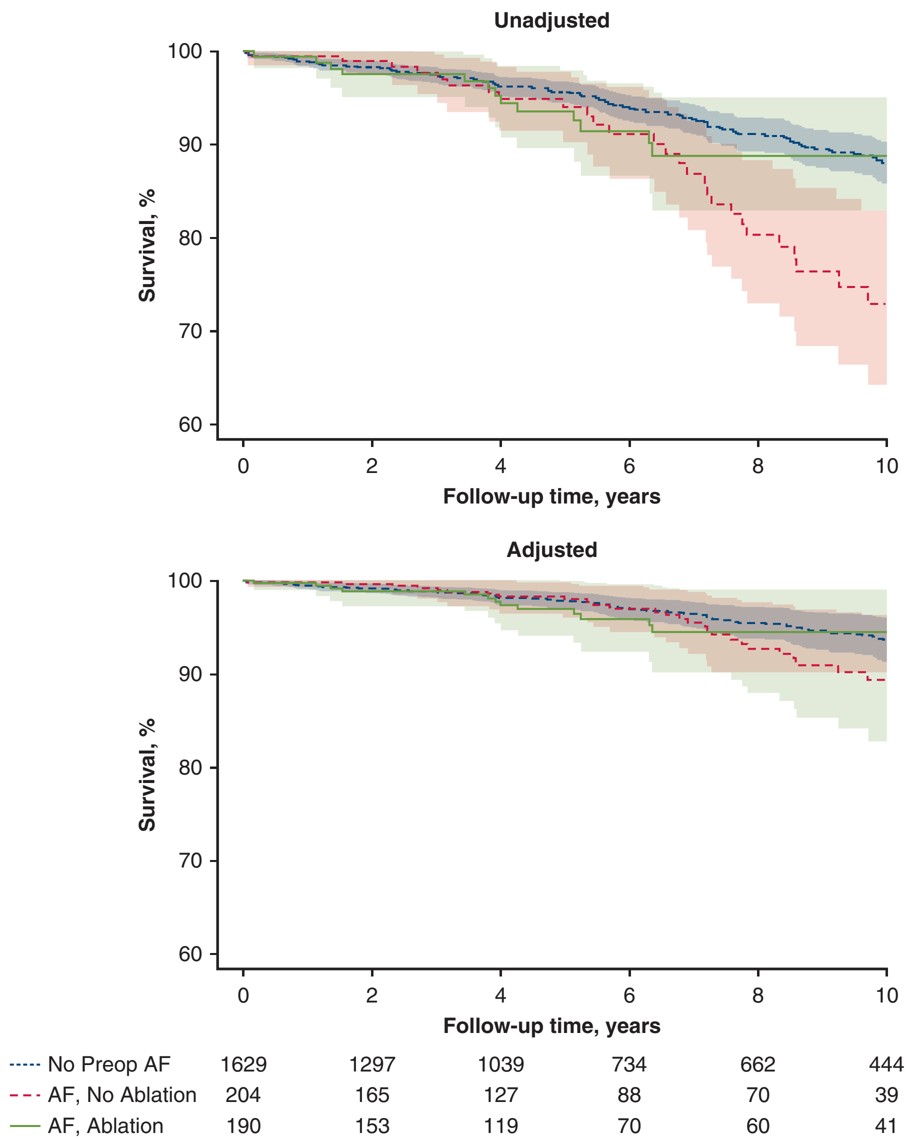


FIGURE 2. Survival according to both AF and concomitant surgical ablation at the time of septal myectomy. After adjustment for multiple comorbidities, long-term survival in patients who underwent surgical ablation of AF (HR, 1.31; 95% CI, 0.79-2.15; $P = .291$) did not differ significantly from those without preexisting AF, whereas unablated AF trended toward significantly worse survival (HR, 1.40; 95% CI, 0.94-2.09; $P = .102$). *AF*, Atrial fibrillation.

characteristics, Cox regression analysis showed no significant association of early new-onset AF with long-term survival (HR, 1.28; 95% CI, 0.89-1.84; $P = .180$) (Figure 4).

