Radiofrequency catheter ablation for atrial flutter and atrial fibrillation : new insights

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Radiofrequency catheter ablation for
atrial flutter and atrial fibrillation
new insights

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Radiofrequency catheter ablation for atrial flutter and atrial fibrillation new insights

PROEFSCHRIFT

ter verkrijging van de graad van doctor
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Prof. dr. A.C. Nieuwenhuijzen Kruseman,
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen
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*tasrnāḁ asaktāḥ satatūḁ
kāryaḁ karma samācara
asakto hy ācaraḁ karma
param āpnoti pūruṣaḥ*

karmayogo nāma tṛtīyo 'dhyāyah, Bhagavadgītā

Therefore, without attachment,
perform always the work that has to be done,
for man attains to the highest by doing work
without attachment.

3rd Chapter, Karma Yoga or the Method of Work, the Bhagvad Gita

Dedicated to
Aai and Baba,
my brother, Shailesh
and my wife, Vaishali
for allowing me to remain engaged in this effort.

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Introduction

Atrial flutter (AFL) is a unique arrhythmia, electrocardiographically characterized by an intriguing monotony in rate (300 beats/min) and morphology (inverted “saw tooth” or “picket fence”) of the atrial deflections (Figure 1).^{1,2} Atrial flutter was first described by Jolly and Ritchie in 1911.³ The incidence of this arrhythmia is uncertain, but is more common in men.⁴ Patients with AFL may have associated structural cardiovascular lesions (like hypertension, coronary artery disease, mitral or tricuspid valve disease or congenital cardiac disease). It may also occur following open heart surgery (like the Mustard or Fontan procedure), or in the presence of a systemic illness (like chronic obstructive pulmonary disease).^{1,2} Atrial flutter is usually paroxysmal and not life-threatening, unless associated with conditions like pulmonary edema or 1:1 atrioventricular (AV) conduction as in presence of Wolff-Parkinson-White syndrome.² Recently, a 7% overall embolic event rate was observed at 2 year follow-up in patients with AFL, which calls attention to a risk of thrombo-embolism seemingly higher than previously thought.⁵

Several animal models have followed the one described by Rosenblueth and Garcia-Ramos, and they have contributed valuable insights into the mechanisms of AFL.^{6,7,8,9} These experimental studies suggest that AFL is predominantly a right atrial (RA) reentrant arrhythmia, with a clockwise (CW) or counterclockwise (CCW) movement around the tricuspid valve (TV) annulus. It may occur in the presence or absence of an anatomical obstacle. Electrophysiological studies, including activation mapping and entrainment techniques pioneered by Puech et al.,¹⁰ and Waldo et al.,¹¹ supported that AFL in humans is based on a RA macro-reentry movement with an excitable gap.^{12,13} The bulk of evidence currently available confirms that in 80-85% of cases, human AFL circuit is in RA (Figure 2).¹⁴ The unique arrangement and orientation of the atrial muscle fibers between inferior vena caval (IVC) orifice and TV orifice¹⁵ may promote nonuniform anisotropic conduction in the so called “isthmus” thus providing a zone of slow conduction in the AFL circuit.^{16,17,18} During type I AFL, double potentials have been recorded along the crista terminalis suggesting that the crista forms a posterior barrier of the flutter circuit^{19,20} while the TV annulus forms an anterior barrier.²¹ Thus, the anatomical barriers provided by the endocardial architecture

Figure 1. The 12-lead ECG shows typical atrial flutter (AFL), with regular and sharp negative atrial deflections in the inferior leads and positive deflections in lead V1.

seems to determine the location of AFL circuit in RA. The left atrium seems to be not essential in the reentry circuit.

Currently, type I (the common or typical) AFL includes the isthmus dependent flutter with either CCW- or CW- RA activation in the frontal plane.^{14,22} Non-fluoroscopic mapping¹⁷ and studies using multiple endocardial electrograms (Figure 3) during pacing induced entrainment of AFL²³ have identified the type I AFL circuit completely. *In a CCW AFL* (Figure 4, Panel A), a broad band of peri-tricuspid activation enters the isthmus, slows in its medial part, ascends up the septum, reaches the root of the superior vena cava, usually crossing it anteriorly and rarely fusing around it to descend down the free wall.¹⁷ Clockwise AFL (Figure 4, Panel B), while running in the opposite direction, shares the same circuit with the same endocardial borders as the CCW-AFL and is therefore best considered as type I

Figure 2. A schematic representation showing the localization of the type I AFL macro-reentry circuit in the right atrium (RA). The panel on the left represents a clockwise (CW) AFL circuit. The activation wavefront is seen to propagate along the atrial septum craniocaudally, followed by mediolateral activation of the tricuspid valve (TV) - inferior vena cava (IVC) isthmus and caudocranial activation of the lateral RA wall (crista terminalis). The panel on the right represents a counterclockwise (CCW) AFL circuit. In this case, the atrial activation wavefront is seen to propagate craniocaudally along the lateral RA wall (crista terminalis), followed by lateromedial activation of the TV - IVC isthmus and caudocranial activation of the atrial septum. In either rotation, the activation wavefront could propagate anterior (A) or posterior (B) to the coronary sinus (CS).

AFL.^{14,24,25} Generally, the CCW-AFL is associated with negative “saw-tooth” flutter waves in leads II, III and aVF and positive flutter waves in lead V1.^{2,19,22,26} This ECG pattern is noted in 2/3rds of all AFLs.²⁶ Positive flutter waves in leads II, III and aVF and negative flutter waves in lead V1 are seen with CW-AFL (Figure 5).^{24,26} However, Saoudi et al., have reported the combination of negative flutter waves in inferior leads with negative flutter waves in lead V1 in a majority of their patients with CW-AFL.¹⁴ Furthermore, some positive flutter waves in inferior leads are due to CCW-RA circuits^{24,26} while some occur in left atrial reentry circuits.²⁵

In an experimental setting, Allesie et al., showed that AFL could occur at numerous places in the atria.^{7,27} During clinical electrophysiologic studies findings like heterogenous electrocardiographic morphology of the flutter wave, shorter cycle length, difficulty in entrainment and tendency for frequent transition to atrial fibrillation (AF) are considered as suggestive for “atypical AFL”.^{25,28} Left atrial²⁹⁻³² and surgical scar related^{33,34} flutter are considered as “atypical” since they do not involve the classical “type I” flutter circuit. Recently, double-wave reentry³⁵ and lower loop reentry³⁶ have been described as subtypes of type I AFL, to explain the mechanisms of more rapid and irregular AFLs.

Figure 3. Fluoroscopic 30° right anterior (Panel A) and 60° left anterior (Panel B) oblique projections showing: a duodecapolar Halo catheter placed around the tricuspid annulus (HALO, 1-2 to 19-20 represent the 10 bipoles of the Halo catheter), a decapolar catheter in the CS, a quadripolar catheter in the His bundle position (HIS) and a radiofrequency ablation catheter (RF) in the posterior RA isthmus.

Figure 4. Intra-atrial activation pattern during CCW (Panel A) and CW (Panel B) rotation of AFL. ECG leads II, III, aVF and V1 are shown. The intracardiac electrograms include, electrograms from the His bundle (distal, HISD and proximal, HISP), 10 bipoles of the Halo catheter (H0102 - H1920) and the CS.

Acute treatment of AFL to restore sinus rhythm includes antiarrhythmic drug (AAD) therapy,^{37, 38} rapid atrial pacing or DC cardioversion.² No drug given intravenously can predictably ensure successful rapid conversion to sinus rhythm. A study comparing the effects of a class III AAD, dofetilide with a class I AAD, flecainide, reported the superiority of dofetilide in conversion of AFL to sinus rhythm.³⁷ Recently, another study comparing the acute effects of class I and class III AADs on the circuits of type I AFL, reported conversion rates with ibutilide, propafenone and amiodarone to be 67%, 33% and 33% respectively.³⁹ Class IA (e.g. quinidine, procainamide, disopyramide), class IC (e.g. flecainide, propafenone) or class III (e.g. amiodarone, sotalol) AADs have been in clinical use for chronic prevention of paroxysms of AFL.² In recent studies, successful interruption by radiofrequency (RF) ablation of isthmus conduction resulted in cure of AFL in > 95% of cases.⁴⁰⁻⁴² The recurrence rate was < 10% when complete

Figure 5. The 12-lead ECG shows AFL, with positive atrial deflections in the inferior leads and negative deflections in lead V1. This patient had a clockwise AFL.

bidirectional isthmus conduction (BIC) block was achieved.⁴⁰⁻⁴² Catheter ablation of type I AFL is clearly the treatment of choice not only in patients with AFL non-responsive to antiarrhythmic medication, but also in patients preferring this curative therapy above AAD therapy, termination by overdrive pacing, or repeated electrical cardioversion.^{43,44}

Atrial fibrillation is currently the most frequent, sustained, symptomatic tachyarrhythmia in patients with or without structural heart disease requiring hospitalization and has been of growing interest to the electrophysiologist in recent years.^{1,45-49} The incidence of this arrhythmia increases with age, estimated to occur in nearly 5% by age 60, over 10% by age 70, and nearly 20% by the age of 80 years and is twice as common in males as females.^{50,51} Mechanistically speaking, mapping of electrical excitation during AF has showed that AF is frequently based on multiple wavelets wandering around natural anatomical obstacles and functional arcs of conduction block (random reentry).^{52,53} In some cases the wavelets seem to be an offspring (daughter wave) of a single reentrant circuit (mother wave).^{52,54} Recently, reports have been published of the

successful ablation of repetitively firing atrial foci resulting in AF.^{55,56} Clinically, the 3 most important consequences of AF are increased risk of thromboembolism,⁵⁷ tachycardiomyopathy⁵⁸ and heart failure. Restoration and maintenance of sinus rhythm is therefore superior to persistence of ventricular rate control by pharmacological or nonpharmacological intervention together with anticoagulation.⁵⁹ Rate control can be achieved pharmacologically, with agents that impair AV nodal conduction directly and/or by increasing the parasympathetic/sympathetic balance, or anatomically by modifying or ablating the AV nodal region.^{49,58} Return to sinus rhythm can be achieved by electrical or pharmacological conversion followed by pharmacological (or occasionally ablative) therapies.^{55,60-63}

Atrial flutter and AF may be considered to represent a spectrum of intra-atrial reentry.^{1,2} Based on the wavelength concept, the wavelength of AFL (≈ 9.7 cm) is longer than that of AF (≈ 7.8 cm).⁶⁴ The clinical co-existence of AFL and AF has been estimated to be 25–33%.^{65,66} Atrial fibrillation is often the transitional rhythm for initiating AFL.^{67,68} Atrial flutter and AF may occur at different times in the same patient⁶⁵ and in fact the presence of AFL and AF in different parts of atria at the same time has been shown in patients whose surface ECG suggests AFL.⁶⁹ A number of experimental^{70,71} and clinical studies^{72,73} have observed that the length of the functional block along the RA free wall (pectinate muscle bundles) determines the transition between AF and AFL. Also, AF is not entirely random as indicated by the periods of “organization” which tend to occur predominantly along the crista terminalis in a craniocaudal direction.^{52,74} Such an “organization” is facilitated by AADs.⁷⁴ The likelihood for “organization” of paroxysmal versus chronic AF is uncertain.⁶³

The class IC AADs, propafenone and flecainide, have been recommended as first line maintenance therapy to prevent AF recurrences in patients with paroxysmal and persistent AF having no or minimal structural heart disease.⁷⁵ “Transformation” of AF to AFL under class IC medication is well-known.^{66,76-79} Increase in the wavelength due to increase in the atrial refractory period in a tachycardia dependent manner,^{80,81} probably explains the class IC antiarrhythmic mediated conversion of AF to AFL. So far, such a conversion to AFL has been considered a proarrhythmic effect due to the risk of 1:1 AV conduction. Ortiz et al.,⁷⁰ remarked that “...of some interest is the recognition that type IC antiarrhythmic agents, when used to suppress recurrent AF in patients, sometimes “convert” subsequent episodes to AFL; i.e., a patient who previously presented with AF in the absence of drug therapy may now present with sustained stable AFL, having been treated with a type IC antiarrhythmic agent to suppress episodes of AF”. The incidence of class IC antiarrhythmic agent mediated conversion to AFL is suggested to be 3.5 to 20%,^{77,78} but may be higher when observed systematically. Recently Huang et

al.,⁸² showed clinical benefit following a “hybrid” strategy of RA isthmus ablation and AAD therapy, in patients who experienced conversion of AF to AFL while taking AAD therapy. Most of the patients in that study developed AFL when amiodarone was prescribed for AF.

We define “**class IC atrial flutter**” as a new AFL developing in patients receiving class IC AADs for recurrent episodes of AF. Our hypothesis was, that successful RF ablation of the RA isthmus in patients with resistant AF who develop AFL while receiving class IC antiarrhythmic therapy could favorably modify the “natural” course of AF. The short-term results of this “hybrid” approach (n = 14 patients) are presented in **Chapter II** of this thesis. Another group, using the same approach obtained equivalent results with regard to AF recurrences.⁸³

Linear ablation of the RA isthmus is an effective and curative therapy for type I AFL.⁸⁴ High procedural success (>95%) and low recurrence (<10%) rate are reported following documentation of BIC block.^{40-42,85,86} Long-term success of RF ablation of AFL may be undone by the occurrence of AF, either preexisting or developing *de novo*.^{87,88} A recent study found that palpitations following successful RA isthmus ablation for type I AFL are mostly due to AF and not due to AFL recurrences.⁸⁹ The risk of postablation AF recurrences is higher (8-30%) in patients with a history of spontaneous AF, structural heart disease, enlarged left atrial size, left ventricular ejection fraction < 50%, a higher number of previously failed AADs, and inducible AF following AFL ablation.^{86,88,90} In **Chapter III**, we tested the hypothesis that at least in some patients with coexisting type I AFL, maintenance of AF may be based on a macro-reentry around the TV orifice, including the RA isthmus. The entire patient population (n = 82), who underwent RF ablation of the RA isthmus by an anatomical approach, was divided into 4 groups after a careful review of the available ECGs and 24-hour Holter recordings. These 4 groups were: Group I, only AFL; Group II, AFL>AF; Group III, AF>AFL and Group IV, “class IC AFL”. Long-term occurrence of AF following successful ablation of the RA isthmus was examined.

Antiarrhythmic drugs,^{65,82,91,92} including class IC agents,^{76-79,83} convert AF to AFL by slowing conduction and causing prolongation of the atrial refractory period, thereby creating functional lines of inter- and intra-atrial block thus leading to transformation of random reentry into organized stable reentry. In the literature, reports on ablation of AFL which developed while taking AAD therapy for recurrent AF, suggest a predominant occurrence of typical AFL.^{82,83} In few patients, atypical ECG and intracardiac electrogram patterns have been documented.^{82,83} The aim of the study presented in **Chapter IV** (n = 24 patients) was 2-fold: 1) to describe the ECG morphology and electrophysiologic findings during RF ablation of “class IC AFL” and 2) to report long-term success

following RA isthmus ablation, in relation to their ECG pattern during AFL. The usefulness of the “hybrid” approach will depend upon the results obtained at long-term.

