Long-Term Risk of Ischemic Stroke After the Cox-Maze III Procedure for Atrial Fibrillation

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Background. **The long-term risk of stroke after surgical treatment of atrial fibrillation is not well known. We performed an observational cohort study with long follow-up after the "cut-and-sew" Cox-maze III procedure (CM-III), including left atrial appendage excision. The aim was to analyze the incidence of stroke/transient ischemic attack (TIA) and the association to preoperative CHA_2DS_2-VASc (age in years, sex, congestive heart failure history, hypertension history, stroke/TIA, thromboembolism history, vascular disease history, diabetes mellitus) score.**

Methods. **Preoperative and perioperative data were collected in 526 CM-III patients operated in four centers 1994 to 2009, 412 men, mean age of 57.1 ± 8.3 years. The incidence of any stroke/TIA was identified through analyses of the Swedish National Patient and Cause-of-Death Registers and from review of individual patient records. The cumulative incidence of stroke/TIA and association with CHA_2DS_2-VASc score was estimated using methods accounting for the competing risk of death.**

Results. **Mean follow-up was 10.1 years. There were 29 patients with any stroke/TIA, including 6 with intracerebral bleedings (2 fatal) and 4 with perioperative strokes (0.76%). The remaining 13 ischemic strokes and six TIAs occurred at a mean of 7.1 ± 4.0 years postoperatively, with an incidence of 0.36% per year (19 events per 5,231 patient-years). In all CHA_2DS_2-VASc groups, observed ischemic stroke/TIA rate was lower than predicted. A higher risk of ischemic stroke/TIA was seen in patients with CHA_2DS_2-VASc score 2 or greater compared with score 0 or 1 (hazards ratio 2.15, 95% confidence interval: 0.87 to 5.32) but no difference by sex or stand-alone versus concomitant operation. No patient had ischemic stroke as cause of death.**

Conclusions. **This multicenter study showed a low incidence of perioperative and long-term postoperative ischemic stroke/TIA after CM-III. Although general risk of ischemic stroke/TIA was reduced, patients with CHA_2DS_2-VASc score 2 or greater had a higher risk compared with score 0 or 1. Complete left atrial appendage excision may be an important reason for the low ischemic stroke rate.**

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Atrial fibrillation (AF) is associated with substantial rates of morbidity and mortality, mainly due to the increased risk of cardioembolic stroke. The Cox-maze III procedure (CM-III) was introduced by James Cox more than 25 years ago as an open heart procedure for medically refractory AF [1], and it is still considered the gold standard for surgical treatment of AF. The original aim of CM-III was to eliminate macro-reentrant circuits sustaining AF by strategically placed surgical incisions in both atria, thereby restoring sinus rhythm and atrioventricular synchrony. Excellent results of the CM-III have been reported with 70% to 96% freedom from AF up to 5 years postoperatively [2, 3].

The left atrial appendage (LAA) has been increasingly recognized as the predominant source of thrombus formation and embolic stroke in nonvalvular AF [4]. Complete excision of the LAA has been a fundamental part of CM-III from the beginning. In theory, a successful CM-III operation, with return of sinus rhythm and with excision of the LAA, should reduce the risk of stroke. An early evaluation by Cox and colleagues [5] showed a low incidence of perioperative and postoperative stroke up to 11.5 years. In general, however, the long-term risks of stroke after surgical treatment of AF have been difficult to assess because of variations in patient characteristics, surgical techniques, and methods of follow-up. In

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addition, postoperative anticoagulation therapy protocols have varied between centers.

The Swedish Arrhythmia Surgery Group was formed to promote multicenter research of surgical AF procedures. Long-term results in a nationally assembled cohort of 536 Swedish CM-III patients have been presented regarding long-term mortality and clinical follow-up of cardiac rhythm and arrhythmia symptoms [6, 7]. Pet and colleagues [8] showed a low long-term risk of stroke in 389 patients after CM-III, unrelated to $CHADS_2$ (congestive heart failure history, hypertension history, age $\geq$75 years, diabetes mellitus history, stroke or transient ischemic attack [TIA] symptoms previously) score. However, the more contemporary use of CHA_2DS_2-VASc (age in years, sex, congestive heart failure history, hypertension history, stroke/TIA, thromboembolism history, vascular disease history, diabetes mellitus) score [9] may be more sensitive, particularly in low-risk patients. Therefore, we performed an observational cohort study in Swedish CM-III patients with the aim to evaluate the long-term incidence of postoperative ischemic stroke and TIA and to investigate if preoperative CHA_2DS_2-VASc score was associated with the long-term risk of stroke.