DISCUSSION

In the present study, the prevalence of AF and results of surgical ablation were investigated in a large cohort of patients with obstructive HCM undergoing septal myectomy. AF is a common arrhythmia associated with HCM, reported in approximately 20% of patients, but its effect on survival is controversial.[1,2] The etiology of AF in HCM may be due to impaired diastolic function, left atrial hypertension/enlargement, and intrinsic atrial fibrosis.[14] In the setting of obstructive HCM, mitral valve regurgitation mediated by systolic anterior motion of the valve leaflets likely increases the risk of developing AF.

The prevalence of AF in our study cohort with obstructive HCM was similar to data from the general population of patients with HCM.[1,2] Siontis and associates[1] reported that among patients evaluated in a specialized HCM center, AF was present in 16% of patients with obstructive HCM and 22% of patients with nonobstructive HCM.[1] In the present surgical cohort, AF was recorded in 19.5% of patients. It is possible that atrial arrhythmias may trigger symptoms in patients with both obstructive and nonobstructive HCM, leading to evaluation.

Increased LA size is an important substrate for AF in patients with HCM. Papavassiliu and associates[14] found that

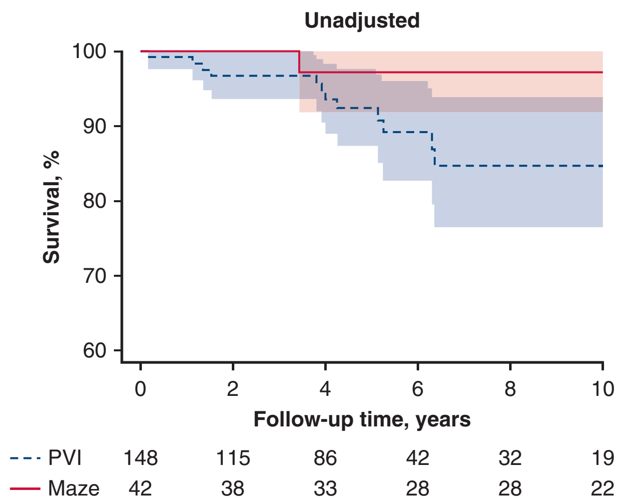


FIGURE 3. Survival of 190 ablated patients undergoing PVI or Cox-maze procedure. The analysis shows an unadjusted HR of 0.37 (95% CI, 0.10-1.33; P = .127) for patients undergoing Cox-maze procedure (vs PVI). *PVI*, Pulmonary vein isolation.

in patients with HCM, LA enlargement was the strongest determinant of AF prevalence and was related to the extent of late gadolinium enhancement in the LV, irrespective of LV mass.[15] Furthermore, McCready and colleagues[15] reported that greater LA size was the only independent risk factor for recurrence of AF in patients with HCM undergoing catheter ablation.[14,15] In our patients, preoperative AF was associated with enlarged LA size but was also associated with older age and male gender. Because chronic mitral valve regurgitation may contribute to enlargement of the LA in patients with obstructive HCM, early myectomy to eliminate systolic anterior motion and associated mitral valve leakage may mitigate the progression of LA enlargement and thereby reduce the risk of AF.[16]

Although 19.5% of our study cohort had AF before myectomy, not all patients underwent surgical ablation at the time of myectomy. The arrhythmia was paroxysmal in approximately 90%, and among these patients, 20% had only 1 episode before operation. In some patients, AF was well controlled medically before myectomy, whereas others had undergone successful catheter ablation.[17] We have generally reserved concomitant surgical ablation for patients who are highly symptomatic with the arrhythmia preoperatively, those with persistent AF, and patients with AF and a history of embolic stroke or inability to maintain chronic anticoagulation. This study includes patients who underwent surgery from 2001 to 2016, and our understanding of AF and the practice of surgical ablation have changed considerably. Use of PVI for persistent AF was performed in some patients in the earlier era, but we now prefer the Cox-maze III procedure for persistent AF and high-burden paroxysmal AF. Survival of patients undergoing the Cox-maze procedure appears to be more favorable than survival of patients having PVI in unadjusted analysis, but it should be noted that the number of patients available for this comparison is relatively small, and the difference was not statistically significant. Additionally, this analysis did not control for potential confounding factors, and we did not collect information on subsequent treatment. PVI with left atrial appendage amputation remains our preferred procedure for those with paroxysmal AF and low AF burden. We generally withhold surgical ablation for patients who have only 1 or 2 episodes of AF that resolve spontaneously and are well tolerated.

