Research Highlight

Performance of the Cox Maze procedure—a large surgical ablation center's experience

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Overview

Our cardiac surgical program performs 1,200 cardiopulmonary bypass (CPB) procedures annually with approximately 100-120 [50% of patients who present with atrial fibrillation (AF)] of these patients undergoing an AF surgical ablation (SA) procedure concomitant to their cardiac surgical operation. Furthermore, we also perform stand-alone surgical ablation for AF as an isolated procedure for patients that are either referred or have chosen to have surgical ablation. Our ablation program was started in late 2005. To date we have performed over 800 SA procedures with the Cox Maze III/IV procedure as the procedure of choice in over 80% of the SA procedures (1-4).

The large and diverse cardiac surgical program gives rise to the opportunity to perform SA procedures in high risk patients with very acceptable and reasonable results. In one published report, we discussed our results for patients considered high risk (Additive EuroSCORE >6). Using data from our local Society of Thoracic Surgeons Adult Cardiac Surgical Database (STSACSD) and our unique AF registry, we propensity-score matched patients who underwent a SA procedure to patients with AF who did not undergo an ablative procedure (n=178 per group). This study suggested that the addition of SA to a high risk case did not result in a higher complication rate but did result in a higher rate of five-year cumulative survival (74.4% *vs.* 69.7%) (*Tables 1,2* and *Figure 1*). We concluded that high surgical risk should not be the only decision factor when evaluating a patient for SA (5).

We have also studied the performance of SA in a subset of high risk patients, those with low ejection fractions (<40%), heart failure and AF (6). In this study we had complete follow-up on 42 patients who met the criteria of low ejection fraction, heart failure and AF (Additive

Table 1 Preoperative patient characteristics comparing surgical ablation group to non-ablative group after propensity-score matching. Data represent mean ± SD or frequency (%)

	Surgical ablation group, n=178	Non-ablative group, n=178	P value
Age	72.8±9.7	72.7±10.4	0.98
Ejection fraction (%)	52.6±13.3	53.7±13.5	0.43
EuroSCORE (additive)	8.7±1.7	9.1±1.9	0.06
EuroSCORE (logistic)	13.4±7.8	15.2±9.5	0.06
Female	80 [45]	80 [45]	1.00
Diabetes mellitus	43 [24]	37 [21]	0.45
Hypertension	142 [80]	142 [80]	1.00
Chronic pulmonary disease	42 [24]	42 [24]	1.00
Congestive heart failure	89 [50]	87 [49]	0.83
Serum creatinine >2 mg/dL	6 [3]	5 [3]	0.77
Pulmonary hypertension	5 [3]	1 [1]	0.22
Peripheral vascular disease	31 [17]	34 [19]	0.68
CABG	86 [48]	79 [44]	0.46
Valve	133 [75]	137 [77]	0.62
CPB time	160.9±47.1	152.6±59.7	0.15

CABG, coronary artery bypass surgery; CPB, cardiopulmonary bypass.

Table 2 Perioperative outcomes. Data represent median (IQR) or frequency (%)

	Surgical ablation group, n=178	Non-ablative group, n=178	P value
Length of stay [days]	7 [6-11]	7 [5-12]	0.15
Prolonged ventilation [>24 hours]	19 [11]	26 [15]	0.34
Permanent stroke or TIA	3 [1.7]	9 [5]	0.14
Pneumonia	12 [7]	7 [4]	0.35
Deep sternal wound infection	1 [0.6]	1 [0.6]	1.00
Reoperation for bleeding	6 [3]	7 [4]	1.00
Perioperative renal failure	10 [6]	14 [8]	0.53
Dialysis required	9 [5]	7 [4]	0.80
30-day readmissions	21 [12]	23 [13]	0.75
Operative mortality (<30 days)	4 [2]	7 [4]	0.54

IQR, interquartile range; TIA, transient ischemic attack.