Patients and Methods

A total of 536 patients underwent CM-III in four Swedish cardiothoracic centers (Sahlgrenska University Hospital, Gothenburg; University Hospital, Uppsala; Karolinska University Hospital and Huddinge University Hospital, Stockholm) between 1994 and 2009. Of these, 10 patients were living abroad and could not be included in the register follow-up, leaving 526 patients in the study cohort. Preoperative, perioperative, and early postoperative (30 days) data were collected through review of patient records and analyzed in a collaborative clinical database. The baseline characteristics, outlined in Table 1, were used to calculate preoperative CHA_2DS_2-VASc score [9]. There were 412 men and 114 women with mean age of 57.1 $\pm$ 8.3 years. In all, 78% underwent stand-alone CM-III, and 22% underwent CM-III concomitantly to other procedures, mainly mitral valve surgical procedures or coronary artery bypass grafting. Six patients underwent surgical procedures for mitral stenosis and were defined as having valvular AF preoperatively. The remaining patients were considered to have nonvalvular AF. In calculating the CHA_2DS_2-VASc score, vascular disease was defined as occurrence of previous myocardial infarction or coronary disease.

All patients, stand-alone or concomitant, underwent the classic "cut-and-sew" CM-III through a median sternotomy and with the aid of cardiopulmonary bypass. The LAA was completely excised in the same session in all patients.

Every Swedish citizen is allocated a unique personal identity number at birth. This was used in all 526 patients to retrieve information from the Swedish National Patient Register (NPR) and from the National Cause-of-Death Register at the Swedish National Board of Health and Welfare. The resulting study cohort database was then anonymized according to health authority regulations. The NPR covers all diagnoses as defined by the International Classification of Disease version 9 and 10 (ICD-10) for all patients admitted to Swedish hospitals from 1987 and onward [10]. The validity of the diagnosis of stroke in the NPR has been evaluated, with a positive predictive value of 98.6% [11]. For the present study, hospitalization under ICD-10 codes I60 to I69 were selected for definition of postoperative stroke, and ICD-10 code G45.9 for TIA.

All deaths in Sweden are reported to the National Board of Health and Welfare, with a cause-of-death form submitted by the responsible physician. Such data have been used in the National Cause-of-Death Register since 1952, currently classified according to the ICD-10 system. For the present study, cardiovascular deaths corresponded to codes I00 to I99 and cerebrovascular deaths to codes I60 to I69.

The occurrence of any stroke/TIA or death from the date of individual operation to the end of follow-up (December 31, 2013) was identified in the registers. These events were further analyzed in detail by reviews of individual patient charts. Patients with cerebral bleeding events were excluded from further analysis. In addition, procedure-related strokes were excluded, because these events were assessed to have a different cause than AF-associated cardioembolic stroke [12].

The Regional Ethic Committee in Stockholm collectively approved the study for all participating centers.

Statistical Analysis

Patient characteristics are presented as frequencies and percentages for categorical variables and as means and SDs for continuous variables. Patients were categorized into two groups, depending on CHA_2DS_2-VASc score, and comparisons between the groups were based on *t* tests for continuous variables and χ^2 tests for categorical variables. The primary outcome measure was ischemic stroke or TIA. Person-time in days was counted from the date of operation until the date of ischemic stroke/TIA, date of death, or end of follow-up. Because death was considered a competing risk, that is, an event that would impede the event of interest (ischemic stroke/TIA), we used competing risk regression based on the Fine-Gray proportional subhazards model [13] to calculate subdistribution hazard ratios (HRs) and 95% confidence intervals (CIs) according to CHA_2DS_2-VASc category (score $\geq$2 versus score 0 or 1). The cumulative incidence function was used to graph the rate of ischemic stroke or TIA, thus accounting for the competing risk of death. Data management and statistical analyses were performed using Stata 14.0 (Stata Corp, College Station, TX) and R version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Mean follow-up was 10.1 years. In total, 29 patients with a postoperative diagnosis of any stroke/TIA were identified. Four strokes were perioperative (0.76%), three at the time of CM-III and one in relation to a reoperation for

