Effects of inadvertent atrioventricular block on clinical outcomes during cryoablation of the slow pathway in the treatment of atrioventricular nodal re-entrant tachycardia

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Aims The study aimed at evaluating the long-term effects of transient atrioventricular (AV) block on clinical outcomes during atrioventricular nodal re-entrant tachycardia (AVNRT) cryoablation.

Methods and results In 150 consecutive patients (39 ± 14 years, ineffective anti-arrhythmic drugs 1.9 ± 1.3), slow-pathway cryoablation for AVNRT was performed. A 7 Fr 6 mm-tip cryocatheter was used. After successful cryomapping (~30 C), defined as jump abolition or AV nodal refractory period prolongation, cryoablation (~80 C for 4 min) was applied if no AV block occurred. Atrioventricular nodal re-entrant tachycardia inducibility was checked after 30 min. Acute success (AVNRT non-inducibility) was achieved in 142 patients (95%). Overall, after a follow-up of 18 ± 10 months, 118 of 150 patients (79%) were recurrence-free (including 2 patients for whom the procedure was unsuccessful). Among successful procedures, 116 of 142 (82%) patients were recurrence-free. During cryoablation, inadvertent transient AV block of varying degrees occurred in 34 patients (22.7%), namely, increased PR duration in 17 patients and a 2nd–3rd AV block in the remaining 17. In 24 patients, AV block occurred at the last effective site (increased PR in 13 patients and a 2nd–3rd AV block in 11). In the study population as a whole, univariate predictors of recurrence in the follow-up were AVNRT inducibility (P < 0.001), increased PR at the last effective site (P < 0.001), residual jump (P < 0.02), and small Koch’s triangle (X-ray distance < 11 mm between the His and coronary sinus ostium catheters; P < 0.02). Atrioventricular nodal re-entrant tachycardia inducibility (P < 0.03), increased PR (P < 0.01), and small Koch’s triangle (P < 0.04) were independently significant. For attempts at the last effective site, 3 groups of patients were compared: 13 patients with increased PR duration (Group A), 11 with a 2nd–3rd AV block (Group B), and 126 without AV block (Group C). Cryo-application time was 277 ± 203 s in Group A, 75 ± 87 s in Group B, and 253 ± 135 s in Group C (A vs. B, P < 0.01; B vs. C, P < 0.001; and C vs. A, P = NS). There was no statistical difference among groups in the atriogram/ventriculogram amplitude ratio at the site of the last attempt, unsuccessful acute procedure, small Koch’s triangle, and residual jump. Actuarial incidence of recurrence-free status at 12 months was 38% in A, 82% in B, and 82% in C (A vs. B, P < 0.05; B vs. C, P = NS; and C vs. A, P < 0.001).

Conclusion All AV blocks occurring during cryoablation were transient, confirming the safety of this method. An increased PR duration at the last effective site is associated with a higher recurrence rate, whereas a 2nd–3rd degree AV block has a recurrence rate similar to that of patients without AV block despite a shorter cryo-application time at the last site.

Introduction

Radiofrequency ablation is a highly effective treatment for atrioventricular nodal re-entrant tachycardia (AVNRT), but it is associated with a small risk of inadvertent
non-reversible AV block, a disastrous event, especially in young patients.\textsuperscript{1,2} Within the last several years, interest in cryo-energy for slow-pathway ablation of AVNRT has been growing\textsuperscript{3–11}. In comparison with radiofrequency, cryoablation is thought to provide a clear safety advantage, especially in preventing non-reversible AV block. Using a technique known as cryomapping, cryoablation offers the possibility of testing a target site by creating a reversible effect using a less critical temperature and therefore assessing a risk of AV block.\textsuperscript{10–11} Nevertheless, adverse but reversible effects on AV conduction may be observed during cryomapping even with no evidence of previous deleterious effects of cryomapping.\textsuperscript{10–11} In our experience\textsuperscript{10} inadvertent AV block can imply, in some cases, (especially a 2nd–3rd degree AV block), interruption of the procedure; in less frequent cases, it can persist at the end of the procedure as a first-degree AV block with delayed but complete AV conduction recovery. This study was designed to evaluate the effects of varying degrees of AV block on acute and long-term clinical outcomes.

