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Original Article

Detection of sequential activation of left atrium and coronary sinus musculature in the general population

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A B S T R A C T

Background: The direction of impulse propagation across the coronary sinus (CS) musculature (CSM) is an important piece of the mechanistic puzzle underlying atrial tachyarrhythmias. We hypothesized that in the general population, the sequence of left atrial (LA) to CSM electrograms recorded in the CS reflects the direction of impulse propagation over the CSM.
Methods: We studied 19 patients with atrioventricular (AV) reentrant tachycardia (RT) utilizing a left-sided accessory pathway (AP) and 21 patients with typical counterclockwise atrial flutter (AFL). Conduction through the CSM during AVRT and AFL is from the left atrial (LA) to the right atrial (RA) and from the RA to LA direction, respectively. CS recordings of retrograde conduction over the AP and of AFL were analyzed in search of far-field, LA potentials.
Results: Among 19 patients with AP, LA potentials were visible in 7 (37%), all in an LA → CSM activation sequence, while among the 21 patients with AFL, LA potentials were visible in 14 (67%), all in a CSM-LA activation sequence ($P < 0.0001$). The prevalence of LA potentials was similar between both study groups ($P = 0.1119$), and the overall prevalence was 53%.
Conclusions: Far-field LA potentials are often recorded in the CS during sequential LA and CSM activation in the general population. The timing of LA potentials in CS recordings reflected the direction of conduction across the CSM.
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1. Introduction

The coronary sinus (CS) musculature (CSM), which is electrically connected to both atria, [1,2] plays the important role of synchronizing their activation during sinus rhythm, [3] as well as perpetuating some atrial tachyarrhythmias [4–6]. Since the direction of wavefront propagation across the CSM varies among atrial tachyarrhythmias, its analysis and elucidation is a critical step toward an accurate interpretation of their mechanisms. For example, during atrioventricular (AV) reentrant tachycardia (RT) utilizing a left-sided AV accessory pathway (AP), the wavefront propagates via a left atrial (LA) connection into and through the CSM toward the right atrium, whereas during typical counterclockwise (CCW) atrial flutter (AFL), the wavefront propagates into and through the CSM in a right atrial (RA) → LA direction (Fig. 1).

A multipolar electrode catheter is usually needed during electrophysiological studies and ablation procedures in order to record the activation sequence from inside the CS. Because of the multiple muscle bundles connecting the CSM and LA, [2] the activation of the CSM and adjacent LA myocardium appears simultaneously. However, we previously found that, in patients whose LA-CSM connections are particularly weak, the far-field LA activation during retrograde conduction over a left-sided AP only, was separated from the near-field activation of the CSM on the CS recordings [7]. If the activation sequence of LA and CSM could be analyzed on the CS recordings of the general population, regardless of differences in conductive properties between LA and CSM, it could be used as an electrophysiological marker of the wavefront propagating across the CSM. Therefore, the present study was conducted to verify our hypothesis that (1) the far-field LA potential recorded in the CS is universally visible in the general population, and (2) the activation sequence of the LA and CSM potentials reflects the direction of impulse propagation over the CSM.

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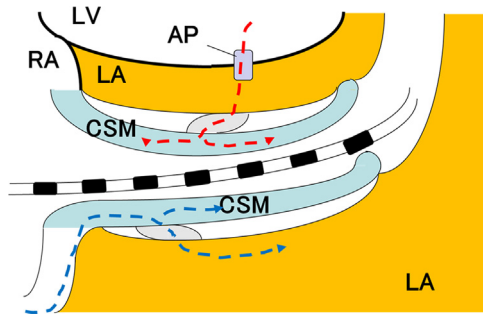
Fig. 1. Representative illustration of activation sequences of LA and CSM during retrograde conduction over left-sided AV AP (red dashed arrow) versus counter-clockwise typical AFL (blue dashed arrow). LV=left ventricle; RA=right atrium.

2. Material and methods

We studied 19 patients (51 ± 18 years old, 12 men) presenting with AVRT utilizing a left-sided AP, and 21 patients (67 ± 11 years old, 18 men) presenting with CCW AFL, who all underwent successful catheter ablation. All of ablation procedures were performed from a submitral approach, confirming the presence of an AP. As briefly mentioned earlier, during AVRT utilizing a left-sided AP, the wavefront, after retrograde conduction over the AP, propagates via LA → CSM connections into and through the CSM in a LA → RA direction, and reaches the RA via the ostium of the CS. During typical CCW AFL, the wavefront rotating around the tricuspid annulus propagates via the ostium of the CS into and through the CSM in a RA → LA direction and reaches the LA via CSM → LA connections. Thus, the wavefront across the interatrial connection at the CS propagates in a left → right direction during ongoing AVRT and in a right → left direction during typical AFL (Fig. 1).