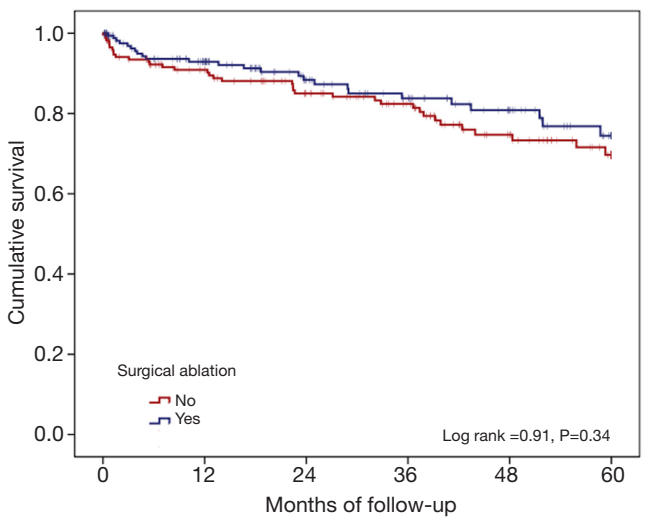

Figure 1 Survival over time comparison between high risk patients who underwent surgical ablation and those that did not.

EuroSCORE 7.5±3.1). We determined in this unique high risk group that SA was performed safely and effectively. Our conclusion was based on the following results: a return to sinus rhythm rate of 86% at the time of their follow-up echo; an improvement of the average ejection fraction

Table 3 Patient demographics (n=42)

Mean age (SD)	61.6 (12.9) years
Gender number	Male =31 (74%)
Preoperative ejection fraction (mean ± SD %)	29.9 (5.0)
Preoperative NYHA classification	I-9 (21%); II-13 (31%); III-16 (38%); IV-4 (10%)
History of preoperative hypertension	52%
Mean CHADS score	1.7 (1.2)
Type of atrial fibrillation prior to surgery	
Paroxysmal	3 (7%)
Persistent	20 (48%)
Long-standing persistent	19 (45%)
Additive EuroSCORE (mean ± SD)	7.5 (3.1)
Type of surgeries	
Stand-alone Cox Maze procedure	8 (19%)
CABG	8 (19%)
Valve (MVR and or AVR)	19 (45%)
CABG/valve	7 (17%)
Left atrial size >5.5	12 (29%)
Ejection fraction <35%	29 (69%)
Preoperative pacemaker	6 (14%)
Preoperative myocardial infarction	7 (17%)

AVR, aortic valve replacement/repair; CABG, coronary artery bypass surgery.

from (30±5.0)% to (45±13.0)%; a significant decrease in the NYHA classification from an average of 2.8 to 1.1 at the time of the echo; a significant increase in patients' self-report of their health-related quality of life physical functioning scores, which surpassed the national norms for people living with heart disease, as well as a significant decrease in their reported AF symptom burden and an event-free survival of 87% at two years (events considered were valve replacement, VAD or death) (*Table 3*, *Figures 2-4*) (6).

Older age is a significant deterrent to performing an additional surgical procedure, even though patients over the age of 80 years have a 1 in 9 chance of developing AF in their lifetime. In addition, patients are now presenting to cardiac surgery older, and in many cases sicker (7-10). Therefore, we studied another subset of high risk patients, those over the age of 75 who presented to cardiac surgery with AF. At the time of this study, we had 44 patients who