Table 1. Baseline Characteristics in 526 Patients Who Underwent the Cox-Maze III Procedure, Stratified by CHA_2DS_2-VASc Score

Characteristic	All Patients	CHA_2DS_2-VASc = 0 or 1	CHA_2DS_2-VASc ≥2	*p* Value
Patients, n (%)	526 (100)	358 (68)	168 (32)	
Age at operation, years	57.1 ± 8.3	55.2 ± 7.9	61.3 ± 7.5	<0.001
Sex				<0.001
Male	412 (78.3)	312 (87.2)	100 (59.5)	
Female	114 (21.7)	46 (12.8)	68 (40.5)	
Center				0.033
A	61 (11.6)	39 (10.9)	22 (13.1)	
B	41 (7.8)	21 (5.9)	20 (11.9)	
C	231 (43.9)	169 (47.2)	62 (36.9)	
D	193 (36.7)	129 (36.0)	64 (38.1)	
Operative period				0.012
1994–1999	134 (25.5)	91 (25.4)	43 (25.6)	
2000–2004	181 (34.4)	137 (38.3)	44 (26.2)	
2005–2009	211 (40.1)	130 (36.3)	81 (48.2)	
Type of operation				<0.001
Stand alone	408 (77.6)	308 (86.0)	100 (59.5)	
Concomitant	118 (22.4)	50 (14.0)	68 (40.5)	
Prior stroke/TIA	48 (9.1)	0 (0.0)	48 (28.6)	<0.001
Diabetes mellitus	63 (12.0)	19 (5.3)	44 (26.2)	<0.001
Hypertension	80 (15.2)	24 (6.7)	56 (33.3)	<0.001
Heart failure	80 (15.2)	35 (9.8)	45 (26.8)	<0.001
Other structural heart disease	57 (10.8)	26 (7.3)	31 (18.5)	<0.001
LVEF				<0.001
≥50%	385 (79.7)	281 (85.4)	104 (67.5)	
30%–49%	93 (19.3)	46 (14.0)	47 (30.5)	
<30%	5 (1.0)	2 (0.6)	3 (1.9)	
AF class				0.54
Paroxysmal	201 (38.2)	140 (39.1)	61 (36.3)	
Nonparoxysmal	325 (61.8)	218 (60.9)	107 (63.7)	
AF duration, years	8.0 ± 6.7	8.4 ± 7.0	7.1 ± 5.9	0.046
Valvular AF (ie, mitral stenosis)	6 (1.1)	3 (0.8)	3 (1.8)	0.340

Data are n (%) or mean ± SD.

AF = atrial fibrillation; CHA_2DS_2-VASc = age in years, sex, congestive heart failure history, hypertension history, stroke/TIA, thromboembolism history, vascular disease history, diabetes mellitus; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.

aortic valve replacement 6 years after CM-III. Five of the postoperative events were cerebral bleedings, one of which was fatal (subarachnoidal hemorrhage). One event was incorrectly registered as a postoperative stroke. The remaining study cohort consisted of 13 patients with postoperative ischemic stroke and 6 with TIA (Table 2). The mean time-interval between operation and event was 7.1 ± 4.0 years. On-going anticoagulant medication at the time of event was none (47%), aspirin (37%), warfarin (11%), and unknown (5%). Rhythm at the time of event was sinus (53%), AF/atrial flutter (21%), pacemaker (5%), and unknown (21%). No patient with valvular AF had a recorded ischemic stroke/TIA. No patient had ischemic stroke as a recorded cause of death, but one of the patients with ischemic stroke later experienced a fatal intracerebral bleeding.

All 526 patients were stratified into two groups, either CHA_2DS_2-VASc score 0 or 1, or 2 or greater, based on preoperative characteristics. Consequently, there were significant differences between groups regarding age, sex, prior stroke, diabetes, hypertension, and heart failure (Table 1). In all, there were 19 events of ischemic stroke/TIA in 5,231 patient-years of follow-up, translating into a yearly rate of 0.36% (Table 3). The number of postoperative events according to different preoperative CHA_2DS_2-VASc scores are listed in Table 4. Although relatively few patients, there were no observed strokes in patients with CHA_2DS_2-VASc greater than 3.