Methods

Inclusion/exclusion criteria

All patients referred to our centre from January 2004 to October 2007 for AVNRT cryoablation and treated with a 6 mm-tip cryocatheter were included. Patients with associated atrial fibrillation/flutter or supraventricular arrhythmias other than AVNRT were excluded as well as those who required β-blocking agents and those with severe underlying heart disease.

Procedure

After granting informed consent, patients were investigated in the fasting state without sedation. Anti-arrhythmic (AA) drugs were discontinued for at least five half-life periods. A standard electrophysiology (EP) study was performed. Dual AV nodal physiology was identified by a sudden AH or HA jump of at least 50 ms in response to programmed atrial or ventricular extra-stimulation. Antroventricular nodal re-entrant tachycardia was diagnosed on the basis of standard diagnostic criteria.\textsuperscript{15} If sustained AVNRT could not be induced, isoproterenol was infused to facilitate tachycardia induction. A combination of intra-cardiac electrograms and anatomical approaches was conducted to identify appropriate target sites for ablation of the slow pathway in the Koch’s triangle.\textsuperscript{16,17} Ablation was performed using a 7 Fr cryocatheter (Freezor\textsuperscript{®} Xtra, CryoCath Technologies, Quebec, Canada) with a 6 mm-tip electrode.

Cryomapping was carried out first at a temperature of \(-30^\circ\text{C}\) for a maximal duration of 30 s to test the electrophysiological effect on the target sites using programmed stimulation that reproducibly demonstrated dual nodal physiology or induced AVNRT. In the case of ineffective results or AV block, cryomapping was terminated and then performed at new target sites. When AV block occurred during cryomapping, the catheter was moved posteriorly or moved in search of a minor atrio-ventriculogram (A/V) amplitude ratio or both. Cryoablation, which created a permanent lesion by induced, isoproterenol was infused to facilitate tachycardia induction. A combination of intra-cardiac electrograms and anatomical approaches was conducted to identify appropriate target sites for ablation of the slow pathway in the Koch’s triangle.\textsuperscript{16,17} Ablation was performed using a 7 Fr cryocatheter (Freezor\textsuperscript{®} Xtra, CryoCath Technologies, Quebec, Canada) with a 6 mm-tip electrode.

Cryomapping was carried out first at a temperature of \(-30^\circ\text{C}\) for 4 min, was initiated immediately following successful cryomapping, which was defined as non-inducibility of AVNRT (or complete elimination of fast-pathway ablation was attempted. Procedural success was defined as non-inducibility of AVNRT (complete elimination of the slow pathway in the case of AVNRT non-inducibility during the EP study) at the end of the last waiting period, baseline, and during isoproterenol administration.

Post-ablation management and follow-up

After cryoablation, all AA drugs were withdrawn, including in those patients for whom the procedure was not successful. During the follow-up, patients underwent assessment of symptoms, rest ECG, and 24 h Holter recording at 1, 3, and 6 months in our centre or by their referring physicians. Relapse was defined as recurrence of index arrhythmia-typical symptoms of tachycardia with sudden onset or tachycardia documented with ECG or 24 h Holter recording. The minimal observation period was set at 6 months.

Statistical analysis

Continuous variables were expressed as mean \(\pm SD\). Comparisons for coupled data used the two-tailed paired \(t\)-test. Comparisons within groups were conducted by ANOVA and comparisons among groups were corrected by Bonferroni’s test. Discrete variable comparisons within and among groups were evaluated using the \(\chi^2\) test. Univariate and multivariate analyses of acute procedural variables were performed with the logistic regression model. Correlation between long-term results in the follow-up and the different variables used Cox’s regression model for univariate and multivariate analyses. Following univariate analysis, factors with an associated \(P\)-value of <0.10 were tested in multivariate analysis. A stepwise regression procedure was used to determine independent predictors. The \(P\)-values for entry or removal of a variable from the regression model were 0.05 and 0.10, respectively. Actuarial graphs of survival were generated using the Kaplan–Meier method, with differences among groups assessed by the log-rank test. A \(P\)-value of <0.05 was considered significant.