In this cohort, there were no early deaths after AF ablation at the time of septal myectomy. These findings support the safety of the procedure as reported in other smaller cohorts of patients undergoing septal myectomy.[9,10,18] Therefore, the major considerations for concomitant surgical ablation of AF are the long-term success in arrhythmia control and potential impact on late survival, which may be affected by thromboembolic stroke related to the arrhythmia. The present study provides new information

TABLE 3. Characteristics of 1629 patients without preoperative atrial fibrillation according to postoperative atrial fibrillation status

Parameters	No postoperative AF (n = 1175)	Postoperative AF (n = 454)	*P* value
Age (y)	52.0 (41.2-62.9)	62.5 (53.8-68.9)	<.001
Male	631 (53.7%)	265 (58.4%)	.090
BSA (m^2)	2.01 (1.82-2.18)	2.02 (1.84-2.19)	.213
BMI (kg/m^2)	30.2 (26.6-34.4)	30.5 (27.2-34.9)	.151
Septal thickness (mm)	18 (14-21)	17 (14-20)	.027
PW thickness (mm)	13 (11-15)	13 (12-15)	.014
LA volume index (mL/m^2)	44.0 (36.0-54.3)	46.7 (37.8-60.0)	<.001*
Concomitant procedure	258 (22.0%)	142 (31.3%)	<.001
MV operation	77 (6.6%)	54 (11.9%)	<.001

For discrete and continuous variables, respectively, values are reported as n (%) and median (IQR), and *P* value is by Pearson chi-square test or Kruskal–Wallis test unless indicated otherwise. *AF*, Atrial fibrillation; *BSA*, body surface area; *BMI*, body mass index; *PW*, posterior wall; *LA*, left atrium; *MV*, mitral valve. **P* value is from a stratified proportional odds ordinal logistic regression model to adjust for variation across measurement techniques.