Ablative therapy for AFL has made tremendous progress in the nineties, and is currently considered as curative management of type I AFL.⁸⁴ There has been a progressive shift in the ablation techniques; from DC shocks⁹³ to RF energy,^{14,25,40-42,84-86,94-103} and from an electrophysiological (focal)^{94,95} to an anatomical (linear) approach.^{14,25,40-42,84-86,96-101} The IVC - TV annulus was identified as the “isthmus” yielding maximum procedural success.^{41,84-86,98-101} This was followed by the recognition of septal isthmus.⁴² Complete BIC block was found to be a superior criterion of successful flutter ablation resulting in low recurrence rate^{41,84-86,101} as compared to noninducibility alone.⁹⁴⁻⁹⁹ It was also shown that ablation during sinus rhythm^{41,85,101} should be preferred as compared to ablation during AFL.⁹⁴⁻⁹⁹ Furthermore, it is now understood that CW-AFL uses the same circuit and isthmus as CCW type I AFL and can be ablated successfully by the same approach.^{14,102} Finally, AFL recurrences can easily be re-ablated by detecting “gaps” in the isthmus conduction.¹⁰³

Present day concerns during the ablation of type I AFL are related to the use of multiple RF applications, which may be delivered at unintended sites¹⁰⁴ and could be potentially proarrhythmic.¹⁰⁵ Risks related to long radiation exposure need careful consideration in planning the ablation procedure.^{106,107} Langberg et al.,¹⁰⁸ and more recently Otomo et al.,¹⁰⁹ reported an 8-mm tip as a more optimal RF electrode size for making linear lesions. The orientation of the ablation electrode determines the electrode-tissue interface and therefore the size of lesion created.^{109,110} The available clinical experience with the use of large tip electrodes for RF ablation of AFL is small and observational.^{41,42,87,88,111} These issues made us decide to compare an 8-mm split-tip electrode with two integrated thermocouples allowing independent temperature monitoring (Cerablate®plus Flutter, Dr Osypka GmbH) with a 4-mm tip electrode ablation catheter, for RF ablation of type I AFL, in a prospective randomized manner. The purpose of this prospective study was to answer the question “*Should we prefer a long tip electrode to perform radiofrequency ablation of type I atrial flutter?*” That study is presented in **Chapter V**. Currently, several other methods to produce deeper and wider isthmus lesions are being evaluated, both in clinical and in experimental setting. They include the use of the irrigated-tip catheter,¹¹² microwave energy¹¹³ and the bipolar two catheter technique.¹¹⁴

Atrial flutter recurrences are associated with failure to achieve complete BIC block at the end of the ablation procedure.⁸⁶ A complete BIC block is a superior endpoint as compared to unidirectional isthmus conduction block or BIC delay.^{41,85,86,101} Repeat electrophysiologic studies in patients with an AFL recur-

Figure 6. Evaluation of bidirectional isthmus conduction (BIC) during electrophysiological study. Panel A (pacing at CS orifice) and B (pacing at low lateral RA) represent pacing during sinus rhythm before ablation. Dual wave front of RA activation with BIC is seen. Panel C (pacing at CS orifice) and D (pacing at low lateral RA) show BIC block. Surface ECG lead III is shown. Intracardiac electrograms recorded include His bundle electrograms (HIS), H1.2 to H19.20 represent 10 bipoles of the duodecapolar Halo catheter placed along the tricuspid annulus, and CS1.2 to CS7.8 represents 4 bipoles of the decapolar catheter placed in the CS.

rence show regression or complete disappearance of isthmus conduction block.⁸⁵ A BIC block is confirmed by pacing alternately from the coronary sinus and low lateral RA at a constant cycle length (600 or 500 ms) (Figure 6).⁴¹ A mediolateral isthmus conduction block¹¹⁵ is defined by an entirely craniocaudal activation of the lateral RA wall during proximal CS (CS7.8) pacing with terminal activation of the Halo 1.2 bipole and prolongation of the CS7.8 - Halo1.2 interval. A lateromedial isthmus conduction block¹¹⁵ is defined by a caudocranial activation of the lateral RA wall and craniocaudal activation of the atrial septum with terminal activation of CS7.8 following activation of the His bundle during low lateral RA pacing. Resumption of isthmus conduction due to reversal of block has been observed within 30 minutes and sometimes as late as 1 hour following the last RF application.^{40,101} At times, AFL may remain inducible despite apparent BIC block.¹¹⁶ These observations may be based on: misinterpretation of isthmus conduction slowing as a block or rate dependent isthmus conduction block,^{41,97,101,117} or anatomical reasons: presence of “gaps”⁹⁸ or alteration in the propagation of the flutter circuit around the coronary sinus ostium.^{42,118} Efforts to obtain a complete and permanent line of BIC block, include demonstration of a complete line of double potentials,¹¹⁹ bipolar electrogram polarity mapping,¹²⁰ recording from a closely spaced multipolar catheter placed in the isthmus¹²¹ or use of non-fluoroscopy CARTO™ (Biosense Ltd, Israel)^{119,122} or non-contact electrode (MEA, Endocardial solutions, Minneapolis, MN)¹²³ mapping systems. The purpose of the study described in **Chapter VI** was to test the persistence of BIC block following isoproterenol administration and to evaluate the importance of this finding for AFL recurrences.

Chapter VII reports two previously unpublished observations made during an electrophysiological study: 1) induction of idiopathic ventricular tachycardia by AF, and 2) the presence of fusion and capture beats during two simultaneously occurring arrhythmias, AF at the atrial level and idiopathic ventricular tachycardia at the ventricular level.

References

1. Josephson ME. Atrial flutter and fibrillation. In: Josephson ME, ed *Clinical Cardiac Electrophysiology: Techniques and Interpretations*. Philadelphia, Lea and Febiger 1993:275-310.
2. Waldo AL. Atrial flutter: mechanisms, clinical features, and management. In: Zipes DP, Jalife J, eds: *Cardiac Electrophysiology: From Cell to Bedside*. WB Saunders Co., Philadelphia, 1995:666-681.
3. Jolly WA, Ritchie WJ. Auricular flutter and fibrillation. *Heart* 1911;2:177-221.

4. Bellet S. *Clinical disorders of the heart beat*. Philadelphia, Lea and Febiger, 1963:144-145.
5. Seidl K, Hauer B, Schwick NG, Zellner D, Zahn R, Senges J. Risk of thromboembolic events in patients with atrial flutter. *Am J Cardiol* 1998;82:580-583.
6. Rosenblueth A, Garcia-Ramos J. Studies on flutter and fibrillation. II. The influence of artificial obstacles on experimental auricular flutter. *Am Heart J* 1947;33:677-684.
7. Allesie MA, Lammers WJEP, Bonke FIM, Hollen J. Intratrial reentry as a mechanism for atrial flutter induced by acetylcholine in rapid pacing in the dog. *Circulation* 1984;70:123-135.
8. Frame LH, Page RL, Hoffman BF. Atrial reentry around an anatomic barrier with a partially refractory excitable gap. A canine model of a atrial flutter. *Circ Res* 1986;58:495-511.
9. Frame LH, Page RL, Boyden PA, Fenoglio JJ Jr, Hoffman BF. Circus movement in the canine atrium around the tricuspid ring during experimental atrial flutter and during reentry in vivo. *Circulation* 1987;76:1155-1175.
10. Puech P, Latour H, Grolleau R. Le flutter et ses limites. *Arch Mal Coeur* 1970;63:116-144.
11. Waldo AL, MacLean WAH, Karp RB, Kouchoukos NT, James TN. Entrainment and interruption of atrial flutter with atrial pacing: studies in man following open heart surgery. *Circulation* 1977;56:737-745.
12. Della Bella P, Marenzi G, Tondo C, Cardinale D, Giralaldi F, Lauri G, Guazzi M. Usefulness of excitable gap and pattern of resetting in atrial flutter for determining reentry circuit location. *Am J Cardiol* 1991;68:492-497.
13. Callans DJ, Schwartzman D, Gottlieb CD, Dillon SM, Marchlinski F. Characterization of the excitable gap in human type I atrial flutter. *J Am Coll Cardiol* 1997;30:1793-1801.
14. Saoudi N, Nair M, Abdelaziz A, Poty H, Daou A, Anselme F, Letac B. Electrocardiographic patterns and results of radiofrequency catheter ablation of clockwise atrial flutter. *J Cardiovasc Electrophysiol* 1996;7:931-942.
15. Cabrera JA, Sanchez-Quintana D, Ho SY, Medina A, Anderson RH. The architecture of the atrial musculature between the orifice of the inferior caval vein and the tricuspid valve: the anatomy of the isthmus. *J Cardiovasc Electrophysiol* 1998;9:1186-1195.
16. Olshansky B, Okumura K, Hess PG, Waldo AL. Demonstration of an area of slow conduction in human atrial flutter. *J Am Coll Cardiol* 1990;16:1639-1648.
17. Shah DC, Jaïs P, Haïssaguerre M, Chouairi S, Takahashi A, Hocini M, Garrigue S, Clémenty J. Three-dimensional mapping of the common atrial flutter circuit in the right atrium. *Circulation* 1997;96:3904-3912.
18. Fenelon G, Brugada P. Unipolar waveforms and monophasic action potentials in the characterization of slow conduction in human atrial flutter. *Pacing Clin Electrophysiol* 1998;21:2580-2587.

19. Olgin JE, Kalman JM, Fitzpatrick AP, Lesh MD. Role of right atrial endocardial structures as barriers to conduction during human type I atrial flutter: activation and entrainment mapping guided by intracardiac echocardiography. *Circulation* 1995;92:1839-1848.
20. Tai CT, Chen SA, Chen YJ, Yu WC, Hsieh MH, Tsai CF, Chen CC, Ding YA, Chang MS. Conduction properties of the crista terminalis in patients with typical atrial flutter: basis for a line of block in the reentrant circuit. *J Cardiovasc Electrophysiol* 1998;9:811-819.
21. Kalman J, Olgin J, Saxon L, Fisher WG, Lee RJ, Lesh M. Activation and entrainment mapping defines the tricuspid annulus as the anterior barrier in typical atrial flutter. *Circulation* 1996;94:398-406.
22. Shah DC, Haïssaguerre M, Jaïs P, Takahashi A, Clémenty J. Atrial flutter: Contemporary electrophysiology and catheter ablation. *Pacing Clin Electrophysiol* 1999;22:344-359.
23. Arribas F, López-Gill M, Cosío F, Núñez A. The upper link of human common atrial flutter circuit: definition by multiple endocardial recordings during entrainment. *Pacing Clin Electrophysiol* 1997;20:2924-2929.
24. Cosío FG, Goicolea A, López-Gil M, Arribas F, Barroso JL, Chicote R. Atrial endocardial mapping in the rare form of atrial flutter. *Am J Cardiol* 1990;66:715-720.
25. Kalman JM, Olgin JE, Saxon LA, Lee RJ, Scheinman MM, Lesh MD. Electrocardiographic and electrophysiologic characterization of atypical atrial flutter in man: use of activation and entrainment mapping and implications for catheter ablation. *J Cardiovasc Electrophysiol* 1997;8:121-144.
26. Cosío FG, Arribas F, López-Gil M, Palacios J. Atrial flutter mapping and ablation I. Studying atrial flutter mechanisms by mapping and entrainment. *Pacing Clin Electrophysiol* 1996;19:841-853.
27. Allesie M, Lammers W, Smeets J, et al. Total mapping of atrial excitation during acetylcholine-induced atrial flutter and fibrillation in the isolated canine heart. In: Kulbertus HE, Olsson SB, Schlepper M, eds: Atrial fibrillation. Molndal, Sweden, AB Hasell, 1982:4-59.
28. Arenal A, Almendral J, Román DS, Delcan JL, Josephson ME. Frequency and implications of resetting and entrainment with right atrial stimulation in atrial flutter. *Am J Cardiol* 1992;70:1292-1298.
29. Jaïs P, Haïssaguerre M, Shah D, Takahashi A, Lavergne T, Clémenty J. A new electrophysiological substrate for spontaneous left atrial flutters. *Circulation* 1998;98 (Suppl):I-19. Abstract.
30. Natale A, Richey M, Tomassoni GF, Beheiry S, Rajkovich K, Wides B, Nickell D, Leonelli FM. Clinical characteristics and ablation of left sided atrial flutter. *J Am Coll Cardiol* 1999;33(Suppl):116A.Abstract.
31. Kall JG, Lin AC, Johnson T, Cooke P, Kopp D, Burke M, Verdino R, Wang Z, Fuomo M, Wilber D. Characteristics of conduction within non-incisional atypical atrial flutter circuits. *J Am Coll Cardiol* 1999;33(Suppl):116A.Abstract.

32. Bogun F, Bender B, Li YG, Hohnloser SH, Goethe JW. Concealed entrainment in radiofrequency catheter ablation of atypical atrial flutter in patients without prior cardiac surgery. *J Am Coll Cardiol* 1999;33(Suppl):116A.Abstract.
33. van Hare GF. Electrical-anatomical correlations between typical atrial flutter and intra-atrial reentry following atrial surgery. *J Electrocardiol* 1998;30:77-84.
34. Li W, Somerville J. Atrial flutter in grown-up congenital heart (GUCH) patients: definition of characteristics. *J Am Coll Cardiol* 1999;33(Suppl):533A.Abstract.
35. Cheng J, Scheinman MM. Characteristics of double-wave reentry induced by programmed stimulation in patients with typical atrial flutter. *Circulation* 1998;97:1589-1596.
36. Cheng J, Cabeen WR, Scheinman MM. Right atrial flutter due to lower loop reentry. Mechanisms and anatomic substrates. *Circulation* 1999;99:1700-1705.
37. Crijns HJGM, van Gelder IC, Kingma JH, Dunselman PHJM, Gosselink ATM, Lie KI. Atrial flutter can be terminated by a class III antiarrhythmic drug but not by a class IC drug. *Eur Heart J* 1994;15:1403-1408.
38. Ellenbogen KA, Stambler BS, Wood MA, Sager PT, Wesley RC, Meissner MD, Zoble RG, Wakefield LK, Perry KT, Vanderlught JT for the Ibutilide Investigators. Efficacy of intravenous ibutilide for rapid termination of atrial fibrillation and atrial flutter: a dose-response study. *J Am Coll Cardiol* 1996;28:130-136.
39. Tai CT, Chen SA, Feng AN, Yu WC, Chen YJ, Chang MS. Electropharmacologic effects of class I and class III antiarrhythmia drugs on typical atrial flutter. Insights into the mechanism of termination. *Circulation* 1998;97:1935-1945.
40. Cauchemez B, Haïssaguerre M, Fischer B, Thomas O, Clémenty J, Coumel P. Electrophysiological effects of catheter ablation of inferior vena cava - tricuspid annulus isthmus in common atrial flutter. *Circulation* 1996;93:284-294.
41. Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter: further insights into various types of isthmus block: application to ablation during sinus rhythm. *Circulation* 1996;94:3204-3213.
42. Nakagawa H, Lazzara R, Khastagir T, Beckman KJ, McClelland JH, Imai S, Pitha JV, Becker AE, Arruda M, Gonzalez MD, Widman LE, Rome M, Neuhausser J, Wang X, Calame JD, Goudeau MD, Jackman WM. Role of tricuspid annulus and eustachian valve/ ridge on atrial flutter. Relevance to catheter ablation of the septal isthmus and a new technique for rapid identification of ablation success. *Circulation* 1996;94:407-424.
43. Griffith MJ, Gammage MD. Radiofrequency ablation of macro-reentrant arrhythmias: cure or adjunctive therapy. *Lancet* 1998;352:1404-1405.
44. Morady F. Radiofrequency ablation as treatment for cardiac arrhythmias. *N Engl J Med* 1999;340:534-544.
45. Olsson SB. Atrial fibrillation - new aspects of mechanism and treatment. *J Int Med* 1996;239:3-15.
46. Pritchett ELC. The case for just "plain atrial fibrillation". *Pacing Clin Electrophysiol* 1997;21:637-640.