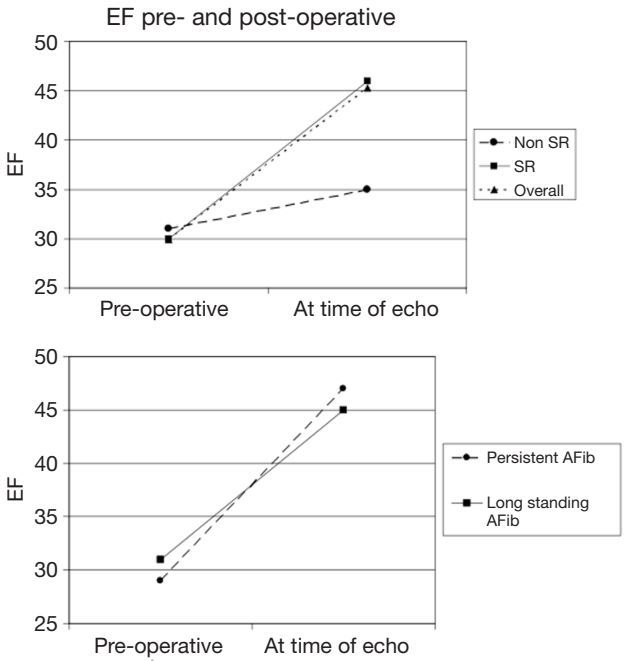

Figure 2 Ejection fraction pre-surgery and at time of echo post-surgery in patients considered high risk, with a low ejection fraction and heart failure.

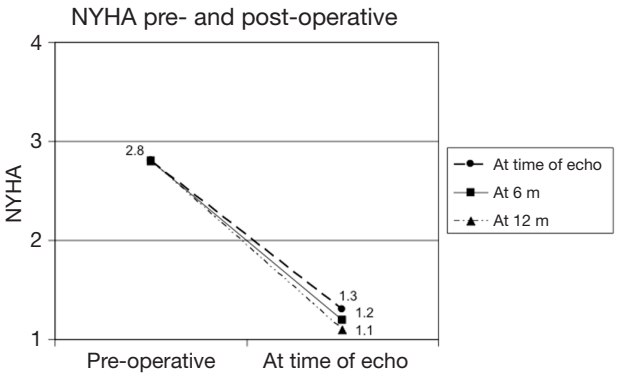

Figure 3 New York Heart Association (NYHA) classification pre-surgery and at time of echo post-surgery for patients considered high risk, with a low ejection fraction and heart failure.

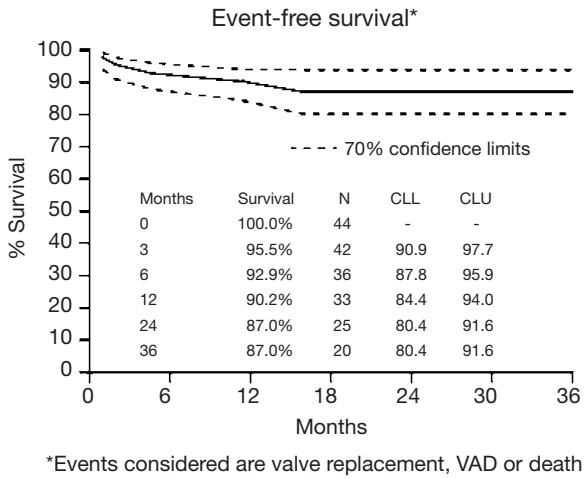

Figure 4 Event-free survival following surgery and ablation in patients considered high risk, with a low ejection fraction and heart failure.

met the inclusion criteria of being over the age of 75 years old and undergoing a full Cox Maze III/IV procedure (7). The average age for this population was 79.5±3 years with a mean additive EuroSCORE of 9±2.1 (very high risk). The majority (93%) of the patients underwent a concomitant valve procedure (*Tables 4,5*). The rate of return to sinus rhythm at 6 and 12 months was 90% and 85% respectively. Two year cumulative survival was 89.6% and there were no embolic strokes or major bleeding incidents in this group (*Figure 5*). We again concluded that advanced age alone should not be a discriminating factor when considering whether to perform the Cox Maze III/IV procedure.