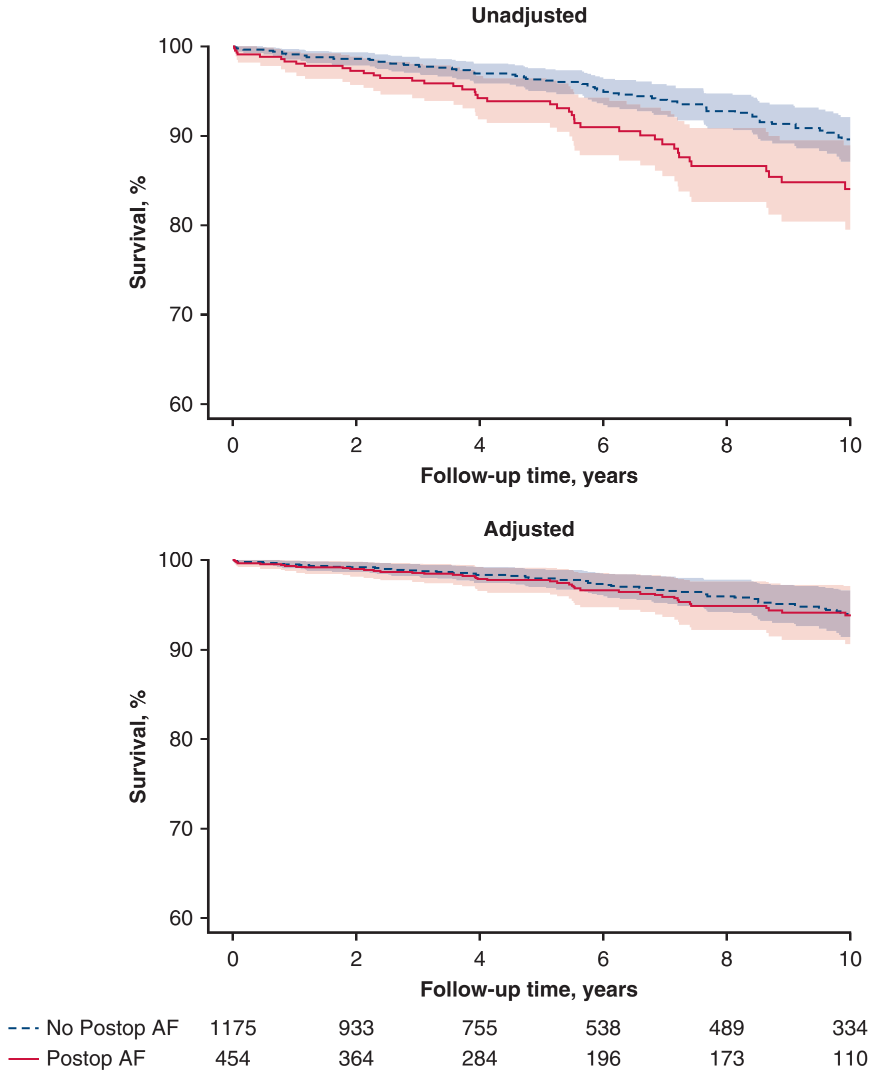


FIGURE 4. Impact of early postoperative AF on survival in 1629 patients who had no preoperative AF. Early postoperative AF shows no impact on survival after adjustment for comorbidities (HR, 1.28; 95% CI, 0.89-1.84; $P = .180$). *AF*, Atrial fibrillation.

on the impact of preoperative AF on patient survival after septal myectomy. Compared with patients without preexisting AF, patients with preoperative AF had reduced long-term survival ($P = .07$); the survival of patients without preoperative AF and those with concomitant surgical ablation was similar. Reduced mitral valve regurgitation[11] and associated remodeling of the LA[12] after myectomy may not be sufficient to prevent the deleterious impact of AF. The improved survival of patients undergoing myectomy and AF ablation is consistent with the findings regarding concomitant surgical ablation at the time of many other cardiac operations.[19] Our data support the latest Society of Thoracic Surgeons clinical practice guidelines for the surgical treatment of AF.[20] However, it is important to note the survival differences did not appear until the fifth year postoperatively, which has practical implications for the design of future surgical AF ablation studies.

In this cohort, we routinely performed PVI procedures for patients with preoperative paroxysmal AF and reserved the standard maze procedure (cut and sew) for those with a high burden of AF. In our opinion, PVI may produce less injury to the atrium and may better preserve atrial function compared with the standard maze procedure as described by Cox and colleagues.[21] However, our experience shows the standard maze procedure as a concomitant operation yields the best results with regard to rhythm control.[22] In the present study, we did not have sufficient follow-up of patients' rhythm. However, it is interesting to note that unadjusted survival after AF ablation showed equivocal effects of procedure type, but the magnitude and direction of this effect seemed to favor the maze procedure over PVI (HR, 0.37; $P = .127$). Further studies are needed to establish the optimal lesion sets and techniques for surgical ablation of HCM-related AF.

ADULT

In this cohort, the incidence of new-onset AF during the first 30 days postoperatively was similar to that in patients undergoing other cardiovascular surgery.[23] The impact of new-onset AF on later survival after cardiovascular surgery has been controversial. In patients undergoing coronary artery bypass grafting, new-onset AF also increases short- and long-term mortality.[24] A smaller study of patients with HCM undergoing septal myectomy suggested that perioperative AF increased short-term composite end point events.[25] In the present study, neither new-onset AF nor early recurrent AF affected early and late outcomes. Early postmyectomy AF is likely a temporary surgical complication and has minimal influence on later mortality.