Results

Patient characteristics

A total of 150 consecutive patients, of mean age 39 \(\pm\) 14 years, 104 female and 46 male, with frequent drug-refractory AVNRT episodes, were included (see Table \(\text{1}\)). Nine patients had arterial hypertension. Symptom duration was 127 \(\pm\) 104 months, number of previously ineffective AA drugs 1.9 \(\pm\) 1.3, and body weight 68 \(\pm\) 15 kg. Eight patients had undergone unsuccessful radiofrequency attempts in other institutions. A slow–fast AVNRT was diagnosed in 134 patients, fast–slow in 8, and slow–slow in 8. The mean AVNRT cycle length was 333 \(\pm\) 70 ms.
Clinical and electrophysiological procedural variables: baseline characteristics and procedural variables

Atrioventricular nodal re-entrant tachycardia was induced in 139 patients and a jump elicited in 129. In 11 patients, AVNRT was not induced (despite a clearly documented EP diagnosis of AVNRT at the referring centre). Twenty-five patients had a small Koch’s triangle (defined as an X-ray distance <11 mm between the His and coronary sinus ostium catheter in a right anterior oblique (RAO) 30° view). In 34 patients, the effective cryoablation site was located at mid-septum (defined as the portion between the His catheter and an ideal line above the coronary sinus ostium in a RAO 30° view, using the cryocatheter to define the upper ridge); in the remaining patients, at the lower part anteriorly to the coronary sinus ostium. The number of cryomapping applications per patient was 7 ± 7.1 and cryoablation 5.3 ± 5.2. Mean cryo-application duration was 932 ± 791 s. The mean A/V ratio at the last effective site was 1 ± 0.6. A freezing–thawing–freezing cycle of 4 ± 4 min was performed in 34 patients. The procedure and fluoroscopy times were 147 ± 47 min and 24 ± 17 min, respectively. There were no procedure-related complications (see Table 2).

**Table 1** Patients characteristics

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39 ± 14</td>
</tr>
<tr>
<td>M/F ratio (patients)</td>
<td>46/104</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>68 ± 15</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>127 ± 104</td>
</tr>
<tr>
<td>Ineffective AA drugs before cryoablation (n)</td>
<td>1.9 ± 1.3</td>
</tr>
<tr>
<td>Slow-fast, fast-slow, slow-slow AVNRT (patients)</td>
<td>134 ± 8-8</td>
</tr>
<tr>
<td>Previous ineffective radiofrequency attempt (patients)</td>
<td>8</td>
</tr>
</tbody>
</table>

AA, anti-arrhythmic; AVNRT, atrioventricular nodal re-entrant tachycardia.

**Table 2** Procedural variables

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AVNRT induction (patients)</td>
<td>139</td>
</tr>
<tr>
<td>Baseline jump (patients)</td>
<td>129</td>
</tr>
<tr>
<td>Small Koch’s triangle (patients)</td>
<td>25</td>
</tr>
<tr>
<td>Effective mid-septal site (patients)</td>
<td>34</td>
</tr>
<tr>
<td>Procedural time (min)</td>
<td>147 ± 47</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>24 ± 17</td>
</tr>
<tr>
<td>Cryomapping (n)</td>
<td>7 ± 7.1</td>
</tr>
<tr>
<td>Cryoablation (n)</td>
<td>5.3 ± 5.2</td>
</tr>
<tr>
<td>Cryoablation duration (s)</td>
<td>932 ± 791</td>
</tr>
<tr>
<td>A/V ratio at last effective site</td>
<td>1 ± 0.6</td>
</tr>
<tr>
<td>Freezing-thawing-freezing cycle (patients)</td>
<td>34</td>
</tr>
<tr>
<td>Inadverstent AV block during cryoablation (patients)</td>
<td>34</td>
</tr>
<tr>
<td>AV block at last effective site (patients)</td>
<td>24</td>
</tr>
<tr>
<td>Post-cryoablation jump (patients)</td>
<td>33</td>
</tr>
<tr>
<td>Post-cryoablation AVNRT induction (patients)</td>
<td>8</td>
</tr>
</tbody>
</table>

AVNRT, atrioventricular nodal re-entrant tachycardia; AV, atrioventricular; A/V, atriogram/ventriculogram.