47. Gallagher MM, Camm AJ. Classification of atrial fibrillation. *Pacing Clin Electrophysiol* 1997;20:1603-1605.
48. Peters NS. Atrial fibrillation: towards an understanding of initiation, perpetuation, and specific treatment. *Heart* 1998;80:533-534.
49. Blitzer M, Costeas C, Kassotis J, Reiffel JA. Rhythm management in atrial fibrillation - with a primary emphasis on pharmacological therapy. Part I. *Pacing Clin Electrophysiol* 1998;21:590-602.
50. Kannel WB, Abbot RD, Savage DD, McNamara PM. Epidemiologic features of atrial fibrillation. The Framingham Study. *N Engl J Med* 1982;306:1018-1022.
51. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population based cohort. The Framingham Heart Study. *JAMA* 1994;171:840-844.
52. Konings KTS, Kirchhoff CJHJ, Smeets JLRM, Wellens HJJ, Penn OC, Allessie MA. High-density mapping of electrically induced atrial fibrillation in humans. *Circulation* 1994;89:1665-1680.
53. Allessie MA, Lammers WJEP, Bonke FIM, Hollen SJ. Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation. In: Zipes DP, Jalife J, eds: *Cardiac Electrophysiology: From Cell to Bedside*. WB Saunders Co., Philadelphia, 1995:265-275.
54. Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone CM, Smith PK, Corr PB, Boineau JP. The surgical treatment of atrial fibrillation. II. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. *J Thor Card Surg* 1991;101:406-426.
55. Jaïs P, Haïssaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M, Clémenty J. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997;95:572-576.
56. Haïssaguerre M, Jaïs P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Mouroux AL, Métayer PL, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659-666.
57. Schlepper M. Identification of patients with atrial fibrillation at risk for thromboembolism. In: Olsson SB, Allessie MA, Campbell RWF, eds. *Atrial Fibrillation. Mechanisms and Therapeutic Strategies*. Armonk, NY: Futura Publishing Co., 1994;15-24.
58. Rodriguez LM, Smeets JLRM, Bayan Xie, de Chillou C, Cheriex EC, Pieters F, den Dulk K, Wellens HJJ. Improvement of left ventricular function by ablation of atrioventricular nodal conduction in selected patients with lone atrial fibrillation. *Am J Cardiol* 1993;72:1137-1141.
59. Watkare JEP, Camm AJ. Acute treatment of atrial fibrillation: why and when to maintain sinus rhythm. *Am J Cardiol* 1998;81:3C-15C.
60. Costeas C, Kassotis J, Blitzer M, Reiffel JA. Rhythm management in atrial fibrillation-with a primary emphasis on pharmacological therapy: Part 2. *Pacing Clin Electrophysiol* 1998;21:742-752.

61. Kassotis J, Costeas C, Blitzer M, Reiffel JA. Rhythm management in atrial fibrillation—with a primary emphasis on pharmacological therapy:Part 3. *Pacing Clin Electrophysiol* 1998;21:1133–1145.
62. Haïssaguerre M, Jaïs P, Shah DC, Gencel L, Pradeau V, Garrigues S, Chouairi S, Hocini M, Métayer PL, Roudaut R, Clémenty J. Right and left atrial radiofrequency catheter therapy of paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 1996;7:1132–1144.
63. Gaita F, Riccardi R, Calò L, Scaglione M, Garberoglio L, Antolini R, Kirchner M, Lamberti F, Richiardi E. Atrial mapping and radiofrequency catheter ablation in patients with idiopathic atrial fibrillation: electrophysiological findings and ablation results. *Circulation* 1998; 97:2136– 2145.
64. Rensma PL, Allesie MA, Lammers WJEP, Bonke FIM, Schalij MJ. Length of excitation wave and susceptibility to reentrant atrial arrhythmias in normal conscious dogs. *Circ Res* 1988;62:395–410.
65. Tunick PA, McElhinney L, Mitchell T, Kronzon I. The alternation between atrial flutter and atrial fibrillation. *Chest* 1992;101:34–36.
66. Murdock CJ, Kyles AE, Yeung-Lai-Wah JA, Anzhen Q, Vorderbrugge S, Kerr CR. Atrial flutter in patients treated for atrial fibrillation with propafenone. *Am J Cardiol* 1990;66:755–757.
67. Watson RM, Josephson ME. Atrial flutter. I. Electrophysiologic substrates and modes of initiation and termination. *Am J Cardiol* 1980;45:732–741.
68. Waldo AL, Cooper TB. Spontaneous onset of type I atrial flutter. *J Am Coll Cardiol* 1996;28:707–712.
69. Gomes JAC, Kang PS, Matheson M, Gough WB, El-Sherif N. Co-existence of sick sinus rhythm and atrial flutter-fibrillation. *Circulation* 1981;63:80–86.
70. Ortiz J, Niwano S, Abe H, Rudy Y, Johnson NJ, Waldo AL. Mapping the conversion of atrial flutter to atrial fibrillation and atrial fibrillation to atrial flutter. Insights into mechanisms. *Circ Res* 1994;74:882–894.
71. Wu TJ, Yashima M, Xie F, Athill CA, Kim YH, Fishbein MC, Qu Z, Garfinkel A, Weiss JN, Karaguezian HS, Chen PS. Role of pectinate muscle bundles in the generation and maintenance of intra-atrial reentry. Potential implications for the mechanism of conversion between atrial fibrillation and atrial flutter. *Circ Res* 1998;83:448–462.
72. Emori T, Fukushima K, Saito H, Nakayama K, Ohe T. Atrial electrograms and activation sequences in the transition between atrial fibrillation and atrial flutter. *J Cardiovasc Electrophysiol* 1998;9:1173–1179.
73. Roithinger FX, Karch MR, Steiner PR, SippensGroenewegen A, Lesh MD. Relationship between atrial fibrillation and typical atrial flutter in humans. Activation sequence changes during spontaneous conversion. *Circulation* 1997;96: 3484– 3491.
74. Roithinger FX, SippensGroenewegen A, Karch MR, Steiner PR, Ellis WS, Lesh MD. Organized activation during atrial fibrillation in man: endocardial and electrocardiographic manifestations. *J Cardiovasc Electrophysiol* 1998;9:451–461.

75. Pratt CM. Impact of managed care on the treatment of atrial fibrillation. *Am J Cardiol* 1998;81:30C-34C.
76. Feld GK, Chen PS, Nicod P, Fleck P, Mezer D. Possible atrial proarrhythmic effects of class IC antiarrhythmic drugs. *Am J Cardiol* 1990;66:378-383.
77. Marcus FI. The hazards of using type IC antiarrhythmic drugs for the treatment of paroxysmal atrial fibrillation. *Am J Cardiol* 1990;66:366-367.
78. Falk RH. Proarrhythmic responses to atrial antiarrhythmic therapy. In: Falk RH, Podrid PJ, eds. Atrial fibrillation: Mechanisms and Management. New York: Raven Press Ltd., 1992:283-305.
79. El-Harari MB, Adams PC. Atrial flutter with 1:1 atrioventricular conduction caused by propafenone. *Pacing Clin Electrophysiol* 1996;21:1999-2001.
80. Crijns HJGM. Clinical manifestations of use- and reverse-use dependence. In: Crijns HJGM, ed. Changes of intra-cardiac conduction induced by antiarrhythmic drugs: Importance of use- and reverse-use dependence. Groningen, Netherlands: BV Knoop Haren; 1993:38-105.
81. Matsuo K, Kumagai K, Annoura M, Ideishi M, Arakawa K. Mechanism of antiarrhythmic effects of class Ic drugs in paroxysmal atrial fibrillation in man. *Cardiology* 1998;89:119-123.
82. Huang DT, Monahan KM, Zimetbaum P, Papageorgiou P, Epstein LM, Josephson ME. Hybrid pharmacologic and ablative therapy: a novel and effective approach for management of atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9:462-469.
83. Schumacher B, Jung W, Lewalter T, Vahlhaus C, Wolpert C, Lüderitz B. Radiofrequency ablation of atrial flutter due to administration of class IC antiarrhythmic drugs for atrial fibrillation. *Am J Cardiol* 1999;83:710-713.
84. Poty H, Saoudi N, Aziz AA, Nair M, Letac B. Radiofrequency ablation of type I atrial flutter. Prediction of late success by electrophysiological criteria. *Circulation* 1995;92:1389-1392.
85. Schumacher B, Pfeiffer D, Tebbenjohanns J, Lewalter T, Jung W, Lüderitz B. Acute and long-term effects of consecutive radiofrequency applications on conduction properties of the subeustachian isthmus in type I atrial flutter. *J Cardiovasc Electrophysiol* 1998;9:152-163.
86. Tai CT, Chen SA, Chiang CE, Lee SH, Wen ZC, Huang JL, Chen YJ, Yu WC, Feng AN, Lin YJ, Ding YA, Chang MS. Long-term outcome of radiofrequency catheter ablation for typical atrial flutter: risk prediction of recurrent arrhythmias. *J Cardiovasc Electrophysiol* 1998;9:115-121.
87. Phillipon F, Plumb VJ, Epstein A, Kay GN. The risk of atrial fibrillation following radiofrequency catheter ablation of atrial flutter. *Circulation* 1995;92:430-435.
88. Paydak H, Kall JG, Burke MC, Rubenstein D, Kopp DE, Verdino RJ, Wilber DJ. Atrial fibrillation after radiofrequency ablation of type I atrial flutter: time to onset, determinants, and clinical course. *Circulation* 1998;98:315-322.
89. Anselme F, Saoudi N, Poty H, Douillet R, Cribier A. Radiofrequency catheter ablation of common atrial flutter. Significance of palpitations and quality-of-life evaluation in patients with proven isthmus block. *Circulation* 1999;99:534-540.

90. Frey B, Kreiner G, Binder T, Heinz G, Baumgartner H, Gössinger HD. Relation between left atrial size and secondary atrial arrhythmias after successful catheter ablation of common atrial flutter. *Pacing Clin Electrophysiol* 1997;20:2936-2942.
91. Chen TO. Atrial flutter during quinidine therapy of atrial fibrillation. *Am Heart J* 1956;52:273-289.
92. Brugada J, Gürsoy S, Brugada P, Atié J, Guiraudon G, Andries E. Cibenzoline transforms random re-entry into ordered reentry in the atria. *Eur Heart J* 1993;14:267-272.
93. Saoudi N, Atallah G, Kirkorian G, Touboul P. Catheter ablation of the atrial myocardium in human type I atrial flutter. *Circulation* 1990;81:762-771.
94. Feld GK, Fleck RP, Chen PS, Boyce K, Bahnson TD, Stein JB, Calisi CM, Ibarra M. Radiofrequency catheter ablation for the treatment of human type I atrial flutter. Identification of a critical zone in the reentrant circuit by endocardial mapping techniques. *Circulation* 1992;86:1233-1240.
95. Cosío F, López-Gil M, Goicolea A, Arribas F, Barroso JL. Radiofrequency ablation of the inferior vena cava - tricuspid valve annulus isthmus in common atrial flutter. *Am J Cardiol* 1993;71:705-709.
96. Kirkorian G, Moncada E, Chevalier P, Canu G, Claudel JP, Bellon C, Lyon L, Touboul P. Radiofrequency ablation of atrial flutter. Efficacy of an anatomically guided approach. *Circulation* 1994;2804-2814.
97. Calkins H, Leon AR, Deam G, Kalbfleisch SJ, Langberg JJ, Morady F. Catheter ablation of atrial flutter using radiofrequency energy. *Am J Cardiol* 1994;73:353-356.
98. Fischer B, Haïssaguerre M, Garrigues S, Poquet F, Gencel L, Clémenty J, Marcus F. Radiofrequency catheter ablation of common atrial flutter in 80 patients. *J Am Coll Cardiol* 1995;25:1365-1372.
99. Steinberg JS, Prasher S, Zelenkofske S, Ehlert FA. Radiofrequency catheter ablation of atrial flutter: procedural success and long-term outcome. *Am Heart J* 1995;130:85-92.
100. Chen SA, Chiang CE, Wu TJ, Tai CT, Lee SH, Cheng CC, Chiou CW, Ueng KC, Wen ZC, Chang MS. Radiofrequency catheter ablation of common atrial flutter: comparison of electrophysiologically guided focal ablation technique and linear ablation technique. *J Am Coll Cardiol* 1996;27:860-868.
101. Schwartzman D, Callans DJ, Gottlieb CD, Dillon SM, Movsowitz C, Marchlinski FE. Conduction block in the inferior vena cava - tricuspid valve isthmus: association with outcome of radiofrequency ablation of type I atrial flutter. *J Am Coll Cardiol* 1996;28:1519-1531.
102. Tai CT, Chen SA, Chiang CE, Lee SH, Ueng KC, Wen ZC, Chen YJ, Yu WC, Huang JL, Chiou CW, Chang MS. Electrophysiologic characteristics and radiofrequency catheter ablation in patients with clockwise atrial flutter. *J Cardiovasc Electrophysiol* 1997;8:24-34.
103. Shah DC, Haïssaguerre M, Jaïs P, Fischer B, Takahashi A, Hocini M, Clémenty J. Simplified electrophysiologically directed catheter ablation of recurrent common atrial flutter. *Circulation* 1997;96:2505-2508.

104. Epstein LM, Mitchell MA, Smith TW, Haines DW. Comparative study of fluoroscopy and intracardiac echocardiography guidance for the creation of linear atrial lesions. *Circulation* 1998;98:1796-1801.
105. Avitall B, Helms RW, Chiang W, Periman BA. Non-linear atrial radiofrequency lesions are arrhythmogenic: a study of skipped lesions in the normal atria. *Circulation* 1995;92(suppl):I-265.Abstract.
106. Rosenthal LS, Mahesh M, Beck TJ, Saul JP, Miller JM, Kay N, Klein LS, Huang S, Gillette P, Prystowsky E, Carlson M, Berger RD, Lawrence JH, Yong P, Calkins H. Predictors of fluoroscopy time and estimated radiation exposure during radiofrequency catheter ablation procedures. *Am J Cardiol* 1998;82:451-458.
107. Wah! MR, Cusma JT, Stevens CL, Packer D. Radiation exposure and associated cancer mortality risk due to fluoroscopy in RF catheter ablation of atrial fibrillation. *Circulation* 1998;98(Suppl):I-181.Abstract.
108. Langberg JJ, Gallagher M, Strickberger A, Amirana O. Temperature guided radiofrequency catheter ablation with very large distal electrodes. *Circulation* 1993;88:245-249.
109. Otomo K, Yamanashi WS, Tondo C, Antz M, Bussey J, Pitha JV, Arruda M, Nakagawa H, Wittkampf FHM, Lazzara R, Jackman WM. Why a large tip electrode makes a deeper radiofrequency lesion: effects of increase in electrode cooling and electrode-tissue interface area. *J Cardiovasc Electrophysiol* 1998;9:47-54.
110. Chugh SS, Chan RC, Johnson SB, Packer DL. Catheter tip orientation affects radiofrequency ablation size in the canine left ventricle. *Pacing Clin Electrophysiol* 1999;22:413-420.
111. Iesaka Y, Takahashi A, Goya M, Yamane T, Tokunaga T, Amemiya H, Fujiwara H, Nitta J, Nogami A, Aonuma K, Hiroe M, Marumo F, Hiraoka M. High energy radiofrequency catheter ablation for common atrial flutter targeting the isthmus between the inferior vena cava and tricuspid annulus using a super long tip electrode. *Pacing Clin Electrophysiol* 1998;21:401-409.
112. Jaïs P, Haïssaguerre M, Shah DC, Takahashi A, Hocini M, Lavergne T, Stéphane L, Mouroux AL, Fischer B, Clémenty J. Successful irrigated-tip catheter ablation of atrial flutter resistant to conventional radiofrequency ablation. *Circulation* 1998;98:835-838.
113. Liem BL, Mead RH. Microwave linear ablation of the isthmus between the inferior vena cava and tricuspid annulus. *Pacing Clin Electrophysiol* 1998;21:2079-2086.
114. Anfinson OG, Kongsgaard E, Foerester A, Aass H, Amile JP. Radiofrequency current ablation of porcine right atrium: increased lesion size with bipolar two catheter technique compared to unipolar application in vitro and in vivo. *Pacing Clin Electrophysiol* 1998; 21:69-78.
115. Barold SS, Shah D, Jaïs P, Takahashi A, Haïssaguerre M, Clémenty J. Nomenclature and characterization of transisthmus conduction after ablation of typical atrial flutter. *Pacing Clin Electrophysiol* 1997;20:1751-1753.