This study complied with the guidelines of the Declaration of Helsinki and was approved by the institutional review board of the Gunma University Hospital (approval date; Jun 30, 2010, No. 774). Written informed consent to participate in this study was obtained from all patients.

2.1. Electrophysiological studies and electrogram analyzes

Electrophysiological studies were performed before catheter ablation. A 6-Fr duodecapolar or decapolar electrode catheter with 5-mm interelectrode spacing was placed in the CS via the right subclavicular or femoral vein for the CS recordings. Other multipolar electrode catheters were placed in the high RA, His bundle region, and at the right ventricular apex in patients presenting with AVRT; and at the tricuspid annulus and His bundle region in patients presenting with AFL. Bipolar intracardiac electrograms and a 12-lead surface electrocardiogram were recorded and stored in an EP Work Mate™ system (EP MedSystems, Inc., West Berlin, NJ), after signal filtering between 30 and 500 Hz, and were analyzed at a paper speed of 100 and 400 mm/s. When the activation sequence in the CS during ongoing AVRT was identical to that during ventricular stimulation, the CS recordings were analyzed during ventricular extrastimulation. In patients with AFL, the CS recordings were made during ongoing AFL. The CSM potentials recorded from inside the CS are characteristically high-frequency and near-field, whereas the LA potentials are far-field, low-amplitude, low-frequency signals, with a gradual onset and gradual return to baseline. Based on these characteristics, all CS electrograms during tachycardia and sinus rhythm were scrutinized in search of LA potentials preceding or following the CSM potentials by 2 cardiologists. When there was disagreement regarding the presence of LA potentials and the sequence of LA and CSM potentials, the cardiologists discussed the results to reach an agreement. The amplitude of LA potentials and the intervals between the onset of LA potential and the end of CSM potential or between the onset of CSM potential and the end of LA potential were measured.

2.2. Statistical analysis

Continuous measurements are expressed as mean $\pm$ SD. Categorical variables were compared by using Fisher's exact test. The statistical analyzes were performed with the Ekuseru-Toukei 2012 statistical software package (Social Survey Research Information Co., Ltd). A P value < 0.05 was considered statistically significant.

3. Results

As shown in Table 1, the amplitude, and the onset or the end of LA potentials were successfully determined via visual inspection. Among 19 patients with AP, LA potentials were detected in 7 (37%), all in an LA → CSM activation sequence (Fig. 2). In contrast, among 21 patients with CCW AFL, LA potentials were visible in 14 (67%), all in a CSM → LA activation sequence (Fig. 3). This difference was highly significant ($P < 0.0001$). The prevalence of LA potentials was not significantly different between both study groups ($P=0.1119$), and the overall prevalence was 53%. In the left anterior oblique fluoroscopic projection, most LA potentials were located between 3 and 6 o'clock in patients with AP and between 4 and 5 o'clock in patients with AFL (Fig. 4).

In a single case with left-sided AP presenting CS double potentials, we compared the relative timing of far-field LA potentials in the CS recordings with LA potentials directly recorded during successful ablation procedure, by using trans-septal approach (Fig. 5). The far-field potential was recorded simultaneously with LA potential at the successful ablation site during retrograde conduction over AP, whereas no far-field potential was observed after the elimination of AP, providing further confirmation that the far-field potentials in the CS recordings reflect LA activation. Furthermore, although not enrolled in the present study, we present two interesting cases in which unique CS double potentials were observed. The diagnosis of the first case was a manifest Wolff-Parkinson-White (WPW) syndrome and AVRT attributable to ventricular-CS connection that was confirmed by its successful ablation inside a mid-cardiac vein [8]. During ventricular pacing before the ablation, LA potentials following CSM potentials were noticed in the proximal CS recordings (Fig. 6). The second case had typical clockwise (CW) AFL that was electrophysiologically confirmed. During the ongoing tachycardia, in contrast to typical CCW AFL, LA potentials preceding CSM potentials were registered on the proximal CS recordings (Fig. 7).

Table 1
Electrogram measurements.