Electrophysiological modifications after cryoablation

Acute procedural success was achieved in 142 patients (95%). In eight patients, cryoablation failed; in two patients, the procedure was interrupted for repeated transient PR prolongation (AV conduction repeatedly recovered during the waiting period with AVNRT still inducible); in the six other patients, the last cryo-application was transiently successful (and always preceded by a successful cryomapping), but the AVNRT was repeatedly inducible during waiting periods. A residual jump was elicited in 33 patients. Atrioventricular nodal effective refractory period (279 ± 55 vs. 316 ± 61 ms; P < 0.01) and Wenckebach AV block cycle length (348 ± 75 vs. 405 ± 99 ms; P < 0.001) were significantly increased. No junctional ectopy occurred during cryomapping or cryoablation. There were no predictors of acute procedural success.

Inadvertent atrioventricular block during cryoablation

During cryoablation, inadvertent AV block of varying degrees was encountered in 34 patients (22.7%): increased PR duration in 17 patients (152 ± 22 vs. 202 ± 29 ms; P < 0.01), and a 2nd–3rd degree AV block in the other 17. There was no overlap between the two groups (PR prolongation always occurred progressively, whereas the 2nd–3rd degree AV block occurred abruptly). Application of cryo-energy at mid-septum was correlated with all types of AV block (P < 0.001), whereas A/V ratio was not. A His potential was recorded in three patients with increased PR duration, and one with a 2nd–3rd degree AV block (P = NS). Time to AV block (from the beginning of cryo-application to AV block occurrence) was significantly longer (125 ± 93 vs. 63 ± 97 ms; P < 0.05) in patients with increased PR than in those with a 2nd–3rd degree AV block. All AV blocks fully recovered after cryoablation interruption. In fact, AV block lasted between 10 s and 4 days (generally, a few minutes) in patients with increased PR, and between 2 and 30 s (except one for 6 min) in those with a 2nd–3rd degree AV block. Using a semi-quantitative evaluation (0 ≥ 1 s; 1 ≥ 1 min; 2 ≥ 3 h; and 3 ≥ 1 day), time to AV node conduction recovery (from the end of the cryo-application to complete AV conduction recovery) was significantly longer in patients with increased PR duration than in those with a 2nd–3rd degree AV block (1.2 ± 1 vs. 0.06 ± 0.24; P < 0.001).

No correlation was found between increased AV block degree and acute procedural success.

Follow-up

At hospital discharge, all AA drugs were withdrawn, including those patients with unsuccessful procedures. During follow-up of 18 ± 10 months, 118 of 150 patients (79%) were recurrence-free (including 2 patients with an unsuccessful procedure for whom the duration of follow-up exceeded 24 months). In 18 patients, AVNRT recurrence was documented by standard ECG or 24 h Holter recording; while in the remaining 14, it was clinically diagnosed on the basis of symptoms strongly suggestive of recurrence. Time to first recurrence was 3.5 ± 3.4 months. Among successful procedures, 116 of 142 (82%) patients were
recurrence-free. After the first debilitating recurrence, an AA drug was reintroduced in 27 patients (with no relapse in five patients and reduction in AVNRT duration frequency in other five). Five patients had a reduction of AVNRT duration frequency without any treatment. Twelve patients without improvement despite reintroduction of an AA drug underwent a further cryoablation procedure, after which nine had no recurrence. Globally, after the second procedure, 127 of 150 (85%) patients were recurrence-free without any AA drug.

There was no correlation between the degree of AV block and AVNRT subtypes in terms of acute and long-term results.