A higher incidence of ischemic stroke/TIA was seen in patients with CHA_2DS_2-VASc score 2 or greater compared with score 0 or 1 (HR 2.15, 95% CI: 0.87 to 5.32, $p = 0.097$) (Fig 1). No difference in ischemic stroke/TIA rate was found by sex or type of operation (stand-alone CM-III versus concomitant procedures) (Fig 2), or in relation to time of operation (1994 to 2001 versus 2002 to 2009). Throughout all CHA_2DS_2-VASc scores, the observed rates of ischemic stroke/TIA were clearly lower for these CM-III patients than predicted rates stated in

Table 2. Characteristics of Patients With Ischemic Stroke or TIA After the Cox-Maze III Procedure

Characteristic	Value
Stroke/TIA, n	13
TIA, n	6
Sex	
Male	15 (79)
Female	4 (21)
Age at operation, years	60.5 ± 6.9
Type AF	
Paroxysmal	11 (58)
Nonparoxysmal	8 (42)
Preoperative stroke/TIA	2 (10.5)
Type of operation	
Stand alone	15 (79)
Concomitant	4 (21)
ASD patch/suture, n	2
MV repair, n	1
MV repair + CABG, n	1
Interval operation to stroke/TIA event, years	71 ± 4.0
Death at follow-up	5 (26)
Cancer, n	2
Motorneuron disease, n	1
Intracerebral bleeding, n	1
Infection, n	1

Values are n (%) or mean ± SD, unless otherwise specified.

AF = atrial fibrillation; ASD = atrial septal defect; CABG, coronary artery bypass grafting; MV = mitral valve; TIA = transient ischemic attack.

guidelines or in a recent study comparing stroke risk scores in Swedish AF patients [9, 14] (Fig 3).

Comment

By means of register analyses, this study attempted to evaluate the true long-term incidence of ischemic stroke and TIA in a multicenter cohort of patients after the cut-and-sew CM-III procedure, including LAA excision. Moreover, it aimed to compare observed with predicted stroke outcome, based on the CHA_2DS_2-VASc score. The main findings were a low incidence of perioperative stroke and a low incidence of late postoperative ischemic stroke/TIA. Patients with CHA_2DS_2-VASc score 2 or greater had a doubled risk of having a postoperative ischemic stroke compared with score 0 or 1, but observed rates were lower than predicted rates for all CHA_2DS_2-VASc groups.

Because of the development of catheter ablation for AF, the cut-and-sew CM-III could be regarded as a historical operation, but it is still considered the gold standard for surgical treatment of AF. In theory, a successful CM-III, with return of sinus rhythm and with elimination of the risk of thrombus forming in the LAA, should reduce the risk of AF-associated stroke. Although previous reports of stroke after surgical treatment of AF may sometimes be hard to evaluate, the present study showed comparable results with others. First, the incidence of perioperative stroke was 0.76%. Cox and associates [5] reported in 1999 a similar low incidence of perioperative stroke (0.7%) in 306 CM patients. The CM-III is an open heart procedure of considerable length and technical difficulty, but these perioperative stroke rates are lower than those reported for comparable contemporary valve procedures [15]. Second, the long-term incidence of postoperative stroke was 0.36% per patient-year. Cox and colleagues [5] found a similar long-term stroke rate of 0.38%, although the follow-up was done by interview method. In more recent patients followed prospectively after surgical biatrial ablation, Ad and colleagues [16] reported a yearly stroke rate of 0.51%. Hwang and colleagues [17] followed patients undergoing concomitant CM-III with mitral valve repair and found a low incidence of postoperative stroke after 5 years (0.06% per patient-year), even without anticoagulant therapy.

In general, a postoperative ischemic stroke rate of 0.36% is lower than the expected risk for AF patients with CHA_2DS_2-VASc score 0 [9, 14]. This could in part be because these Swedish CM-III patients were relatively young and otherwise healthy (78% had stand-alone CM-III). In the perspective of 10 to 15 years of follow-up, most patients in this study will have reached the age for an increased CHA_2DS_2-VASc score. Interestingly, the long-term risks of stroke/TIA after CM-III are comparable with those after catheter ablation for AF. In patients with maintained sinus rhythm after catheter ablation, stroke rates of 0.7% per year have been observed, even after discontinuation of anticoagulant therapy [18]. In a German study of more than 2,000 catheter ablation patients followed to 18 months, 16 events of stroke/TIA/systemic embolism were reported within 30 days of ablation and 15 events (0.72%) during the follow-up period [19].