Aortic valve replacement/repair (AVR) and coronary artery bypass surgery (CABG) are two of the most common surgeries performed. However, patients who have AF and are undergoing these surgical procedures are less likely to have a SA procedure performed (11,12). Therefore, we investigated whether operative risk was increased when adding the Cox Maze III/IV procedure to AVR or CABG surgery (13). Using propensity-score matching, we matched 95 patients who underwent a full Cox Maze III/IV procedure concomitant to an AVR, CABG and AVR/CABG procedure (Cox Maze III/AVR =30; Cox Maze III/CABG =47; Cox Maze III/AVR/CABG =18) to patients without a history of AF but underwent an AVR, CABG or AVR/CABG procedure. There were no differences between groups in perioperative outcomes except that the Cox Maze group was on CPB longer and had more pacemakers implanted. However, survival was not different between the groups in a mean follow-up of 35 months. The Cox Maze group had a return to sinus rhythm rate of 94% with 81% off Class III anti arrhythmic medications by 12 months, and both groups had significant improvement in their reported health-related quality of life (13) (*Tables 6,7* and *Figure 6*). This study is of importance as less than 30% of the patients who presented to surgery with AF and these concomitant pathologies are being offered SA in North America. This is despite the data suggesting that leaving the patients in AF is associated with lower long-term survival and higher morbidity that is

Table 4 Patient preoperative characteristics

	Cox-Maze III/IV procedure*, N=44
Age	79.5±3.0
Male	23 (52%)
Additive EuroSCORE	9.0±2.1
Logistic EuroSCORE	15.1±10.7
Type of concomitant surgery	
CABG	3 (7%)
Valve	31 (70%)
CABG & valve	10 (23%)
Thromboembolic event prior to surgery	8 (18%)
CHADS2 score	2.7±0.9
Hemorrhagic score**	2.6±1.0
Long-standing AF	31 (70%)
History of myocardial infarction	5 (11%)
Diabetes	6 (14%)
Previous cardiovascular surgery	5 (11%)
History of renal failure with dialysis	0
Hypertension	35 (80%)
Ejection fraction (%)	57.7±11.6
Congestive heart failure	28 (64%)
NYHA heart failure class**	
I	2 (5%)
II	10 (23%)
III	14 (32%)
IV	2 (5%)
None	16 (36%)
Prior cerebrovascular accident	3 (7%)
Chronic lung disease	8 (18%)
Perfusion time (minutes)	187.1±58.3
Cross-clamp time (minutes)	132.5±45.7

CABG, coronary artery bypass surgery; *, data presented as mean ± SD or frequency (%); **, hemorrhagic score calculated as: [1.6× age.60 (0,1)]+[1.3× female (0,1)]+[2.2× history of malignancy (0,1)]—higher score indicates increased risk for bleeding (max score =5.1). **, The percentage add to greater than 100% due to rounding

Table 5 Post-operative complications

	Cox-Maze III/IV procedure*, N=44
Deep sternal wound infection	0
Permanent cerebrovascular accident	0
Prolonged ventilation (>24 hours)	9 (21%)
Renal failure in hospital	4 (9%)
Reoperation for bleeding	3 (7%)
Readmit to intensive care unit	0
Length of stay (days)	8 [6-12.75]
Operative mortality	1 (2%)
Readmission <30 days	3 (7%)

*, data presented as median (IQR) or frequency (%). IQR, interquartile range.

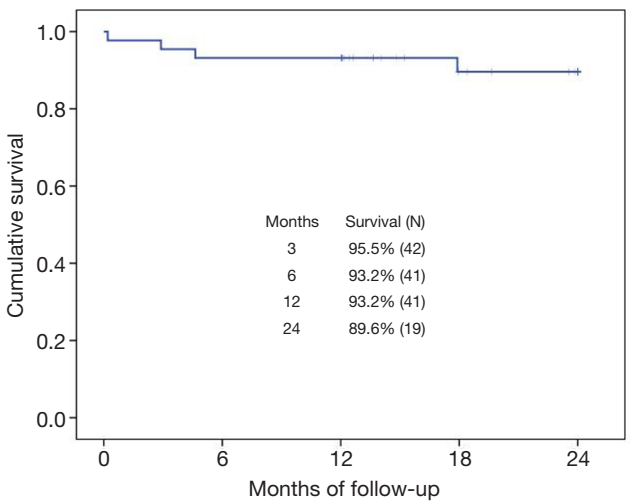

Figure 5 Survival over time for patients >75 years old who underwent a surgical ablation.

mainly associated with Coumadin and embolic events (12,14). We concluded that the Cox Maze procedure should be considered in patients who present for cardiac surgery in AF and will undergo CABG and or AVR procedure.

