Atrial flutter: arrhythmia circuit and basis for radiofrequency catheter ablation

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The term atrial flutter was introduced 90 years ago for an arrhythmia with a unique electrocardiographic pattern. The development of endocardial mapping techniques in the last decade allowed the detailed characterization of the tachycardia circuit and the identification of the cavotricuspid isthmus as its critical part. This review stresses the position of atrial flutter in the new classification of atrial tachycardias and focuses on its unique electrophysiological characteristics and different variants described in humans. Transcatheter radiofrequency ablation across the cavotricuspid isthmus constitutes a feasible and safe therapy, which prevents flutter recurrences during the long-term follow-up. This paper describes the different techniques that validate bidirectional isthmus block, which is an important endpoint for successful ablation.

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Introduction

The term atrial flutter was introduced by Jolly and Ritchie[1] in 1911. Until the 1970s the mechanism of this arrhythmia remained controversial, with protagonists and antagonists of reentry versus ectopic focus theories[2]. The development of clinical and experimental electrophysiology (both animal and human studies) supported the concept of atrial flutter as a macroreentrant wave reentry confined to the right atrium[3-9].

On the basis of the new classification, atrial tachycardia is defined as a regular atrial rhythm at a constant rate ≥ 100 b/min, originating outside the sinus node[10]. The mechanism can be focal or reentrant. The well characterized macroreentrant atrial tachycardias include: 1) typical atrial flutter, 2) reverse typical atrial flutter, 3) lesion macroreentrant tachycardia, 4) lower loop flutter, 5) double wave reentry, 6) right atrial free wall macroreentry without atriotomy, and 7) left atrial macroreentrant tachycardia. Atrial flutter refers to a regular atrial tachycardia with a rate ≥ 240 b/min (cycle length ≤ 250 ms, < 2% cycle to cycle variation)[11], lacking an isoelectric baseline between the deflections on the ECG.

A proposal of an updated classification of atrial flutter could be that reported in table I.

The most common typical atrial flutter ECG characteristics are: a "sawtooth" pattern in leads II, III and/or aVF (Fig. 1A). This consists of a downsloping segment followed by a sharper negative deflection, then a sharp positive deflection with a positive overshoot leading to the next downsloping plateau. Lead V_1 often shows a positive deflection, but biphasic or negative deflections may be seen in some cases. The relative size of each component may vary markedly. The reverse typical atrial flutter may be recognized with a high degree of reliability in the presence of a broad, positive deflection in the inferior leads (Fig. 1B), although morphologies similar to that of typical atrial flutter have been reported. The polarity of the F waves in the surface ECG leads II, III, aVF, V_1 and V_6, especially the wide negative deflections in V_1, are the most sensitive features in distinguishing counter-clockwise and clockwise typical atrial flutter[12,13].

Atrial flutter circuit

The importance of barriers, either functional or anatomical in the genesis and perpetuation of atrial arrhythmias in both animal models and in humans has long been recognized[14]. Atrial flutter results from a right atrial macroreentrant circuit bounded anteriorly by the tricuspid orifice, and posteriorly by the arrangement of anatomical obstacles [orifices of

Table I. Proposal of an updated classification of atrial flutter (AF).

Typical AF (cavotricuspid isthmus-dependent)
Counter-clockwise (common AF)
Clockwise (reverse AF)

Atypical AF
- Right atrial AF
  Lower loop reentry AF
  Upper loop reentry AF
  Right atrial free wall macroreentrant AF without atriotomy
  Incisional reentrant tachycardia (atriotomy incision)
- Left atrial macroreentrant tachycardia
  AF after linear catheter ablation
  AF in diseased left atria
  Idiopathic (very rare)

