Acute resumption of conduction in the cavotricuspid isthmus after catheter ablation in patients with common atrial flutter

Real-time evaluation and long-term follow-up

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Aims Cavotricuspid isthmus conduction (CIC) is closely associated with the maintenance and recurrence of common atrial flutter (AFL). This study systematically sought to assess the prevalence and characteristics of acute CIC recovery during AFL ablation and to define its predictors and its relationship with the results of long-term follow-up.

Methods and Results A total of 124 consecutive patients (105 men, 19 women, mean age 58 ± 11 years) who underwent successful AFL ablation were included. The procedure endpoint was defined as complete bi-directional CIC block. During an observation period of 30 min, the incidence of CIC restoration was 34.7% in patients and 39.8% in applications. It increased with increasing block time and decreased over time during the observation period. Block time in successful burns followed by persistent block was shorter than in those followed by CIC resumption (12 ± 6 vs 33 ± 12 s, P<0.0001). A negative correlation between block time and resumption time was found (r = -0.57, P<0.001). Patients with permanent pacemakers had a higher incidence of acute CIC resumption than those without pacemakers (5/7 vs 29/117, P=0.007). The AFL recurrence rate was 4.8% during a mean follow-up period of 21 ± 8 months. Our results suggest that acute CIC resumption may be a potential risk for clinical AFL recurrence during long-term follow-up.

Conclusions Acute CIC resumption in common AFL ablation varies in terms of incidence and time course. Block time has a predictive value for acute CIC recovery. Observation time can be shortened if block time is short. With longer block time, it is essential to observe for a longer period in order to minimize CIC resumption.

Key Words: Atrial flutter, radiofrequency, ablation, mapping.

Introduction

Radiofrequency ablation is a highly effective method of treating patients with common atrial flutter (AFL)¹–⁷. Cavotricuspid isthmus conduction (CIC) is intimately related to the induction and maintenance of AFL, suggesting that bi-directional conduction block in the isthmus should be the aim of the ablation pro-


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The aim of this study was to evaluate the prevalence and characteristics of acute CIC resumption using a multi-electrode catheter during AFL ablation and to identify its predictive factors and its impacts on AFL recurrence during long-term follow-up.

**Methods**

**Study population**

The study population consists of 124 consecutive symptomatic patients (105 men and 19 women, mean age of 58±11 years) admitted for catheter ablation of drug-resistant common AFL. Non-predominant episodes of paroxysmal atrial fibrillation presented in 57 patients (46.0%). Forty-four patients (35.5%) had structural heart disease including coronary heart disease (n=17), valvular heart disease (n=10), hypertensive cardiomyopathy (n=12), congenital atrial septal defect (n=3) and hypertrophic cardiomyopathy (n=2). Prior to the ablation procedure, 7 patients had a pacemaker implanted either for sick sinus syndrome (n=1) or for atrioventricular block (n=6). Antiarrhythmic drugs were interrupted for at least five half-lives, except for amiodarone, which was terminated one week or more before the ablation procedure, but was not withdrawn in case of associated atrial fibrillation.

**Electrophysiological study and ablation procedure**

A 24-pole mapping catheter (Orbiter®, Bard Inc., 2–7–2 mm electrode spacing) was positioned in the right atrium with its distal poles in the coronary sinus and proximal poles around the tricuspid annulus (Fig. 1). With this position, there were always two adjacent pairs of electrodes bracketing the ablation line created within the isthmus. These provided the real-time assessment of isthmus conduction, block and resumption. Endocardial bipolar electrograms were band-pass filtered between 30 and 500 Hz, recorded on a CardioLab system (Prucka Engineering, Inc.) and analyzed at a chart speed of 100 mm/s.

A deflectable 7F quadripolar catheter (Cordis Webster, Johnson & Johnson Inc., 2 mm electrode spacing, 4 mm tip electrode) or a deflectable 8F quadripolar catheter (EP technologies, Boston Scientific Inc., 2.5 mm electrode spacing, 8 or 10 mm tip electrode) was used for mapping and ablation in 102 and 22 patients, respectively. In addition, a quadripolar catheter (Bard Inc., 10 mm electrode spacing) was used to record in the His bundle region. A Stockert-Cordis radiofrequency generator was used and energy was applied in a temperature-controlled mode with a cutoff at 65°C. The ablation line was performed from the ventricular side progressively to the inferior vena cava under fluoroscopic control [2,5,6,18]. At each new position, radiofrequency energy was delivered for 60 s. If CIC block was obtained at a certain site, the application time was prolonged to 120 s. Ablation was performed with patients either in AFL or in sinus rhythm. When in sinus rhythm, the ablation was performed with a pacing cycle length of 600 ms in the proximal coronary sinus.

