Cryoblation of superoparaseptal and septal accessory pathways: a single centre experience

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Aims

Radiofrequency (RF) catheter ablation in the septum close to the atrioventricular (AV) node or His bundle has an increased risk of irreversible complications. Cryothermal energy has the advantages of reversible cryomapping and increased catheter stability. This study evaluates the usefulness of cryoablation in superoparaseptal and septal accessory pathways (APs).

Methods and results

Twenty-seven consecutive patients (16 men, 11 women, median age 29 years, range 15–65) underwent cryoablation for APs either located in the superoparaseptal (n = 18) or septal (n = 9) area. Cryomapping, using exclusively a 6 mm tip catheter, at −30 °C was performed before ablation with a goal temperature of −80 °C for 240 s. Acute success was achieved in 26 out of 27 patients (96%). Total procedure and fluoroscopy time was 163 ± 61 and 30 ± 22 min, respectively. During a follow-up for a mean of 996 ± 511 days, seven patients (27%) had recurrences of arrhythmia. Five out of these seven underwent a second cryoablation with successful results, giving a total success rate of 89%. Two patients developed transient second degree AV block during cryoablation; however, no permanent AV block was observed. The recurrence rate was significantly higher in patients with procedure-related transient mechanical AP block (6/7; 86%) due to catheter trauma compared with those without mechanical block (5/20; 25%; P = 0.006).

Conclusion

Cryoablation of the superoparaseptal and septal APs is a safe and effective alternative to RF therapy. Procedure-related transient mechanical AP block predicts worse late outcome.

Keywords

Cryomapping • Cryoablation • Atrioventricular re-entrant tachycardia • Accessory pathways • Radiofrequency

Introduction

Radiofrequency (RF) catheter ablation is the routine treatment of accessory pathways (APs) at various sites along the atrioventricular (AV) annuli.1,2 However, RF ablation of pathways near the His bundle or the AV node (such as superoparaseptal or septal APs) is associated with a risk for inadvertent AV block.3–6 Recently, cryoablation of supraventricular arrhythmias has emerged as an alternative to RF ablation.7,8 Cryothermal energy has advantages such as reversibility of cryothermal energy lesions during cryomapping, decreased thrombus risk, and increased catheter stability.9–11 Furthermore, cryomapping seems to predict the effectiveness and safety of the ablation of APs near the AV node or His bundle. However, few published reports focus on these issues.9,10 In the present study, we wanted to study the safety, efficacy, and possible predictors of recurrence using cryoablation for superoparaseptal and septal APs.

Methods

Patients and materials

The study population consisted of all patients undergoing a first transvenous catheter ablation procedure of a superoparaseptal or septal AP using cryothermal energy between January 2004 and December 2008. During this 5-year period, 464 patients underwent transvenous catheter ablation of AP at our institution. Twenty-seven (5.8%) of these patients had an AP located either in the superoparaseptal (n = 18) or in the septal (n = 9) region and seven (26%) of these patients had previously undergone an electrophysiological (EP) study with aborted RF ablation attempt due to an estimated high risk of
complications. Patient characteristics are summarized in Table 1. Superoparaseptal and septal APs (Table 2) were defined as follows.

**Superoparaseptal accessory pathway**
Pathways were classified as superoparaseptal if an AP activation potential as well as a His bundle potential were simultaneously recorded from a mapping catheter placed at the His bundle region. At fluoroscopy, the tip of the mapping catheter was near the His-catheter in different radiological views (Figure 1).

**Septal accessory pathway**
Pathways were classified as right septal if either the earliest anterograde ventricular activation or an AP potential was recorded from a catheter located in an area bounded superiorly by the tip electrode of the His bundle catheter and inferiorly by the coronary sinus ostium, excluding atrioventricular nodal re-entrant tachycardia (AVNRT), and septal or parahissian ectopic atrial tachycardias.

**Electrophysiological study and ablation procedure**
Anti-arrhythmic drug medication was discontinued five half-lives before the study. All procedures were performed under light sedation, under local anaesthesia, and in the fasting state. Heparin was given routinely. A 12-lead surface electrocardiogram (ECG) during pre-excitation was obtained and analysed. The delta-wave morphology was used to predict the site of origin.12,13

A conventional EP study was performed using three electrode catheters that were positioned in the right ventricle apex, in the coronary sinus, and in the His position. The left atrium was mapped in four patients using a transeptal approach. Both AV conduction and refractoriness in the anterograde and retrograde direction were evaluated by mapping catheter placed at the His bundle region. At fluoroscopy, the tip of the mapping catheter was near the His-catheter in different radiological views (Figure 1).