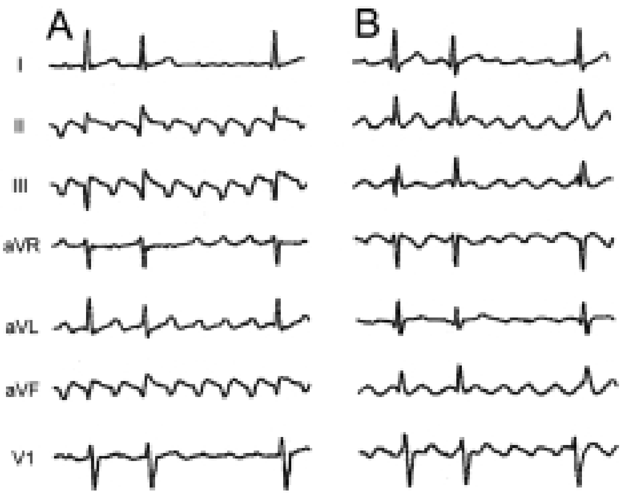

Figure 1. *ECG recordings during typical counter-clockwise* (A) *and typical clockwise (reversal) atrial flutter* (B). *Note the "sawtooth" pattern of the F waves and the absence of an isoelectric line in leads II, III and/or aVF.*

the superior and inferior vena cava (IVC) and Eustachian ridge][15-17] and functional barriers (region of the crista terminalis)[9,18-20]. In humans, the most common direction of activation of the flutter circuit (90%) is the following: the wavefront proceeds in a lateral to septal direction along the isthmus between the IVC and the tricuspid valve (TV) and then proceeds along the septum in a caudocranial direction. This has been described as counter-clockwise reentry, when viewed from a left anterior oblique fluoroscopic perspective. The opposite direction of activation (clockwise direction, reversal typical flutter) occurs in approximately 10% of clinical cases.

The superior pivot point of the circuit is not well defined. Current data suggest that in most cases it includes the right atrial roof anterior to the superior vena cava orifice, including the initial portions of Bachmann's bundle[21,22]. However, sometimes the activation can also cross the superior end of the crista terminalis[23] or even lower along this structure (lower loop reentry-LLR)[24]. The inferior pivot point is the area bounded anteriorly by the inferior part of the TV and posteriorly by the IVC. This area, the target of the ablation procedure, has been called the cava-tricuspid isthmus, sub-Eustachian isthmus, inferior isthmus or simply flutter isthmus.

This isthmus frequently has a heterogeneous anatomy with a high prevalence of a non-uniform arrangement of the trabecular muscles[25]. A posterior sector of the isthmus close to the IVC consists mainly of fibrous and fatty tissue with rare muscle fibers. This could explain the low amplitude voltage in this area[26,27]. Anatomical studies have shown that its width from the TV to the IVC varies from 18-50 mm (mean 31 ± 7 mm)[28]. The anatomy and in particular the length of the Eustachian ridge, which in effect forms the posterior boundary of the so-called septal isthmus also varies (21-50 mm, mean 34 ± 8 mm) affecting the functional width of the isthmus[29]. Studies using conventional[30,31] or non-fluoroscopic[23] mapping techniques found that the conduction velocity within the isthmus is slower than in the rest of the human right atrium. When the right atrial conduction times were compared during sinus rhythm in patients with or without a history of typical flutter, lower conduction velocities were found in the TV-IVC isthmus in patients with flutter by the some investigators, but not by others[32]. Recent data of Schilling et al.[33] obtained using a non-contact mapping system led to the conclusion that the conduction velocity within the isthmus may be slower than in the rest of the atrial flutter circuit.

Septal isthmus and variations of the crista terminalis conduction. The Eustachian valve forms a line of conduction block extending from the IVC to the coronary sinus (CS) ostium, which, combined with the TV, forms a protected channel within the reentrant circuit of typical and reverse typical atrial flutter. The lateral end of this channel forms the "posterior isthmus" (between the IVC and the TV) and its medial end forms the "septal isthmus" (between the CS ostium and the TV)[16].