Since conduction was continuously monitored during energy delivery, CIC block was always demonstrated with an abrupt change in the activation sequence on the Orbiter® catheter appearing from one beat to the next (Fig. 2A). Conduction recovery was detected in the same
way (Fig. 2B). Bi-directional conduction block defined the end-point of the ablation procedure. The methods for assessment of bi-directional isthmus block were both activation sequence mapping and multiple-site pacing on both sides of the ablation line, as described previously. Thirty minutes were taken to monitor CIC resumption with persistent proximal coronary sinus pacing at a cycle length of 600 ms after CIC block was obtained. CIC resumption re-initiated the ablation procedure until complete bi-directional block was obtained again, and re-confirmed after another 30-min observation period. We used atrial fractional potentials as a target for ablation of acute CIC resumption. The bi-directional conduction pattern was evaluated in sinus rhythm either pre-ablation or when AFL was converted peri-ablation, and always in sinus rhythm post-ablation. This was carried out sequentially with bipolar pacing at the proximal coronary sinus and low lateral right atrium.

**Definitions**

Block time (BT) was defined as the duration from the onset of burn to the moment of CIC block occurring during the successful ablation application. Resumption time (RT) was defined as the duration from the end of the application creating CIC block, to the moment of CIC recovery. CIC block or recovery occurring during the same application, and CIC block created by mechanical pressure of catheters, were excluded from the analysis.

While pacing in the proximal coronary sinus before CIC block, there was always a collision of clockwise and counterclockwise wave fronts on the lateral right atrial wall. The distance from collision to the ablation line was calculated from the Orbiter catheter.

**Follow-up**

Patients were monitored for 24–48 h post-ablation. No antiarrhythmic drug therapy was prescribed except for some patients with a history of atrial fibrillation. The patients were followed on an outpatient basis by clinical evaluation and 24-h Holter recording. Documented recurrences of AFL promoted a second electrophysiological study and CIC recurrence led to a repeat ablation procedure. Undocumented events, however, first required proof of isthmus conduction and AFL inducibility before a repeat ablation was attempted. The induction programme consisted of atrial pacing at two cycle lengths with one to three extrastimuli, as well as burst pacing.

**Statistical analysis**

Continuous variables are expressed as mean±SD and compared using the unpaired Student’s t-test or Mann–Whitney test. Chi-square analysis and Fisher exact test were used to compare the proportions. The curve estimation regression was applied to evaluate the correlation. Values for P<0.05 were considered statistically significant.

**Results**

**General characteristics of the patients (Table 1)**

There were no significant differences between patients with and without CIC resumption with respect to age, proportion of gender, structural heart disease, left atrial enlargement, or whether the ablation procedure was begun in AFL or in sinus rhythm. The proportion of multiple-sessions in patients with CIC resumption was statistically lower than those without CIC resumption; and the proportion of patients with permanent pacemakers was higher in the CIC resumption group.

**Incidence of acute CIC resumption**

During a 30-min observation period after CIC block was obtained, CIC resumed 82 times in 43/124 patients (34·7%); once in 21 (16·9%), twice in 11 (8·9%), 3 times in 7 (5·6%), 4 times in 3 (2·4%) patients and 6 times in 1 (0·8%) patient. Of all 82 episodes of CIC resumption which were included in this analysis, RT was less than 2 min in 39 (47·5%), between 2 and 5 min in 21 (25·6%), 14 (17·1%) were between 5 and 15 min and 8 (9·8%) were longer than 15 min. In 4 patients, there was bi-directional CIC block after interruption of AFL, but CIC was subsequently restored. Resumption of medial to lateral CIC was always accompanied by recovery of lateral to medial CIC and no unidirectional block was observed. (The RT was too short to permit full evaluation of CIC pattern in 22 episodes of resumption.)