Study Limitations

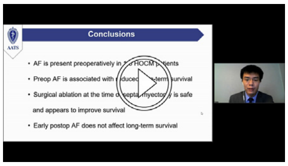
The present study was limited by the number of patients with AF, which made it difficult to detect possible differences in survival in some subgroup analyses. Lack of follow-up data on rhythm maintenance also limited the evaluation of surgical ablation. Moreover, the effect of later transcatheter ablation was not able to be excluded, which might improve the survival of patients who did not undergo surgical ablation.

CONCLUSIONS

The prevalence of preoperative AF in patients with obstructive HCM is 19.5%. After myectomy, risk of death was increased in patients with preoperative AF (HR, 1.36; $P = .07$), but survival of patients receiving concomitant AF ablation with septal myectomy did not differ significantly from patients without preoperative AF.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/20AM/Presentations/Does%20Ablation%20of%20Atrial%20Fibrillation.mp4.



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: atrial fibrillation, hypertrophic cardiomyopathy, septal myectomy, surgical ablation

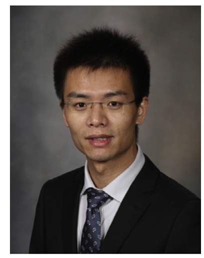
Discussion

Presenter: Dr Hao Cui

Dr Nicholas G. Smedira *(Cleveland, Ohio)*. Presented today is a series of approximately 2000 patients undergoing myectomy and some form of ablation for AF. Dr Cui correctly points out that the impact of AF on the long-term survival of patients with HCM and hypertrophic obstructive cardiomyopathy is unclear, and there's little doubt for those of us who commonly treat these patients that AF definitively impacts their quality of life and need to access medical care. As he also noted, it's prevalent—as many as 1 in 5 patients will develop AF over their lifetime. It's easy to understand how a rapid and irregular heart rate is deleterious to patients with left ventricular outflow tract obstruction or diastolic dysfunction. Noteworthy is the authors show really outstanding surgical results.

One of the major challenges we faced interpreting reviews of interventions for AF is that the guideline definitions of AF that are generated by the various societies, which were appropriately used to classify the patients in this study, do not consistently reflect clinical AF burden. As an example, in your article, 10% of patients undergoing surgical ablation had a prior ablation procedure. Conversely, 6.4% of patients not having a surgical ablation at the time of the myectomy had a prior ablation.

I often think of needing a catheter ablation as reflecting a greater AF burden, but if it cures the patient of AF and you see the patient in the setting of outflow tract obstruction and they have not had AF in let's say 18 months, are they cured of their AF? From this article, I cannot tell what the timeframe was for identifying when the patient had their last AF episode. Could you clarify whether a patient could have had an ablation and no recurrence and still be included in this study?



Dr Hao Cui *(Rochester, Minn)*. Yes. Generally, we include all of the patients with a history of AF in the AF group. They include even those patients who had a prior catheter ablation, although we're not sure if the patients are really free from AF.

Regarding the surgical treatment, usually we decide on the basis of recent episodes of AF. If the patient had a transcatheter ablation 3 years ago and this patient has had no recurrences of AF, usually we don't perform ablation on this patient. If the patient had a prior ablation and then has recurrent episodes, we usually perform a surgical ablation for this patient.

Dr Smedira. So, if I understand correctly, if they don't have recurrence, you would not perform an ablation at the time of myectomy?

Dr Cui. No.

Dr Smedira. Okay. In your article, there's no mention of antiarrhythmic medications as a risk factor and they were not included in your in your analysis. It's my impression that the presence of some of these medications, many of them toxic—amiodarone or Tikosyn—is a reflection of the AF burden, and often patients want to come off those medications as part of the desire to have a surgical ablation. Did you look at the use of these medications? Do you think it would have been helpful in your analysis?

