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Atrial fibrillation inducibility during cavo-tricuspid isthmus dependent atrial flutter ablation for the prediction of clinical atrial fibrillation☆

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ABSTRACT

Background: Atrial fibrillation (AF) and cavo-tricuspid isthmus (CTI) dependent atrial flutter (AFL) are two separate entities that coexist in a significant percentage of patients.
Methods: We sought to investigate whether AF inducibility during CTI AFL ablation predicted the occurrence of AF at follow up after AFL ablation. Univariate and multivariate analyses were performed.
Results: A total of 154 patients (male: 72%, age: 61 ± 13) with AFL and without history of AF were included. All patients underwent successful CTI dependent AFL ablation demonstrated by bidirectional block. During ablation, AF was seen or induced in 28 (18%) patients. After a mean follow up of 34 ± 24 months a total of 50 patients (32%) were noted with clinically manifest AF. From the patients who had inducible AF during AFL ablation, 50% developed post-procedural AF. From those in whom AF could not be induced, only 29% were documented with AF after ablation. Univariate and multivariate analyses revealed that only age and AF inducibility during AFL ablation were predictors of AF. Univariate analysis (age $p = 0.038$ and inducible AF $p = 0.032$ with odds ratio of 1.030 [95% CI (1.002–1.059)] and 2.500 [95% CI (1.084–5.765)], respectively) and multivariate analyses (age $p = 0.011$ and inducible AF $p = 0.016$ with adjusted odds ratio of 1.043 [95% CI (1.010–1.077)] and 3.293 [95% CI (1.250–8.676)], respectively).
Conclusion: AF inducibility in patients undergoing CTI AFL without history of AF is a strong predictor of AF occurrence in the future. Appropriate cardiology follow-up must be encouraged in this high-risk population as stroke prevention strategies can be appropriately introduced in a timely matter especially in patients with elevated CHA_2DS_2-VASc scores (≥2).

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1. Introduction

The prevalence of atrial fibrillation (AF) in the US is expected to rise to 5.6–12.0 million by 2050. In 2010 the estimated prevalence of AF in the same demographic area ranged from 2.7 million to 6.1 million. Worldwide, AF is the most common arrhythmia in the elderly population (>65 years old) [1–4].

Compared to AF, the development of new onset atrial flutter (AFL) is significantly less frequent in the general population. The estimated incidence of AFL in the US is 200,000 new cases per year, out of which 80,000 are thought to have isolated AFL. This arrhythmia is seen 2.5 times more in men than in women. Some of the risk factors that can be attributable to AFL onset include systolic or diastolic heart failure, chronic obstructive pulmonary disease, and atrial fibrillation [5–8].

As shown by long-term low recurrence rates, typical or cavotricuspid isthmus dependent (CTI) AFL is curable with radiofrequency (RF) catheter ablation [5,9–13].

Prior data in patients who were followed 6 to 40 months after AFL ablation estimate the rates of AF in this population to be between 15 and 82% [9,11,12,14–18]. The progressive occurrence of AF after AFL

Abbreviation: AFL, atrial flutter; AF, atrial fibrillation; CTI, cavo-tricuspid isthmus; PVI, pulmonary vein isolation; EPS, electrophysiology study; ECG, electrocardiogram; BMI, body mass index; gtTSH, thyroid stimulating hormone; MRMVR, mitral regurgitation (moderate or severe) or previous mitral valve replacement; TRTVR, tricuspid regurgitation (moderate or severe) or previous tricuspid valve replacement.

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ablation has been associated with pre-ablation AF, age <65 years and mitral regurgitation [16,18–24].

Despite having a 6% cumulative incidence of stroke during a mean follow-up of 30 months after ablation for typical AFL, recommendations for anticoagulation or antiarrhythmic therapy for this population are scant [25,26]. Of note, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers and diuretics were associated with less development of AF [27], perhaps given their ability to lower intraventricular filling pressures and prevent or decrease left atrial remodeling, and treating comorbidities that predispose to AF such as hypertension and heart failure. However, larger randomized studies are required to propose this intervention [28–30].