**Atrioventricular block at last effective site**

In 24 patients, AV block occurred at the last effective site: increased PR duration in 13 (151 ± 20 vs. 200 ± 19 ms; P < 0.01), and a 2nd–3rd degree AV block in 11. Cryo-application was interrupted at the time of AV block in 18 patients (seven with increased PR duration, and all patients with a 2nd–3rd degree AV block; AVNRT was still inducible in only one patient with transient increased PR). In the remaining six patients, the procedure was difficult: frequent cryo-application interruptions for inadvertently increased PR at the only effective site, and PR recovery during the waiting periods with further AVNRT induction repeatedly occurring. In these six difficult cases, the last cryo-application was not interrupted despite an increased PR duration, and an entire freezing–thawing–freezing cycle of 4 + 4 min was performed. At the end of the procedure, AVNRT was non-inducible in five of these patients with a stable prolonged PR duration at the end of the procedure. However, complete AV conduction fully recovered after a few hours in two patients and after a few days in three patients. During the follow-up, four patients had recurrence. Time to AV block was longer in patients with increased PR duration (146 ± 97 vs. 75 ± 87 ms; P < 0.03) when compared with those with 2nd–3rd degree AV blocks, as was the case with AV block duration (1.4 ± 1.1 vs. 0.09 ± 0.3; P < 0.001).

**Predictive variables of recurrence in the follow-up in the whole population**

Post-cryoablation AVNRT inducibility (P < 0.001), increased PR duration at the last effective site (P < 0.001), residual jump (P < 0.02), and small Koch’s triangle (P < 0.02) were correlated with recurrence (see Table 3). Post-cryoablation AVNRT inducibility (P < 0.03), increased PR duration at the last effective site (P < 0.01), and small Koch’s triangle (P < 0.04) were independently significant.

**Atrioventricular block degree at last effective site and clinical outcome in the whole population**

Taking into consideration only the attempt at the last effective site, we compared 3 groups of patients: 13 patients with increased PR duration (Group A), 11 with a 2nd–3rd degree AV block (Group B), and 126 without AV block (Group C) (see Table 4 and Figure 1).

There was no statistical difference among groups in the A/V ratio, unsuccessful first cryoablation, small Koch’s triangle, and residual jump. A freezing–thawing–freezing cycle was applied in 6 patients in Group A, 0 in B, and 29 in C (A vs. B, P < 0.05). Cryo-application time at the last effective site was 277 ± 203 s in Group A, 75 ± 87 s in B, and 253 ± 135 s in C (A vs. B, P < 0.01; B vs. C, P < 0.001). During the follow-up, 8 of 13 patients had recurrences in Group A, 2 of 11 in B, and 22 of 126 in C (A vs. B, P < 0.05; C vs. A, P < 0.001).

The number of patients needing AA drugs in the follow-up was: 7 in Group A; 2 in B; and 18 in C (C vs. A, P < 0.001); however, the need for a new cryoablation intervention was comparable among the three groups. Actuarial incidence of recurrence-free status at 12 months was 38% in Group A, 82% in B, and 82% in C (A vs. B, P < 0.05; C vs. A, P < 0.001).

**Predictive variables of recurrence in the follow-up of patients with acute successful procedure (n = 142)**

Increased PR at the last effective site (P < 0.02) and small Koch’s triangle (P < 0.04) were correlated with recurrence in the univariate analysis, but only increased PR (P < 0.04) was independently significant. Actuarial incidence of recurrence-free status at 12 months was 50% in Group A, 82% in B, and 84% in C (C vs. A, P < 0.05).

**Discussion**

**Main findings**

Our results demonstrate that PR prolongation and a 2nd–3rd degree AV block at the last spot during slow-pathway cryoablation for AVNRT are differently correlated with long-term outcomes. All AV blocks were transient, which support the safety profile that characterizes cryoablation.

**Acute and long-term results**

Acute procedural success did not differ from that of other series, but long-term results showed a relatively high incidence of recurrence. In a previous initial experience, we reported an overall recurrence rate of 38% including

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**Table 3** Predictive variables of recurrence in the follow-up in the whole population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>SE</td>
</tr>
<tr>
<td>Post-cryoablation AVNRT inducibility</td>
<td>1.73</td>
<td>0.46</td>
</tr>
<tr>
<td>Residual jump (patients)</td>
<td>0.9</td>
<td>0.37</td>
</tr>
<tr>
<td>Increased PR at last effective site</td>
<td>1.41</td>
<td>0.40</td>
</tr>
<tr>
<td>Small Koch’s triangle (patients)</td>
<td>0.91</td>
<td>0.38</td>
</tr>
</tbody>
</table>