Dr Cui. Yes, I think using the medications would be useful in analysis, but unfortunately, we don't have this data.

Dr Smedira. Survival for patients with AF in your study was worse than for patients without AF. Survival tends to improve to the point of approaching the survival curves of patients without AF only for patients undergoing a cut-and-sew maze procedure, but not PVI. I'm trying to determine why a cut-and-sew is so advantageous. Do you have any data on whether your patients remained in sinus rhythm after the cut-and-sew procedure? Is it obtaining sinus rhythm that's important to the survival advantage? The reason I ask that is that in Rowin and colleagues' article that you quoted out of New York, 36% of their patients at 8 years had symptomatic recurrence, and we have an article that we hope will be published soon in which I looked at my cut-and-sew maze experience, and we had a 50% rate of AF recurrence at 8 years. Do you know what rhythm the patients were in when you did the analysis?

Dr Cui. No, we don't have the rhythm follow-up in this study, because usually they need consecutive 72-hour monitoring of the heart rhythm, and for that reason, we were unable to do such follow-up. Regarding the maze and PVI, we are not clear if there's any difference in the rhythm control.

Dr Smedira. One interesting aspect of Rowin and colleagues' article, when they looked at the natural history of AF in these patients, was that the cause of death in the few patients who died was thromboemboli, specifically cerebral thromboemboli. We know one of the distinct advantages of the cut-and-sew maze procedure is the elimination of the left atrial appendage. Do you have any information on the cause of death? When you did the exclusion of the left atrial appendage in the PVI, was that with a clip or did you over-sew internally inside the LA? We know that oversewing may be associated with recurrence of opening of the LA and increase thromboemboli.

Dr Cui. Yes. I think from Rowin and colleagues' article, embolic events may be the major cause of death in patients with AF. We don't have the cause of death in this study. With the left atrial appendage, from the recent decade, we usually use amputation rather than ligation.

Dr Smedira. Okay, so it's unlikely that was the oversewing. My last question is, have you continued to use the cut-and-sew or have you migrated to the Cox-maze IV, and would you recommend that surgeons should use a cut-and-sew in the HCM patient population?

Dr Cui. In our clinic, we prefer Cox-maze III, the cut-and-sew technique. We think that the cut-and-sew technique may have more reliable transmurality. An important consideration for choosing the cut-and-sew technique or other energy source for ablation is the crossclamp time added to the septal myectomy. In this study, in patients undergoing isolated septal myectomy plus Cox-maze III procedure, the average crossclamp time is 47 minutes, and I think it's acceptable to continue to use it.

Dr Smedira. I agree. Dr Schaff and I have shared the same opinion. I don't know what Dr McCarthy's opinion is, but I always thought the cut-and-sew was the definitive way to go in these patients since it's so problematic. However, my personal data comparing the 2, the IV and III, haven't supported that, although the numbers are small.

Dr Patrick M. McCarthy *(Chicago, Ill)*. This is an excellent article and another outstanding report from Mayo with excellent results for HCM surgery. I have a comment and a question. It's interesting that AF ablation in valve surgery and in coronary bypass has now been shown in multiple studies to improve survival. But it didn't have that response here. As Dr Smedira commented, it's hard to get a good result in patients with HCM. That group of patients have a very thick left atrial wall. Unlike patients with degenerative mitral valve disease, the LA may be 1 cm or more thick. If you perform radiofrequency ablation for the pulmonary veins, as I assume you did, or if you do cryoablation, it doesn't work well in thick tissue and you don't have a reliably transmural lesion. That may explain why the cut-and-sew technique had better results. Those 2 curves diverged significantly, so if you had enough patients, I expect it would have been a significant difference in survival. Do you know where the failures are? If we have patients who fail after AF ablation, we try to map them and then do an ablation. By doing that, we learn where we failed. I would anticipate in this group, if you mapped them, that you might find that you had failed because of nontransmural lesions.