Using intracardiac echocardiography, Olgin et al.[15,34] found that the crista terminalis was the posterolateral boundary in human atrial flutter. In contrast, Friedman et al.[35], using the same method, demonstrated that a functional line of block was present at the posterior (sinus venosa) region during atrial flutter. Similarly, Cheng et al.[24] assessed in a study the conduction of the crista terminalis and found that nearly half of flutter patients presented with crista terminalis permeability. Additionally, Schilling et al.[33], using a non-contact mapping system, demonstrated that the line of block represented by the crista terminalis was not necessarily complete in all patients. These data suggest a variability in the crista terminalis conduction in patients with atrial flutter.

Flutter circuit mapping

Entrainment mapping. In 1977 Waldo et al.[8] first described that high right atrial pacing at a rate faster than the spontaneous flutter rate caused acceleration of the flutter or "entrainment". Since then entrainment mapping is applied to localize the critical part of the circuit, which is generally formed by a narrow protected isthmus of conduction. Pacing within such an isthmus will demonstrate entrainment with concealed fusion (no evidence of change in the activation sequence with pacing and a long delay between the stimulus artifact and the flutter wave), while the first flutter wave after the last paced beat returns to the tachycardia cycle length (Fig. 2).

Activation mapping. This technique implies the use of a multielectrode catheter for which a specifically preformed shape (e.g. halo) facilitates anteroinferior right atrial positioning (Fig. 3)[18,36]. In the clinical setting, bipolar recordings with a short interelectrode distance (≤ 2 mm) offer sufficient spatial resolution, since the reentrant circuit size is generally large (several cm in diameter). The limitation of atrial mapping as well as of tachycardia definition include the inaccessibility of some endocardial atrial recording sites as well as the inability to map the epicardium using traditional catheter electrode techniques.

Double potentials. Early investigations[20,37-40] have shown that a line of conduction block in the atrium is

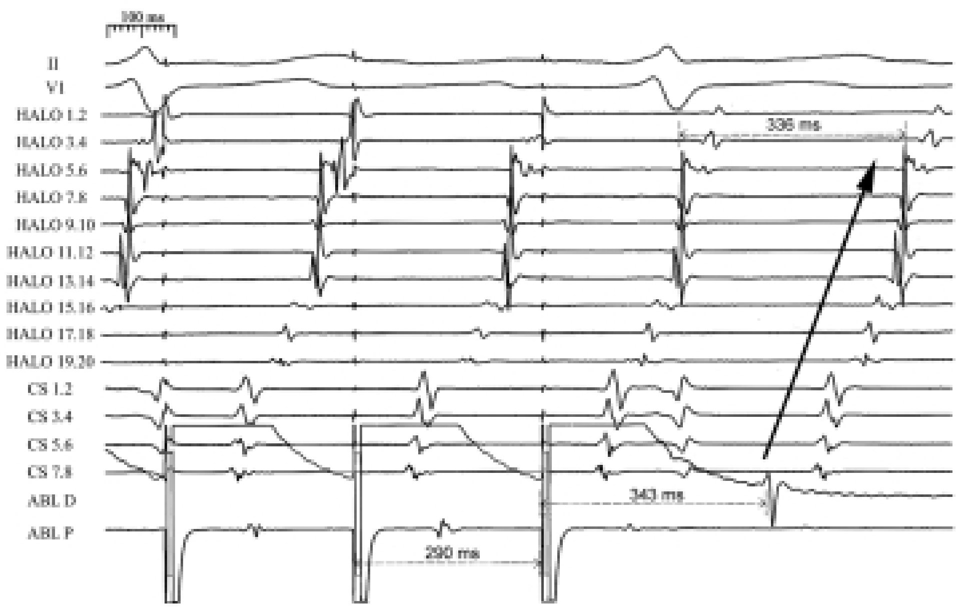

Figure 2. *Electrograms demonstrating entrainment with concealed fusion within the cavotricuspid isthmus. During atrial flutter with a cycle length of 336 ms, pacing from the catheter positioned on the isthmus (Abl) at a faster rate (290 ms) was employed to verify the participation of the isthmus in the circuit. The tachycardia beats are advanced by the stimulation. Note that the activation sequence in the coronary sinus (CS) and the halo (HALO) catheter is the same in the paced beats and first spontaneous tachycardia beat* (arrow). *The interval between the last stimulated and the first spontaneous cycle recorded in the ablation catheter (post-pacing interval) is 343 ms, only 7 ms longer than the tachycardia cycle length, which proves that the flutter isthmus is an active part of the reentrant circuit.*