AVNRT, atrioventricular nodal re-entrant tachycardia.
unsuccessful procedures and a small group of patients treated by a 4 mm-tip cryocatheter. It has recently been demonstrated that cryoablation with 6 mm-tip catheters is associated with fewer recurrences on long-term follow-up compared with the 4 mm-tip catheter.10, Better results in this study may be due to the exclusion of patients treated with a 4 mm-tip cryocatheter, exclusion of patients with other arrhythmias or structural heart disease (potential source of false positive recurrence in the follow-up), and a learning curve effect. Patients referred to our centre were generally younger and some presented with difficult anatomies, contributing to less favourable results.18 However, in other studies higher rates of recurrence have also been reported.9–22

Two patients were recurrence-free in the follow-up despite an unsuccessful cryoablation procedure. This development may be due to peri-lesional fibrosis and the fact that a partial slow-pathway lesion may be enough to ensure no recurrence. A clustered pattern of AVNRT access is less probable because the follow-up in these two patients was very long.

### Table 4: Atrioventricular-block at last effective site and clinical outcome in the whole population

<table>
<thead>
<tr>
<th>Group</th>
<th>A Increased PR</th>
<th>B 2nd–3rd AV block</th>
<th>C No AV block</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>13</td>
<td>11</td>
<td>126</td>
<td></td>
</tr>
<tr>
<td>Unsuccessful first cryoablation (patients)</td>
<td>2</td>
<td>0</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Small Koch’s triangle (patients)</td>
<td>3</td>
<td>2</td>
<td>20</td>
<td>NS</td>
</tr>
<tr>
<td>Residual jump after cryoablation (patients)</td>
<td>4</td>
<td>0</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>Cryo-application time at last effective site (s)</td>
<td>277 ± 203**</td>
<td>75 ± 87†</td>
<td>253 ± 135</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recurrence in the follow-up (patients)</td>
<td>6*</td>
<td>0</td>
<td>28</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>AA drugs given after the first recurrence (patients)</td>
<td>7</td>
<td>2</td>
<td>18†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cryoablation after recurrence (patients)</td>
<td>3</td>
<td>1</td>
<td>8</td>
<td>NS</td>
</tr>
</tbody>
</table>

AV, atrioventricular; AA, anti-arrhythmic.

*P < 0.05; A vs. B.
**P < 0.01; A vs. B.
†P < 0.001; B vs. C.
‡P < 0.001; C vs. A.

**Figure 1:** Actuarial graphs of atrioventricular nodal re-entrant tachycardia recurrence-free status depending on atrioventricular block degree at the last effective site during slow-pathway cryoablation. Group A, increased PR duration; Group B, 2nd–3rd atrioventricular block; Group C, no atrioventricular block (A vs. B, P < 0.05; B vs. C, P = ns; C vs. A, P < 0.001).

### Inadvertent atrioventricular block and cryomapping

It has been stated that the cornerstone of cryoablation is the capability of testing for effect with a reversible interruption of cellular activity at less critical temperatures, thus permitting the assessment of the risk of AV block. Cryoadhesion prevents catheter-tip dislodgment, thereby preventing accidental energy delivery at the compact AV node or His bundle. Junctional ectopy, a sensitive marker of successful radiofrequency ablation,20 does not occur during cryoablation, which facilitates the monitoring of the completeness of the fast pathway. Nevertheless, despite negative cryomapping, inadvertent AV block occurrence seems relatively frequent, between 7 and 20% in the literatures.4–8,10,11 In this study, we confirm this incidence of inadvertent AV block during cryoablation. This experience demonstrates that the lesion created during cryoablation may expand relative to that suggested by cryomapping, suggesting the need for vigilance also when ablating with cryo-energy instead of radiofrequency. However, no permanent AV block occurred, also in patients with increased PR duration at the end of the procedure in whom a complete recovery of AV conduction required hours or days in some cases. Not surprisingly, the only predictor of an increased risk of AV block was application of cryo-energy at the mid-septum.

### Atrioventricular block degree and clinical outcome

While the degree of AV block during cryoablation did not affect acute results, this is not the case concerning long-term outcomes. In fact, inadvertent transient 2nd–3rd degree AV block at the last effective site assured not only a complete acute success but also an optimal long-term result similar to patients without AV block. Conversely, the presence of an increased PR at the last effective site was associated with a higher incidence of recurrence in the follow-up, although it ensured AVNRT non-inducibility in the vast majority of patients.