**Table 1 Patient characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>27</td>
</tr>
<tr>
<td>Men</td>
<td>16 (59%)</td>
</tr>
<tr>
<td>Women</td>
<td>11 (41%)</td>
</tr>
<tr>
<td>Age (years); median (range)</td>
<td>29 (15–65)</td>
</tr>
<tr>
<td>No underlying heart disease</td>
<td>24 (89%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
</tr>
<tr>
<td>VOC</td>
<td>1</td>
</tr>
</tbody>
</table>

VOC, Vitium organicum cordis.

**Table 2 Procedural characteristics**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>n</th>
<th>Cryo success</th>
<th>Procedural time (min); median (range)</th>
<th>Fluoroscopy time (min); median (range)</th>
<th>Cryoablation time (s); median (range)</th>
<th>Recurrence rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All AP</td>
<td>27</td>
<td>26 (96%)</td>
<td>150 (70–330)</td>
<td>21 (6–81)</td>
<td>450 (240–2464)</td>
<td>7/26 (27%)</td>
</tr>
<tr>
<td>Superoparaseptal</td>
<td>18</td>
<td>17</td>
<td>150 (80–330)</td>
<td>20 (6–80)</td>
<td>401 (240–2464)</td>
<td>4/17 (23%)</td>
</tr>
<tr>
<td>Septal</td>
<td>9</td>
<td>9</td>
<td>165 (70–220)</td>
<td>30 (7–81)</td>
<td>480 (240–1031)</td>
<td>3/9 (33%)</td>
</tr>
</tbody>
</table>

AP, Accessory pathway; Cryo, Cryothermal ablation.

Cryoablation of superoparaseptal and septal accessory pathways 973

Follow-up
Clinical follow-up was based on outpatient visit (n = 27), medical records, and telephone contacts. A 12-lead surface ECG was obtained in all patients at long-term follow-up. Holter monitoring or EP study were used depending on the presented symptoms. In addition, a symptom questionnaire was sent to all patients. Patients were queried whether they were totally free from arrhythmia symptoms, significantly better, somewhat improved, or if the symptoms were unchanged or had deteriorated. They were also asked about the
frequency of symptoms: daily, several times per week, once per week, or less. Furthermore, if they had experienced a recurrence of arrhythmia symptoms, they were asked to describe these symptoms. Finally, the patients were asked about current anti-arrhythmic drug therapy. If recurrence were suspected, the patient was subjected to further investigation. Recurrence was defined as ECG-documented tachycardia, relapse of pre-excitation (delta-wave), or return of clinical symptoms identical to those before cryoablation.

Statistics

Data are given as median and range or mean ± SD as appropriate. Continuous data were compared using the Mann–Whitney U-test or Student’s t-test. For categorical data, proportions were analysed using the χ² test. P < 0.05 was considered significant. Statistical analyses were performed using commercially available software (Statistica version 8.0, StatSoft Scandinavia AB).

Results

Acute procedural success was achieved in 26 out of 27 patients (96%). The patient who did not have a successful treatment declined a new ablation attempt due to absence of symptoms on low-dose Sotalol treatment. Four patients had dual APs with the associated APs located in left inferoparaseptal (n = 2), left posterior (n = 1), and right anterior (n = 1) position. Because the location of the additional APs was considered safe, these APs were successfully treated by conventional RF current application.

After a mean follow-up of 956 ± 511 days, seven patients (27%) had recurrences. Five of these 7 (71%) underwent a second successful cryoablation. One patient underwent a new ablation attempt by RF with a late recurrence. The remaining patient experienced substantial improvement after cryoablation and because of a prolonged refractoriness of the AP (APERP = 500 ms) during a new EP study no new intervention was performed. No further recurrences were seen during 786 ± 484 days in the five patients with a redo procedure. The final success rate was 89%, 24 out of 27 (Figure 2). Total procedure and fluoroscopy time was 163 ± 61 and 30 ± 22 min, respectively. The procedural characteristics are summarized in Table 2.

Transient catheter-induced mechanical block of the AP was observed in 11 patients (41%) with pre-excitation, seven with superoparaseptal, and four with septal APs. No patient showed prolongation of the AH interval during cryomapping. However,
despite negative cryomapping, two patients, one with a superoparaseptal and the other with a septal located AP, developed transient second degree AV block during cryoablation that lasted 10 and 25 s, respectively. No permanent PR interval prolongation was observed at long-term follow-up.

