A More Specific Anticoagulation Regimen Is Required for Patients After the Cox-Maze Procedure

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Background. **Long-term management of oral anticoagulation (OAC) after ablation for atrial fibrillation (AF) is an ongoing challenge. Heart Rhythm Society (HRS) guidelines provide no specific recommendations for OAC after surgical ablation. The purpose of this study was to determine the necessity of OAC protocols after surgical ablation.**

Methods. **Patients (N = 691) who underwent the Cox-Maze procedure with left atrial appendage (LAA) management were followed prospectively. All patients were discharged on OAC unless contraindicated. Cardiac rhythm, bleeding, and embolic stroke or transient ischemic attack (TIA), or both, were verified during follow-up.**

Results. **Over a mean follow-up of 47.3 ± 30.3 months, stroke/TIA was reported in 14 patients (5.1 cases per 1,000 person-years) and major bleeding events were found in 46 patients (16.9 cases per 1,000 person-years). Patients with major bleeding events had higher median $CHADS_2$ (Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack) scores (2 [range, 1–3] versus 1 [range, 1–2]; $p = 0.012$), but no association was found between incidence of stroke/TIA and median $CHADS_2$ score (1 [range, 0–2.25] versus 1 [range, 1–2]; $p = 0.377$). Patients with $CHADS_2$ scores of 2 or greater had the same rates of stroke/TIA ($p = 0.787$) but a higher incidence of major bleeding ($p = 0.009$) as did patients with $CHADS_2$ scores less than 2. Adjusting for OAC discontinuation and stable sinus rhythm, patients with $CHADS_2$ scores of 2 or greater did not have higher stroke/TIA risk (hazard ratio [HR], 0.84; $p = 0.759$).**

Conclusions. **Our results indicate that the decision to discontinue OAC after the Cox-Maze procedure should not be based solely on $CHADS_2$ scores; rather, rhythm status, echocardiographic findings, and patient risk for bleeding should be considered. These findings underscore the need for an OAC protocol for patients who have undergone the Cox-Maze procedure with appropriate LAA management.**

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Despite advances in surgical approaches to atrial fibrillation (AF) treatment, the management of oral anticoagulation (OAC) in patients after surgical ablation remains unclear. There are no widely accepted guidelines specifically for the management of patients after the Cox-Maze procedure; guidelines from the Heart Rhythm Society (HRS) and other organizations provide recommendations that are more aligned with catheter-based interventions [1–3]. In a previous study, we published the significant limitation in applying only the $CHADS_2$ (Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack) score in the decision to maintain anticoagulation treatment after the Cox-Maze procedure [4]. In the present study, we examined the impact of OAC treatment on the incidence of stroke or transient ischemic attack (TIA), or both, and major bleeding after the Cox-Maze procedure to determine the need for a specific protocol for OAC after this operation.

Patients and Methods

All consecutive patients who underwent the full Cox-Maze procedure for AF at our center between January 2005 and September 2013 were followed prospectively (N = 691). The study was approved by our institutional review board (IRB No. 06.095 and 12.055), and a waiver of consent was given. Detailed information on clinical, medication, and rhythm status was collected prospectively before and after operative treatment, and follow-up data were collected at 3, 6, 9, 12, 18, and 24 months after operation and then yearly thereafter. Follow-up data for the present analyses include the first 5 years after the surgical procedure. Rhythm status was verified by electrocardiography and 24-hour Holter monitoring at each follow-up point. The HRS definition of failure (all documented atrial arrhythmias lasting > 30 seconds) was used to determine return to sinus rhythm [3]. Data collected as

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Abbreviations and Acronyms

AADs = anti-arrhythmic drugs
AF = atrial fibrillation
HR = hazard ratio
HRS = Heart Rhythm Society
IQR = interquartile range
LAA = left atrial appendage
OAC = oral anticoagulation
OR = odds ratio
SR = sinus rhythm
STS = The Society of Thoracic Surgeons
TIA = transient ischemic attack

part of our prospective study were merged into our local Society of Thoracic Surgeons (STS) database. All but 15 patients, in whom operative death occurred (within 30 days after operation), were eligible to be followed for postsurgical outcomes, although not all patients chose to participate at every time point. Not every follow-up point was complete on all patients because of deaths during follow-up or patients not yet reaching the time point. Patients were considered to be in stable sinus rhythm if all available time points indicated that the patient was in sinus rhythm.