**BT and acute CIC resumption rate**

There were overall 206 applications that created CIC block in the 124 patients studied. Of these applications, 124 (60·2%) were followed by persistent CIC block and 82 (39·8%) applications were followed by acute CIC resumption. There was no CIC recovery when BT<10 s (P<0·01 compared with the other periods), whereas all applications were followed by CIC resumption when BT≥50 s (Fig. 3A). Cumulative resumption rates were 0%, 8·1%, 20·0%, 29·3%, 37·1% and 39·8% while BTs were <10, <20, <30, <40, <50 and <60 s, respectively. If a value of ‘BT≥20 s’ is employed as a criterion, the positive predictive value for CIC recovery is 93·6%, the sensitivity is 89·0% and the specificity is 90·7%.

**Correlation between BT and RT**

Among the patients with CIC resumption, BT was 33±12 s (range 12–56) in the applications followed by...
Figure 2  (A) During the 17th ablation application, an abrupt change occurred with complete reversal of the atrial depolarization sequence on the Orbiter catheter during proximal coronary sinus pacing. The ablation line was located between ORB 4 and ORB 5. The collision of clockwise and counterclockwise wave fronts was at ORB 11. Note: the atrial waves at ORB 5 and ORB 6 were even later than ventricular activation. (B) 3 min after the successful burn, there was an abrupt change with the atrial depolarization sequence return on the Orbiter catheter during proximal coronary sinus pacing. Note: the collision of clockwise and counterclockwise wave fronts had shifted to ORB 9. ORB 1 to ORB 12 denote the 12 pairs of electrodes from distal to proximal. Abbreviations as in Fig. 1.
Table 1  Clinical characteristics of patients

<table>
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<tr>
<th></th>
<th>Patients with CIC resumption n=43</th>
<th>Patients without CIC resumption n=81</th>
<th>Overall n=124</th>
<th>P value*</th>
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<tr>
<td>Age, years</td>
<td>59 ± 11</td>
<td>59 ± 10</td>
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<td>Female/male</td>
<td>8/35</td>
<td>11/70</td>
<td>19/105</td>
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<td>Heart disease</td>
<td>16 (37·2)</td>
<td>28 (34·6)</td>
<td>44 (35·5)</td>
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<td>Enlargement of left atrium</td>
<td>14 (32·6)</td>
<td>23 (28·4)</td>
<td>37 (29·8)</td>
<td>0·630</td>
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<td>Multiple-session</td>
<td>3 (7·0)</td>
<td>17 (21·0)</td>
<td>20 (16·1)</td>
<td>0·044</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>5 (11·6)</td>
<td>2 (2·5)</td>
<td>7 (5·6)</td>
<td>0·035</td>
</tr>
<tr>
<td>Atrial flutter at start of ablation procedure</td>
<td>28 (65·1)</td>
<td>39 (48·1)</td>
<td>67 (54·0)</td>
<td>0·071</td>
</tr>
</tbody>
</table>

CIC: cavotricuspid isthmus conduction. Multiple-session: patients had previous ablation. Percentages are shown in parentheses. *Comparing between patients with and without CIC resumption.

acute CIC return. BT in the last burn followed by persistent CIC block was 12 ± 6 s (range 3–32) (P<0·001). In the patients without CIC resumption, BT in the last successful application was 14 ± 9 s (range 3–45) (P=0·089, compared with those with CIC restoration). RT ranged from 0·5 to 28 min (mean 5 ± 7, median 2). A negative correlation between BT and RT was found (r= −0·57, P<0·001, Fig. 3B).

Electrophysiological data and ablation results

During proximal coronary sinus pacing, there was always a collision of counterclockwise and clockwise wave fronts in the lateral wall. In the patients with CIC restoration, distance from the collision to the ablation line just before CIC block occurred was 43 ± 14 mm. Just after CIC resumed, it shortened to 38 ± 16 mm (P=0·027, Fig. 2).

The mean number of ablation applications was 19 ± 12 in all patients, and 17 ± 12 in the patients without CIC restoration. In the patients with CIC restoration, the total number of applications was 23 ± 11 (P=0·009, compared with those without CIC restoration). After the first CIC resumption, a further 5 ± 5 applications were needed to obtain the final successful CIC block. On analysing the 43 last applications which created the eventually successful CIC block, only 4 were located at the tricuspid annulus side of the isthmus, 22 in the middle of the isthmus, and 17 were located on the sub-Eustachian ridge. In addition, the final successful ablation site was located just underneath the ventricular lead in 3 of 5 patients with pacemaker who had acute CIC resumption.