Symptom questionnaire
Out of 27 patients, 25 (92%) responded to the questionnaire, and 88% of the patients reported that the procedure had completely abolished (n = 15) or significantly improved (n = 7) their symptoms without taking anti-arrhythmic medication and that the ablation had been a success. Three patients did not experience a procedural success although all three indicated some improvement of their symptoms. Two of them had a documented relapse of pre-excitation. One was offered a new EP study, but declined due to the improvement of symptoms with low-dose Sotalol. In the other patient, no new ablation attempt was performed as a new EP study revealed a significant prolongation of refractoriness of AP and considering the high-risk location. This patient continued medical therapy with bisoprolol. Holter monitoring and a new EP study in the third patient did not show any sign of recurrence.

Predictors of recurrence
Compared with those without mechanical block (5/20, 25%; \( P = 0.006 \)), recurrence was more likely in patients with catheter-induced transient AP block (6/7, 86%) due to catheter manipulation. Furthermore, recurrence rate was higher in those who had a previous RF ablation attempt (\( P = 0.03; \) Table 3).

Table 3 Comparison of patients with and without accessory pathway recurrence

<table>
<thead>
<tr>
<th></th>
<th>Recurrence ( (n = 7) )</th>
<th>No recurrence ( (n = 20) )</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (males %)</td>
<td>3/7 (43%)</td>
<td>13/20 (65%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Age</td>
<td>31 ± 8</td>
<td>35 ± 17</td>
<td>0.57</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>162 ± 41</td>
<td>163 ± 68</td>
<td>0.82</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>27 ± 24</td>
<td>31 ± 22</td>
<td>0.80</td>
</tr>
<tr>
<td>Cryoablation (n)</td>
<td>2 ± 1</td>
<td>4 ± 5</td>
<td>0.37</td>
</tr>
<tr>
<td>Dual APs</td>
<td>1/7 (14%)</td>
<td>3/20 (15%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Mechanical block in AP</td>
<td>6/7 (86%)</td>
<td>5/20 (25%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Previous aborted RF</td>
<td>4/7 (57%)</td>
<td>3/20 (15%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Site of AP (superoparaseptal)</td>
<td>4/7 (57%)</td>
<td>14/20 (70%)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Data are given as mean ± SD.

Discussion

Main findings
The present study investigates the usefulness of cryoablation, using exclusively a 6 mm tip catheter, in superoparaseptal and septal APs and is to the best of our knowledge the largest consecutive series with the longest follow-up period published so far. Acute procedural success was achieved in 96% of the patients with a recurrence rate of 27% during a median follow-up period of 33 months and without any ablation related long-term
complications. Importantly, the majority (71%) of the patients with recurrences underwent a new successful cryoablation, giving a total success rate of 89% after a second cryoablation procedure. Thus, acute and long-term results are similar to those described for RF but without any complications.

Superoparaseptal and septal accessory pathways

Superoparaseptal and septal APs constitute less common APs with 1.4–1.6% for superoparaseptal and 2–5% for septal pathways. The present study, these APs accounted for 6% of all APs ablated during the study period. These high-risk located arrhythmia substrates pose particular challenges to the electrophysiologist. The major challenge is to avoid any damage to the normal conduction system, damage that sometimes requires a permanent pacemaker. Published data of RF ablation of superoparaseptal and septal APs have shown primary success rates ranging from 71 to 100%, with recurrence rates of 15–25% and the risk for AV block varying between 0 and 36%. The use of low-energy RF has been recommended to reduce the risk for AV block, but this technique is associated with a higher incidence of recurrences.

Cryothermal energy

Cryothermal energy has been suggested as a safe alternative to RF energy whereas ablating close to perinodal structures such as the slow pathway in AVNRT. The safety profile is due to the ability of cryomapping, a process that creates reversible lesions at potential ablation sites as well as cryoadherence, which prevents catheter dislodgement during ablation. The superoparaseptal and septal APs account for only a minority of all APs, a finding that might explain the limited data regarding the usefulness of cryoablation for the treatment of perinodal APs.