Likewise, there have been remarkable benefits shown from ablation of AF and AFL, when both are present [31]. Small initial trials of prophylactic AF ablation during typical AFL ablation have evidenced double rate of long-term freedom from recurrent arrhythmias after 20 month follow-up [32,33]. Current AHA/ACC guidelines exclude this prophylactic approach, probably due to the highly complex and potentially life-threatening complications (e.g., atrioesophageal fistula, cardiac tamponade, phrenic nerve injury, pulmonary vein stenosis, stroke) as well as the need for transseptal puncture during AF ablation. The objective of this study was to determine which factors can predict post-procedural AF in patients undergoing AFL ablation, particularly AF inducibility during the procedure.

2. Methods

2.1. Study population

Two hundred seventy-three consecutive patients with an ECG proven CTI AFL, who underwent CTI AFL radiofrequency ablation from July 1, 2006 to June 31, 2011 were included in this analysis. One hundred and nineteen (43%) patients were excluded since they had evidence of AF prior to AFL ablation or there was incomplete data in the chart. Patients were also excluded if they had a previous unsuccessful CTI AFL ablation, pulmonary vein isolation (PVI) or were under 21 years old. To determine prior history of AF, we searched the patient's medical chart, and reviewed all electrocardiograms (ECGs), 24-hour Holter monitors and event monitors available. No patient had implantable loop recorders in this study. Clinical data and comorbidities were obtained from chart review using Montefiore Medical Center's electronic health records.

2.2. Electrophysiology study (EPS) and inducibility

All patients provided written informed consent before EPS and CTI AFL ablation. Patients were asked to stop all antiarrhythmic drugs (AAD) at least 5 half-lives prior to ablation and if patients were on amiodarone, this was stopped at least one month in advance as per arrhythmia service protocol in this institution. Procedure data was collected from EPS reports. Access was obtained through the right and/or left femoral veins and the right internal jugular vein. Quadripolar catheters were advanced under fluoroscopy to the bundle of His and the right ventricle. A CS-L catheter was advanced to the coronary sinus. A duodecapolar catheter 10-2-10 mm was looped in the right atrium under fluoroscopic guidance, with distal electrodes at the CTI. A Biosense ThermoCool irrigated 4-mm tip ablation catheter or a 8-mm tip non-irrigated catheter was advanced under fluoroscopy to the right atrium (RA). This was used to create RA anatomy as well as to perform activation maps in the RA. This catheter was subsequently positioned on the tricuspid valve/inferior vena cava isthmus for the ablation procedure. An RA map was constructed using either the EnSite navigation system (St Jude, St Paul, MN, USA), Carto XP or Carto 3 mapping system (Biosense Webster, Inc., Diamond Bar, Calif.). The electroanatomic map was also used to guide catheter positioning during the ablation. Rapid atrial pacing was performed to induce AFL if a patient was in normal sinus rhythm at the beginning of the procedure. Entrainment mapping around the tricuspid annulus with post-pacing intervals minus tachycardia cycle length <30 ms confirmed isthmus-dependent RA clockwise or counterclockwise flutter in all cases. The ablation catheter was initially advanced into the RV, curved and pulled back to seat it on the isthmus. The position of the catheter was confirmed in both the RAO and LAO fluoroscopic views and with electroanatomic mapping. Radiofrequency ablation (RFA) lesions were applied for 60 s at a maximum power of 40 W and maximum temperature of 42 °C for irrigated catheters and at a maximum power of 50 W and maximum temperature of 55 °C for non-irrigated catheters along the isthmus (i.e., tricuspid valve annulus to inferior vena cava). Loss of electrogram following radiofrequency delivery was confirmed at each site. Determining bidirectional conduction block across the isthmus (>130 ms cut-off) was performed in all cases by noting a change in activation in the duodecapolar catheter electrograms in the RA and conduction times by pacing in the lateral RA and coronary sinus. Atrial burst pacing was carried out to induce AFL before and after ablation. We performed formal decremental pacing (atrial burst) and atrial pacing at two cycle lengths with single and double extrastimuli to intentionally try to induce AFL. AF inducibility was defined as sustained AF over 30 s either due to catheter manipulation or due to pacing protocols performed to induced AFL. If AF did not spontaneously convert to sinus rhythm, the patient was electrically cardioverted. Anti-arrhythmic medications, which were held prior to the procedure and atrioventricular nodal blockers, were permanently discontinued after RFA. Chronic anticoagulation for stroke prevention in patients with high CHADS and CHA_2DS_2-VASc score was discontinued after one to three months of the ablation in all patients.