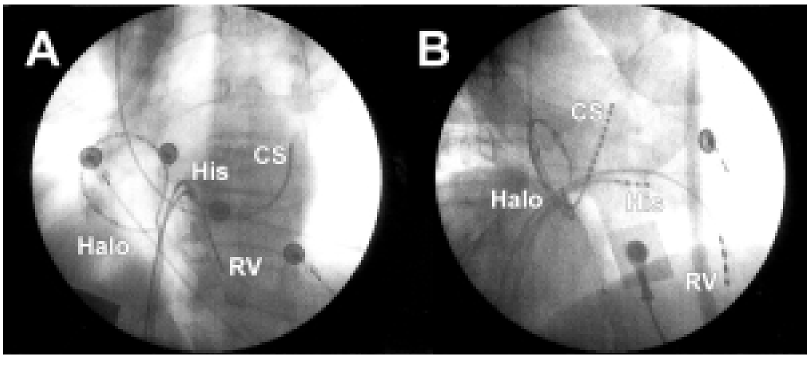

Figure 3. *Fluoroscopic image showing the catheter position in the left anterior oblique* (A) *and right anterior oblique* (B) *views. The halo catheter (Halo) is placed in the anteroinferior position around the tricuspid valve. CS = coronary sinus catheter; His = catheter positioned on the His bundle; RV = catheter in the right ventricle.*

manifested by double potentials separated by an isoelectric interval. The first potential is due to the arrival of the atrial impulse on one side of the line of block, whereas the second potential is due to the later atrial activation on the other side of the line of block. However, double potentials may also be recorded from areas of local block outside the reentrant circuit. The interpretation of double potentials has to be made in the context of the general activation sequence and of the response of the entrainment pacing.

Additional techniques. Recent new technologies have provided additional or corroborative data about the anatomical and electrophysiological properties of the flutter circuit. These include non-contact (EnSite) and contact electroanatomical (CARTO) mapping systems (Fig. 4). Both techniques allow for better spatial resolution as well as an enhanced mapping precision[23,33,41-44]. Additionally, intracardiac echocardiography permits the correlation of electric signals with intracardiac structures[15,34].

Variations of human atrial flutter

Double wave reentry. In 1998 Cheng and Scheinman[45] first described the double wave reentry, a subtype of atrial flutter. In this tachycardia two activation wavefronts circulating simultaneously in the typical flutter circuit are present, while there are no changes in the flutter wave morphology on the surface ECG. Double

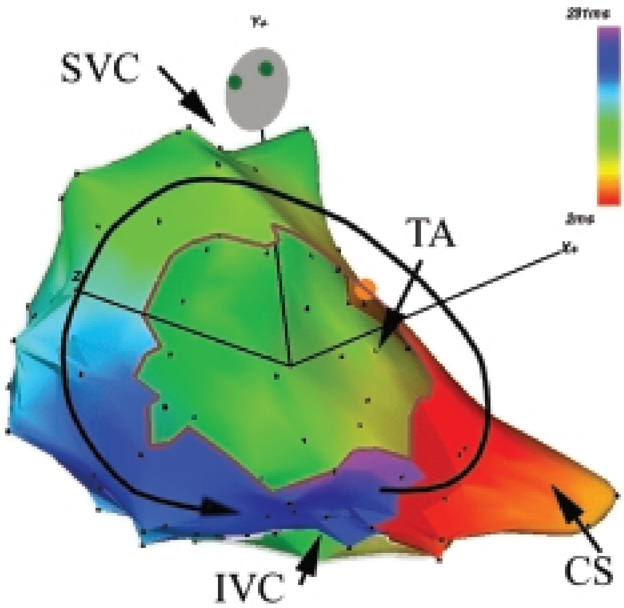

Figure 4. *Electroanatomical activation map of the right atrium in the left anterior oblique projection during typical counter-clockwise flutter. The activation times are color coded as displayed on the scale. The tachycardia circuit encircles the tricuspid annulus (TA)* (arrow). *The latest activation* (violet) *encounters the earliest* (red) *on the posterior isthmus closing the tachycardia circuit. CS = coronary sinus; IVC = inferior vena cava; SVC = superior vena cava.*

wave reentry is a transient arrhythmia with a more rapid and irregular rate compared to typical atrial flutter.