	Patients with AP ($n=19$)		Patients with AFL ($n=21$)	
	LA-CSM, ms	Amp (LA), mV	CSM-LA, ms	Amp (LA), mV
6 o'clock	32.5 ± 0.7	0.28 ± 0.01	62.0 ± 20.6	0.12 ± 0.06
5 o'clock	39.2 ± 3.6	0.21 ± 0.21	55.0 ± 9.4	0.17 ± 0.08
4 o'clock	41.7 ± 6.9	0.33 ± 0.07	46.3 ± 2.6	0.15 ± 0.03
3 o'clock	47.3 ± 12.1	0.18 ± 0.08	48.0 ± 1.4	0.08

Amp (LA)=the amplitude of LA potentials; CSM-LA=the interval between the onset of CSM and the end of LA potentials; LA-CSM=the interval between the onset of LA and the end of CSM potentials.
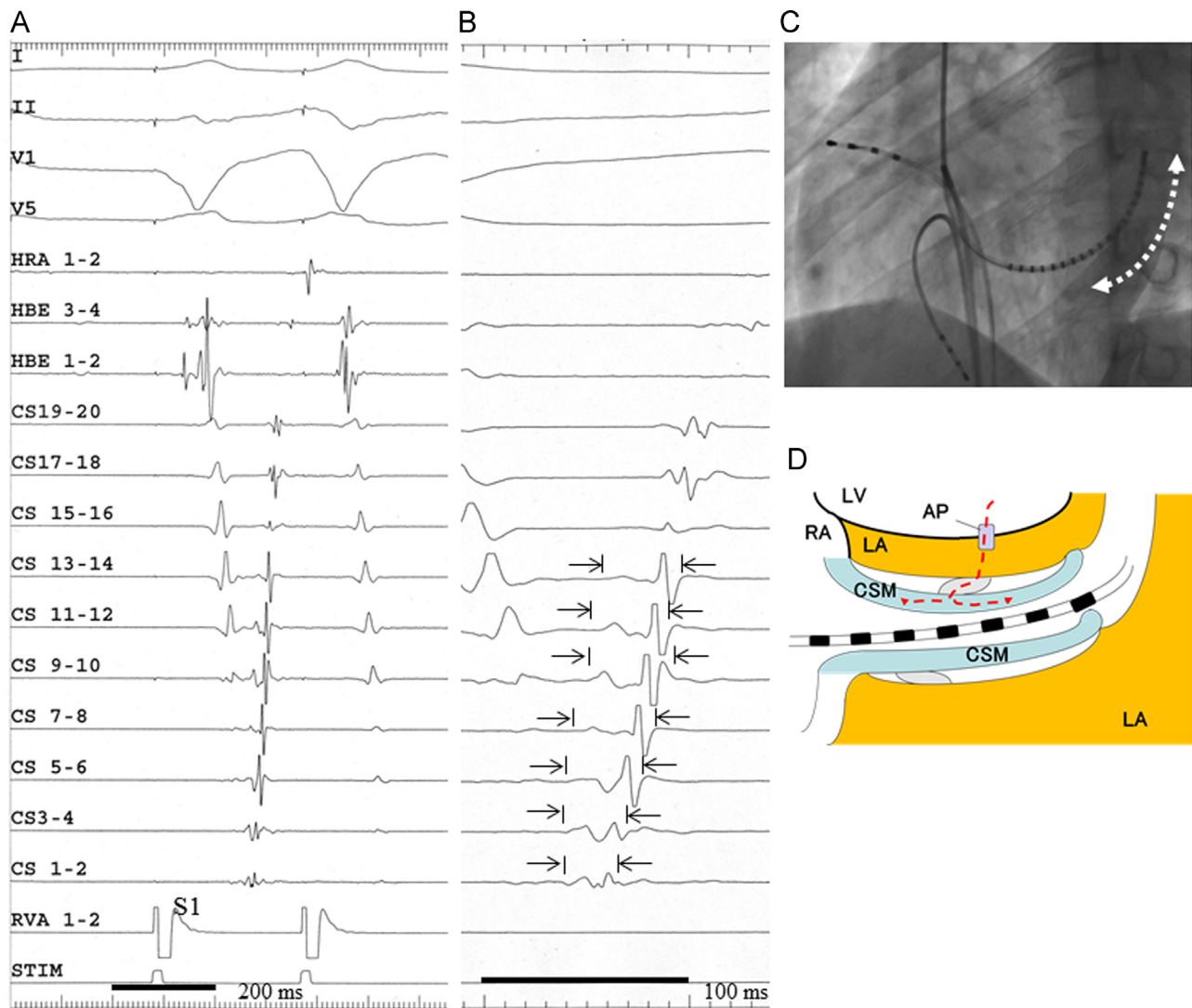
Fig. 2. Example of left lateral AP in a 17-year-old man. (A) Intracardiac recording of right ventricular (RV) extrastimulus (S2) following an S1-S1 pacing at 600 ms cycle length. Note the absence of LA potentials following conduction block at AP after S2, which made it easier to discriminate the far-field LA activation with far-field ventricular activation. 100 mm/s paper speed. (B) Intracardiac recordings at 400 mm/s paper speed, immediately following the delivery of S1. Right- and left-pointing arrows mark the onset of the LA potentials and the end of the CSM potentials, respectively. (C) Fluoroscopic view in left anterior oblique projection showing the position of CS catheter. Bidirectional dotted arrow between 3 and 6 o'clock indicates the location of LA potentials recordings. (D) Illustration of activation sequences. I, II, V1, and V5=surface ECG; HRA=high right atrium; HBE1-2 and 3-4=distal to proximal His-bundle region; CS19-20 to 1-2=proximal to distal coronary sinus (CS) recording. Abbreviations and symbols as in Fig. 1.