We can speculate that, in patients with a 2nd–3rd degree AV block (occurring always abruptly), the site of the cryolesion was the compact AV node, and that rapid AV conduction recovery after cryoablation interruption was due to the relatively resistant nature of the compact AV node to
cryothermal lesions\textsuperscript{23} in combination with an immediate cryo-application interruption. Nevertheless, the slow pathway was eliminated with AVNRT non-inducibility in all patients; only a few patients had recurrence in the follow-up. Although in some cases, cryo-application time at the effective site was prolonged enough to account for this positive effect on the slow pathway, in the majority of these patients cryo-energy application time was very short. A low recurrence rate may be explained for an effective cryo-lesion involving the compact AV node and the site of connection with the slow pathway (whatever its anatomical and functional substrate), in this case more fragile or limited in size.

Conversely, in patients with increased PR, the incidence of recurrence was higher, despite acute successful procedures in most of them (no intentional fast-pathway lesion was attempted). This type of AV block occurred after a longer period of cryo-application time than in patients with 2nd–3rd degree AV blocks, and progressively. This fact may indicate a minor degree of proximity to the compact AV node. Anyway, AV conduction recovered in all patients, suggesting that if or when the fast pathway is involved in the lesion, it becomes more difficult to ablate using cryo-energy than the slow pathway. However, a higher recurrence rate indicates that the slow pathway also recovered in some patients during follow-up— an event for which a clear explanation is difficult to formulate.

Safety of cryoablation

In our study and in other published studies in which inadvertent AV block was reported, no permanent AV block occurred. In addition, the A/V ratio at the effective site using cryo-energy was higher than the A/V ratio usually recommended in AVNRT radiofrequency ablation.\textsuperscript{15} Globally, these experiences support the claim of enhanced safety for perinodal cryoablation. However, it is important to underline that experiences evaluating the feasibility of AV node cryoablation in humans have shown conflicting results. Pérez-Castellano et al.\textsuperscript{24} performed cryoablation in 15 patients referred for AV nodal junction ablation with a 6 mm-tip cryocatheter. Overall, persistent complete AV block resulted with cryo-energy in only one patient, and in two additional patients AV conduction remained modified. Nevertheless, in a previous study in humans, Dubuc et al.\textsuperscript{25} performed cryoablation of the AV node using a 4 mm-tip cryocatheter in 12 patients with refractory atrial fibrillation. Complete AV block resulted in 10 patients. After 6 months of follow-up, 8 of 10 initially successful patients remained in complete block, whereas 1 had partial recovery of AV conduction, and 1 fully recovered AV conduction. However, whatever the rate of persistent AV conduction impairment observed with attempts to cryoablate the AV node, permanent AV node cryoablation is clearly possible. This fact confirms the need to avoid aggressive strategies when ablating near the AV node.

In one animal model, the minimal application of cryo-energy needed to obtain complete nodal AV block was 10 s.\textsuperscript{26} Thus, although cryo-energy appears to be safer than radiofrequency, vigilance when ablating with cryo is still required.

Clinical implications

Atrioventricular block is often not guaranteed by negative cryomapping. Direct short cryo-applications may be performed without preliminary cryomapping, at least in the posterior septum, reserving the use of cryomapping to ablations in the mid-septum or close to the His bundle.

An increased PR duration at the effective site appears to be a negative prognostic factor in the follow-up. When it results in rapid transience, with the AVNRT still inducible during the waiting period, the electrophysiologist should look for a better site.

Interuption of the procedure for a 2nd–3rd degree AV block at the effective site, when AVNRT non-inducibility is assured during the entire waiting period, does not affect long-term outcome, implying that, at least in this case, a short cryo-application time can be effective with no need for further cryo-applications.

Conclusion

All AV blocks occurring during cryoablation were transient, confirming the safety profile of this method. A prolonged PR duration at the last effective site appears to be associated with a higher recurrence rate in the follow-up, whereas a 2nd–3rd degree AV block has a recurrence rate similar to patients without AV block despite a shorter cryo-application at the last site.

Conflict of interest: none declared.

References