Atrioventricular block

In high risk APs, the main advantage of cryothermal energy is increased safety as a vast majority of these patients are young (median age of 29 years in this study) and otherwise healthy individuals. Two patients, one with a superoparaseptal and the other with a septal located AP, developed transient second degree AV block during cryoablation. Long-term follow-up of these two patients did not show any indication of delayed AV block development and no permanent AV conduction disturbances were seen. This finding agrees with our previous findings in patients with transient AV-block during cryoablation of AVNRT and ectopic foci in the vicinity of the AV node. Therefore, it seems that transient AV-block during cryoablation is a benign phenomenon with no or very low risk for long-term complications.

Accelerated junctional rhythm during RF energy delivery has been reported in up to 5% of patients undergoing ablation of septal or superoparaseptal APs. Cryomapping/ablation does not result in accelerated junctional rhythm. Importantly, just because this rhythm is absent during cryothermal therapy does not mean that the risk for damage to the AV node or His bundle is absent. Our data demonstrate that AV block may develop during cryoablation despite negative cryomapping. Therefore, this underlines the importance of close monitoring of AV conduction during the entire cryoablation.

Mechanical trauma to pathways

In the present study, catheter-induced trauma resulted in transient mechanical AP block in 11 out of 27 (41%) patients. The high incidence of catheter-induced trauma caused by cryocatheter in this study was comparable with previous studies, using different RF catheters. Belhassan et al. reported as much as 38% block of AP conduction in one or both directions due to catheter manipulation in right superoparaseptal (anteroseptal) APs. Haissaguerre et al. reported transient mechanical block in right superoparaseptal (anteroseptal) APs in as much as 42% of the cases. The superficial subendocardial location of perinodal APs, particularly the right superoparaseptal APs, makes these pathways susceptible to mechanical trauma. Our experience shows a less favourable late outcome with significantly higher recurrence in patients with catheter-induced AP block compared with those without block. This is consistent with previous observations, suggesting that cryothermal energy was actually delivered to a location different from where the mechanical block was encountered. In contrast to the RF catheter, the tip of the cryoablation catheter adheres to the endocardium during energy delivery and does not move, whereas the tip of an RF ablation catheter moves across the endocardial surface with each heartbeat, increasing the surface area affected. Generally, APs are very small discrete structures. RF ablation of such structures may be possible even when the catheter tip is not precisely on the target. As the cryolesions are more focused due to cryoadherence, it is important that the cryocatheter tip is located exactly on the target to achieve success.

Clinical implications

Radiofrequency ablation is used in the majority of patients with APs; however, RF ablation of perinodal APs has an increased risk of inadvertent damage of the normal conduction system. This knowledge may influence both the patient’s decision to undergo an ablation procedure and the electrophysiologist’s decision to complete the procedure when the risk for complication is perceived to be high. In fact, 26% of the patients in this study had previously been subject to RF therapy that was aborted due to the risk for AV block. These patients subsequently underwent successful cryoablation(s) without any permanent complications, a finding that suggests that cryoenergy may enable curative treatment for almost all patients with perinodal APs. Bar-Cohen et al. found a higher recurrence rate with cryoablation in a series of patients with perinodal APs compared with our data. A possible explanation for the higher recurrence rate in that study could be the predominant use of a 4 mm tip cryoablation catheter, whereas we exclusively used a 6 mm tip. The recurrence rate in this study may be higher than what one may expect from high energy RF, but is in the same range as for low-energy RF ablation. The acute and a reasonable long-term outcome together with absence of complications in this and previous studies supports the conclusion that high risk APs, such as superoparaseptal and septal APs, are arrhythmias well-suited for cryoablation treatment.
Limitations

Our study is limited by its observational, non-controlled design, and the limited sample size. However, to the best of our knowledge, this is the largest series of cryoablation, using exclusively a 6 mm tip catheter, in high-risk located APs so far. Randomization between different ablation approaches would not be possible for many of our patients in whom RF-energy was aborted due to high estimated risk of AV block.

In non-symptomatic patients, EP studies were not routinely performed during the follow-up. Therefore, the recurrence rate might have been underestimated although the clinical importance of this is probably minimal as the patients were clinically arrhythmia free. However, a 12-lead surface ECG was obtained in all patients with pre-excitation.

Catheter-mediated mechanical block to pathways with anterograde conduction is generally easy to diagnose. However, in patients with concealed APs, the diagnosis of catheter-induced AP block requires either orthodromic tachycardia or ventricular pacing. Therefore, it is possible that mechanical block due to catheter manipulation in patients with concealed APs is actually more frequent than reported in this study.

Conclusion

Cryoablation is a safe and effective alternative therapy for superoparaseptal and septal APs. Procedure-related mechanical AP block predicts a higher recurrence rate.

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