4. Discussion

Until recently, most clinical electrophysiologists believed that the CS electrograms reflected strictly the LA activation. However, the recognition of far-field LA potentials distinct from the near-field potentials of the CSM has gradually increased, after a detailed human anatomical study revealed a distinct spatial relationship of the CSM and the LA such that the former is near and the latter is away from the catheter located inside the CS [2]. Kasai et al. first reported that the far-field LA and near-field CSM potentials recorded from the CS, which seemed to be fused, could be separated by functional block over the CSM → LA connection caused by extrastimulation [9]. We reported the recording of double CS potentials, consisting of LA and CSM potentials, visible only during retrograde AP conduction in patients in whom there were few LA → CSM connections, except in the proximal CS [7,10]. The activation pattern of the double potentials varies, depending on the differences in the conductive properties of the LA-CSM connections [7,10,11]. Double potentials were also recorded inside the CS during atrial fibrillation, and during typical or perimitral AFL in patients with LA → CSM connections that were impaired by an ablation attempt [11–14]. Nevertheless, far-field LA electrograms distinct from CSM potentials have been much less reported than expected. However, they were visible in approximately 50% of patients in this study, suggesting that, if persistently looked for during sequential LA → CSM activation, far-field LA potentials adjacent to near-field potentials are not rare, regardless of individual variations in the LA-CSM connections. In other words, even if multiple LA-CSM connections are present, activation of LA and CSM is not strictly simultaneous, and as noticed in the subjects included in the present study, a far-field LA potential is not fully superimposed on near-field CSM potential during sequential activation of LA and CSM. That is, at least the onset of LA potential not superimposed on CSM potential is visible during retrograde conduction over left-sided AP, and at least the offset of LA potential not superimposed on CSM potential is visible during CCWAFL. When the activation direction of CSM potential is identical to that of LA potentials as shown in Fig. 2, it is possible that multiple LA-CSM connections are present. Under these conditions,
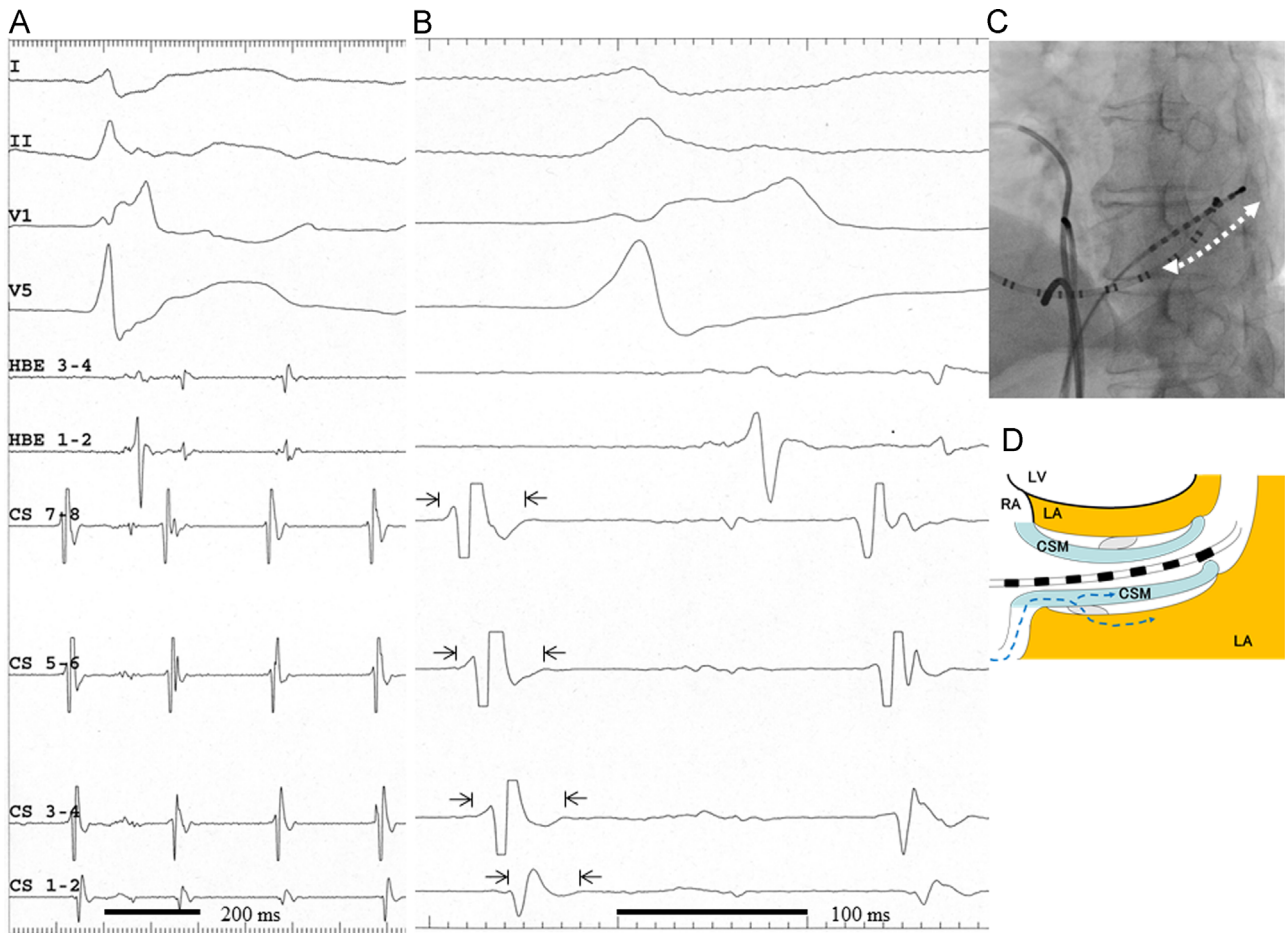
Fig. 3. Example of typical CCW AFL in a 48 year-old man. (A and B) Intracardiac recordings of AFL at paper speeds of 100 and 400 mm/s, respectively. Right- and left-pointing arrows in panel B mark the onset of the CSM potential and the end of the LA potential, respectively. (C) Bidirectional dotted arrow indicates the sites of recordings between 3 and 6 o'clock. Other abbreviations and symbols as in Fig. 2. D: Illustration of activation sequences. Abbreviations and symbols as in Fig. 1.
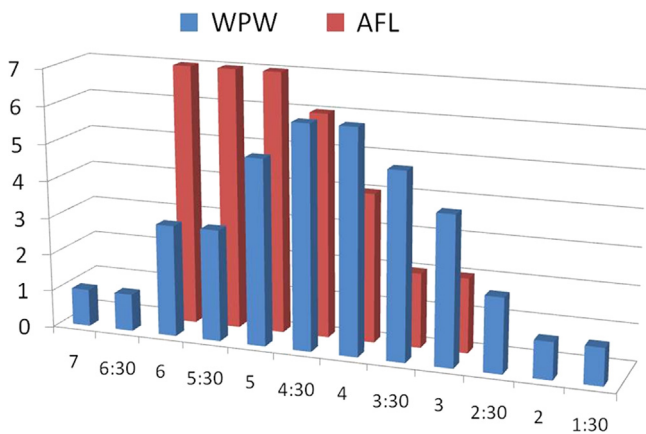
Fig. 4. Recording sites of the far-field LA potential. Red and blue bars indicate the number of LA potential recordings in patients with WPW syndrome and AFL, respectively.