Post-ablation AF was usually found either based on new symptoms,; or incidentally during a hospital admission or regular clinic appointment with the treating physician. On these situations, a 12 lead ECG or Holter monitoring was performed to confirm the diagnosis. Routine ECGs were performed at every outpatient follow up visit. The primary clinical endpoint was the development of ECG-proven AF, regardless of symptoms. A secondary endpoint was the recurrence of CTI-dependent AFL. Outcomes were determined through chart review. The study was approved by the Institutional Review Board of Montefiore Medical Center and Albert Einstein College of Medicine.

2.3. Statistical analysis

Continuous and categorical variables were expressed as the mean and standard deviation (SD) or number and percentage, respectively. Risk factors previously demonstrated to be associated with atrial AF (age, gender, body mass index (BMI), heart failure, hypertension, chronic obstructive pulmonary disease, obesity hypoventilation syndrome, hyperthyroidism), echocardiographic variables (ejection fraction, presence of mitral regurgitation or mitral valve replacement-MRMVR- and tricuspid regurgitation or tricuspid valve replacement-TRTVR-), and the provocation of AF during the procedure were included. The main outcome was the diagnosis of AF post AFL ablation. The cohort was stratified in those who were diagnosed with AF and those who were not. Univariate and multivariate logistic regression was used to compute odds ratios (OR) and 95% confidence intervals, using the aforementioned variables. All analyses were performed using SPSS version 21.0 (IBM, Armonk, NY).

3. Results

3.1. Study population

Data from 273 consecutive patients who underwent ablation of CTI-dependent AFL at our institution from July 2006 until June 2011 was reviewed. Fifty-eight patients (21%) were excluded due to prior AF history and sixty-one patients (22%) were excluded due to incomplete data in the chart. A total of 154 patients with AFL and without history of AF composed the study population included in the statistical analysis. All patients underwent successful AFL ablation without any complications. The mean age was 60.9 years (SD 13.4 years) with a male-to-female ratio was 7:3 and a mean BMI of 31 kg/m^2 (SD 7.7 kg/m^2). Relevant recorded past medical history included heart failure (35%), hypertension (62%), chronic obstructive pulmonary disease (11%) and obesity hypoventilation syndrome (20%). Echocardiographic findings included a mean left ventricular ejection fraction (LVEF) of 47.8% (SD 15.9%), MRMVR (29%) and TRTVR (26%). AF was documented/induced during ablation in 28 patients (18%).

3.2. AFL ablation: procedural details AFL

Complete bidirectional TV-IVC block was achieved with no periprocedural complications observed in all patients. The average fluoroscopy time was 24 min (SD 16.2 min) and the average procedure time was 181.9 min (SD 101.7 min) for all patients combined.

3.3. Post-procedural AF occurrence

After a mean follow-up of 34 ± 23.5 months, a total of 50 (32%) patients with isolated AFL were documented with AF. Patients that were identified to have developed AF were found to be older compared to those who did not develop AF (OR 1.030, 95% CI 1.002–1.059; adjusted OR 1.043, 95% CI 1.010–1.077). In addition, although comorbidities appeared to be less prevalent in the group that developed AF compared to those who did not, there were no significant differences between groups in both, univariate and multivariate analysis (Tables 2 and 3).

During ablation of CTI AFL, AF was documented/induced in 28 (18%) patients and half of those (14, 50%) developed AF during follow-up. Only 29% of non-inducible patients had documented AF at follow up.

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