Table 3. Absolute and Relative Risks of Ischemic Stroke or TIA After the Cox-Maze III Procedure in 526 Patients Stratified by CHA_2DS_2-VASc Score

Stroke/TIA	All Patients	CHA_2DS_2-VASc 0 or 1	CHA_2DS_2-VASc ≥2
Events/PY	19/5,231	10/3,716	9/1,514
Crude rate per 1000 PY (95% CI)	3.6 (2.3–5.7)	2.7 (1.4–5.0)	5.9 (3.1–11)
sHR (95% CI)		1.00	2.15 (0.87–5.32)

CHA_2DS_2-VASc = age in years, sex, congestive heart failure history, hypertension history, stroke/TIA, thromboembolism history, vascular disease history, diabetes mellitus; CI = confidence interval; PY = person-years; sHR = subdistribution hazard ratio; TIA = transient ischemic attack.

Table 4. Number of Patients and Ischemic Stroke/TIA According to CHA_2DS_2-VASc Score

CHA_2DS_2-VASc Score	All (n = 526)	No Stroke (n = 507)	Stroke or TIA (n = 19)
0	218	215	3
1	140	133	7
2	96	90	6
3	40	37	3
4	24	24	0
5	5	5	0
6	3	3	0

CHA_2DS_2-VASc = age in years, sex, congestive heart failure history, hypertension history, stroke/TIA, thromboembolism history, vascular disease history, diabetes mellitus; TIA = transient ischemic attack.

The CM-III has been associated with excellent long-term rhythm results, with 75% of patients in sinus rhythm after 10 years [20]. In a recent electrocardiographic follow-up of the same cohort of Swedish CM-III patients as the present study, 82% had sinus or other regular supraventricular rhythm more than 9 years postoperatively [7]. However, the true prevalence of asymptomatic paroxysmal AF remains unknown, and the low rate of ischemic stroke/TIA after CM-III may not be attributed solely to freedom from AF. Instead, the removal of the LAA is most likely of significant importance. This surgical step has been a fundamental and nonoptional part of CM-III from the beginning. In fact, CM-III may be the only open-heart surgical procedure that includes complete LAA excision in all patients undergoing the operation. The LAA has traditionally been recognized as a main source of clot formation and embolization in nonvalvular AF. In one review, LA thrombus was found in 17% of nonvalvular AF patients, and 91% of these clots were found in the LAA [21]. Surgical closure of the LAA has been performed for years in many cardiac operations by ligation, over-sewing, or using stapling devices. However, recent studies have shown that traditional surgical closures may often be incomplete, paradoxically increasing the postoperative risk of stroke [22]. The current development in catheter-based LAA occlusion devices underscores the importance of the LAA [4], and at present surgeons are focusing more on complete closure of the LAA using new devices. For the classic cut-and-sew CM-III, a complete LAA excision was performed in all patients, leaving the issue of incomplete closure out of the equation for the present follow-up.

Methods to predict the risk of stroke in different populations with AF are of major importance. The relationship between predicted stroke risk and observed stroke outcome after CM-III has been evaluated in previous studies. Ad and associates [23] found embolic stroke/TIA

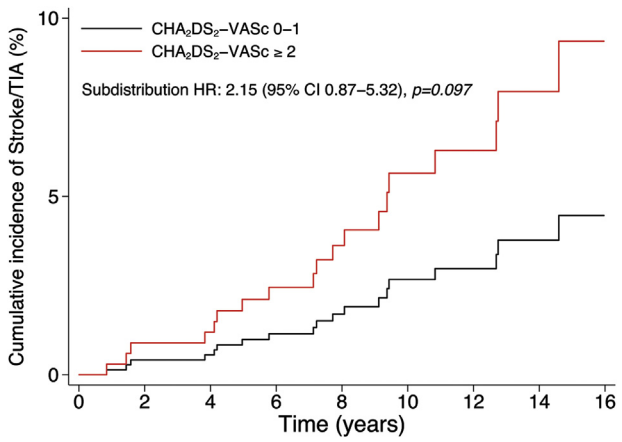

Fig 1. Cumulative incidence of ischemic stroke/transient ischemic attack (TIA) after the Cox-Maze III procedure in patients with preoperative CHA_2DS_2-VASc (age in years, sex, congestive heart failure history, hypertension history, stroke/TIA, thromboembolism history, vascular disease history, diabetes mellitus) score 0 or 1 compared with patients with CHA_2DS_2-VASc score 2 or greater. Note: A competing risk regression model was used to calculate the cumulative incidence function, accounting for the competing risk of death [13]. (CI = confidence interval; HR = hazard ratio.)

