Incremental His-To-Coronary Sinus Maneuver: A Non-Local Electrogram-Based Technique to Assess Complete Cavo-Tricuspid Isthmus Block during Typical Flutter Ablation

Running title: Vallès et al.; Criteria for typical flutter isthmus block assessment

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Abstract

Background - Achievement of complete cavo-tricuspid isthmus (CTI) conduction block reduces typical atrial flutter recurrences after ablation. The lack of increase in the His-to-Coronary sinus ostium (CSO) atrial interval during incremental pacing (IP) from the low lateral right atrium (LLRA) may distinguish slow conduction from complete CTI conduction block.

Methods and Results - Sixty-six consecutive patients (age 65±13 years, 18% female) were prospectively included. A <10ms increase in the His-to-CSO atrial timing during LLRA incremental pacing at cycle length of 600 ms through 300 ms was compared to the previously reported IP maneuver for the confirmation of complete CTI block. On the basis of the IP maneuver complete CTI block (phase 2) was achieved in 59 patients, in 13 of whom an intermediate phase of functional CTI block (phase 1) was observed. In the remaining 7, the IP maneuver did not allow for assessment of complete CTI block due to the presence of inconclusive potentials in the CTI ablation line. As compared to the IP maneuver, the incremental His-to-CSO maneuver was consistent with functional CTI block during phase 1 in all cases and conclusive of complete CTI block in 98% of cases during phase 2.

Conclusions - The incremental His-to-CSO maneuver is analogous to the IP maneuver in distinguishing complete CTI block from persistent CTI conduction. This maneuver may provide confirmation of CTI block in those patients in whom assessment of local electrogram-based criteria is not feasible due to inconclusive potentials in the CTI ablation line.

Key words: typical flutter, ablation, cavo-tricuspid isthmus, complete block, incremental His-to-coronary sinus maneuver, incremental pacing
Introduction

Typical isthmus-dependent atrial flutter (AFL) recurrences after ablative therapy are due to restoration of conduction across the cavo-tricuspid isthmus (CTI). \(^1,2\) Documentation of complete trans-isthmus conduction block after ablation has been proven to be superior to cardioversion in terms of arrhythmia recurrence, and has become the gold-standard endpoint during AFL ablation. \(^1-5\) However, definite proof of complete conduction block is not always evident. Distinction from incomplete block with slow conduction across the CTI is essential in order to achieve a favorable arrhythmia control outcome after ablation. Local electrogram (EGM)-based criteria rely on the observation of a complete corridor of parallel double potentials (DPs) along the isthmus ablation line. \(^6-9\) An inter-DP interval \(\geq 110\) ms with little variation along the ablation line has been associated with conduction block. \(^7\) Assessment of the distance between both components of the DP in response to differential pacing from the distal and the proximal low lateral right atria (LLRA), or between the atrial EGMs in the His bundle region and in the coronary sinus ostium (CSO) during pacing from the LLRA are additional maneuvers that are useful for the diagnosis of CTI block. \(^7,10,11\) Recently, the incremental pacing (IP) maneuver was noted to further improve the ability to determine complete CTI conduction block in the presence of little inter-DP interval variation in response to incremental pacing from both sides of the isthmus line. Briefly, the IP maneuver consists in pacing at a cycle length (CL) of 600 ms down to 250 ms from both the LLRA and the CSO. Persistent CTI conduction is suspected when a \(\geq 20\) ms increase in the interval between the two potentials during IP is observed. In this setting, CTI line re-mapping and further ablation are frequently needed. Complete CTI block is defined by a \(< 20\) increase in inter-DP interval during IP. \(^12\) In fact, confirmation of complete CTI block by IP has been associated with a lower incidence of AFL recurrences after ablation. \(^12,13\) One limitation of such
maneuver, however, is that it requires the identification of two distinct potentials in the CTI ablation line during ablation, which is not always feasible, since multiple and/or fragmented potentials are commonly observed in relation to a broad or nonlinear ablation. We therefore developed a novel simple maneuver analogous to the IP maneuver based on examination of the atrial EGMs at the His and CSO regions, thus avoiding the need for evaluation of local EGMs throughout the CTI ablation line. We hypothesized that no or mild increase in the His-to-CSO timing of atrial EGMs during incremental atrial pacing from the LLRA would serve as a surrogate of the previously established IP maneuver for the diagnosis of complete CTI block after AFL ablation.