the detection of the LA potentials may depend on the distance between the LA wall and the recording catheter inside the CS. No detection of an LA potential suggests that the recording catheter inside the CS is not located adjacent to the LA wall, and does not mean that the LA muscle near CS is absent or injured. As shown in Fig. 4, there seemed to be a difference in recording sites of LA potentials between the two groups, probably because the difference

might be attributable to the conductive direction of the LA wavefront relative to the axis of the CS recording catheter. The bipolar recording with the standard CS catheter could detect the LA wavefront that propagated almost parallel to the recording catheter, such as during CCW AFL. It may be less incident to record the LA wavefront that propagated nearly perpendicular to the catheter, such as during retrograde conduction over the left-sided AP. We did not routinely insert a distal tip of the CS catheter into a great cardiac vein to record LA potential only of which the recording may make it easier to differentiate LA potential from CSM potentials. In addition, we did not record the CS electrograms with a low sensitivity setting to observe the whole CSM potentials, instead, we always recorded those with a high sensitivity setting in order to detect tiny LA potentials.

In the present study, the timing of the LA potentials in respect to the timing of the CSM potentials depended closely on the direction of impulse propagation across the interatrial connection at the proximal CS. Thus, a LA → CSM activation sequence was observed only when the wavefront traveled through the proximal CSM in left-to-right direction as during retrograde conduction over left-sided AP or the ongoing typical CW AFL., The CSM → LA activation sequence was observed only when it propagated in the right-to-left direction as during the ongoing CCW AFL, confirming our hypothesis. This also confirmed that the far-field LA potentials were identified on the basis of their morphologies. It was of a particular clinical interest to know whether the timing of the LA potentials on the CS electrogram recordings helps in clarifying the electrophysiological mechanism of various supraventricular tachyarrhythmias. This point has been the