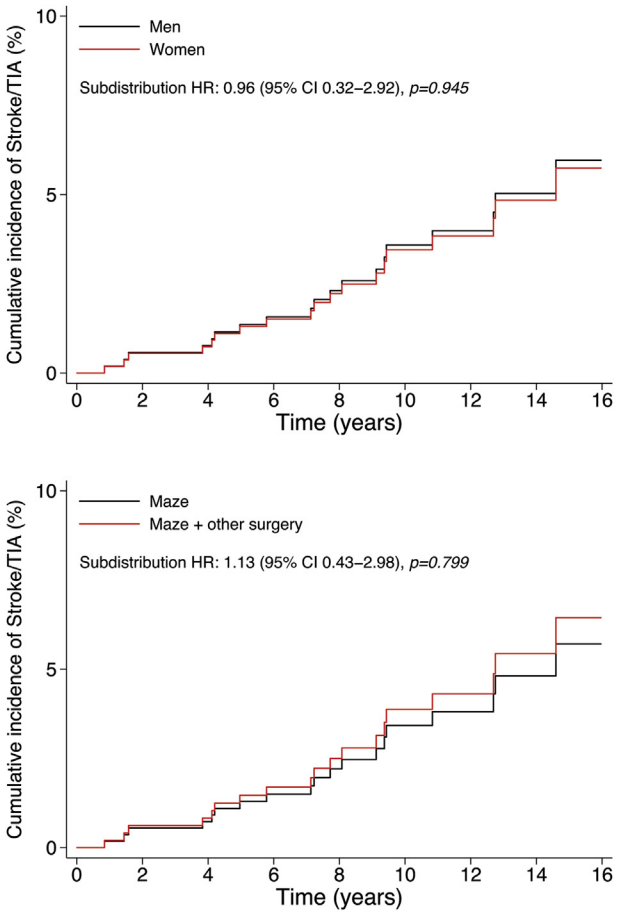

Fig 2. Cumulative incidence of ischemic stroke/transient ischemic attack (TIA) after the Cox-Maze III procedure (CM-III) in men compared with women (upper panel), in patients who underwent a stand-alone CM-III compared with CM-III concomitant with other cardiac procedures (lower panel). (CI = confidence interval; HR = hazard ratio.)

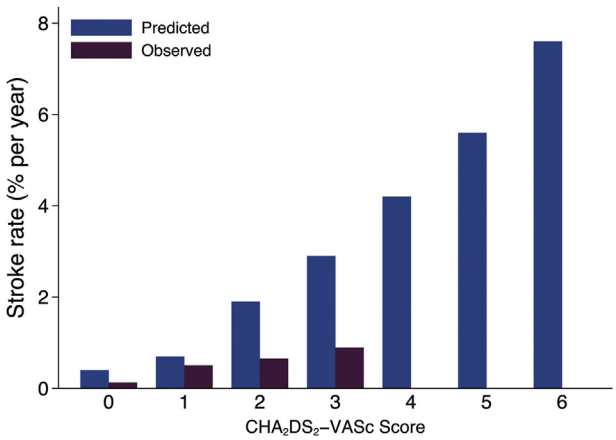

Fig 3. Observed and predicted [14] ischemic stroke rate (% per year) according to CHA_2DS_2-VASc (age in years, sex, congestive heart failure history, hypertension history, stroke/transient ischemic attack, thromboembolism history, vascular disease history, diabetes mellitus) score in patients who underwent the Cox-Maze III procedure. Note that there were no observed strokes in patients with a CHA_2DS_2-VASc score greater than 3.