116. Mecca AL, Gou H, Olshansky B. Apparent bidirectional conduction block: not a foolproof marker of success in atrial flutter ablation. *Pacing Clin Electrophysiol* 1998;21(Suppl, Part II):984.Abstract.
117. Arenal A, Almendral J, Alday JM, Villacastín J, Ormaetxe JM, Sande JLM, Perez-Castellano N, Gonzalez S, Ortiz M, Delcan JL. Rate-dependent conduction block of the crista terminalis in patients with typical atrial flutter. Influence on evaluation of cavotricuspid isthmus conduction block. *Circulation* 1999;99:2771-2778.
118. Okishige K, Azegami K, Satoh T, Goseki Y, Ohira H, Yamashita K, Satake S. Alternation in the flutter wave morphology during radiofrequency catheter ablation for common atrial flutter. *Jpn Circ J* 1998;62:795-800.
119. Shah DC, Haïssaguerre M, Jaïs P, Takahashi A, Hocini M, Clémenty J. High-density mapping of activation through an incomplete isthmus ablation line. *Circulation* 1999;99:211-215.
120. Yamabe H, Okumura K, Misumi I, Fukushima H, Ueno K, Kimura Y, Hokamura Y. Role of bipolar electrogram polarity mapping in localizing recurrent conduction in the isthmus early and late after ablation of atrial flutter. *J Am Coll Cardiol* 1999;33:39-45.
121. Willems S, Weiss C, Hoffmann M, Meinertz T. Atrial flutter ablation using a technique for detection of conduction block within the posterior isthmus. *Pacing Clin Electrophysiol* 1999;22:750-758.
122. Nakagawa H, Jackman WM. Use of three-dimensional, non-fluoroscopic mapping system for catheter ablation of typical atrial flutter. *Pacing Clin Electrophysiol* 1998;21:1279-1286.
123. Goyal R, Zivin A, Souza F, Flemming M, Knight BP, Man KC, Strickberger A, Morady F. Endocardial mapping of typical atrial flutter using a noncontact mapping system. *Circulation* 1998;98:I-73. Abstract.

CHAPTER II

Radiofrequency ablation of “class IC atrial flutter” in patients with resistant atrial fibrillation

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ABSTRACT

Background: Atrial fibrillation (AF) organizes to atrial flutter (AFL) in 3.5-20% of patients on class IC antiarrhythmic drugs (AAD), the so called "*class IC atrial flutter*". We investigated if radiofrequency ablation (RFA) of "*class IC AFL*" can modify the "natural" course of AF.

Methods: Fourteen patients (age = 53.7 ± 13.9 years, 12 males) with daily recurrences of therapy resistant (median = 3 AADs) AF, paroxysmal ($n = 8$) or chronic persistent ($n = 6$), who developed "*class IC AFL*" (cycle length = 230 ± 28 ms) while on propafenone ($n = 9$) or flecainide ($n = 5$) therapy for a median duration of 3 months, underwent RFA of AFL by the anatomical approach. Counterclockwise AFL (2 patients had an additional clockwise AFL) and/or evidence of bidirectional isthmus conduction (BIC) was documented in all patients.

Results: Radiofrequency ablation was successful (AFL non-inducible and BIC block) in 12 patients, partially successful (AFL non inducible but no BIC block) in 1 patient and failed (operated Ebstein's anomaly) in 1 patient. The mean procedure and fluoroscopy time was 191.2 ± 48.1 and 49.9 ± 23.9 minutes, respectively. All, but 1 patient continued class IC AAD. At a mean follow-up of 4 months (range, 2 to 13 months) following successful RFA ($n = 13$, including 1 partial success), 9 patients are symptom free and 2 patients have had a few (1 and 4 each), short-lasting AF recurrences. Thus 11 of 13 (85%) patients improved clinically after RFA. The last two patients underwent successful repeat RFA for AFL recurrence but later had AF recurrences, albeit less frequent.

Conclusion: In patients with AF who develop AFL during treatment with class IC AADs, RFA of the isthmus results in a clinical improvement in 85% of the patients. A larger prospective study with a longer follow-up is required to validate its benefits.

Introduction

Class IC antiarrhythmic drugs (AAD) are recommended as the initial therapy in patients with lone atrial fibrillation (AF).¹ In some of these patients, AF converts or recurs as persistent atrial flutter (AFL).² Radiofrequency ablation (RFA) of typical AFL by the anatomic approach has good procedural³ and long term results.⁴ In the present study we evaluated the hypothesis that successful RFA of the right atrial isthmus in patients with resistant AF who develop AFL while receiving class IC AAD therapy could favorably modify the "natural" course of AF.

Methods

Study patients: Fourteen consecutive patients with drug-resistant AF who developed AFL during treatment with an oral class IC AAD, so called "*class IC atrial flutter*" were offered RFA of AFL (Table 1). Inclusion in the study required documentation of typical AFL with negative flutter waves in the inferior leads. The mean patient age was 53.7 ± 13.9 years (range 22 to 78), and there were 12 men. All the patients had disabling palpitations because of chronic (6 patients) or frequently recurring episodes (8 patients) of AF. The median duration from symptom onset was 3.5 years (range 1 month to 20 years). The mean left atrial size was 4.6 ± 0.3 cm. Four patients had mild to moderate mitral regurgitation, 1 tricuspid regurgitation, and 1 decompensated left ventricular function (left ventricular ejection fraction 40%) as a consequence of the tachycardia. One patient had a repaired Ebstein's anomaly. Antiarrhythmic drugs (median 3, range 1 to 4) were ineffective in preventing recurrences. Two patients had an implantable Atrioverter (MetrixTM 3020 device, InControl, Redmond, Washington). Patients were treated with either oral propafenone (450 - 900 mg/day, 9 patients) or flecainide (100 - 300 mg/day, 5 patients) for a median duration of 3 months (range, 2 to 8) before transformation to AFL was noted (Figure. 1). One patient with "*class IC AFL*" receiving flecainide had a collapse due to transient 1:1 atrioventricular (AV) response confirmed by the episode log of the Atrioverter.

Electrophysiological study and RFA: Electrophysiologic study and RFA was performed after informed, written consent. Class IC AADs were continued. At the time of study, 9 patients were in sinus rhythm and 5 had sustained AFL. The mean flutter cycle length was 230 ± 28 ms with a predominant 2:1 AV response. Counterclockwise AFL was documented in all patients, and 2 patients also had a clockwise AFL. The mean anterograde (lateromedial) and retrograde

Table 1. Clinical Characteristics of 14 Patients With "Class IC Atrial Flutter"

No	Age (yr)	Sex	Type AF	AF duration (yr)	Additional Heart Disease	No. of Failed AADs	Class IC AADs (mg)
1	22	M	paroxysmal	3 mo	-	1	Propafenone (450)
2	40	M	persistent	10	Repaired Ebstein's	2	Flecainide (100)
3	40	M	paroxysmal	1	-	3	Flecainide (100)
4	48	F	persistent	3	Tachycardia-myopathy	2	Propafenone (450)
5	51	M	paroxysmal	8	-	2	Propafenone (450)
6	51	M	paroxysmal	19	Atrial septal aneurysm	1	Propafenone (900)
7*	53	M	persistent	3	-	4	Propafenone (450)
8	56	M	paroxysmal	8 mo	-	1	Propafenone (900)
9	57	M	paroxysmal	4	-	2	Propafenone (450)
10	59	M	paroxysmal	1	-	1	Flecainide (300)
11	63	M	persistent	17	-	4	Flecainide (100)
12*	67	F	persistent	10	-	2	Flecainide (200)
13	67	M	persistent	2	-	4	Propafenone (600)
14	78	M	paroxysmal	20	Mitral valve prolapse	4	Propafenone (900)

*Patient with Atrioverter

(mediolateral) isthmus conduction times⁵ were 98 ± 25.5 ms and 61 ± 26.8 ms respectively. A 4-mm (Cordis-Webster, Baldwin Park, California) or 8-mm-tip (EP Technology, Mountain View, California; or Cerablate[®] *plus Flutter*, Osypka, Sulzer Medica, Grenzach-Wyhlen, Germany) ablation catheter, passed through an 8Fr long sheath (SAFL or SR0, Daig, Minnetonka, Minnesota) was used. Linear ablation of the posterior isthmus was performed, followed by the ablation of the septal isthmus, when necessary.⁶ Procedural success was defined as inability to induce AFL and demonstration of bidirectional isthmus conduction (BIC) block⁴ during isoproterenol infusion (1 to 3 μ g/min). Follow-up was conducted at 8 and subsequently at 3-month intervals. Patients were advised to continue taking propafenone or flecainide. Holter recordings were requested at pre-discharge, at 8 and 12 weeks after the procedure, and when symptoms suggested an arrhythmia recurrence. The symptom status of all patients was confirmed by telephone at the end of the study.

Figure 1. Twelve-lead ECG showing atrial fibrillation (A) and development of atrial flutter with 2:1 atrioventricular conduction after treatment with propafenone 450 mg (B).

Results

Six patients had sustained AF during the course of the procedure. Sinus rhythm was restored in all patients by intravenous flecainide ($n = 3$), external cardioversion ($n = 1$) or both ($n = 2$). Procedural success was obtained in 12 of 14 (85%) patients. The posterior isthmus was ablated in all, with 4 patients requiring additional septal isthmus ablation. One procedure was classified as a partial success, because AFL was noninducible but no BIC block could be demonstrated. A patient with repaired Ebstein's anomaly had an unsuccessful procedure. A median number of 25 applications (range, 12 - 54), each of 90 seconds duration, were required per procedure. The mean procedure and fluoroscopy times were 191.2 ± 48.1 and 49.9 ± 23.9 minutes, respectively. No patient had in-hospital recurrences. A mean follow-up of 4 months (range, 2 to 13) was available in all 13 patients who had a successful (including 1 partial success) ablation. Nine patients were completely symptom free. Seven of these 9 patients continued taking class IC AADs. One patient also received amiodarone, and flecainide was replaced by atenolol in 1 patient. Two patients had a few (1 and 4 each) short-lasting and well-tolerated symptomatic AF episodes during a follow-up period of 1 and 5 months, respectively. None of the 11 patients had recurrence of AFL. The remaining 2 patients had AFL recurrence at 3 and 7 months, respectively. During the second study, resumption of BIC was documented and the posterior isthmus successfully reablated. Both patients reported AF recurrences at subsequent follow-up. Addition of oral sotalol 80 mg/day resulted in a reduction in symptom frequency (2 to 3 short-lasting episodes per week) in 1 patient. The other patient continued to have frequent AF episodes despite adding 200 mg/day amiodarone to the daily propafenone medication.

Discussion

Class IC AADs affect refractory period duration and conduction velocity of atrial tissue. Depression of conduction velocity by a class IC agent may either prevent reentry by producing complete conduction block or it may facilitate reentry by slowing conduction. Class IC AADs cause a rate-dependent prolongation of the atrial refractory period⁷⁻⁹ and suppress excitability. The increase in atrial refractory period counteracts the drug-induced conduction slowing and prolongs the wavelength.^{7,8} Atrial fibrillation may change into AFL when the combination of electrophysiologic changes induced by class IC agents either prevents the formation of smaller secondary circuits derived from a large "mother" wave or the class IC agent decreases the number and increases the size

of multiple smaller reentrant circuits, resulting in a single macroreentrant loop.⁷ These effects may result in development of "class IC AFL" in patients with AF. There is a wide variation (3.5 to 20%) in the reported incidence^{2,10} of "class IC AFL", at this point we cannot predict in which patients with AF this may develop. The obvious danger is the development of a fast ventricular rate, because the relative slow atrial rate caused by the class IC agent may be followed by 1:1 AV conduction. This was observed in 1 of our patients and stresses the need to be aware of this complication when a patient with AF becomes more symptomatic when treated with a class IC agent.

Previous studies have pointed out the higher risk of postablation AF recurrences in patients with a history of spontaneous AF, structural heart disease, left ventricular ejection fraction < 50%, higher number of previously failed AADs, and AF inducible following AFL ablation.^{11,12,13,14} During follow-up (mean 4 months, range 2 - 13), 9 patients were symptom free and 2 patients had a few, short-lasting and well-tolerated AF recurrences. We may hypothesize that the short-lasting and well-tolerated arrhythmia recurrences in these 2 patients were based on AF, but that the rate-dependent effects of the class IC drug increased the wavelength and the isthmus ablation line caused conduction block, thereby terminating the episode.

Conclusions

We conclude that, in this small series of patients, there was clinical improvement in 11 of 13 patients (85%) after combined class IC AAD and right atrial isthmus ablation. Similar results were reported recently by Huang et al¹⁵; however, most of these patients developed AFL when amiodarone was prescribed for the treatment of AF. This suggests that these changes also may occur when patients are receiving drugs other than class IC agents and stresses the need to carefully evaluate the behaviour of AF after drug administration. The incidence of long-term success of right atrial isthmus ablation in patients who develop AFL requires further study.