Fig. 5. Intracardiac electrograms obtained during successful ablation of the left posterolateral AP by applying radiofrequency (RF) delivered at the earliest atrial activation during RV pacing at a 750 ms during S-S cycle. During retrograde conduction over AP on the 1st and 2nd RV pacing, the far-field LA potentials with the earliest site at CS5-6, followed by near-field CSM activation is observed, almost simultaneously with atrial deflection at the distal pole of ablation catheter (ABL), and the onset is indicated by dot line. On the 3rd and 4th RV pacing, retrograde conduction over AP disappears, instead, retrograde conduction through the AV node evidenced by the earliest atrial activation at His bundle region appears, accompanied by a disappearance of LA potentials preceding CSM potentials. Other abbreviations as in Fig. 2.
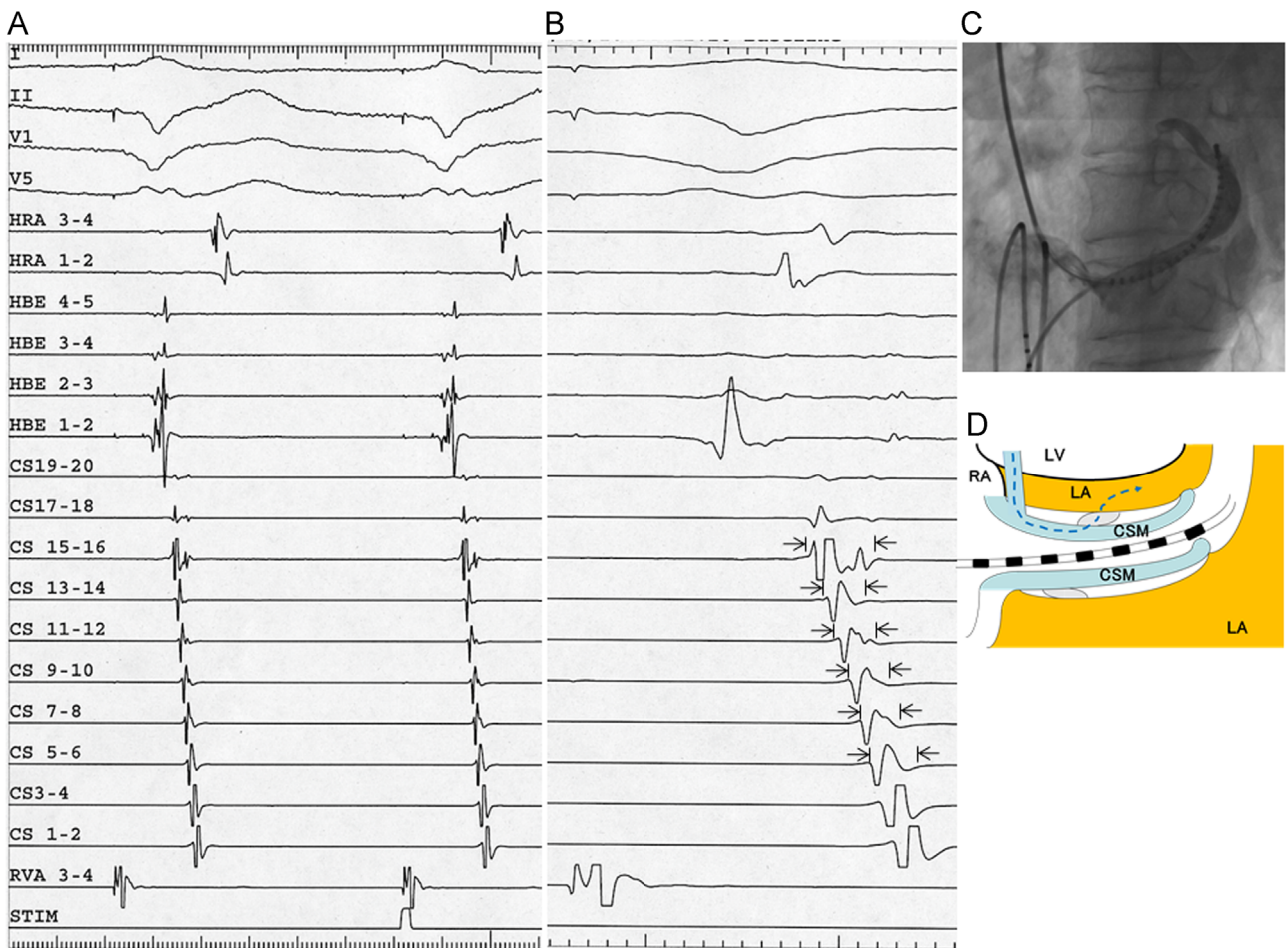
