Scientific letters

Long-term Outcome of Cryoballoon Ablation of Atrial Fibrillation in a Low-volume Center

Resultados a largo plazo de la criobalón para el tratamiento de la fibrilación auricular en un centro de bajo volumen

To the Editor,

Cryoballoon ablation (CBA) accounted for 19% of all ablation procedures for atrial fibrillation (AF) in Spain in 2012. Little information is available on the long-term outcomes of CBA. No data have been reported from low-volume centers, but such information is important because almost 80% of Spanish catheterization laboratories perform fewer than 50 AF ablations per year.

We prospectively analyzed the outcomes of CBA as the first-line technique in a low-volume center. From November 2010 through June 2013, 63 patients were included (12 of whom were women; mean [standard deviation] age, 55 [10] years). Of these patients, 48 (76%) had recurrent paroxysmal AF, and 15 had short-lasting persistent AF (<6 months). The mean left atrial diameter was 41 (4) mm, and 9 patients (14%) had structural heart disease; 11 patients (18%) had a score ≥2 on the CHA2DS2–Vasc score.

Oral anticoagulants were administered for at least 1 month prior to CBA and were continued for 1 month after the ablation procedure. After the first month, the decision to continue or stop anticoagulant therapy was based on the score on the CHA2DS2–Vasc scale. Antiarrhythmic agents were continued for 3 months after the procedure (6 months in persistent AF).

Cryoballoon ablation was initially performed through double transseptal puncture, although single puncture techniques were used once the intraluminal circular catheter became available. The last 19 procedures were performed with the Advance Cryoballoon (Medtronic Inc.), which was the device that achieved the most homogeneous application to the whole circumference of the opening of the pulmonary vein. At least 2 applications were made per vein, with continuous phrenic pacing of the right pulmonary veins during ablation to monitor for the appearance of phrenic paralysis.

Procedure and fluoroscopy times were 168 (22) minutes and 30 (12) minutes, respectively. These times decreased significantly after the first 30 procedures (the procedure time was 189 [18] minutes for the first 30 procedures and 147 [34] minutes for subsequent procedures, while the fluoroscopy time was 35 [7] minutes for the first 30 procedures and 23 [5] minutes for subsequent procedures; P < .001). Electrical isolation was achieved in 224 of the 231 pulmonary veins identified (97%). The vessel most frequently left without isolation was the right inferior vein (4 procedures), in all cases because phrenic paralysis was detected in the superior right pulmonary vein during the application. Six patients had a common chamber (4 left, 2 right).

During the 12 (8) months of follow-up, recurrence of AF was reported in 20 patients (32%), with a rate of sustained sinus rhythm after 1 and 2 years of 69% and 51%, respectively. With antiarrhythmic agents, these rates increased to 94% and 86%, respectively (Figure). Symptomatic arrhythmic episodes persisted in 5 patients, AF was documented in 3 patients, and 2 patients had atrial flutter. All these patients underwent a further ablation procedure, this time with radiofrequency.

On multivariate analysis, the only independent predictor of recurrence of AF after CBA was time in AF prior to the procedure (hazard ratio [HR] = 1.17; 95% confidence interval [CI], 1.035–1.32; P = .012). The number of pulmonary veins isolated was a protective factor (HR = 0.19; 95% CI, 0.072–0.509; P = .001) (Table). Of the 4 patients without application to the right inferior pulmonary vein, 2 experienced recurrence.

Twelve complications were reported (19% of procedures). These were mainly phrenic paralysis in right pulmonary veins during the procedure (7 cases, 11%). These events were always transient, although resolution occurred late in 2 patients (9 and 12 months). After controlling the application times (240–180 seconds) and temperature (limited to −55°C), no phrenic paralyses were reported in the last 28 ablations, with no impact on the efficacy of the procedure (P = .01). In addition, there was 1 transient ischemic attack due to air embolism, 1 asymptomatic thalamic stroke, and 2 minor episodes of hemoptysis. Finally, there was 1 case of atrioesophageal fistula, attributed to application (with the

Figure. Atrial-fibrillation-free survival without (A) and with (B) antiarrhythmic drugs.
new cryoballoon) to the left inferior pulmonary vein. The patient died 1 month after the procedure.

The learning curve for CBA as the treatment of choice for recurrent paroxysmal AF or short-lasting persistent AF in small-volume centers is steep, as indicated by the high initial short-term efficacy and fast decrease in fluoroscopy and procedure times ($P < .001$) in our series. The rates of sustained sinus rhythm with and without antiarrhythmic drugs and the incidence of phrenic paralysis and severe complications (3 out of 63 cases [4.8%]) appear to be similar to those of other series with a larger number of patients.3–5 Although the incidence of complications may seem high, it was driven mainly by transient phrenic paralysis. This complication was eliminated when we limited the application

time and minimum temperature reached ($P = .01$). Importantly, however, changes in the ablation parameters and the small number of patients in the series prevent affirmations about the steepness of the learning curve, particularly regarding the incidence of serious complications.