References

1. Pratt CM. Impact of managed care on the treatment of atrial fibrillation. *Am J Cardiol* 1998;81(5A):30C-34C.

2. Falk RH. Proarrhythmic responses to atrial antiarrhythmic therapy. In: Falk RH and Podrid PJ, eds. *Atrial fibrillation: Mechanisms and Management*. New York: Raven Press Ltd., 1992:283-305.
3. Cosío FG, López-Gill M, Goicolea A, Arribas F, Barroso JL. Radiofrequency ablation of the inferior vena cava-tricuspid annulus valve isthmus in common atrial flutter. *Am J Cardiol* 1993;71:705-709.
4. Poty H, Saoudi N, Aziz AA, Nair M, Letac B. Radiofrequency catheter ablation of type I atrial flutter. Prediction of late success by electrophysiological criteria. *Circulation* 1995;92:1389-1392.
5. Cauchemez B, Haïssaguerre M, Fischer B, Thomas O, Clémenty J, Coumel P. Electrophysiological effects of catheter ablation of inferior vena cava-tricuspid annulus isthmus in common atrial flutter. *Circulation* 1996;93:284-294.
6. Nakagawa H, Lazzara R, Khastagir T, Beckman KJ, McClelland JH, Imai S, Pitha JV, Becker AE, Arruda M, Gonzalez MD, Widman LE, Rome M, Neuhauser J, Wang X, Calame JD, Goudeau MD, Jackman WM. Role of tricuspid annulus and eustachian valve/ridge on atrial flutter. Relevance to catheter ablation of the septal isthmus and a new technique for rapid identification of ablation success. *Circulation* 1996;94:407-424.
7. Crijns HJGM. Clinical manifestations of use- and reverse-use dependence. In: Crijns HJGM, ed. *Changes of intracardiac conduction induced by antiarrhythmic drugs: Importance of use- and reverse use-dependence*. Groningen, Netherlands: BV Knoop Haren; 1993:38-105.
8. O'Hara G, Villemarie C, Talajic M, Nattel S. Effects of flecainide on the rate dependency of atrial refractoriness, atrial repolarization and atrioventricular nodal conduction in anesthetized dogs. *J Am Coll Cardiol* 1992;19:1335-1342.
9. Allesie MA, Janse MJ. Mechanisms of atrial arrhythmias. In: Singh BN, Wellens HJJ, Hiraoka M, eds. *Electropharmacological control of cardiac arrhythmias*. Mount Kisco, NY: Futura, 1994;115-124.
10. Feld GK, Chen PS, Nicod P, Fleck RP, Mezer D. Atrial proarrhythmic effects of class IC antiarrhythmic drugs. *Am J Cardiol* 1990;66:378-383.
11. Philippon F, Plumb VJ, Epstein AE, Neal Kay G. The risk of atrial fibrillation following radiofrequency catheter ablation of atrial flutter. *Circulation* 1995;92:430-435.
12. Movsowitz C, Callans DJ, Schwartzman D, Gottlieb C, Marchlinski FE. The results of atrial flutter ablation in patients with and without a history of atrial fibrillation. *Am J Cardiol* 1996;78:93-96.
13. Tai CT, Chen SA, Chiang CE, Lee SH, Wen ZC, Huang JL, Chen YJ, Yu WC, Feng AN, Lin YJ, Ding YA, Chang MS. Long-term outcome of radiofrequency catheter ablation for typical atrial flutter: risk prediction of recurrent arrhythmias. *J Cardiovasc Electrophysiol* 1998;9:115-121.
14. Paydak H, Kall JG, Burke MC, Rubenstein D, Kopp DE, Verdino RJ, Wilber DJ. Atrial fibrillation after radiofrequency ablation of atrial flutter. Time to onset, determinants, and clinical course. *Circulation* 1998;98:315-322.

15. Huang DT, Monahan KM, Zimetbaum P, Papageorgiou P, Epstein LM, Josephson ME. Hybrid pharmacologic and ablative therapy: a novel and effective approach for the management of atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9:462-469.

Effect of right atrial isthmus ablation on the occurrence of atrial fibrillation:

Observations in four patient groups having type I atrial flutter with or without associated atrial fibrillation

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ABSTRACT

Objective: The goal of this study was to test the hypothesis that the occurrence of atrial fibrillation (AF), in at least some patients with coexisting type I atrial flutter (AFL), is based on macro-reentry around the tricuspid valve orifice including the right atrial (RA) isthmus, by evaluation of AF recurrences following successful ablation of AFL.

Methods: Eighty-two consecutive patients with type I AFL, with or without concomitant AF, underwent radiofrequency ablation (RFA) of the RA isthmus by an anatomical approach. The results were analyzed in 4 groups of patients: group 1 (only AFL; 29 patients), group 2 (AFL > AF; 22 patients), group 3 (AF > AFL; 15 patients) and group 4 (developing AFL while receiving class IC antiarrhythmic drug therapy for AF, the "class IC atrial flutter"; 16 patients).

Results: In all groups, RFA of type I AFL was performed with a high ($\geq 93\%$) procedural success rate. In group 1, only 2 (8%) patients had AF after (18 ± 14 months) AFL ablation. These figures were 38% (20 ± 14 months) and 86% (13 ± 8 months) in groups 2 and 3, respectively. Group 4 patients (4 ± 2 months) had a 73% freedom of AF recurrences with continuation of the class IC agent.

Conclusions: The low incidence of new AF during long-term follow-up after RFA of type I AFL makes it unlikely that radiofrequency lesions promote the development of AF. The impact of isthmus ablation on AF recurrences differs according to the clinically predominant atrial arrhythmia and suggests a possible role of the RA isthmus in the occurrence of AF in some patients. Ablation of class IC AFL in patients with therapy-resistant AF is a novel approach to management of this patient subset. Careful classification of AF patients plays a role in the selection of the site of ablation therapy.

Introduction

Atrial flutter (AFL) and atrial fibrillation (AF), which are both intra-atrial reentrant arrhythmias with differing complexity in their activation pattern and mechanisms, are frequently seen to coexist in clinical practice. Long-term success of radiofrequency ablation (RFA) of AFL may be undone by the occurrence of AF, either preexisting or developing *de novo*. Few studies have evaluated the incidence of AF after successful RFA of type I AFL.¹⁻³ We evaluated the hypothesis that at least in some patients with coexisting type I AFL, maintenance of AF might be based on macro-reentry around the tricuspid valve orifice, including the right atrial (RA) isthmus. We therefore evaluated the long-term occurrence of AF following a successful RFA of the RA isthmus for type I AFL.

Methods

Study population: Eighty-two consecutive patients with type I AFL, identified by negative flutter waves in the inferior leads and positive flutter waves in lead V1,⁴ who underwent RFA of the RA isthmus by an anatomical approach were included. All procedures were performed between November 1994 and April 1998. Patients having documentation of additional episodes of AF were also considered for RFA. The patient population was divided into 4 groups after careful review of the available ECGs and 24-hour Holter recordings. Group 1 consisted of patients who had documented episodes of AFL alone. Patients included in group 2 predominantly had episodes of AFL and 1 to 3 isolated episodes of AF; thus, AFL as their most frequently occurring arrhythmia. Patients included in group 3 had predominant documentation of AF. In these patients, 1 or 2 episodes of AFL were detected. Patients with therapy-resistant AF and no previous documentation of AFL but who developed AFL on oral class IC antiarrhythmic drug (AAD) (propafenone or flecainide) were placed in group 4. We called this new AFL the “class IC atrial flutter”. After a median treatment duration of 3 months (range, 2 – 8 months) class IC AFL occurred. The characteristics of the 82 patients are summarized in Table 1. Every patient was symptomatic with intermittent palpitations despite AAD therapy. Coronary artery disease was the most common structural heart disease amongst patients in groups 1 ($n = 14$), 2 ($n = 3$) and 3 ($n = 2$) and was considered an exclusion criterion for patients in group 4. Tachycardiomyopathy was diagnosed in 3 patients in group 1, 2 patients in group 3 and 1 patient each in groups 2 and 4. Six patients had previously undergone coronary bypass surgery (1 in group 1, 2 in group 2 and 3 in group 3), whereas repair of atrial septal defect (group I) and Ebstein’s anomaly

Table 1. Characteristics of the 82 Patients Divided into the 4 Groups Studied*

	Group 1 (n = 29)	Group 2 (n = 22)	Group 3 (n = 15)	Group 4 (n = 16)	P
Age, y	60.5 ± 15.5	55.9 ± 16.4	50.8 ± 15.7	53.7 ± 13.9	NS
Sex, M/F	24/5	21/1	13/2	14/2	NS
Structural heart disease, n (%)	18 (62)	5 (23)	4 (27)	2 (13)	0.002
Median symptom duration, (range)	3y (3mo-10y)	5.5y (6mo-30y)	5y (4mo-13y)	3.5y (1mo-20y)	
Failed AADs (median), n	2 (1 - 6)	3 (1 - 7)	3.5 (1 - 8)	3 (1 - 4)	
Left atrial size, cm	4.4 ± 0.5	4.7 ± 0.8	4.2 ± 0.4	4.6 ± 0.3	0.04
LVEF < 50 %, n	9	2	3	1	NS
AF (paroxysmal / persistent), n	-	22/0	6/9	8/8	

* Every patient had at least one documented episode of type I AFL.

(group 4) was performed in 1 patient each. Fifteen patients (9 in group 1, 2 in group 2, 3 in group 3 and 1 in group 4) had a left ventricular ejection fraction (LVEF) < 50%. Compared with patients in other groups, patients in group 1 had a higher incidence ($P = 0.002$) of structural heart disease, whereas patients included in group 2 had a larger ($P = 0.04$) mean left atrial size. Devices implanted before ablation included a pacemaker ($n = 4$, 2 each in group 1 and 3) and an Atrioverter (Metrix™ 3020 device, InControl; $n = 3$: 1 in group 3 and 2 in group 4).⁵ All patients in group 2 had paroxysmal AF, whereas a greater (9 of 15) or an equal (8 of 16) proportion of patients in groups 3 and 4, respectively, had chronic persistent AF.

Electrophysiology study and RFA: Informed written consent was obtained. In patients with frequent arrhythmia recurrences, AADs were continued. Bidirectional isthmus conduction (BIC) and collision of dual wavefronts was demonstrated,⁴ and programmed atrial stimulation was performed to induce AFL. Anatomically guided linear ablation of the RA isthmus was performed^{2-4,6-10} using either a 4mm-tip (Cordis Webster) or an 8mm-tip (EP Technology or Cerablate® *plus Flutter*, Osypka, Sulzer Medica) ablation catheter stabilized through an 8Fr long sheath (SAFL or SR0, Daig Corp.). Radiofrequency pulses were delivered with the temperature preset to 55°C (Osypka HAT 300S) or 70°C (Stockert GmbH) for 90 seconds. Ablation of the posterior and/or septal isthmus was performed. Initially, noninducibility of AFL^{2,7-9} was considered a procedural success. Later, we sought to achieve isthmus conduction block, initially unidirectional (confirmed by coronary sinus [CS] pacing) and currently bidirectional,^{1,4,6,10} at the conclusion of every procedure. Procedural success was always confirmed under isoproterenol infusion (1 to 3 µg/min). A 24-hour Holter recording was made before discharge. At follow-up, patients in group 1

discontinued AADs, and patients in groups 2 and 3 received AAD therapy to prevent AF recurrences. Patients in group IV continued either propafenone or flecainide. If the first procedure was not successful, repeat RFA was advised.

Follow-up: Follow-up was conducted at the arrhythmia clinic, initially at 8 weeks and subsequently at 3-month intervals. Patients with successful RFA of AFL were eligible for follow-up analysis. Holter recordings were made at 8 and 12 weeks and when symptoms were suggestive of an arrhythmia recurrence. Patients with a documented AFL recurrence underwent repeated RFA. Patients with recurrent AF were managed with AADs and/or by nonpharmacological alternatives. Current symptom status of all patients was confirmed by telephone.

Statistical analysis: Results are expressed as mean $\pm$ S.D, median and range. Mean values were compared by 1-way ANOVA, and the χ^2 test (or Fisher's exact test) was used for testing homogeneity in contingency tables. Results were considered to be significant at the 5% critical level ($P < 0.05$).

Results

Electrophysiology study and RFA procedure: The results of electrophysiology study and RFA procedures in the 82 patients are summarized in Table 2. During the electrophysiology study, more patients in group 1 ($P = 0.01$) presented with incessant AFL. One patient in group 1 and 3 patients in group 2 were successfully ablated after a second procedure. A second attempt failed to ablate AFL in 1 patient (group 3). The mean AFL cycle length in the 4 groups varied from 230 ± 28 ms to 257 ± 37 ms. Predominantly, a counterclockwise AFL was induced in all 4 groups. More ablation procedures were performed during CS pacing in patients from groups 1 through 4, whereas a preference for ablation performed during AFL was noted from groups 4 through 1 ($P = 0.003$). Although statistically not significant, posterior RA isthmus was found to be most frequently ablated in the 4 study groups. However a relatively greater percentage of patients in groups 2 through 4 required additional septal isthmus ablation. Successful RFA could be performed in $\geq 93\%$ patients (93% in group 1, 96% in group 2, 93% in group 3 and 94% in group 4). A higher ($P = 0.02$) mean number of radiofrequency pulses per successful procedure was required in group 4 patients (27 ± 13) and was related to achieving a BIC block in all successful procedures but 1 ($P = 0.001$). One patient (group 3) developed complete atrioventricular (AV) block during septal isthmus ablation and needed a pacemaker. This patient had BIC block and AFL noninducibility after the last RF pulse and was classified as a successful ablation.

Table 2. Results of Electrophysiology Study and RFA Procedures in the 82 Patients According to the 4 Groups Studied.

	Group 1 (n = 29)	Group 2 (n = 22)	Group 3 (n = 15)	Group 4 (n = 16)	P
No. of procedures, * n	30	25	16	16	
Initial rhythm during study, n(%)					
Sinus	10 (33)	14 (56)	11 (69)	10 (63)	0.01
AFL	20 (67)	11 (44)	3 (19)	6 (27)	
AP	0	0	2 (12)	0	
AFL cycle length, ms	257 ± 37	251 ± 37	239 ± 28	230 ± 28	NS
AFL, n					
Induced† (CCW/CW)	25 (21/5)	19 (17/6)	11 (11/2)	16 (16/2)	
Not induced	4	3	4	0	
Rhythm during RFA, n (%)					
CS pacing	4 (13)	8 (32)	7 (44)	11 (69)	0.003
AFL	22 (74)	11 (44)	6 (37)	5 (31)	
CS pacing + AFL	4 (13)	6 (24)	3 (19)	0	
RA isthmus ablated, n (%)					
Posterior	20 (67)	14 (56)	8 (50)	10 (63)	NS
Septal	3 (10)	3 (12)	1 (6)	0	
Posterior + Septal	7 (23)	8 (32)	7 (44)	6 (27)	
Successful RFA of AFL, n (%)	27/29 (93)	21/22 (96)	14/15 (93)	15/16 (94)	NS
Criteria of successful RFA, n (%)					
NI	4 (15)	6 (29)	3 (21.5)	1 (7)	<0.001
NI + UIC block	15 (55)	6 (29)	8 (57)	0	
NI + BIC block	8 (30)	9 (42)	3 (21.5)	14 (93)	
Radiofrequency pulses/procedure, n	16 ± 8	22 ± 14	21 ± 10	27 ± 13	0.02
Procedure time, min	162 ± 74	199 ± 53	189 ± 70	191 ± 48	NS
Fluoroscopy time, min	43 ± 28	50 ± 26	36 ± 14	50 ± 24	NS

CCW indicates counterclockwise; CW, clockwise; NI, noninducibility; UIC, Unidirectional isthmus conduction; BIC, Bidirectional isthmus conduction.

*One patient each in groups 1 and 3 and 3 patients in group 2 required 2 ablation procedures.

† Both CCW- and CW-rotation AFL was induced in 1, 4, 2 and 2 patients in groups 1 through 4, respectively.

Recurrence of AFL: Follow-up was available in all but one patient (n = 76) after successful RFA of AFL (Table 3). Nine patients (12%) developed an AFL recurrence. No differences were noted ($P = NS$) in the recurrence rate of AFL in the 4 groups, and all AFL recurrences except 1 occurred within 6 months of ablation. In 7 patients, a recurrence after successful ablation judged by either non inducibility (n = 2 patients) or noninducibility and unidirectional isthmus conduction block (n = 5 patients). In the latter 5 patients, there was a demonstrable isthmus conduction delay, indicating regression of isthmus conduction

Table 3. Follow-up Results of AFL Recurrence After Successful RFA in the 76 Patients* According to the 4 Groups Studied.