Operative Approach

The Cox-Maze procedure was performed by multiple surgeons as previously described [5, 6]. The left atrial appendage (LAA) was managed in all patients; the approach for management (ie, complete excision, endocardial suturing, clip device) was left to the surgeon's discretion. Closure of the appendage was confirmed by echocardiography. Our center does not perform left atrial size reduction procedures on any patients. The energy source used for the Cox-Maze procedure was cryothermia alone (CryoFlex, Medtronic, Minneapolis, MN) in 63% of patients and a combination of bipolar radiofrequency and cryothermia in the other 37% of patients.

Postoperative Clinical Management

We have developed an intensive follow-up program and clinical protocols for patients after surgical ablation for AF to address issues related to rhythm or management of antiarrhythmic drugs (AADs) and OAC [7]. Briefly, OAC and AADs are continued postoperatively for all patients unless contraindicated or not tolerated. If the patient is in sinus rhythm at 3 months, as confirmed by 24-hour Holter monitoring, discontinuation of AADs is recommended. At 6 months, the patient undergoes 7 days of Holter monitoring with no AADs, and it is determined whether the patient is in sinus rhythm according to HRS guidelines (ie, no atrial arrhythmia episode lasting $>$ 30 seconds). Echocardiography is used to confirm no stasis in the left atrium and a well-managed LAA. If all these criteria are met, a recommendation is made to the presiding cardiologist to discontinue OAC therapy if there are no other clinical indications (eg, deep vein thrombosis, pulmonary embolism, mechanical valve).

Definitions

The $CHADS_2$ score is used to estimate the risk for stroke in patients with AF by assigning a score based on the following high-risk conditions: congestive heart failure, hypertension, age of 75 years or older, diabetes mellitus, and previous stroke/TIA [8]. Each condition receives 1 point except for previous stroke/TIA, which receives 2 points. HRS guidelines recommend OAC therapy for all patients with AF and a $CHADS_2$ score of 2 or greater and do not distinguish between those who have and those who have not had their AF corrected with ablative techniques. For these analyses, 2 groups were formed based on these guidelines: patients with $CHADS_2$ scores less than 2 (lower risk) and patients with $CHADS_2$ scores of 2 or greater (higher risk).

The $HEMORR_2HAGES$ (Hepatic or Renal Disease, Ethanol Abuse, Malignancy, Older Age, Reduced Platelet Count or Function, Rebleeding, Hypertension, Anemia, Genetic Factors, Excessive Fall Risk and Stroke) risk score provides clinical predictive rules for bleeding events in patients with AF to balance the benefit of OAC against the risk for bleeding events [9]. The score assigns 2 points to patients with a previous bleeding event and 1 point each for hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count or function, hypertension, anemia, genetic factors, excessive fall risk, and stroke.

Stroke/TIA events were defined as thromboembolic events diagnosed through patient-reported symptoms, physical examination, and computed tomography or magnetic resonance imaging at the time of the event. Major bleeding events were defined as the receipt of blood products for a bleeding event, stroke or death caused by brain hemorrhage, or a large hematoma requiring medical intervention.

Statistical Analysis

Continuous data are presented as mean $\pm$ standard deviation or median (interquartile range [IQR]), and categorical data are presented as frequency (percentage) unless otherwise noted. Group comparisons for categorical variables were conducted with the χ^2 or Fisher's exact test, and comparisons for continuous variables were conducted with the Student's t test or the Mann-Whitney U test based on test assumption requirements. Spearman's correlation was performed to examine the nonparametric correlation between $CHADS_2$ and $HEMORR_2HAGES$ scores. Multivariate logistic regression was used to determine predictors of receiving OAC therapy at 1 and 2 years after operation and included the following factors: age, $CHADS_2$ score, nonstable sinus rhythm during follow-up, concomitant valve operations, and preoperative left atrial size (in centimeters). Kaplan-Meier survival analysis was conducted to examine event-free survival during follow-up and univariate comparisons between $CHADS_2$ score groups. Cox regressions were used for multivariate analyses of event-free survival. All analyses were conducted using SPSS Statistics, version 17.0 (SPSS