Methods
Patient population
Sixty-six consecutive patients undergoing CTI radiofrequency catheter ablation for typical isthmus-dependent AFL were prospectively included. The ablation procedure was performed after informed consent was obtained. All oral antiarrhythmic drugs were discontinued 5 half-lifes prior to the procedure, except for amiodarone, which was interrupted 48 hours before ablation.

Electrophysiological Study and CTI Ablation
Cavo-tricuspid isthmus ablation was performed in the fasting state under local anesthesia and conscious sedation. A diagnostic steerable 6F catheter was placed via the right femoral vein in the lateral right atrium; this included a steerable quadripolar catheter in 34 patients and a steerable 20-pole catheter in 32 patients. A diagnostic steerable quadripolar catheter was introduced through the right femoral vein into de CSO in all patients. Bipolar EGMs were filtered through a band pass of 30 to 500 Hz and were recorded on a multi-channel polygraph...
Radiofrequency ablation was performed during atrial pacing from the CSO or during AFL. The ablation line was drawn from the tricuspid annulus edge, with local large ventricular and small atrial EGMs, to the inferior vena cava edge. Radiofrequency energy was delivered with a power limit of 35 to 40W.

**Identification of CTI conduction block**

The CTI ablation line was identified as a continuous corridor of double potentials separated by an isoelectric line during pacing from the CSO. Previously established criteria for the diagnosis of CTI block were then assessed. These included loss of the caudo-cranial atrial activation in the LLRA during pacing from the CSO, observation of an interval of >40 ms between the atrial EGMs at His and CSO during pacing at a CL of 600 ms from the LLRA, and confirmation by local EGM-based criteria (Table 1).

Upon accomplishment of at least one of these criteria, the IP maneuver was performed from both the CSO and the LLRA, as described elsewhere. The IP maneuver was used as the gold-standard method for the definition of complete CTI block and for validation of the new incremental His-to-CSO maneuver. Therefore, only patients with DPs identifiable along the ablation line in whom the IP maneuver could be performed were included. In those cases in which a >20 ms increase in the interval between the two potentials during IP was observed by pacing from either the LLRA or the CSO, persistent counterclockwise or clockwise CTI conduction was suspected, respectively (Phase 1). In this setting, the CTI line was re-mapped in the search of conduction gaps and additional radiofrequency pulses applied until a <20 increase in inter-DP interval was achieved (phase 2).
Incremental His-to-CSO maneuver

Before AFL ablation, the atrial EGM registered in the CSO region during pacing from the LLRA, anterior to the Crista Terminalis and in the vicinity of the isthmus line, results from counterclockwise conduction of the stimulus across the CTI through the right posteroseptal region. In contrast, the atrial signal registered in the His-bundle region is secondary to conduction of the stimulus through the anterior and anteroseptal aspect of the tricuspid annulus.

After CTI ablation, counterclockwise conduction is interrupted at the CTI level during pacing from the LLRA, and activation would be expected to travel sequentially from His to CSO, with a His-to-CSO EGM interval that has been reported of >40 ms.\(^5\) We hypothesized that, in the presence of slow conduction and/or functional CTI block after ablation, the His-to-CSO interval would significantly increase (≥10 ms) in response to IP from the LLRA. Conversely, during complete CTI conduction block, the His-to-CSO interval should not significantly vary (<10 ms) during incremental LLRA pacing (Figures 1 and 2). Incremental LLRA pacing was started at a CL of 600 ms, followed by pacing at 500 ms, 400 ms, and 300 ms for at least 5 pulses for each CL. We chose the cut-off value of 10 ms based on data on His-to-CSO atrial conduction time that we obtained in a separated cohort of age and gender-matched patients without structural heart disease and normal atrio-ventricular conduction pattern undergoing electrophysiological study for another purpose. In this population, we evaluated the His-to-CSO interval during incremental atrial pacing from the His-bundle area, observing an average increment of His-to-CSO conduction time of 3 ± 3 ms. Measurements were taken by two blinded investigators, with no differences between them (data not shown).