	Group 1 (n = 26)	Group 2 (n = 21)	Group 3 (n = 14)	Group 4 (n = 15)	P
AFL recurrence, n (%)	6 (23)	0	1 (7)	2 (13)	NS
Time to recurrence, n					
< 6 mo	5	–	1	2	
> 6 mo	1	–	0	0	
Success criteria during first RFA					
NI	2	–	0	0	
NI + UIC block	4	–	1	0	
NI + BIC block	0	–	0	2	
Repeat RFA of AFL					
1 procedure	4	–	1	2	
2 procedures	2	–	0	0	

Abbreviations as in Table 2.

*RFA of AFL was successful in 77 patients. Follow-up was available in all but 1 patient.

block (n = 2 patients) or resumption of isthmus conduction (n = 3 patients). The remaining 2 patients with BIC block had resumption of isthmus conduction bidirectionally. After a repeated RFA requiring either 1 (n = 7) or 2 (n = 2) sessions, all patients are free of AFL recurrences at the long term.

Atrial fibrillation following RFA of type I AFL: The mean follow-up duration was as follows: group 1, 18 ± 14 months; 2, 20 ± 14 months; and 3, 13 ± 8 months. Patients in group 4 had a significantly ($P < 0.001$) shorter mean follow-up (4 ± 2 months). Two patients in group 1 had episodes of paroxysmal AF during the postoperative period after coronary bypass surgery. No other patient in this group developed AF. In group 2, 13 of 21 (62%) patients, including 10 patients in whom AADs were discontinued, were free of AF recurrences. Furthermore, in 5 patients (24%), AF recurrences were controlled better with AADs that previously failed. Thus, 86% patients in group 2 had long-term improvement of concomitant AF. The remaining 3 patients had frequent AF recurrences resistant to multiple AADs. One patient underwent AV nodal ablation with pacemaker implantation, another had a surgical Maze procedure, while the third continues to be symptomatic despite AADs. In contrast, only 2 (14%) patients in group 3 were free of AF recurrences after withdrawal of AAD treatment. In 6 patients (43%), control of AF was achieved by an AAD that had failed before the ablation. This means that 57% of patients in this group had easier control of AF recurrences after RFA of AFL. The remaining 6 patients remained symptomatic despite trials with different AADs (n = 4 patients) and non pharmacological methods (n = 2 patients). After successful RFA of class IC AFL and

continuation of propafenone or flecainide, 11 patients (73%) in group 4 had no AF recurrences. Two patients had few short-lasting and well-tolerated AF recurrences confirmed by the episode log of the Atrioverter. Thus, at a short-term follow-up, definite improvement occurred in 87% patients. When the 4 groups were compared for incidence of AF recurrences following RFA of AFL, patients in group 1 had significantly ($P < 0.01$) less risk of AF recurrences.

Follow-up was available in all but one patient from group 1 in the subgroup of 15 patients with LVEF $< 50\%$. Three patients (0 in group 1 and 4, 1 in group 2 and 2 in group 3) had AF recurrences. In comparison, 23 of 62 (37%) patients with LVEF $\geq 50\%$ had an AF recurrence ($P = 0.13$).

Discussion

The study population consisted of 82 consecutive patients who underwent linear ablation of RA isthmus for type I AFL. Both the ablation protocol and the criteria of procedural success evolved during the study period between November 1994 to April 1998. As shown by the longer duration of mean follow-up a greater number of patients in groups 1 (AFL, no AF) and 2 (AFL $>$ AF) were considered for RFA during our early experience. More patients in groups 3 (AF $>$ AFL) and 4 (class IC AFL) were offered an RFA procedure later; hence, a shorter mean follow-up was available.

Anatomically guided RFA of type I AFL: High procedural success rates (86% to 98%) have been reported after RA isthmus ablation for type I AFL.^{1-4,6-10} In the present study, RFA of AFL was successful in $\geq 93\%$ of patients in all 4 groups. Initially, ablation procedures were performed during AFL, and non inducibility^{2,7-9} was accepted as a procedural success. Later, following the introduction of isthmus conduction block as a criterion, ablation procedures were performed during sinus rhythm with CS pacing.⁶ Therefore, in the present study, there was an increasing use of ablation procedures being performed during CS pacing from groups 1 through 4. This change in ablation protocol was related to later recruitment of patients in groups 3 and 4. In all groups, procedural success was more frequent after ablation of the posterior isthmus (50% to 67%) compared with septal isthmus ablation alone ($\leq 10\%$). This may relate to the ease of achieving a stable catheter position at the posterior isthmus. Interestingly, a greater proportion of patients in groups 2 through 4, involving patients with concomitant AF, underwent an additional septal isthmus ablation. A potential benefit of ablating the septal isthmus in patients with concomitant AF could be modification of the posterior AV nodal input,¹¹ resulting in better ventricular rate control and therefore better tolerance of AF recurrences. During ablation of the

septal isthmus, 1 patient developed complete AV block and required a pacemaker. Single cases of this complication have been reported.¹⁰ It indicates the small but definite risk of RFA of the septal isthmus.

Recurrence of AFL: Nine out of 76 patients (12%) had a recurrence of AFL. Most recurrences ($n = 7$) were in patients in whom noninducibility alone or noninducibility and a unidirectional isthmus conduction block was considered as a success. Higher recurrences (10% to 55%) have been reported after noninducibility alone as a criterion for successful ablation.^{2,7-9} The recurrence rates are lower (6 to 9%) in patients with complete BIC block compared with patients with a unidirectional isthmus conduction block or BIC delay at the conclusion of a successful ablation.^{1,4,6,10} All but 1 recurrence of AFL occurred within initial 6 months after ablation. This stresses the need for close follow-up in the months immediately after a successful ablation. Regression ($n = 2$ patients) or complete disappearance ($n = 5$ patients) of isthmus conduction block was demonstrated during a repeat study, as previously reported.^{1,6,10} Recently, a complete line of double potentials has been advocated as a new success criterion to avoid misinterpretation of isthmus conduction delay as block.¹² A successful repeated RFA in all 9 patients resulted in long-term freedom from arrhythmia recurrences.

Outcome of AF following successful RFA of type I AFL: A variable number (8% to 30%) of patients have been reported to develop AF following RFA of AFL.^{2,3,8,9} In group 1, only 2 patients developed AF, both during the postoperative course of coronary bypass surgery. This finding does not support that in patients with AFL, an RA isthmus radiofrequency lesion could be proarrhythmic for the development of AF.

On the basis of our current understanding, at least 3 mechanisms could be responsible for clinical coexistence of type I AFL and AF in patients included in groups 2 and 3: (1) RA leading circle re-entry (type I AFL) with atrial dissociation and AF in the left atrium;¹³ (2) RA leading circle re-entry (type I AFL) which becomes unstable and degenerates into multiple wavelets of AF;¹⁴ or (3) temporal dissociation of AFL and AF, with a tendency for significant periods of organization along the trabeculated RA in a craniocaudal direction during AF.¹⁵ During the first 2 mechanisms, AF is secondary to a type I AFL circuit and consequently should cease after RA isthmus ablation, which interrupts the flutter circuit. In AF resulting from the third mechanism, we may speculate, that ≥ 1 wavefronts propagating along the trabeculated RA would extinguish on encountering the RA isthmus ablation line. This may reduce the critical number of wavelets necessary to sustain AF, which then terminates. The extent of "organization" in paroxysmal *versus* chronic AF is controversial.^{15,16} The chance of reducing or eliminating AF recurrences after ablation of type I AFL is greater in patients with the initial 2

mechanisms as the basis for atrial arrhythmias and less in case of the third mechanism. Radiofrequency ablation of the RA isthmus for type I AFL in combination with a previously ineffective AAD therapy was found to result in longer arrhythmia free intervals in a greater proportion of patients (86%) in group 2 (AFL > AF) as compared with group 3 (57%) (AF > AFL). From the above reasoning, it is attractive to postulate that a greater proportion of patients in group 2 had coexisting AFL and AF mediated via the first two mechanisms and consequently derived a larger clinical benefit. Undoubtedly, the electrophysiological basis of the inter-relation between AF and AFL needs further elucidation. On the other hand, the explanation for our data may be simple because ablation of the RA isthmus interrupts a major pathway for impulse conduction between the left and RA. This may affect the ability of AF to remain sustained. In summary, what seems certain is the fact that the chance of lowering AF recurrences appears definitely higher in the subgroup of patients with AFL as their predominant clinical arrhythmia.

Patients included in group 4 (class IC AFL) had AF that was nonresponsive to multiple AADs. Rate-dependent prolongation of atrial refractory period by class IC agents effected an increase in the wavelength and facilitated the conversion of AF (multiple smaller reentry circuits) to AFL (a single macro-reentrant loop).¹⁷ After a RA isthmus ablation and continuation of class IC therapy, 87% of patients were either symptom free or had only short lasting, well controlled AF recurrences. A similar successful “hybrid” therapy in patients who were treated primarily with amiodarone for AF was recently reported by Huang et al.¹⁸

A small subgroup ($n = 15$, 18.2%) of our patients had LVEF < 50%. Following AFL ablation, 3 of 14 patients (in 1 patient, we have no follow-up) had AF recurrences. Paydak et al.³ found that a history of spontaneous AF and LVEF < 50% were significant independent predictors of subsequent AF after AFL ablation. When both characteristics were present, 74% of their patients had AF recurrences.³

Study Limitations

Our study population was classified into 4 groups on the basis of documentation of AFL alone or in combination with AF. The exact incidence of arrhythmia episodes, especially those that were asymptomatic, is not known and may have affected our classification. Although every procedure involved an RA isthmus ablation, the ablation protocol and the criteria for procedural success have changed over the study period in keeping with advances in our knowledge. A complete isthmus conduction block at the conclusion of a successful procedure

was not obtained in all patients. This has obvious implications for analysis of arrhythmia recurrences.

Conclusions

Radiofrequency ablation of type I AFL can be performed, regardless of concomitant AF, with a high primary success rate and low overall AFL recurrences. A low incidence of new AF after RFA of type I AFL indicates that those radiofrequency lesions do not or rarely lead to development of AF. In patients with type I AFL as their predominant clinical arrhythmia, RA isthmus ablation reduces recurrences of AF over a long period of follow-up. This procedure is less successful in patients with AFL and more frequent episodes of AF. Patients with therapy-resistant AF who develop a type I AFL while receiving class IC therapy also seem to profit, showing a reduced incidence of AF recurrences after AFL ablation. Our findings contribute to the growing conviction to individualize the site and extent of RFA(s) in patients with AF.^{16,19} Our ultimate goal in RFA for AF should be to apply the interventions only to the site(s) resulting in the greatest amount of success and the least amount of damage to atrial function.

References

1. Tai CT, Chen SA, Chiang CE, Lee SH, Wen ZC, Huang JL, Chen YJ, Yu WC, Feng AN, Lin YJ, Ding YA, Chang MS. Long-term outcome of radiofrequency catheter ablation for typical atrial flutter: risk prediction of recurrent arrhythmias. *J Cardiovasc Electrophysiol* 1998;9:115-121.
2. Philippon F, Plumb VJ, Epstein A, Kay GN. The risk of atrial fibrillation following radiofrequency catheter ablation of atrial flutter. *Circulation* 1995;92:430-435.
3. Paydak H, Kall JG, Burke MC, Rubenstein D, Kopp DE, Verdino RJ, Wilber DJ. Atrial fibrillation after radiofrequency ablation of type I atrial flutter: time to onset, determinants, and clinical course. *Circulation* 1998;98:315-322.
4. Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter: further insights into the various types of isthmus block : application to ablation during sinus rhythm. *Circulation* 1996;94:3204-3213.
5. Wellens HJJ, Lau CP, Lüderitz B, Akhtar M, Waldo AL, Camm AJ, Timmermans C, Tse HF, Jung W, Jordaens L, Ayers G, for the Metrix Investigators. The atrioverter: an implantable device for treatment of atrial fibrillation. *Circulation* 1998; 98:1651-1656.
6. Poty H, Saoudi N, Aziz AA, Nair M, Letac B. Radiofrequency catheter ablation of type 1 atrial flutter: prediction of late success by electrophysiological criteria. *Circulation* 1995;92:1389-1392.

7. Cosío FG, López-Gil M, Goicolea A, Arribas F, Barroso JL. Radiofrequency ablation of the inferior vena cava- tricuspid valve isthmus in common atrial flutter. *Am J Cardiol* 1993;71:705-709.
8. Kirkorian G, Moncada E, Chevalier P, Canu G, Claudel JP, Bellon C, Lyon L, Touboul P. Radiofrequency ablation of atrial flutter: efficacy of an anatomically guided approach. *Circulation* 1994;90:2804-2814.
9. Fischer B, Haïssaguerre M, Garrigues S, Poquet F, Gencel L, Clémenty J, Marcus FI. Radiofrequency catheter ablation of common atrial flutter in 80 patients. *J Am Coll Cardiol* 1995;25:1365-1372.
10. Schumacher B, Pfeiffer D, Tebbenjohanns J, Lewalter T, Jung W, Lüderitz B. Acute and long-term effects of consecutive radiofrequency applications on conduction properties of the subeustachian isthmus in type I atrial flutter. *J Cardiovasc Electrophysiol* 1998;9:152-163.
11. Klug D, Lacroix D, Franc LP, Kouakam C, d'Hautefeuille, Dennetierre S, Pecheux M, Kacet S. Linear isthmus block for atrial flutter radiofrequency ablation modifies AV nodal inputs during low lateral atrial pacing. *Pacing Clin Electrophysiol* 1998; 21 (Part II): 833.Abstract.
12. Shah DC, Takahashi A, Haïssaguerre M, Jaïs P, Clémenty J. Definitive criteria of cavo-tricuspid isthmus block. *Pacing Clin Electrophysiol* 1998;21:832.Abstract.
13. Yamauchi S, Boineau JP, Schuessler RB, Cox JL. Varying types of circus movement reentry with both normal and dissociated contralateral conduction causing different right and left atrial rhythms in canine atrial flutter. *Jpn Circ J* 1998;62:201-210.
14. Wu TJ, Yashima M, Huang H-LA, Kim YH, Athill CA, Karaguezian HS, Chen PS. Atrial wavefront instability induced by progressive action potential duration shortening: a mechanism of conversion from atrial flutter to atrial fibrillation. *J Am Coll Cardiol* 1998; Suppl 31(2):158A.Abstract.
15. Roithinger FX, SippensGroenewegen A, Karch MR, Steiner PR, Ellis WS, Lesh M. Organized activation during atrial fibrillation in man: endocardial and electrocardiographic manifestations. *J Cardiovasc Electrophysiol* 1998;9:451-461.
16. Gaita F, Riccardi R, Calò L, Scaglione M, Garberoglio L, Antolini R, Kirchner M, Lamberti F, Richiardi E. Atrial mapping and radiofrequency catheter ablation in patients with idiopathic atrial fibrillation: electrophysiological findings and ablation results. *Circulation* 1998;97:2136-2145.
17. Crijns HJGM. Clinical manifestations of use- and reverse-use dependence. In: Crijns HJGM, ed: Changes of intracardiac conduction induced by antiarrhythmic drugs: Importance of use- and reverse-use dependence. Groningen, Netherlands: BV Knoop Haren;1993:38-105.
18. Huang DT, Monahan KM, Zimetbaum P, Papageorgiou P, Epstein LM, Josephson ME. Hybrid pharmacologic and ablative therapy: a novel and effective approach for the management of atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9:462-469.
19. Jaïs P, Haïssaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M, Clémenty J. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997; 95:572-576.