Julio Martí-Almor, Victor Bazan,* Ermengol Vallés, Begona Benito, Miguel Eduardo Jauregui-Abularach, and Jordi Bruguera-Cortada

Unidad de Arritmias, Servicio de Cardiología, Hospital del Mar, Universidad Autónoma de Barcelona, Barcelona, Spain

*Corresponding author:
E-mail address: vbazan@hospitaldelmar.cat (V. Bazan).
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**Table**

Predictors of Atrial Fibrillatory Recurrence After Cryoballoon Ablation of Atrial Fibrillation

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal AF</td>
<td>0.899 (0.299-2.700)</td>
<td>.851</td>
</tr>
<tr>
<td>LA diameter</td>
<td>1.071 (0.959-1.197)</td>
<td>.221</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.943 (0.863-1.031)</td>
<td>.199</td>
</tr>
<tr>
<td>Age</td>
<td>1.012 (0.963-1.064)</td>
<td>.641</td>
</tr>
<tr>
<td>AF duration</td>
<td>1.168 (1.035-1.318)</td>
<td>.012</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>0.859 (0.199-3.710)</td>
<td>.838</td>
</tr>
<tr>
<td>Ablation of atrial flutter combined with CBA</td>
<td>0.892 (0.322-2.476)</td>
<td>.825</td>
</tr>
<tr>
<td>CHA2DS2–VASc $&gt; 2$</td>
<td>0.996 (0.332-2.989)</td>
<td>.994</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.819 (0.273-2.458)</td>
<td>.819</td>
</tr>
<tr>
<td>Use of Artic Front Advance device*</td>
<td>0.454 (0.101-2.032)</td>
<td>.301</td>
</tr>
<tr>
<td>Number of applications</td>
<td>1.064 (0.824-1.372)</td>
<td>.633</td>
</tr>
<tr>
<td>Number of PVs isolated</td>
<td>0.192 (0.072-0.509)</td>
<td>.001</td>
</tr>
<tr>
<td>Anatomic variants of PV</td>
<td>1.545 (0.512-4.661)</td>
<td>.440</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; CBA, cryoballoon ablation; CI, confidence interval; HR, hazard ratio; LA, left atrial; LV, left ventricle; PV, pulmonary veins. Statistical significance was set at $P < .05$. 

**Prognostic Value of the INTERHEART-Cholesterol Risk Score in Patients Hospitalized for Chest Pain**

**Valor pronostico de la escala INTERHEART-cholesterol para pacientes que ingresan por dolor torácico**

**To the Editor,**

Predicting the incidence of and/or mortality associated with ischemic heart disease is of crucial importance in public health and consequently a number of scoring systems have been developed to estimate the risk of this disease, such as the Framingham equation1 or the SCORE chart.2 In 2011, the investigators in the INTERHEART study described a specific scoring system to predict the incidence of acute infarction, with a variant based on both low-density and high-density lipoprotein cholesterol.3 The objective of our study was to analyze the prognostic value of the INTERHEART-cholesterol score in patients admitted to hospital for chest pain. This score is based on a prospective observational registry of all the patients hospitalized consecutively for chest pain in a single cardiology department over a 19-month period. In all, 1312 consecutive patients were recruited, of which 1240 (94.5%) were included in the study, after exclusion of those whose analytical results were not available. The enrolled patients were classified according to a diagnosis of acute coronary syndrome (ACS) or nonischemic chest pain. The INTERHEART-cholesterol score3 was calculated for each participant on the basis of age (> 55 years for men and > 65 years for women, 2 points), low-density lipoprotein cholesterol (77–116 mg/dL, 1 point; 177–150 mg/dL, 2 points; > 151 mg/dL, 5 points), high-density lipoprotein cholesterol (< 40 mg/dL, 2 points), tobacco use (ex-smoker, 2 points; smoker of 1-5 cigarettes/d, 2 points; smoker of 6-10 cigarettes/d, 4 points; smoker of > 11-20 cigarettes/d, 7 points; smoker of > 20 cigarettes/d, 11 points), diabetes mellitus (7 points), and hypertension (6 points); the patients were divided into tertiles depending on their individual scores. After hospital discharge, the patients were followed up for at least 1 year.

The statistical analysis was carried out with SPSS 20.0 for Mac (SPSS Inc., Chicago, Illinois, United States). Categorical variables were evaluated with the chi-square test and continuous variables with Student’s $t$ test and analysis of variance (ANOVA). The survival analysis was performed using Cox proportional hazards regression by means of forward selection; for this analysis, we considered the lowest tertile as the reference variable and analyzed the variables not included in the INTERHEART score but having clinical implications for prognosis or those that obtained a $P$ value $\leq .25$ in the univariate analysis. $P$ values $< .05$ were considered to indicate statistical significance.

Of the 1240 patients studied, 467 (37.7%) had non-ST-segment elevation ACS, 189 (15.2%) had ST-segment elevation ACS, and 584 (47.1%) had nonischemic chest pain. The mean score...