Statistical analysis

Categorical variables were compared using Fisher’s exact test in the event of an \(n \leq 5\) for one or
more values (all analyses). Continuous variables (expressed as mean ± SD) were compared using a paired Student t-test. A P value ≤0.05 was considered statistically significant. Sensitivity and specificity were determined for each maneuver taking the IP maneuver as the reference maneuver. All analyses were performed using Numbers '09 software, version 2.3 (Apple Inc., Cupertino, California).

Results

Study population

Patient population characteristics are summarized in Table 2. Most patients were male and had no structural heart disease. Only 18 out of the 66 patients were in sinus rhythm at the time of the procedure. Before ablation, the His-to-CSO timing did not change significantly during IP from the LLRA in patients in sinus rhythm (from 18 ± 13 ms at pacing CL of 600 ms to 20 ± 14 ms at 300 ms, p = 0.65). This increase in the His-to-CSO interval was of <10 ms in all cases, supporting the validity of the pre-defined cut-off value for this increase. The proximal delay during IP (between the pacing stimulus and the His region) was measured as a marker of absence of significant intra-atrial conduction disturbances in our population, with an average increment of 2 ± 1 ms (data not shown).

Incremental His-to-CSO maneuver during Phase 1 CTI block

During CTI ablation, an intermediate phase of functional CTI block (Phase 1) confirmed by IP was observed in 13 out of the 66 patients, despite other established maneuvers suggesting CTI block (Table 3). In all these cases the His-to-CSO interval during pacing from the LLRA at a CL of 600 ms was >40 ms (49 ± 18 ms). However, during IP a >10 ms increase in the His-to-CSO interval was registered in all 13 patients, suggesting persistent CTI conduction, with a statistically significant average value of 26 ± 21 ms (p = 0.020).
Incremental His-to-CSO maneuver during Phase 2 CTI block

At the end of the procedure, complete CTI block according to the IP maneuver could be confirmed in 59 out of the 66 patients. In the remaining 7 patients (11%), the ablation line could not be appropriately assessed due to the presence of inconclusive/multiple/fractionated potentials. These patients were withdrawn from the final analysis and in these cases CTI block was defined by classical criteria.

Among the 59 patients, 91% and 87% fulfilled classical criteria of clockwise and counterclockwise CTI block according to the activation sequence when pacing from the CSO and from the LLRA, respectively (Table 4). The peak-to-peak inter-DP interval was >110 ms in 72%, and the isoelectric interval between them was >70 ms in 80% of patients. Finally, the mean His-to-CSO interval during pacing at a CL of 600 ms from the LLRA was 51 ± 15 ms. Importantly this interval was <40 ms in 6 patients.

The incremental His-to-CSO maneuver showed a <10 ms increment in the His-to-CSO interval when pacing from 600 ms down to 300 ms in 58 out of the 59 patients (98%), with a mean increment of 1 ± 3 ms (p = 0.58). When using the IP maneuver as a reference for both phases 1 and 2, the proposed incremental His-to-CSO maneuver showed a 98% sensitivity and 100% specificity for the diagnosis of complete CTI block.