A unique aspect of our program is that patients have the opportunity to undergo the full Cox Maze procedure through a minimally invasive approach. In a recent report, we shared the results of patients who underwent a stand-alone minimally invasive procedure for non-paroxysmal atrial fibrillation (15). Using a small right mini-thoracotomy incision (6 cm) and femoral cannulation and fibrillating heart with no cross clamp, a full Cox Maze III/IV procedure was performed on 104 patients at the time of the study. This population was younger, with a mean age of 55.9±9.0 years, the vast majority of the patients being male (91%), and 78% having long-standing persistent AF. Almost half of the patients had undergone at least one

Table 6 Perioperative characteristics of all patients (N=4,350)

	Cox Maze III procedure, n=95	No Cox Maze III procedure, n=4,255	P value
Age	68.2±9.0	63.6±10.9	<0.001
Female	20 (21%)	955 (22%)	0.75
Body mass index	28.9±4.6	29.3±8.0	0.64
NYHA Class 3 & 4	7 (7%)	453 (11%)	0.40
Ejection fraction	57±11	54±11	0.03
History of MI	18 (19%)	1,742 (41%)	<0.001
Chronic pulmonary disease	16 (17%)	569 (13%)	0.36
Diabetes	24 (25%)	1,563 (37%)	0.02
EuroSCORE (additive)	6.33±2.49	4.85±3.36	<0.001
Previous valve surgery	2 (2%)	27 (0.6%)	0.13
Previous CABG	4 (4%)	141 (3%)	0.56
Emergent surgery	0	224 (5%)	0.02
Redo surgery	6 (6%)	159 (4%)	0.18
Aortic valve surgery	48 (51%)	737 (17%)	<0.001
CABG	65 (68%)	3,833 (90%)	<0.001
Number of bypass grafts	2.5±1.0	3.1±1.0	<0.001
Perfusion time	164.4±39.9	97.4±35.2	<0.001

CABG, coronary artery bypass surgery.

Table 7 Results of multivariate analyses of the full sample (N=4,350) to determine the effect on perioperative outcomes from the addition of the Cox Maze III/IV procedure to the AVR and CABG procedures

	OR	95% CI	P value
Permanent stroke	0.55	0.07-4.35	0.57
Prolonged ventilation (>24 hours)	0.78	0.31-1.93	0.59
Pneumonia	3.80	1.27-11.38	0.02
Renal failure requiring dialysis	0.76	0.09-6.20	0.80
Reoperation for bleeding	2.09	0.81-5.41	0.13
Length of stay (Days)	t=2.52	0.42-3.36	0.01
Readmissions within 30 days	1.24	0.64-2.39	0.53
Operative death	0.34	0.04-2.72	0.31

AVR, Aortic valve replacement/repair; CABG, coronary artery bypass surgery.