Fig. 6. Example of coronary sinus-ventricular connection in a 79-year-old man. (A and B) Intracardiac recordings of right ventricular (RV) stimulation (S) at 100 and 400 mm/s paper speed, respectively, which reveals the far-field LA activation following near-field CSM activation. (C) Left anterior oblique fluoroscopic view of the position of the CS catheter during CS venography. Abbreviations and symbols as in Fig. 2. (D) Illustration of activation sequences. Abbreviations and symbols as in Fig. 1.
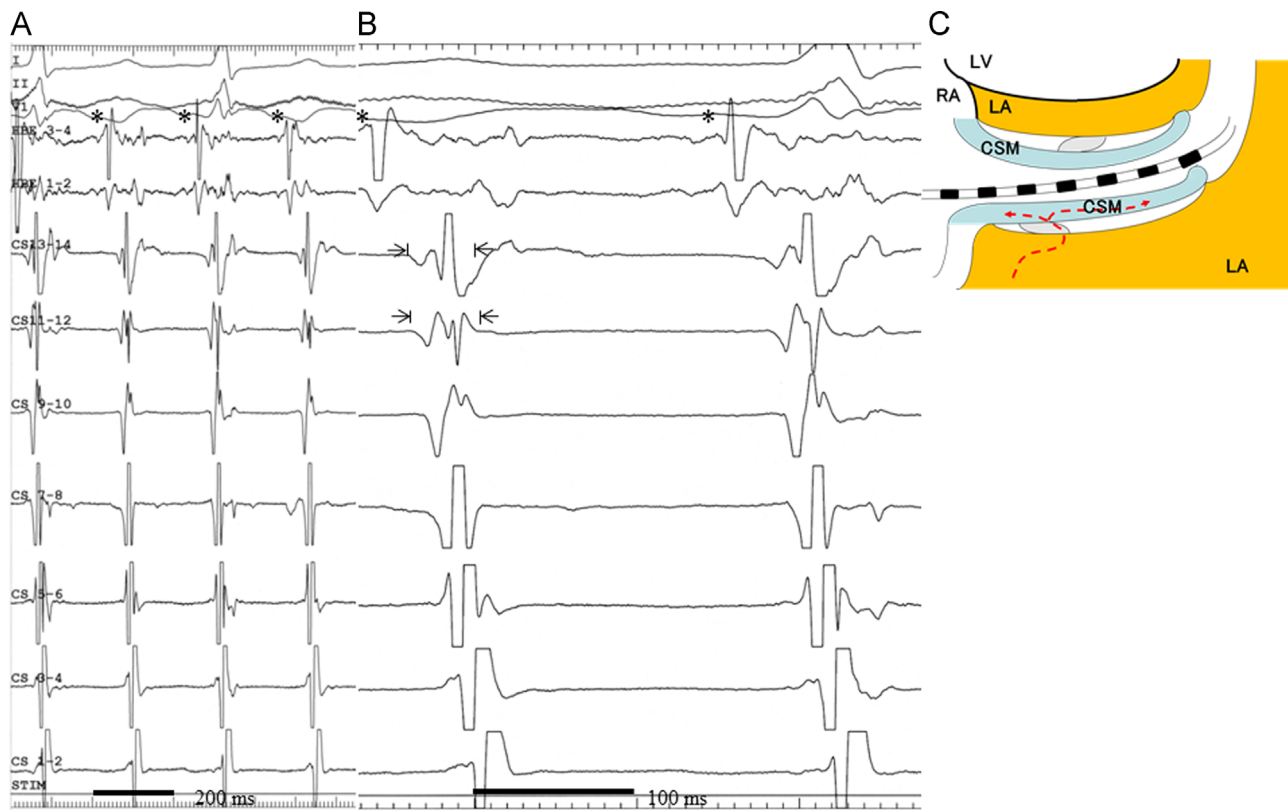
Fig. 7. Example of typical CW AFL in a 64-year-old man. (A and B) Intracardiac recordings of AFL at paper speed of 100 and 400 mm/s, respectively. Right- and left-pointing arrows in panel B mark the onset of the LA potential and the end of the CSM potential, respectively. Asterisks indicate atrial deflections. (C) Bidirectional dotted arrow indicates the sites of recordings between 4:30 and 6:00 o'clock. Other abbreviations and symbols as in Fig. 2. (D) Illustration of activation sequences. Abbreviations and symbols as in Fig. 1.