Discussion

The present study validates a novel maneuver to identify complete CTI conduction block during ablation of typical isthmus-dependent AFL. We demonstrate that the incremental His-to-CSO maneuver is feasible and analogous to the previously reported IP maneuver, allowing for discrimination between complete CTI conduction block and residual slow conduction through the CTI. This distinction is crucial since demonstration of CTI block is necessary to prevent...
AFL recurrences.\textsuperscript{12,13} Our data show that little (<10 ms) variation in the His-to-CSO atrial EGM interval in response to progressively faster (from 600 ms to 300 ms) pacing from the LLRA is indicative of complete CTI block, whereas a >10 ms increase of the His-to-CSO atrial interval with IP would support slow conduction and/or functional block across the CTI. The correlation of this technique to the previously validated IP maneuver appears excellent.

The Incremental His-to-CSO maneuver does provide advantages over the IP maneuver. First, the incremental His-to-CSO maneuver does not require the identification of 2 differentiated potentials within the CTI ablation line. Identification of DPs is an important limitation of all diagnostic maneuvers that rely on CTI line mapping (local EGM-based criteria and IP pacing \textsuperscript{6–12}) because of inconclusive, multiple or fragmented potentials corresponding to bystander slow conduction areas due to non-linear CT ablation, which are frequently observed (in 7 out of the 66 patients in our series, in 10 out of 55 patients in a previously reported series from our group\textsuperscript{12}, and in up to 39\% of patients in other groups reported series).\textsuperscript{14} For these cases it might be of interest the measurement of the stimulus-to-atrial signal just lateral to the ablation line during incremental CSO pacing, but since this maneuver, which is mechanistically very similar to the IP maneuver, is not validated, we did not perform it in our protocol.

Another potential advantage of the incremental His-to-CSO maneuver over the IP maneuver relies on the possibility of Crista Terminalis and intra-atrium conduction delay in some patients presenting with AFL. The latter is especially important in the setting of anti-arrhythmic drugs. In this setting, a >20 ms increase in the interval between both CTI potentials during IP may be due to intra-atrial conduction delay of the second potential rather than to actual CTI slow persistent conduction. Although we did not specifically assess this issue, it is plausible that the incremental His-to-CSO maneuver would be less influenced by this potential
phenomenon since it relies on timing measurements restricted to a very limited atrial region. This observation, however, requires further investigation.

**Previously established criteria for the diagnosis of CTI block**

The present study demonstrates that during linear radiofrequency CTI ablation, achievement of previously reported criteria may not always indicate complete CTI block. This circumstance indicates the necessity of a more specific criterion for confirmation. Moreover, despite His-to-CSO interval at a fixed pacing cycle length showed a good sensitivity, with >40 ms in 53 out of 59 patients (90%) with complete block, still there were 10% of cases with true block and a shorter His-to-CSO interval. In this setting, the incremental His-to-CSO maneuver had a sensitivity of 98% and a specificity of 100%. Furthermore previously established criteria such as peak-to-peak inter-DP interval or inter-DP isoelectric line interval only showed limited sensitivity (72% and 80% respectively). Whether the IP maneuver or other previously reported maneuvers should serve as the gold standard for the diagnosis of complete CTI block has not been elucidated.

**Limitations**

Not all previously reported criteria for the diagnosis of CTI block were assessed. However, the purpose of our study was to validate the incremental His-to-CSO maneuver as an accurate non-local EGM-based surrogate of the IP maneuver. In this sense the IP maneuver was used as the gold standard method to diagnose complete CTI block. The use of other previously established criteria would not have affected the positive correlation between the two proposed maneuvers based on incremental atrial pacing. It is important to note that the incremental His-to-CSO maneuver is only confirmatory of counterclockwise conduction block. No clockwise conduction block can be proven by this technique. As it was acknowledged previously in the description of
the IP maneuver a significant delay in the His-to-CSO interval after ablation may still theoretically be due to functional Crista Terminalis block. Finally, no follow-up data are provided in the present study. It has been shown that confirmation of complete CTI block by means of the IP maneuver is accompanied by a reduced incidence of typical flutter long-term recurrences.\textsuperscript{12,13} It remains unproven whether application of the incremental His-to-CSO maneuver might also result in a reduction of AFL recurrences during follow-up.