Eight or 10 mm tip ablation catheters were used in 22 patients, and 4 mm tip catheters were employed in the other 102 patients to achieve CIC block. The incidence of acute CIC resumption was 27·3% and 36·3% respectively for 8 or 10 mm tip and 4 mm tip catheters (P=0·421).

Acute CIC resumption in patients with pacemakers

Seven patients (6 men, 1 woman, mean age 69 ± 8 years) had permanent pacemakers at the time of the AFL ablation procedure. Pacemaker modes were DDD (n=3), DDDR (n=3) and VDD (n=1). Mean time from implantation was 5 ± 2 (range 3–9) years. The mean CIC resumption population, the pacemaker patients were older (68 ± 8 vs 58 ± 11, P<0·05), had more CIC resumption numbers and total application numbers were 2 ± 2 (range 0–6) and 23 ± 14, respectively. Acute CIC resumption was observed in 5 patients. The patient with VDD mode pacemaker had CIC resumption 6 times. The incidence of acute CIC resumption in patients with pacemakers was significantly higher than in those without pacemakers (5/7 vs 29/117, P=0·007). In the CIC resumption population, the pacemaker patients were older (68 ± 8 vs 58 ± 11, P<0·05), had more CIC resumption numbers (median 3 vs 1, P<0·01), and needed more additional applications (median 6 vs 3, P<0·05) to get final CIC block after the first resumption, than those without pacemakers. There was no statistically significant difference with respect to BT (32 ± 11 vs 34 ± 13 s), RT (4 ± 7 vs 5 ± 7 min) and total ablation numbers (median 31 vs 18·5) between the two groups (P>0·05). The functional parameters of pacemakers did not change after ablation.

Follow-up

No significant complications occurred during the ablation procedure and hospital stay. At a mean follow-up period of 21 ± 8 months (range 7–34), 6 of 124 patients (4·8%) experienced at least one symptomatic episode of AFL, starting 1, 3, 7, 8, 8 and 10 weeks, respectively, after hospital discharge. In all these 6 patients, a further electrophysiological study showed CIC return with induction of AFL. Using the same protocol as described above, a second ablation procedure was successfully performed. Recordings from the first ablation procedures of these 6 patients showed that 4 had had previous acute CIC resumption with 1, 2, 2
Figure 3  (A) Percentage of CIC resumption in different block time periods in a total of 206 applications that created CIC block. (B) Correlation between block time and resumption time in 43 patients having a total of 82 applications followed by CIC recovery. CIC: cavotricuspid isthmus conduction.
and 4 times, respectively. In the groups with and without acute CIC resumption, the AFL recurrence rates were 4/43 (9.3%) and 2/81 (2.5%), respectively \( P = 0.181, \) Odds ratio=4/05 (95% confidence interval 0·71; 23·09), Risk ratio=2·02 (95% confidence interval 1·08; 3·75). A further 19 patients underwent a repeat electrophysiological study 3 to 8 months after the ablation procedure, because of non-documented recurrent palpitations. In all of these patients, the study showed persistent CIC block and noninducibility of AFL with programmed atrial stimulation and burst pacing.

**Discussion**

This study investigated the prevalence and electrophysiological characteristics of acute CIC restoration during ablation and its relationship to the results of long-term follow-up. Traditional routine electrophysiological study does not offer evaluation of CIC pattern. Even if a multi-electrode catheter was used and only positioned on the lateral wall in the right atrium, the assessment could not correctly\(^8,9,18\) be made. Our technique allows continuous CIC monitoring, enabling real-time evaluation of isthmus conduction or block to be performed, as well as CIC restoration.

Several reports have described the phenomenon of CIC recovery after initial block has been obtained\(^9,10,18\). The incidence of acute restoration ranged from 15·9% to 50\%\(^{17,20}\), while the time course of recovery might take more than an hour\(^9\). The main reasons for the variability in results may be the different methods of assessment and the location of the ablation lines. Since the acute CIC resumption rate increased with longer BT and a negative correlation between BT and RT was found in the present study, BT may be used as an indicator to predict the acute CIC restoration. In view of the fact that no application with BT<10 s was followed by acute CIC return (Fig. 3A), we recommend that observation time in these patients can be greatly shortened. Potential reduction in procedure time would be 30 min (waiting time) \( \times \) 42 (number of burns with BT<10 s)=1260 min (i.e. average 10·2 min per patient); On the contrary, the observation time should be at least 30 min if BT\( \geq 10\) s. In Fig. 3B, if one extrapolates the curve towards low BT values then RT values should accordingly increase. This probability is quite low based on the low recurrence (2·5%), during long-term follow-up in patients without CIC resumption, in whom most BT values were <15 s.