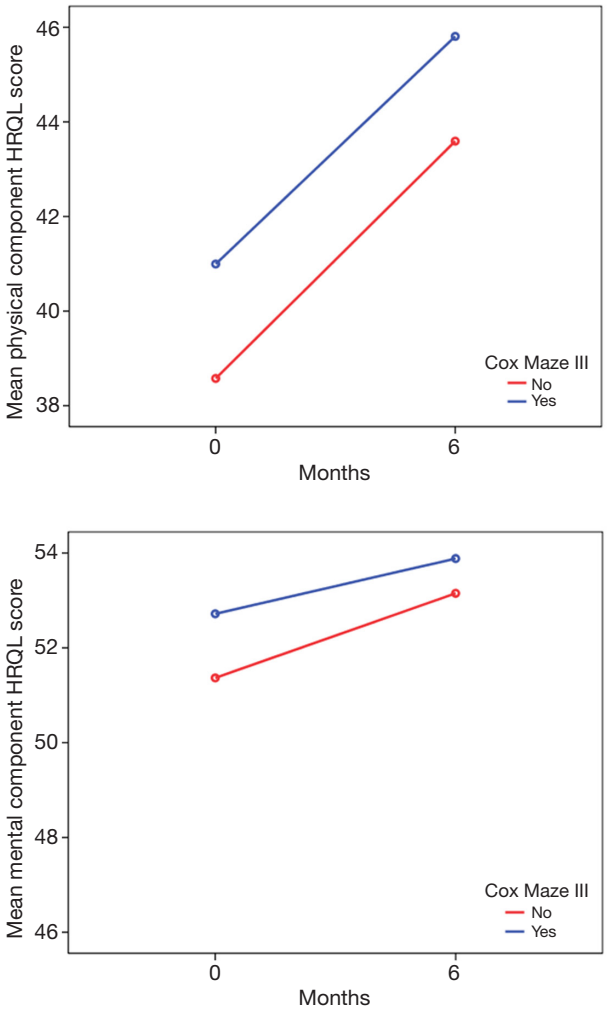

Figure 6 Comparison of health-related quality of life scores between those that underwent the Cox Maze procedure and those that did not for patients who underwent an aortic valve replacement/repair (AVR) and coronary artery bypass surgery (CABG).

percutaneous catheter ablation prior to their SA. The left atrial size was significantly higher than normal (average left atrium size was 5.0±1.1 cm). The return to sinus rhythm rate was >90% at all time points through to the last follow-up of 36 months (6, 12, and 24 months), with at least 80% off anti-arrhythmic drugs at each time point respectively. A longer duration of AF was a predictor of failure of the procedure. Arrhythmia-free survival for the first five years after surgery was 81% (*Figure 7*). Patients reported a significant increase in their health-related quality of life, especially when compared to age group national norms (*Tables 8,9* and *Figure 8*). However, we did discern that there

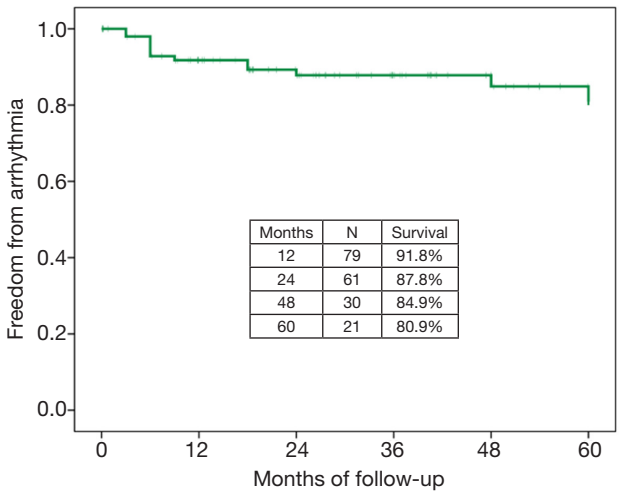

Figure 7 Freedom from atrial arrhythmia over time following minimally invasive surgical ablation.

Table 8 Baseline patient characteristics

	MI standalone Maze, N=104
Age (years)	55.9±9.0
Female	9
Type of AF	
Long-standing persistent	81
Persistent	23
Median (IQR) AF duration (months)	49.9 (22.7-92.6)
Left atrial diameter (cm; range)	5.0±1.1 (2.6-9.9)
Left atrial size >6 cm	13
Previous ablation	46

AF, atrial fibrillation; IQR, interquartile range.