in 4 of 385 patients (0.42% per year) followed prospectively for 3 years, but a higher incidence of bleeding events (7.3% per year). The investigators found no significant correlation between $CHADS_2$ score and embolic stroke/TIA in these patients. Pet and colleagues [8] showed a low postoperative stroke rate in 389 CM-III patients after a mean of 6.6 years (0.2%) with no association to $CHADS_2$ score or the use of warfarin. In our study, the observed stroke rate was clearly lower than predicted for all CHA_2DS_2-VASc scores. The cumulative incidence of ischemic stroke/TIA was approximately 6% at 10 years for patients with CHA_2DS_2-VASc score 2 or greater compared with 2.5% for CHA_2DS_2-VASc score 0 or 1. The relative risk of stroke was about twice as high for CHA_2DS_2-VASc score 2 or greater compared with CHA_2DS_2-VASc score 0 or 1, but this did not reach statistical significance because of the low number of events. In contrast to the study by Pet and colleagues [8], which had a limited follow-up and used the interview method to identify stroke incidence, we do believe there is an association between CHA_2DS_2-VASc and stroke in our patients. A register-based follow-up is more comprehensive and reliable in detecting the true number of strokes, as well as excluding other diagnoses that may simulate stroke symptoms. In addition, the CHA_2DS_2-VASc score is considered more sensitive than the $CHADS_2$ score, especially for low-risk patients. In our study, 68% of patients had a CHA_2DS_2-VASc score of 0 or 1. We also believe the statistical methods used, accounting for the competing risk of death, are more accurate in assessing the long-term risk of stroke.

Currently, the CHA_2DS_2-VASc score is widely used to determine which AF patients benefit from anticoagulant therapy. In the previously referred studies [8, 17, 23], the low number of postoperative strokes and the lack of association between stroke and $CHADS_2$ score caused the investigators not to recommend using $CHADS_2$ for evaluation of anticoagulant therapy. In our study, the low number of strokes observed even in patients with higher CHA_2DS_2-VASc scores may suggest that anticoagulant therapy is not necessary in surgically treated AF patients. However, this study represents a historical cohort of young and quite healthy AF patients. At present, most patients undergoing surgical treatment of AF are older concomitant valve or coronary artery bypass grafting patients with more complex comorbidities. They are now treated with the CM IV procedure using cryoablation or radiofrequency ablation, and we do believe in the appropriateness of using the CHA_2DS_2-VASc score and associated guidelines for postoperative anticoagulation treatment in these patients.

Limitations

This study suffers from the inherent limitations of a retrospective analysis. The results depend on the reliability of register data used, assuming that any postoperative stroke has resulted in a hospitalization and recorded as the correct diagnosis in the NPR. The validity of the diagnosis of stroke is strong in the NPR, with a sensitivity (proportion of patients with actual stroke identified in NPR) of 84% to 98% and a positive predictive value (correct diagnosis in NPR) of 98.6% [11]. Clearly, the number of TIAs postoperatively may be higher, because this is harder to differentiate from other diagnoses, and some patients may not even seek medical care for transient symptoms. In addition, we could not discern the role of postoperative anticoagulation therapy in this study. Medication after CM-III varied between centers and time eras and also on an individual basis according to cardiologist preference. We could not determine the medication history of all patients, especially in most patients who did not have a register-reported stroke or TIA. However, 80% of patients underwent surgical procedures in two centers with a clear policy of discontinuing warfarin immediately after CM-III and instead using aspirin. In the present follow-up, 84% were on aspirin or nothing at the time of their stroke/TIA event. We believe this study reflects the true incidence of ischemic stroke/TIA in CM-III patients without anticoagulant therapy in the ensuing years after the operation. The rhythm of the patients at the time of hospital admission for their event was predominantly sinus rhythm, but this fact is quite insignificant, because the incidence of residual silent paroxysmal AF is unknown. Although not proven, we believe this study indicates that the low incidence of stroke/TIA, regardless of rhythm, may be attributed to excision of the LAA.

Conclusions

We found a low incidence of perioperative and long-term postoperative ischemic stroke/TIA in a multicenter follow-up of AF patients undergoing cut-and-sew CM-III. Although the general risk of ischemic stroke/TIA was low, patients with preoperative CHA_2DS_2-VASc score 2 or greater had a higher risk than CHA_2DS_2-VASc score

0 or 1. Complete LAA excision may be an important reason for reduced ischemic stroke rate.