**Acknowledgments:** We express our appreciation for the editing assistance of Roger Fan, MD.

**Conflict of Interest Disclosures:** None.

**References:**


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Table 1. Assessed criteria for CTI block. Incremental His-to-CSO highlighted in bold.

<table>
<thead>
<tr>
<th>Previously Established Criteria for CTI Block</th>
<th>Incremental Pacing-based Criteria for complete CTI block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descending sequential activation along the lateral wall and the CTI when pacing from the CSO</td>
<td></td>
</tr>
<tr>
<td>Descending sequential activation along the septal wall and the CTI when pacing from the LLRA</td>
<td></td>
</tr>
<tr>
<td>Peak-to-peak time between the two CTI potentials &gt;110ms</td>
<td></td>
</tr>
<tr>
<td>Isoelectric line time between the two CTI potentials &gt;70ms</td>
<td></td>
</tr>
<tr>
<td>His-to-CSO timing of &gt;40ms during pacint at a cycle length of 600 ms from the LLRA</td>
<td></td>
</tr>
<tr>
<td>No or mild increment (&lt;20ms) between the two CTI potentials during incremental pacing (600-300 ms) from both sides of the ablation line (parallel activation of the two potentials)</td>
<td></td>
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<tr>
<td>Incremental His-to-CSO maneuver</td>
<td></td>
</tr>
</tbody>
</table>

No or mild increment (<10ms) in the His-to-CSO interval of atrial EGMs during incremental pacing (600-300 ms) (sequential activation of His and CSO)

CSO: coronary sinus ostium; CTI: cavo-tricuspid isthmus; EGM: electrogram; LLRA: low lateral right atrium

Table 2. Main population characteristics

<table>
<thead>
<tr>
<th>Overall Population (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Gender n (%)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Type of Flutter n (%)</td>
</tr>
<tr>
<td>Paroxysmal</td>
</tr>
<tr>
<td>Persistent</td>
</tr>
<tr>
<td>Structural Heart Disease n (%)</td>
</tr>
<tr>
<td>Left Ventricle Ejection Fraction &lt;55% (%)</td>
</tr>
<tr>
<td>Left Atrium Diameter &gt;40 mm (%)</td>
</tr>
<tr>
<td>53</td>
</tr>
</tbody>
</table>
Table 3. Electrophysiological maneuvers during Phase 1 CTI block.

<table>
<thead>
<tr>
<th>Criteria accomplishment during Phase 1</th>
<th>Number of patients (%)</th>
<th>Average +/- Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descending activation along the lateral wall during pacing from the CSO</td>
<td>11/13 (85%)</td>
<td>CSO-LLRA 131 +/- 52 ms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CSO-P2 146 +/- 49 ms</td>
</tr>
<tr>
<td>Descending activation along the septal wall during pacing from the LLRA</td>
<td>8/8 (100%)</td>
<td>LLRA-CSO 134 +/- 52 ms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LLRA-P2 147 +/- 57 ms</td>
</tr>
<tr>
<td>His-to-CSO interval of &gt;40 ms during pacing at a CL of 600 ms from the LLRA</td>
<td>13/13 (100%)</td>
<td>49 +/- 18 ms</td>
</tr>
<tr>
<td>Non-significant increment (&lt;20 ms) between the two CTI potentials during IP from the CSO</td>
<td>0/13 (0%)</td>
<td>42 +/- 18 ms</td>
</tr>
<tr>
<td>Non-significant increment (&lt;20 ms) between the two CTI potentials during IP from the LLRA</td>
<td>2/11 (18%)</td>
<td>35 +/- 19 ms</td>
</tr>
</tbody>
</table>

CL: cycle length; CSO: coronary sinus ostium; CTI: cavo-tricuspid isthmus; IP: incremental pacing; LLRA: low lateral right atrium; P2: second potential in the CTI line.
Table 4. Electrophysiological maneuvers during Phase 2 CTI block.