Table 9 Postoperative outcomes

	MI standalone Maze, N=104
Perioperative renal failure	0
TIA	1
Reoperation for bleeding	1
Intraoperative blood given	3
Postoperative blood given	4
Operative mortality	0
Readmissions <30 days	13
Perioperative PM for SN dysfunction	1
Median (IQR) ICU stay (hours)	22.9 [8.2-33.3]
Median (IQR) length of stay (days)	4 [3-5]
Mean follow-up (months)	44.9±26.3
Late embolic stroke	1
Warfarin at 12 months	21/86 (24%)
Clinically indicated warfarin	14/21 (67%)
Warfarin at 24 months	9/53 (20%)
Cumulative 4-year survival	97.1%

TIA, transient ischemic attack; PM, pacemaker; SN, sinus node; IQR, interquartile range; ICU, intensive care unit.

was a significant learning curve associated with performing a minimally invasive Cox Maze III/IV procedure after observing that our return to sinus rhythm at one year went from 89% for the first 20 patients to 94% for the remaining patients. Based on these results, we concluded that the Cox Maze procedure can be performed safely and effectively in this very challenging group of patients. However, there is a significant learning curve associated with performing this procedure, and therefore emphasis must be placed on educational opportunities for surgeons to master this technique (15).

All of the studies presented thus far have demonstrated that the Cox Maze III/IV procedure, in contrast to misperception among many surgeons and cardiologists, can be performed very safely and effectively in a wide group of patients. They furthermore suggests that each patient who presents for cardiac surgery while experiencing AF should be evaluated on an individual basis and not just on rote criteria. To investigate this point more thoroughly, we conducted an analysis of our data to determine the impact of clinical presentation and surgeon experience on the decision to perform SA, since our program has multiple surgeons (n=8) who perform AF surgical ablation (16). Overall, we found that the rate of performing SA significantly increased from 31% in 2005 to 49% in 2010 (P<0.001). The greatest chance (OR =5.81) of having a SA procedure occurred when the patient presented with a lower creatinine level whilst undergoing a mitral valve procedure (OR =4.34); however, as the comorbidity score increased, the probability of actually performing a surgical ablation procedure decreased (*Table 10*, *Figure 9*). Surgeon experience was also a predictor, such that there was a 6% greater chance of having SA procedure for every 10 SA cases performed. Surgeons who had ablated >50 patients ablated 57% of the AF patients, while those with <50 cases of experience only ablated 22%.

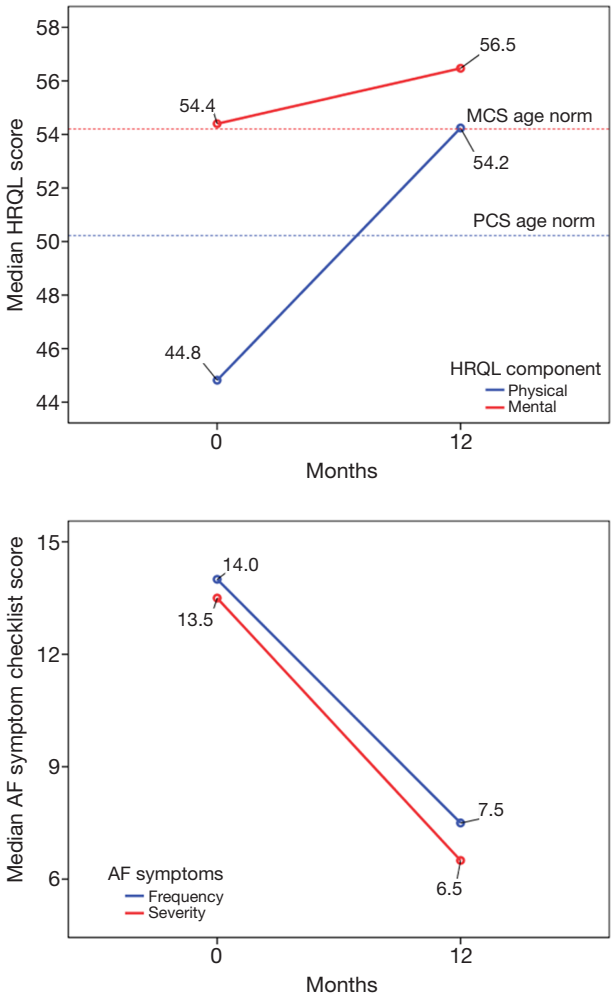

Figure 8 Change in atrial fibrillation health-related quality of life and atrial fibrillation symptoms from pre-surgery to 12 months post surgery in patients who underwent a minimally invasive surgical ablation.