Lower loop reentry. One year later the same group[24] published their observations about another subtype of atrial flutter designated as LLR. During LLR the activation traverses the typical flutter isthmus, activates the posterior right atrium and then skirts the IVC with breakthrough along the low right atrium. This generates two wavefronts which collide and extinguish themselves in the high lateral or septal right atrium. Still, the flutter isthmus forms the critical component, but the superior pivot point is lower compared to that of typical atrial flutter. The 12-lead surface ECG of this type of tachycardia tends to show negative atrial complexes in the inferior leads. In contrast to double wave reentry, LLR has a more stable rhythm that persisted for as long as 4 min compared to double wave reentry, which lasts only for 2 to 12 beats.

Left atrial flutter. Stable macroreentrant atrial tachycardias can also originate from the left atrium. The exact incidence of left atrial flutter in humans is currently unknown, but it may account for 10% of atrial flutters and occurs mainly in patients with underlying structural heart disease[46]. Right atrial mapping typically shows non-reentrant activation patterns with two superior and inferior wavefronts emerging from the intra-atrial septum and merging on the lateral right atrial wall. The activation sequence of the CS is typically from distal to proximal or from the mid CS to both the proximal and distal CS, with cycle length variations in the right atrium.

Jais et al.[46] using conventional right atrial and direct left atrial three-dimensional electroanatomical mapping in 22 patients with atypical flutter demonstrated various left atrial macroreentrant circuits. In most cases, the arrhythmia rotated around the mitral annulus, a zone of block including the pulmonary veins, or an electrically silent area. In some patients, the circuits were more complex, with 2 or 3 loops rotating concomitantly. In their series 50% of patients with left atrial flutter had a left atrial electrically silent area which was probably related to severe atrial fibrosis, a common phenomenon in patients with structural heart disease[47]. The importance of electrically silent areas for the maintenance of left atrial reentrant tachycardias was confirmed in a recent report by Ouyang et al.[48] who, using the electroanatomical mapping system, described different left atrial flutter circuits in 26 patients.

Ablation of atrial flutter

Overall, the various principles of ablative antiarrhythmic therapy for any reentrant arrhythmia are similar: reconstruction of the circuit, identification of the narrowest, but safe to section, part of the circuit and ablation directed to this region resulting in complete conduction block and the elimination of the tachycardia. As with other arrhythmias the catheter DC ablation was preceded by the successful cryosurgical destruction of the region of slow conduction in the low right atrium[49]. The first radiofrequency (RF) catheter ablation for atrial flutter was performed by Cosio et al.[50]. These authors used the "anatomically guided" approach, but other groups attempted focal ablation using entrainment markers of the slow conduction[51] and/or fragmented ECGs as targets[52]. The endpoint was the termination of the flutter during the procedure. An early comprehensive study[53] compared three different target sites: 1) between the IVC and the TV, 2) between the CS ostium and the TV, and 3) between the CS ostium and the IVC. Ablation of the ICV-TV annulus provided the maximum acute success (70%). Later, Tabuchi et al.[54], in canine models of atrial flutter, showed that complete conduction block in the cavotricuspid isthmus well correlates with acute success and that it can be easily verified by right atrial mapping even in sinus rhythm. The similar concept was almost simultaneously developed and applied clinically by two French groups[36,55] and complete bidirectional isthmus conduction block was established as a new endpoint for flutter ablation.