“Class IC atrial flutter”: Electrocardiographic and electrophysiological findings and their importance for long-term outcome after right atrial isthmus ablation

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ABSTRACT

Background: Recent reports suggest clinical benefit, at least short-term, after right atrial (RA) isthmus ablation, in patients showing conversion of atrial fibrillation (AF) to atrial flutter (AFL) while taking antiarrhythmic drug (AAD) therapy. The aim of this study was 1) to describe the electrocardiographic (ECG) and electrophysiologic characteristics of the AFL, developing in patients taking class IC AAD therapy for recurrent AF, the so called "class IC AFL" and 2) to report long-term success following RA isthmus ablation, in relation to their ECG pattern during AFL.

Methods: The 12-lead ECG, findings during electrophysiological study, acute results of RA isthmus ablation, and long-term outcome as to AF recurrences were examined in 24 consecutive AF patients (54 ± 12 years, 19 males) who were diagnosed as developing AFL while taking propafenone ($n=12$) or flecainide ($n=12$).

Results: On retrospective analysis, ECG was considered suggestive of typical AFL, when flutter waves showed a regular rhythm with sharp negative deflections in the inferior leads and positive deflections in lead V1. This was found in 13 patients (54%). The ECG was classified as atypical AFL ($n = 8$) or coarse AF ($n = 3$) in the remaining patients. On electrophysiological study, the RA isthmus conduction time was slower in lateromedial than in mediolateral direction (104 ± 32 ms versus 75 ± 34 ms, $P=0.023$). During the study, a counterclockwise (CCW) AFL was documented in 7 out of 7 and 4 out of 5 patients having typical and atypical AFL respectively. Acute success of ablation was similar in patients with typical (92%) and atypical (100%) AFL. At long-term follow-up (13 ± 6 ; range, 6 - 26 months), continuation of AAD therapy resulted in better control of AF recurrences, in patients with typical than an atypical AFL. Coarse AF ($n = 3$) persisted despite ablating the RA isthmus. At follow-up all 3 patients continued to have frequent recurrences of AF.

Conclusions: This study shows that, in class IC AFL electrocardiographically both typical and atypical AFL morphologies are seen. The AFL circuit was always located in the RA and the isthmus was crucial for maintaining reentry. The best long-term control of AF using the "hybrid" approach was obtained in patients with an AFL ECG pattern of typical AFL. Patients developing coarse AF are no candidates for this strategy.

Introduction

The architecture of the right atrium (RA) provides natural obstacles or barriers promoting the development of atrial flutter (AFL).¹ Indeed, the macro-reentrant circuit of AFL is located in the RA in 80 - 85% of the cases.² Atrial fibrillation (AF) may be based on either a "mother" macro-reentrant circuit with "daughter" waves, random reentry or rapid focal activity.^{3,4} Under antiarrhythmic drug (AAD) therapy, "organization" of AF in craniocaudal direction along the crista terminalis has been observed.⁵ Transformation of AF to AFL requires prolongation of the reentrant wavelength,⁶ resulting in a single macro-reentrant loop. AADs may promote this conversion⁷ by slowing RA isthmus conduction⁸ and by limiting transversal conduction across the crista terminalis.⁹ Although, not studied systematically, the incidence of AFL in patients taking class IC AADs for recurrent AF is estimated to range from 3.5 to 20%.¹⁰

A typical AFL may occur, when patients with AF develop AFL after administration of class IC AADs.^{11,12} However, atypical electrocardiographic (ECG) and intracardiac electrogram patterns of AFL have also been noted.¹² After short-term follow-up, the "hybrid" therapy of isthmus ablation and AADs has been reported to prevent or reduce the recurrences of AF in patients in whom use of AADs resulted in "conversion" of AF to AFL.^{7,11,12} However the usefulness of this approach will depend upon the results obtained during long-term follow-up.

We defined "class IC atrial flutter" as a new AFL developing in patients taking propafenone or flecainide for recurrent episodes of AF.¹¹ The aim of the present study was 1) to describe the ECG characteristics and the electrophysiological findings during radiofrequency (RF) ablation of class IC AFL, and 2) to report long-term success following RA isthmus ablation, in relation to their ECG pattern during AFL.

Methods

Study population: Twenty-four consecutive patients, who underwent electrophysiological study and RF ablation, between March 1997 and January 1999, for the so called class IC AFL were included in the study. Before class IC AAD therapy, every patient was symptomatic with recurrent and disabling episodes of AF, since 8 ± 9 years (3 months - 30 years). AF was paroxysmal in 9 and persistent in 15 patients. Prolonged periods of sinus rhythm could not be maintained, in spite of 3 ± 1.6 (range, 1-6) AADs per patient. In the past, 3 patients had received an atrial defibrillator (Metrix, Atrioverter, InControl Inc, Redmond, WA). A dual chamber pacemaker was implanted in 1 patient for a sick

sinus syndrome. In none of the patients, AFL was documented before the use of class IC therapy. The clinical characteristics of the 24 patients are described in Table 1. An equal number of patients were taking propafenone (450-900 mg/day) or flecainide (100-400 mg/day) when "conversion" to class IC AFL was observed.

ECG: The 12-lead ECG recorded during the clinical AFL episode was classified with regard to the morphology of the flutter waves. Typical AFL was defined as the presence of regular flutter waves showing negative (or predominantly negative with a terminal positive deflection) deflections in the inferior leads and an entirely or predominantly positive flutter wave in lead V1 (Figure 1, A).² AFL, with uniform, regular flutter waves but another morphology, either in the inferior leads or lead V1, was classified as atypical (Figure 1, B). The ECG classification was done in retrospect by one of the investigators (HW), unaware of the findings during the electrophysiologic study

Electrophysiological study and RF ablation procedure: The electrophysiological study and RF ablation was performed after informed consent and the patient in the post absorptive state. Details of the procedure are described elsewhere.^{11,13} The RA activation pattern was recorded from a duodecapolar Halo catheter (Cordis-Webster, Baldwin Park, CA, USA) positioned around the tricuspid annulus, and preferably a multipolar catheter (Cordis-Webster, Baldwin Park, CA, USA) was placed in the coronary sinus (CS) so that its proximal bipole was at the ostium. At the beginning of the study and when possible, bidirectional isthmus conduction (BIC)¹⁴ was evaluated at a pacing cycle length of 600 ms. The AFL induction protocol consisted of up to 3 atrial extrastimuli delivered after a basic 10-beat drive, with 3 different cycle lengths. Incremental atrial pacing was performed, when necessary. Isthmus activation time (time interval between the Halo bipole positioned at the low lateral RA and the proximal CS bipole) was expressed as a percentage of flutter cycle length. We refrained from performing entrainment studies, because in the initial procedures attempts to entrain class IC AFL resulted in induction of sustained AF. In case of a sustained AF induced inadvertently, sinus rhythm was restored by cardioversion. Ablation of the RA isthmus was performed by an anatomical approach.

Acute procedural result: After RA isthmus ablation, success was judged by demonstrating noninducibility of AFL and BIC block. The procedure was considered a partial success if AFL was rendered noninducible in the absence of complete BIC block. The procedure had failed if AFL remained inducible. Procedural success was confirmed under isoproterenol infusion (1 to 3 μ g/min).¹⁵

Follow-up protocol: After the procedure, patients were advised to take propafenone or flecainide. Follow-up was conducted at 8 weeks and then at

Table 1. Clinical Characteristics of the 24 Patients Studied.

Age (years)	54 ± 12
Male / Female, n/n	19 / 5
Structural heart disease, n	
None	17
Mild mitral regurgitation	4
Mild left ventricular dysfunction	1
Small atrial septal defect	1
Corrected Ebstein's anomaly	1
Left atrial size (cm)	4.6 ± 0.4
Duration of AF (years)	8 ± 9 (3 mo - 30 years)
Number of previously failed AADs, n	3 ± 1.6 (1 - 6)

*AAD, Antiarrhythmic drug; AF, Atrial fibrillation.

3-month intervals. Holter recordings were requested predischARGE, at 8 and 12 weeks after the procedure, and when symptoms suggested an arrhythmia recurrence.

Patients having a documented recurrence of AFL were advised to undergo re-ablation. After isthmus ablation, patients having no AF recurrences, asymptomatic recurrences (AF detected only by Holter, Atrioverter or pacemaker device), or symptomatic but short-lasting AF recurrences were considered to be well-controlled. These patients were taking either propafenone or flecainide, and occasionally a class III AAD or calcium antagonist was added for further control of AF recurrences. Patients who continued to have frequent or symptomatic AF recurrences, despite alterations in the AAD regimen, were considered as inadequately controlled.

Statistical analysis: Results were expressed as mean ± SD and range and proportions as percentages. Mean values were compared by 1-way ANOVA test and χ^2 test was used for testing homogeneity in contingency tables. Results were considered to be significant at 5% critical level ($P < 0.05$).

Results

Twelve lead ECG during a clinical recording of class IC AFL: Thirteen patients (54%) were classified as typical AFL. In 8 other patients, the flutter wave deflection was different in the inferior leads and lead V1. They were classified as atypical AFL. The mean AFL cycle length was 268 ± 34 ms (range, 220 - 360 ms). Atrioventricular (AV) conduction was variable in 9 patients, fixed 2:1 in 10, and 1:1 in 1 patient (flutter rate, 360 ms). In the remaining 3 patients there were small differences in interval and configuration of the atrial deflections, and they were classified as fibrillo-flutter or coarse AF (Figure 1, C).

Figure 1. The 12-lead ECG shows A) typical atrial flutter (AFL) with regular and sharp negative atrial deflections in the inferior leads and positive ones in lead V1. B) atypical AFL with positive and rounded atrial deflections in the inferior leads. The deflections in lead V1 are negative and rounded, and C) coarse atrial fibrillation with varying intervals and morphology of the atrial deflections.

Table 2. Findings during Electrophysiological Study.

	Typical AFL (n = 13)	Atypical AFL (n = 8)	Coarse AF (n = 3)
AFL inducibility, n (%)			
Incessantly present	4 (31)	2 (24)	3 (100)
Induced	3 (23)	3 (38)	0
Noninducible	6 (46)	3 (38)	0
Right atrial activation during AFL, n (%)	(n = 7)	(n = 5)	(n = 3)
Counterclockwise	7 (100)	4 (80)	3 (100)
Clockwise	0	1 (20)	0
AFL cycle length stability, n (%)	(n = 7)	(n = 5)	(n = 3)
Yes	6 (86)	4 (80)	1 (33)
No	1 (14)	1 (20)	2 (67)
Left atrial response during AFL, n (%)	(n = 6)	(n = 5)	(n = 1)
1:1	6 (100)	5 (100)	0
AF	0	0	1 (100)
Episodes of sustained AF, n (%)	5 (39)	3 (38)	3 (100)

AF, Atrial fibrillation; AFL, Atrial flutter.

Findings during the electrophysiological study: Prior to RF ablation, BIC could be assessed in 17 patients. The mean lateromedial isthmus conduction time was longer than the mediolateral isthmus conduction time¹⁶ (104 ± 32 ms versus 75 ± 34 ms, $P = 0.023$).

Table 2 summarizes the findings during electrophysiological study. From the beginning of the procedure, AFL was continuously present in 6 patients. In 6 more patients, a sustained AFL could be induced by; programmed atrial premature beats ($n = 3$), atrial premature beats related to catheter manipulation ($n = 1$), and spontaneous transition from on going AF ($n = 2$). AFL could not be induced in 9 (43%) patients. There was no difference as regards inducibility, in patients with typical or atypical AFL. AF was present during most of the procedure, in the 3 patients later classified as coarse AF.

Therefore the intracardiac atrial activation pattern could be studied during AFL in 12 patients. The RA activation pattern was constant and repetitive in every patient (Figure 2). The direction of activation was counterclockwise (CCW) in every patient ($n = 11$), except 1. The mean isthmus activation time constituted $35\% \pm 14\%$ of the flutter cycle length. Most of the patients with typical (6 of 7) and atypical (4 of 5) AFL showed a stable cycle length. As

Figure 2. Intra-atrial activation pattern of the same three patients shown in Figure 1. ECG leads II, III, AVF and V1 are shown. The intracardiac electrograms include: bipoles of the duodecapolar (Halo) catheter positioned around the tricuspid annulus (H0102 - H1920) and the bipole located at the coronary sinus ostium (CSOS). A) shows a clockwise rotation of the AFL (310 ms) B) shows a counterclockwise (CCW) rotation of the AFL (260 ms) C) shows a directionally stable RA activation sequence (viz. CCW). However, there are beat-to-beat variations in the cycle length. Note that the CS electrograms suggest a 1:1 left atrial response in all 3 patients.

Figure 3. An example of class IC AFL. Note that the RA endocardial activation shows CCW rotation (H0506 to H1920). Electrograms from the coronary sinus (CS) suggest left atrial fibrillation.

expected, patients with coarse AF (2 of 3) had a beat-to-beat variation in the atrial cycle length. The atrial cycle length was stable in the remaining 1 patient with coarse AF.

Simultaneous recordings from the CS were available in 12 of the 15 patients mentioned above. The left atrial (LA) response was consistently 1:1 in 11 patients. In the remaining patient, CS electrograms were indicative of LA fibrillation (Figure 3). Multiple recordings from the CS were available in only 5 of the former 11 patients. In 4 of these patients with CCW-AFL, the activation sequence of the CS was; proximal to distal ($n = 1$), distal to proximal ($n = 2$) and simultaneous ($n = 1$). In 1 patient with clockwise AFL, the CS activation was proximal to distal.

Atrial fibrillation during ablation of class IC AFL: Sustained AF was precipitated inadvertently in 8 (38%) patients, including 5 patients with typical and 3 with atypical AFL. During the procedure, at least on 1 occasion, every patient with coarse AF ($n = 3$) showed disorganization of RA activation (absence of repetitive pattern of activation along the Halo catheter). Sinus rhythm was

restored by external (n = 5) or internal (n = 2) electrical cardioversion, intravenous flecainide (n = 1) or overpacing (n = 1). In the remaining 2 patients, a spontaneous reversion to AFL was observed.

Acute procedural result: A linear ablation of the RA isthmus was performed during CS pacing (n = 13), AFL (n = 6) or both rhythms (n = 4). In 1 patient, with recurrent spontaneous induction of AF, the ablation was performed during sinus rhythm (without CS pacing). The results of ablation are included in Table 3.

The ablation was judged as successful, after noninducibility of AFL and BIC block, in 18 out of 21 patients. Success was considered as partial in 2 patients, because of noninducibility alone in 1 patient (typical AFL) and noninducibility and unidirectional isthmus conduction block in another patient (atypical AFL). In the remaining 1 patient who had a typical AFL, ablation was considered unsuccessful. In case of the 3 patients with coarse AF, after ablation of both the RA isthmi, coarse AF was persistently present in 2 patients. It is of some interest that, coarse AF was not inducible after obtaining BIC block in the remaining 1 patient. When the 3 groups were compared, in contrast to patients with coarse AF, the acute effect of isthmus ablation was considered to be successful in a high number of patients with typical (92%) or atypical (100%) AFL.