object of several previous reports, including our own observations. First, the activation sequence of the LA and CSM during retrograde conduction over a left-sided AP may be a clue to differentiate an AV AP from CS-ventricular accessory pathways that connect the atrium and the ventricle via CSM [7,8,15]. A LA → CSM activation sequence suggests the presence of an AV AP (Fig. 2), while, during retrograde conduction over CS-ventricular accessory pathways, the wavefront propagates via CSM before reaching the atrium, thus representing a CSM → LA activation sequence (Fig. 6) [8,16,17]. This information may be useful in choosing the best approach for ablating the left-sided AP. Second, the participation of the LA in the reentry circuit of a slow-fast AVNRT, albeit controversial, is suggested by the observation of a LA → CSM activation sequence during ongoing tachycardia [6]. Third, the activation sequence of the LA and CSM may be influenced by the direction of the reentrant wavefront during ongoing AFL. During typical CW AFL, the sequence of activation is from LA → CSM (Fig. 7), in contrast to typical CCW AFL, where the activation sequence is from CSM → LA (Fig. 3). This is because the CSM is activated by propagation of the wavefront via the superior interatrial connections, including Bachmann's bundle and interatrial septum, reaching the LA from the RA, instead of being activated via the interatrial connection at the proximal CS, as in the case of typical CCW AFL [18]. The activation of the mid or distal CS electrograms during typical AFL is proximal-to-distal because of their RA origin, regardless of the CW or CCW reentrant direction and this sequence does not explain the mechanism of typical AFL. Thus, the timing of LA potentials may be a useful atrial indicator of the mechanism and origin of supraventricular tachyarrhythmias that cannot be mapped, particularly when non-sustained. Further studies, in larger populations are needed to verify this hypothesis.

4.1. Limitations of our study

First, since this was a retrospective study, we did not confirm the activation sequence of the CSM and the LA during both, retrograde conduction over the AP and during ongoing AFL. Second, we did not routinely perform neither differential pacing nor a direct recording of LA potentials to confirm that the far-field potentials in CS recordings truly reflect LA activation. Finally, we could not evaluate the frequency of the LA potentials.

5. Conclusions

Far-field LA potentials are frequently detected on CS recordings during sequential activation of the LA and the CSM in the general population. The timing of these LA potentials recorded through electrograms in the CS reflected the direction of impulse propagation via the CSM. They could be a useful atrial indicator of the mechanism and origin of supraventricular tachyarrhythmias.

Conflict of interest

All authors declare no conflict of interest related to this study.

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