<table>
<thead>
<tr>
<th>Criteria accomplishment during Phase 2</th>
<th>Number of patients (%)</th>
<th>Average +/- Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descending activation along the lateral wall during pacing from the CSO</td>
<td>52/57 (91%)</td>
<td>CSO-LLRA 135 +/- 30 ms CSO-P2 160 +/- 38 ms</td>
</tr>
<tr>
<td>Descending activation along the septal wall during pacing from the LLRA</td>
<td>48/55 (87%)</td>
<td>LLRA-CSO 131 +/- 28 ms LLRA-P2 152 +/- 34 ms</td>
</tr>
<tr>
<td>Peak-to-peak interval between the two CTI potentials &gt;110 ms</td>
<td>42/59 (72%)</td>
<td>120 +/- 28 ms</td>
</tr>
<tr>
<td>Isoelectric line interval between the two CTI potentials &gt;70 ms</td>
<td>47/59 (80%)</td>
<td>88 +/- 24 ms</td>
</tr>
<tr>
<td>His-to-CSO interval of &gt;40 ms during pacing at a cycle length of 600 ms from the LLRA</td>
<td>53/59 (90%)</td>
<td>51 +/- 15 ms</td>
</tr>
<tr>
<td>Non-significant increment (&lt;20 ms) between the two CTI potentials during IP from the CSO</td>
<td>59/59 (100%)</td>
<td>5 +/- 6 ms</td>
</tr>
<tr>
<td>Non-significant increment (&lt;20 ms) between the two CTI potentials during IP from the LLRA</td>
<td>59/59 (100%)</td>
<td>5 +/- 6 ms</td>
</tr>
</tbody>
</table>

CSO: coronary sinus ostium; CTI: cavo-tricuspid isthmus; IP: incremental pacing; LLRA: low lateral right atrium; P2: second potential in the CTI line.
Figure Legends:

**Figure 1.** Rationale of incremental His-to-CSO maneuver. Upper figures show the observed conduction response to IP during damaged but not blocked CTI. The decrease in the conduction velocity across the CTI results in an increment in the interval between the His and the CSO atrial EGMs (left: pacing at a CL of 600 ms; right: pacing at a CL of 300 ms). Bottom figures show the usual response to IP when complete CTI block has been accomplished, with no increment in the interval between the His and the CSO atrial EGMs (left: pacing at 600 ms; right: pacing at 300 ms). CSO: coronary sinus ostium; CTI: cavo-tricuspid isthmus; EGM: electrogram; IP: incremental pacing.

**Figure 2.** Example of the incremental His-to-CSO maneuver. Panels A and B were registered during Phase 1 CTI block and Panels C and D were registered in the same patient after delivery of additional radiofrequency lesions and Phase 2 CTI block was achieved. Each panel shows one paced beat from different pacing trains. The distal bipole of the ablation catheter (ABL D) was placed at the His bundle region. Panel A shows a delay of 35 ms between the atrial EGMs of His and CSO regions during pacing from the LLRA at a CL of 600 ms. Panel B shows an increase in this delay to 58 ms (increment of >10 ms) during IP down to a CL of 300 ms. In comparison, at the end of the procedure the timing delay between His and CSO was 58 ms during pacing from the LLRA at a CL of 600 ms (Panel C) and 60 ms (increment of <10 ms) during IP down to a CL of 300 ms (Panel D). ABL D: distal bipole of the ablation catheter (placed at the His bundle region); ABL P: proximal bipole of the ablation catheter; AD 1-2: distal bipole of the LLRA catheter; AD 3-4: proximal bipole of the LLRA catheter; CL: cycle length; CSO: coronary sinus ostium; CTI: cavo-tricuspid isthmus; EGM: electrogram; IP: incremental pacing; LLRA: low lateral right atrium; SC 1-2: distal bipole of the coronary sinus catheter; SC 3-4: proximal bipole of the coronary sinus catheter.
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