Dr Cui. I think you have a good point. In our study we are increasingly finding that in patients with HCM, we didn't find that the patients with a high resting pressure gradient had a higher prevalence of AF. So, I think the failure of the ablation may be associated with the diastolic dysfunction. I think this is a problem, but whether it's the exact reason, I'm not sure.

Dr McCarthy. It's an interesting point, and I'm not really sure why these patients fail. We haven't treated enough of them or seen enough of them with a cut-and-sew maze to really know exactly where the failures are. Certainly, the diastolic dysfunction causes a lot of the symptoms that Dr Smedira referred to earlier.

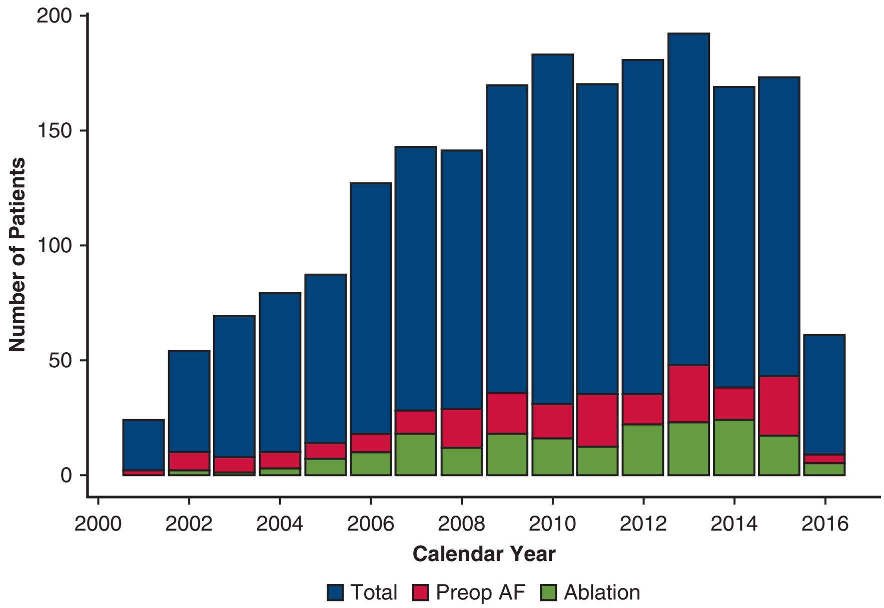


FIGURE E1. Histogram of the surgery years for the study population. *AF*, Atrial fibrillation.

TABLE E1. Association of preoperative atrial fibrillation and other clinical factors with risk of death

Predictor	Comparison*	Unadjusted		Adjusted	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age at surgery	65.6 y: 45.3 y	3.71 (2.88-4.78)	<.001	3.35 (2.55-4.41)	<.001
Gender	Female: Male	1.41 (1.05-1.88)	.020	0.97 (0.71-1.33)	.859
Body mass index†	34.5 kg/m^2 : 26.8 kg/m^2	0.85 (0.71-1.02)	.003	0.96 (0.79-1.16)	<.001
Concomitant operation	Yes: No	2.69 (2.02-3.59)	<.001	1.80 (1.29-2.53)	<.001
LV index	181.4 g/m^2: 120 g/m^2	1.10 (0.93-1.30)	.290	1.07 (0.77-1.48)	.696
MV operation	Yes: No	1.77 (1.17-2.68)	.007	0.86 (0.54-1.39)	.547
NYHA	III: I/II IV: I/II	0.84 (0.57-1.25) 1.90 (1.05-3.46)	.006	0.84 (0.56-1.26) 1.50 (0.81-2.77)	.086
Posterior wall thickness	15 mm: 11 mm	1.13 (0.93-1.36)	.219	1.11 (0.86-1.43)	.407
Septal thickness	21 mm: 14.2 mm	0.91 (0.76-1.10)	.344	1.10 (0.80-1.52)	.567
Year of surgery	2013 : 2007	1.01 (0.75-1.36)	.933	0.98 (0.73-1.33)	.914
Preoperative AF	Yes: No	1.76 (1.27-2.45)	<.001	1.36 (0.97-1.91)	.070