Ablation techniques. The ablation can be performed in patients either in atrial flutter or in sinus rhythm. When in sinus rhythm, the ablation is usually made during continuous pacing from the low lateral right atrium (LLRA pacing) or from the CS ostium (CS pacing). The target area for RF ablation is at the isthmus between the IVC and the tricuspid annulus or between the tricuspid annulus and the Eustachian ridge[16,36,56]. RF energy delivery begins at the ventricular side of the tricuspid annulus when a stable electrogram with small atrial and large ventricular amplitudes is recorded. Then the ablation catheter is dragged progressively (3-4 mm steps), until the ostium of the IVC is reached. At each position, temperature-controlled RF energy is delivered for 30 s to 2 min[53,57-59]. The creation of this linear ablation line may be facilitated by the use of long introducer sheaths for superior stability or non-fluoroscopic imaging techniques[41-43]. The latter allow the reduction of the overall X-ray exposure time without prolonging the duration of the procedure. However, considering cost-effectiveness issues, it may be argued that the routine use of these expensive mapping systems should be reserved for problematic cases (e.g. unstable arrhythmias or resistant flutter) or for recurrences after a prior ablation to better characterize the completeness of the line of block.

The efficacy of RF ablation (the creation of a transmural lesion) varies according to contact, local blood flow, delivered power and myocardial thickness. Data of Shah et al.[60] in this regard suggest that a transmural RF lesion can be recognized by double potentials separated by an isoelectric interval. Additionally, the interindividual variability of the isthmus anatomy[28,29,61] and its electric properties[44] can explain the relatively large variability in the number of RF applications required to create a complete block. Theoretically, larger lesions with each application created by 8-mm tip or irrigated tip ablation catheters may shorten the procedure time[62].

Isthmus conduction block assessment. Different studies in the literature have compared incomplete versus complete and bidirectional versus unidirectional block[36]. Historically, isthmus conduction block was first described using the activation mapping technique[55]. This technique implies the use of a multielectrode halo catheter that facilitates the detailed analysis of the right atrial activation sequence before and after isthmus ablation[36]. Based on activation mapping criteria, complete bidirectional isthmus conduction block is defined by the observation of a pure descending wavefront at the lateral wall down to the low right atrial isthmus during CS pacing (clockwise block) (Fig. 5) and by the observation of a pure descending wavefront at the septal wall down to the septal side of the isthmus during LLRA wall pacing (counter-clockwise block). The term incomplete block refers to persistent, but delayed conduction through the isthmus. Previously, it has been claimed that unidirectional block may correlate with the elimination of the substrate for one variant of typical flutter (clockwise or counter-clockwise). Presently, it appears that the unidirectional block represents different degrees of slow conduction for both directions.

The changed atrial activation after isthmus ablation during pacing is reflected by alterations in the surface ECG. Typically, during LLRA pacing (similarly, but less commonly during CS pacing), a "positivization" of the terminal part of the P wave may be noted in the inferior leads after completion of the conduction block[63]. Unfortunately, the specificity and sensitivity of this simple but indirect method are limited.

Cosio et al.[37] proposed that double potentials separated by an isoelectric line reflect local conduction block. The presence of widely separated double potentials along the ablation line was proposed as a direct criterion for complete isthmus conduction block[64]. One advantage of this technique is that it can be performed using only two catheters (without the need for a halo catheter). However, Anselme et al.[65] found difficulty in recording clear-cut widely separated double potentials with this method. Despite the complete conduction block, the double potentials recorded on the isthmus were considered ambiguous/atypical in 39% of their study population.