Clearly, even in a large center, with a very active ablation center and the knowledge that patients with AF at the time of cardiac surgery have higher morbidity and decreased survival, the decision to ablate AF is still based on several clinical factors and surgeon experience. This also reinforces how it is imperative that surgeons understand the criteria to use when making clinical decisions, as was recently discussed in a publication based on the STS database where it was clearly shown that the decision regarding the invasiveness of a procedure should be based on evidence (12).

Summary

This brief discussion has covered only several of our published manuscripts on our work with patients who have undergone a SA procedure. However, the papers we chose to present were chosen to help demonstrate that SA can be performed safely and effectively even in the most high risk patients. It is our hope that through this discussion, the percentage of patients who are offered and undergo an AF

Table 10 Logistic regression model to predict the performance of concomitant surgical ablation and comparison of surgical groups on variables included in the model. Data presented as mean ± SD or % of group

	OR (CI)	No ablation, N=582	Surgical ablation, n=401
Age	0.99 (0.97-0.998)	69.6±11.5	66.5±11.9
Female	0.77 (0.56-1.08)	31	38
Body mass index (kg/m^2)	1.01 (0.99-1.04)	28.3±5.6	27.9±5.9
Myocardial infarction	0.53 (0.36-0.78)	35	14
Cerebrovascular disease	0.92 (0.44-1.94)	26	14
Unstable angina	0.36 (0.13-0.95)	6	2
Peripheral vascular disease	1.19 (0.60-2.38)	17	9
Previous cardiac surgery	0.29 (0.19-0.45)	25	11
Extracardiac arteriopathy	0.54 (0.24-1.20)	37	19
Chronic pulmonary disease	0.66 (0.45-0.97)	24	16
Ejection fraction (%)	1.02 (1.01-1.03)	50.5±13.1	55.1±11.6
Creatinine <2 mg/dL	4.34 (1.66-11.37)	94	98.5
Critical preoperative state	0.41 (0.19-0.90)	8	3
Concomitant mitral valve surgery	5.81 (4.09-8.25)	21	59
Number of concomitant surgeries >2	0.63 (0.37-1.07)	8	11

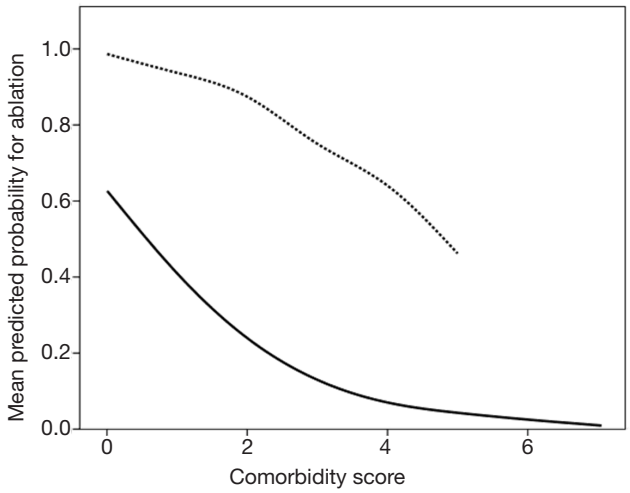

Figure 9 The predicted probability that a surgeon will perform a surgical ablation in relation to the patients comorbidity score.

ablative procedure will increase from the current figure of only 38% (11). However, we feel in order for this increase to occur, there must be a comprehensive approach to educate and train surgeons so that the safety and integrity of the SA procedure will be maintained.

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