"Unadjusted" results were obtained from separately fitted univariable Cox models, and "Adjusted" results were from a multivariable Cox model. All models were fitted on 2023 patients. To account for missing data on body mass index, LV index, New York Heart Association, posterior wall thickness, and septal thickness, we imputed 10 datasets for all regression analyses using multiple imputation. *HR*, Hazard ratio; *CI*, confidence interval; *LV*, left ventricle; *MV*, mitral valve; *NYHA*, New York Heart Association; *AF*, atrial fibrillation. *The HRs (95% CIs) for continuous variables represent an IQR increase (ie, comparing a patient at the 75th percentile of the distribution to a patient at the 25th percentile of the distribution). †Body mass index was fit with a restricted cubic spline to avoid assuming a linear effect; the inclusion of 1.0 in the 95% CI is inconsistent with the significant test of association due to nonlinearities in this relationship.

TABLE E2. Association of atrial fibrillation–related factors with risk of death from separately fitted Cox models

Predictor	Comparison	Unadjusted		Adjusted	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Preoperative AF	Yes: No	1.76 (1.27-2.45)	<.001	1.36 (0.97-1.91)	.070
Preoperative AF and type	Paroxysmal AF: No AF Persistent AF: No AF	1.76 (1.24-2.49) 1.80 (0.84-3.84)	.001 .131	1.37 (0.96-1.96) 1.33 (0.61-2.91)	.084 .480
Preoperative AF and treatment	AF, Ablation: No AF AF, No ablation: No AF	1.43 (0.87-2.34) 2.04 (1.38-3.01)	.155 <.001	1.31 (0.79-2.15) 1.40 (0.94-2.09)	.291 .102
New-onset Postoperative AF	Yes: No	1.94 (1.37-2.73)	<.001	1.28 (0.89-1.84)	.180

"Unadjusted" and "Adjusted" results were obtained from separate univariable and multivariable Cox model fits, respectively; covariates included in each multivariable model are those variables listed in Table E1. All models were fitted on 2023 patients, except the models evaluating new-onset postoperative AF, which were fitted on the subset of 1629 patients without preoperative AF. To account for missing covariate data, we imputed 10 datasets for all regression analyses using multiple imputation. *HR*, Hazard ratio; *CI*, confidence interval; *AF*, atrial fibrillation.

TABLE E3. Variables stratified by type of atrial fibrillation

Variables	No preoperative AF (n = 1629)	Preoperative AF (n = 394)			P value
		Paroxysmal (n = 354)			
		Single episode (n = 76)	Recurrent (n = 278)	Persistent (n = 40)	
Age (y)	55.3 [44.4-65.2]	58.5 [49.5-67.3]			<.001
Male	896 (55.0)	242 (61.4)			.021
Larger LA (OR)	1 (reference)	3.09 (95% CI, 2.51-3.79)			<.001
Larger LA (OR)	-	1 (reference)	1.44 (95% CI, 0.90-2.29)	9.46 (95% CI, 4.55-19.69)	.126 <.001
Ablation	-	12 (15.8)	146 (52.5)	32 (80.8)	
PVI	-	135		13	
Maze	-	23		19	

AF, Atrial fibrillation; *LA*, left atrium; *OR*, odds ratio; *CI*, confidence interval; *PVI*, pulmonary vein isolation.

TABLE E4. Unadjusted model for risk of death in subset of ablated patients

Predictor	Comparison	Unadjusted HR (95% CI)	Unadjusted P value
Ablation type	Maze: PVI	0.37 (0.10-1.33)	.127

Subgroup analysis of ablated patients was limited to unadjusted Cox regression, because the smaller number of patients (190) was insufficient for multivariable regression adjustment. *HR*, Hazard ratio; *CI*, confidence interval; *PVI*, pulmonary vein isolation.