Another technique (differential pacing) has been proposed by Shah et al.[66]. This method assesses the changes in the timing of double potentials recorded by a catheter positioned across the isthmus ablation line. Its principle is based on the presumption that during pacing close to the line of block the first component of

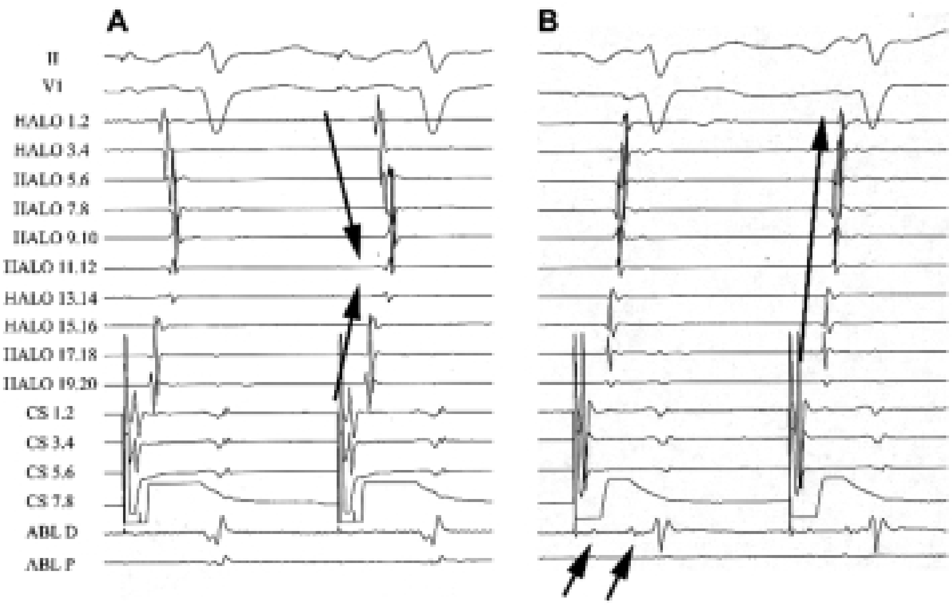

Figure 5. *Electrocardiograms showing the change in the right atrial activation sequence during pacing from the proximal coronary sinus (CS 7-8). The catheters are positioned as depicted in figure 4. In* panel A *the halo (HALO) catheter is activated by two wavefronts: one going up the septum and the second across the cavotricuspid isthmus* (arrows). *Both wavefronts collide on the right atrial lateral wall and the latest activation is in the halo bipoles 11-12.* Panel B *shows activation after the creation of conduction block across the isthmus. The activation in the halo catheter is counter-clockwise and unidirectional from the proximal (19-20) to the distal (1-2) bipoles proving complete clockwise block. Note the wide split double potentials in the ablation (Abl) catheter positioned along the ablation line* (arrows). *The second component of the double potential is recorded after the activation of the distal halo catheter (1-2), which is consistent with complete conduction block.*

the double potential reflects direct activation, while the second component represents activation by the wavefront arriving to the isthmus around the TV. In the presence of complete block, the change of the pacing site to a more distant position from the isthmus will lead to the later timing of the first component (as the distance between the pacing site and the line of block is now longer) and to the earlier timing of the second component (as the distance between the pacing site and the opposite side of the isthmus shortens).

The usefulness of unipolar electrograms in determining complete isthmus conduction block was demonstrated by Villacastin et al.[67]. The RS morphology of a unipolar electrogram is associated with the propagation of the wavefront through the exploring electrode, whereas a R (positive uniphasic) unipolar electrogram is characteristic of the termination of activation. The presence of a positive uniphasic electrogram at the LLRA lateral to the line of block predicted clockwise complete isthmus conduction block with a 100% success rate. The presence of different unipolar electrograms at the proximal CS region as predictors of counter-clockwise complete isthmus conduction block was associated with an 89% sensibility, a 100% specificity and a 100% positive predictive value.

Another simple technique to discriminate between complete and incomplete block based on the prolongation of the transisthmus interval after linear flutter ablation was recently introduced by Oral et al.[68]. The transisthmus interval was defined as the interval between the stimulus artifact and the local atrial activation recorded from the proximal CS electrode during LLRA pacing (counter-clockwise interval) or between the stimulus artifact and the atrial activation recorded from a catheter positioned on the isthmus just lateral to the line during CS pacing (clockwise interval). The study demonstrated that the transisthmus intervals had progressively decreasing conduction properties in both directions. There was no critical transisthmus interval which appeared to discriminate between complete and incomplete bidirectional block. However, the prolongation of the transisthmus conduction by ≥ 50%, as compared with the baseline interval, identified complete block with a 100% sensitivity, an 80% specificity, an 89% positive predictive value, a 100% negative predictive value and a diagnostic accuracy of 92%.