Transmural myocardial lesions in the isthmus are necessary for conduction block. Thicker myocardium and lack of cooling effect from local blood flow prevent myocardial lesion extension and lead to increased BT. The same factors also facilitate CIC recovery. The technique of stepwise ablation might have influenced the incidence of CIC resumption. Sometimes, radiofrequency energy does not result in transmural necrosis in the isthmus. There might only be a loss of side-to-side connections between groups of fibres and intercellular clefts with shrinkage of contractile elements\(^21\) followed by conduction return. The novel irrigated catheter, which produces much deeper lesions, may be capable of solving this kind of problem\(^22\). Experimental models have suggested that a large tip ablation catheter makes a larger and deeper lesion than a small tip catheter\(^23\). However our results show no significant difference in acute CIC resumption rate between them. The volume and size of ablation lesions depend not only on the catheter tip size, but also temperature, power output, cooling effect of blood flow and tissue contact. Our results suggest that the latter may be more important in clinical practice. A morphological study of the isthmus showed that 18/28 of normal heart specimens had a pouch-like area anterior to the orifice of the inferior vena cava and the sub-Eustachian ridge. An additional small recess was found inferior to the coronary sinus orifice in 5/28 specimens\(^24\). The undulating endocardial surface between the tricuspid valve and inferior vena cava probably resulted in difficulty in reaching the residuum of conduction known as the ‘gap’, as was also demonstrated in the present study that 39/43 successful ablation sites for CIC return were located in this region. When the ablation site is close to the gap, CIC could be blocked by the conducted heat effect, and followed by early recovery.

Atrial tachyarrhythmias are frequently complicated by bradycardias\(^25\). The effects of radiofrequency ablation on the function of the implanted permanent pacemaker have earlier been investigated\(^26\). But the impact of pacemaker leads on catheter ablation of AFL has not been studied. The present study showed that the patients with permanent pacemakers had a higher incidence of acute CIC resumption, and needed more applications to obtain the final CIC block. This impact of indwelling pacemaker leads on the ablation procedure is postulated to be firstly, the ablation catheter can not be manipulated to achieve an ideal position because the ventricular lead occupies the target site; secondly, the ventricular lead adhering to the isthmus tissue may increase tissue fibrosis and thus impede penetration of the radiofrequency energy.

During long-term follow-up, only 6 (4·8%) patients suffered from clinical AFL recurrence, which was lower than the prevalence found in earlier reports\(^2,8\). The AFL recurrence rates were 9·3% and 2·5%, respectively in the patients with and without a history of acute CIC resumption. Although the \( P \)-value does not reach a level of statistical significance in this population, the higher values of odds ratio and risk ratio may suggest that the patients with a history of acute CIC resumption have an increased risk of clinical AFL recurrence. Thus, diminishing acute CIC restoration might minimize the clinical AFL recurrence rate during long-term follow-up.

**Limitations**

Induction of AFL was not attempted after CIC resumption, because recent studies\(^8,10–12\) have shown that
complete bi-directional conduction block in the isthmus is by far the best marker for long-term success. No systematic electrophysiological controls were warranted. No information on the persistence of the CIC block is therefore available for this study population. However, in the 19 patients who underwent a repeat electrophysiological study due to palpitations, all demonstrated persistent CIC block. Our study finished after a 30-min period of observation. Further investigation is required systematically to evaluate the long time course of recovery and the results of long-term follow-up. The study on large and small tip ablation catheters was retrospective and non-randomized and the large tip group was small. These factors may limit the results. Furthermore, the location of the final ablation site was verified only under fluoroscopic guidance, as neither atrial angiography nor invasive ultrasound imaging was performed.

Conclusions

Our data suggest that (1) Acute CIC resumption in common AFL ablation varies in terms of incidence and time course. Patients with permanent pacemakers have a higher incidence of acute CIC resumption. (2) Acute resumption rate decreases over time during the 30-min observation period, and increases with increasing BT. BT has a predictive value for acute CIC recovery. (3) If BT<10 s, observation time can be shortened. With longer BT, it is essential to observe for longer in order to minimize CIC resumption. (4) Acute CIC resumption might be a potential risk for clinical AFL recurrence during long-term follow-up.

References