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References

1. Cox JL, Schuessler RB, D'Agostino HJ Jr, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. J Thorac Cardiovasc Surg 1991;101:569–83.
2. Prasad SM, Maniar HS, Camillo CJ, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. J Thorac Cardiovasc Surg 2003;126:1822–8.
3. Ballaux PK, Geuzebroek GS, van Hemel NM, et al. Freedom from atrial arrhythmias after classic maze III surgery: a 10-year experience. J Thorac Cardiovasc Surg 2006;132:1433–40.
4. Holmes DR Jr, Doshi SK, Kar S, et al. Left atrial appendage closure as an alternative to warfarin for stroke prevention in atrial fibrillation: a patient-level meta-analysis. J Am Coll Cardiol 2015;65:2614–23.
5. Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. J Thorac Cardiovasc Surg 1999;118:833–40.
6. Albåge A, Jidéus L, Ståhle E, Johansson B, Berglin E. Early and long-term mortality in 536 patients after the Cox-maze III procedure: a national registry-based study. Ann Thorac Surg 2013;95:1626–32.
7. Albåge A, Johansson B, Kennebäck G, Källner G, Scherstén H, Jidéus L. Swedish Arrhythmia Surgery Group. Long-term follow-up of cardiac rhythm in 320 patients after the Cox-maze III procedure for atrial fibrillation. Ann Thorac Surg 2016;101:1443–9.
8. Pet M, Robertson JO, Bailey M, et al. The impact of $CHADS_2$ score on late stroke after the Cox maze procedure. J Thorac Cardiovasc Surg 2013;146:85–9.
9. January CT, Wann LS, Alpert JS, et al, American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:e1–76.
10. World Health Organization. International Statistical Classification of Diseases and Related Health Problems 10th Revision 2010. Available at: http://apps.who.int/classifications/icd10/browse/2010/en#/VII.
11. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. BMC Public Health 2011;11:450.
12. Bergman P, van der Linden J. Atherosclerosis of the ascending aorta as a major determinant of the outcome of cardiac surgery. Nat Clin Pract Cardiovasc Med 2005;2:246–51.
13. Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. Circulation 2016;133:601–9.
14. Aspberg S, Chang Y, Atterman A, Bottai M, Go AS, Singer DE. Comparison of the ATRIA, CHADS2, and CHA2DS2-VASc stroke risk scores in predicting ischaemic stroke in a large Swedish cohort of patients with atrial fibrillation. Eur Heart J 2016;37:3203–10.
15. LaPar DJ, Mulloy DP, Crosby IK, et al. Contemporary outcomes for surgical mitral valve repair: a benchmark for evaluating emerging mitral valve technology. J Thorac Cardiovasc Surg 2012;143(4 Suppl):S12–6.
16. Ad N, Holmes SD, Massimiano PS, Pritchard G, Stone LE, Henry L. The effect of the Cox-maze procedure for atrial fibrillation concomitant to mitral and tricuspid valve surgery. J Thorac Cardiovasc Surg 2013;146:1426–34; discussion 1434–5.
17. Hwang SK, Yoo JS, Kim JB, et al. Long-term outcomes of the maze procedure combined with mitral valve repair: risk of thromboembolism without anticoagulation therapy. Ann Thorac Surg 2015;100:840–3; discussion 843–4.
18. Ha AC, Hindricks G, Birnie DH, Verma A. Long-term oral anticoagulation for patients after successful catheter ablation of atrial fibrillation: is it necessary? Curr Opin Cardiol 2015;30:1–7.
19. Kornej J, Hindricks G, Kosiuk J, et al. Renal dysfunction, stroke risk scores (CHADS2, CHA2DS2-VASc, and R2CHADS2), and the risk of thromboembolic events after catheter ablation of atrial fibrillation: the Leipzig Heart Center AF Ablation Registry. Circ Arrhythm Electrophysiol 2013;6:868–74.
20. Stulak JM, Dearani JA, Sundt TM III, Daly RC, Schaff HV. Ablation of atrial fibrillation: comparison of catheter-based techniques and the Cox-Maze III operation. Ann Thorac Surg 2011;91:1882–8; discussion 1888–9.
21. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thor Surg 1996;61:755–9.
22. Cullen MW, Stulak JM, Li Z, et al. Left atrial appendage patency at cardioversion after surgical left atrial appendage intervention. Ann Thorac Surg 2016;101:675–81.
23. Ad N, Henry L, Schlauch K, Holmes SD, Hunt S. The CHADS score role in managing anticoagulation after surgical ablation for atrial fibrillation. Ann Thorac Surg 2010;90:1257–62.