Finally, a recent study of Tada et al.[69] evaluated the utility of the reversal of the bipolar electrogram polarity as an indicator of complete isthmus conduction block. Electrograms recorded from two distal electrode pairs (E1 and E2) of the halo catheter positioned just lateral to the ablation line were analyzed during atrial flutter and during CS pacing. Before ablation, the initial polarity of E1 and E2 was predominantly negative during atrial flutter and positive during CS pacing. In each of the patients with complete isthmus conduction block as assessed by the widely separated double potentials along the ablation line, the polarity of E1 and E2 became negative during CS pacing, compared to the incomplete block when the electrogram polarity became reversed either only at E2, or at neither E1 nor E2. Of note, in 10% of patients the atrial activation sequence recorded with the "halo" catheter was consistent with complete isthmus block, but the presence of incomplete block was accurately detectable by the inspection of the polarity of E1 and E2. The authors concluded that the change in electrogram polarity is an accurate indicator of complete isthmus block that can be assessed instantaneously after each RF energy delivery.

Early isthmus conduction recurrence. Early recurrence of isthmus conduction occurs in approximately 25-50% of patients[41,64]. This recovery ranged from 5 s (in 76% within the first 3 min), but may uncommonly occur as late as 1 hour. For this reason, the patients are routinely observed in the electrophysiological laboratory for at least 20 min after successful ablation before the repetition of the electrophysiological study to exclude isthmus conduction recovery.

Resistant flutter. The term "resistant flutter", although commonly used, remains poorly defined in the literature. Cosio et al.[70] proposed this term for an ablation procedure lasting > 4 hours, while others defined it on the basis of the number and extent of RF applications (in a series of Willems et al.[41] more than 21 RF burns). Jais et al.[62] reported a 7.6% incidence of resistant flutter and suggested a practical definition based on the inability to achieve complete isthmus block despite a number of RF applications more two standard deviations above the mean in their series. Different anatomic factors (e.g. dilated right atrium, tricuspid regurgitation) are frequently considered responsible[28], but two factors appear to be especially important: the thickness of the myocardium and the isthmus topography. In case of resistant flutter the use of a long sheath and/or ablation during enforced apnea increase the mechanical stability and may lead to success. Another possibility is to repeat the ablations empirically all along the same line or to create additional lines on either side of the original lesions. Furthermore, the use of an 8-mm ablation catheter tip with a high power RF generator or a cooled tip catheter may be effective and safe in achieving complete bidirectional isthmus block resistant to conventional ablation[62].

Recurrent flutter. With isthmus conduction block as the endpoint of RF ablation, the flutter recurrence rates decreased to about 5.1-9%[41,44,57,64]. In most cases, a recurrence represents the recovery of isthmus conduction after complete block achieved during a prior ablation. Recurrence is mostly noted within 3 months of the initial procedure (however, Schneider et al.[44] described recurrences after 18.8 months) and it is almost always the same as the initial flutter, though there may be variations in the cycle length due to the effects of the ablation on isthmus conduction. Ablation targeting residual gaps guided by conventional or non-fluoroscopic (EnSite, CARTO) mapping techniques is effective and parsimonious in this situation[41-43,60].

Conclusions

Advancements in electrophysiology and the development of endocardial mapping techniques allowed the exact delineation of the tachycardia circuit and the identification of the cavotricuspid isthmus as its critical part. The creation of bidirectional complete block across the isthmus by transcatheter RF ablation represents a feasible and safe therapy, which prevents atrial flutter recurrences during the long-term follow-up. The demonstration of a complete conduction block is an important endpoint for successful ablation. Further advancements in mapping systems and ablation technologies may help to overcome the difficulties which may be encountered in individual patients.

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