Long-term follow-up results: A mean follow-up of 13 ± 6 months (range, 6 - 26) was available (Table 3). After an initially successful ablation, 4 patients (3 with typical and 1 with atypical AFL) had a recurrence of AFL, 9 ± 4 months (range, 3 - 15) later. In these 4 patients, acute success had been judged by: noninducibility alone (n = 1), noninducibility and unidirectional isthmus conduction block (n = 1), and noninducibility and BIC block (n = 2). All 4 patients underwent successful re-ablation, with confirmation of BIC block under isoproterenol infusion. At the last follow-up, all 4 patients were free of AFL recurrences.

Of the 13 patients who underwent ablation for typical AFL, recurrences of AF were prevented in 11 (85%) patients. Class IC AADs were stopped in 2 patients, whereas 9 patients continued taking class IC medication alone (7 patients) or in combination with sotalol (2 patients). Recurrent episodes of AF were found in 2 patients. Out of the latter 2 patients, 1 patient with operated Ebstein's anomaly had an unsuccessful ablation of AFL. The other patient had AF recurrences, after successful RA isthmus re-ablation for an AFL recurrence, in spite of the addition of amiodarone to flecainide. After ablation of atypical AFL (n = 8 patients), 4 patients (50%) showed a reduction in AF recurrences while taking class IC medication alone. Frequency of AF recurrences did not change in other 4 patients. Clearly, more patients with typical as compared to atypical AFL, had an improvement in control of their AF recurrences after ablation of the isthmus. Not surprisingly, all 3 patients who underwent isthmus ablation despite of coarse AF continued to have frequent recurrences of AF.

Table 3. Long-term Results following Right Atrial Isthmus Ablation in the 24 Patients.

No.	Class IC AFL	Class IC AAD used (mg/day)	Acute Result	FU	Recurrence AFL AF	AADs at last follow-up (mg/day)	Control of AF recurrences	
1	Typical	Propafenone (900)	Success NI+BICB	8	No	Few, short-lasting episodes	Propafenone (750)	Well-controlled
2	Typical	Propafenone (450)	Success NI+BICB	21	No	None	Atenolol (25). Propa- fenone stopped.	Well-controlled
3	Typical	Flecainide (200)	Partial NI	9	Yes	Recurrent episodes, external cardioversion X 1	Flecainide (100) + Amiodarone (200)	Not controlled
4	Typical	Flecainide (200)	Success NI+BICB	16	No	Few, short-lasting episoddes. Detected by Atrioverter	Flecainide (200) + Metoprolol (25)	Well-controlled
5	Typical	Propafenone (450)	Success NI+BICB	10	No	None	Flecainide (200)	Well-controlled
6	Typical	Flecainide (100)	Failed	18	No	Recurrent episodes	Flecainide (100)	Not controlled
7	Typical	Propafenone (450)	Success NI+BICB	15	Yes	1 episode, 2 hours, asymptomatic. Detected by Holter	None, Propafenone stopped	Well-controlled
8	Typical	Propafenone (900)	Success NI+BICB	12	No	2 symptomatic episodes, lasting 2 hours and 3 days	Propafenone (450) + Sotalol (80)	Well-controlled
9	Typical	Flecainide (100)	Success NI+BICB	14	No	None	Flecainide (100) + Diltiazem SR(120)	Well-controlled
10	Typical	Propafenone (900)	Success NI+BICB	18	Yes	Few, short-lasting episodes	Propafenone (600) + Sotalol (80)	Well-controlled
11	Typical	Propafenone (450)	Success NI+BICB	9	No	Few episodes on disconti- nuing AADs, re-started.	Propafenone (450) + Atenolol (25)	Well-controlled
12	Typical	Flecainide (150)	Success NI+BICB	6	No	3 symptomatic episodes	Flecainide (150) + Metoprolol (25)	Well-controlled
13	Typical	Flecainide (200)	Success NI+BICB	13	No	Few short-lasting episodes	Flecainide (100)	Well-controlled
14	Atypical	Flecainide (300)	Success NI+BICB	25	No	Few short-lasting & 1 sustained episode	Flecainide (100) + Metoprolol (25)	Well-controlled
15	Atypical	Propafenone (450)	Partial NI+UICB	26	Yes	Recurrent, multiple AADs used & Atrioverter shocks	Amiodarone	Not controlled
16	Atypical	Flecainide (200)	Success NI+BICB	24	No	Amiodarone added, hyper- thyroidism, external cardioversion X 4, recurrent AF	Flecainide (200) + Metoprolol (50)	Not controlled
17	Atypical	Propafenone (600)	Success NI+BICB	11	No	Few, short-lasting recurrences	Propafenone (450) + Metoprolol (50)	Well-controlled
18	Atypical	Propafenone (450)	Success NI+BICB	10	No	Recurrent, multiple Atrioverter shocks	Propafenone (450) + Metoprolol (50)	Not controlled

Table 3. Continued

No.	Class IC AFL	Class IC AAD used (mg/day)	Acute Result	FU	Recurrence AFL	AF	AADs at last follow-up (mg/day)	Control of AF recurrences
19	Atypical	Flecainide (200)	Success NI+BICB	6	No	Few, short-lasting recurrences	Flecainide (200) + Metoprolol (100)	Well-controlled
20	Atypical	Propafenone (450)	Success NI+BICB	8	No	Recurrent episodes.	Amiodarone (200) Propafenone stopped	Not controlled
21	Atypical	Flecainide (400)	Success NI+BICB	11	No	Had AF recurrences on reducing Flecainide (100)	Flecainide (400) + Pindolol (5)	Well-controlled
22	Coarse AF	Flecainide (400)	Failed	9	No	Recurrent episodes. No response to Disopyramide	Flecainide (400) + Metoprolol (50)	Not controlled
23	Coarse AF	Flecainide (200)	NI+BICB	10	No	Recurrent AF, multiple mode switches (DDIR) done by the DDDR pacemaker	Flecainide (200) + Digoxin (0.125) + Metoprolol (50)	Not controlled
24	Coarse AF	Propafenone (450)	Failed	6	No	Chronic permanent AF External cardioversion X 2	Amiodarone (200), Propafenone stopped	Not controlled

AAD, Antiarrhythmic drug; AF, Atrial fibrillation; AFL, Atrial flutter; BICB, Bidirectional isthmus conduction block; FU, Follow-up duration in months; NI, noninducible; UICB, Unidirectional isthmus conduction block.

Discussion

“Class IC AFL”: In the present study, the electrocardiographic morphology of class IC AFL was the typical AFL morphology in $\approx 50\%$ of the patients. The remaining half, based on the morphological characteristics of the atrial deflections in the ECG were classified as showing atypical AFL or coarse AF. The mean flutter rate (268 ± 34 ms) was slow because of the class IC therapy. During the electrophysiological study, no differences between typical and atypical AFL were noted in regard to the pattern of activation during AFL. The flutter circuit was always localized to the RA, having a CCW direction in the majority of patients. The preference for CCW-reentry may be based on a slower isthmus conduction in lateromedial, in comparison to the mediolateral direction (104 ± 32 ms versus 75 ± 34 ms, $P = 0.023$). The mean isthmus activation time was $35\% \pm 14.3\%$ of the flutter cycle length. This was longer, as compared to the isthmus activation time ($25\% - 27\%$) reported in another study,¹⁶ and might support the presence of a macro-reentrant circuit. In most of the patients (11 out of 12), where this was recorded, the LA responded to the RA-reentrant circuit in a 1:1 fashion. This finding is compatible with the argument, that LA is a simple bystander and not essential to the AFL circuit.² The limited recordings from CS

using multiple electrodes do not allow an impression of global LA activation. The importance of the LA activation sequence, in determining the electrocardiographic polarity of flutter wave, has been demonstrated in a canine model of AFL.¹⁷ In the present study, it remains speculative whether differences in LA activation, are responsible for the observed differences in electrocardiographic morphology of class IC AFL. Although a recent study pointed to the lack of correlation between direction of rotation of AFL and the polarity in the inferior leads,¹⁸ our observations suggest that the predominantly negative flutter waves in the inferior leads and positive flutter deflections in lead V1, indicate class IC AFL patients who do well after RA isthmus ablation.

RF ablation of class IC AFL: Every patient underwent a linear ablation of the RA isthmus. Thereafter noninducibility of AFL could be achieved in the majority of patients with either a typical (92%) or atypical (100%) AFL. A majority of patients studied by Huang et al,⁷ developed AFL while receiving amiodarone for recurrent AF. That study reported a better procedural outcome following ablation of typical AFL. In terms of recurrences of AF, our long-term follow-up suggests better late results in patients with typical AFL.

Development of Coarse AF after class IC AAD therapy: Three patients with coarse AF underwent isthmus ablation. Every patient showed a stable RA activation pattern, but a beat-to-beat variation in the cycle length was present in 2 patients. Noninducibility could not be achieved after ablating both the RA isthmi in 2 patients. Furthermore, at long-term, AF recurrences occurred in all 3 patients. These findings confirm that, conduction through the isthmus is not critical to the maintenance of coarse AF. Based on the results of this study, these patients should not be considered candidates for the "hybrid" approach.

Study limitations

Nearly 50% of our patients with class IC AFL had an atypical morphology. In the absence of detailed mapping from the atrial septum and left atrium, the reasons for differences in electrocardiographic morphology of class IC AFL could not be understood. In 9 (43%) patients, AFL could not be induced. In these patients, with noninducible but clinically documented class IC AFL, complete BIC block had to be accepted as an procedural endpoint. In the absence of entrainment studies, determining the location of class IC AFL circuit and its isthmus dependence, based on a circular pattern of RA activation, is a limitation. However, we decided not to attempt entrainment, because of the precipitation of sustained AF early in the series. The frequency of AF recurrences during follow-up is at best an estimate. Asymptomatic recurrences could go undetected

even with the use of Holter monitoring or event recorders. However, the frequency of symptomatic AF recurrences requiring treatment is directly relevant to the patient.

Clinical Implications

This study shows that, after class IC AAD therapy for AF, both typical and atypical AFL-ECG morphologies are seen. The AFL circuit was always located in the RA and the RA isthmus was involved in the reentry mechanism. Long-term success, defined as improvement in control of AF recurrences, with the "hybrid" approach, was higher in patients who underwent RA isthmus ablation for typical AFL. Less patients, when treated by this approach, benefited during long-term, when the RA isthmus ablation was performed for atypical AFL. Patients with coarse AF are no candidates for this strategy.

References

1. Cabrera JA, Sanchez-Quintana D, Ho SY, Medina A, Anderson RH. The architecture of the atrial musculature between the orifice of the inferior vena caval vein and the tricuspid valve: the anatomy of the isthmus. *J Cardiovasc Electrophysiol* 1998;9:1186-1195.
2. Cosío FG, Arribas F, López-Gil M, Goicolea A. Endocardial catheter mapping of atrial arrhythmias. In Shenasa M, Borggreffe M, Breithardt G, eds: *Cardiac Mapping*. Futura Publishing Co, Inc., Mount Kisco, NY, 1993:443-459.
3. Konings KTS, Kirchhoff CHJH, Smeets JLRM, Wellens HJJ, Penn OC, Allesie MA. High-density mapping of electrically induced atrial fibrillation in humans. *Circulation* 1994;89:1665-1680.
4. Jaïs P, Haïssaguerre M, Shah DC, Chourairi S, Gencel L, Hocini M, Clémenty J. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997;95:572-576.
5. Roithinger FX, SippensGroenewegen A, Karch MR, Steiner PR, Ellis WS, Lesh MD. Organized activation during atrial fibrillation in man: endocardial and electrocardiographic manifestations. *J Cardiovasc Electrophysiol* 1998;9:451-461.
6. Matsuo K, Kumagai K, Annoura M, Ideishi M, Arakawa K. Mechanism of antiarrhythmic effects of class Ic drugs in paroxysmal atrial fibrillation in man. *Cardiology* 1998;89:119-123.
7. Huang DT, Monahan KM, Zimetbaum P, Papageorgiou P, Epstein LM, Josephson ME. Hybrid pharmacologic and ablative therapy: a novel and effective approach for the management of atrial fibrillation. *J Cardiovasc Electrophysiol* 1998;9:462-469.

8. Yamashita T, Inoue H, Nozaki A, Tsong-teh K, Usui M, Sugimoto T. Role of anisotropy in determining the selective action of antiarrhythmics in atrial flutter in the dog. *Cardiovasc Res* 1992;26:244-249.
9. Schumacher B, Schmidt H, Fischenbeck C, Lewalter T, Wolpert C, Jung W, Lüderitz B. Pulse propagation through the crista terminalis in patients with atrial fibrillation and atrial flutter. *J Am Coll Cardiol* 1998;32:221A. Abstract.
10. Falk RH. Proarrhythmic responses to atrial antiarrhythmic therapy. In: Falk RH, Podrid PJ, eds. *Atrial fibrillation: mechanisms and management*. NY: Raven Press Ltd., 1992:283-305.
11. Nabar A, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Radiofrequency ablation of "class IC atrial flutter" in patients with resistant atrial fibrillation. *Am J Cardiol* 1999;83:785-787.
12. Schumacher B, Jung W, Lewalter T, Vahlhaus C, Wolpert C, Lüderitz B. Radiofrequency ablation of atrial flutter due to administration of class IC antiarrhythmic drugs for atrial fibrillation. *Am J Cardiol* 1999;83:710-713.
13. Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter: further insights into the various types of isthmus block: application to ablation during sinus rhythm. *Circulation* 1996;94:3204-3213.
14. Barold SS, Shah D, Jaïs P, Takahashi A, Haïssaguerre M, Clémenty J. Nomenclature and characterization of transisthmus conduction after ablation of typical atrial flutter. *Pacing Clin Electrophysiol* 1997;20:1751-1753.
15. Nabar A, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Isoproterenol to evaluate resumption of conduction following right atrial isthmus ablation in type I atrial flutter. *Circulation* 1999;99:3286-3291.
16. Saoudi N, Nair M, Abdelaziz A, Poty H, Daou A, Anselme F, Letac B. Electrocardiographic patterns and results of radiofrequency ablation of clockwise type I atrial flutter. *J Cardiovasc Electrophysiol* 1996;7:931-942.
17. Okumura K, Plumb VJ, Pagé PL, Waldo AL. Atrial activation sequence during atrial flutter in the canine pericarditis model and its effects on the polarity of the flutter wave in the electrocardiogram. *J Am Coll Cardiol* 1991;17:509-518.
18. Lai LP, Lin JL, Lin LJ, Chen WJ, Ho YL, Tseng YZ, Chen CH, Lee YT, Lie WP, Huang SKS. New electrocardiographic criteria for the differentiation between counterclockwise and clockwise atrial flutter: correlation with electrophysiological study and radiofrequency catheter ablation. *Heart* 1998;80:80-85.

Should we prefer a long tip electrode to perform radiofrequency ablation of type I atrial flutter?

Results of a prospective randomized study comparing an 8-mm split-tip versus a 4-mm tip ablation catheter

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ABSTRACT

Aim: Clinical experience using a long tip electrode for radiofrequency (RF) catheter ablation of type I atrial flutter (AFL) is largely observational. We therefore compared a new RF catheter design with an 8-mm split-tip electrode having integrated thermocouples [Cerablate®*plus* Flutter, Dr Osypka GmbH, Grenzach-Wyhlen, Germany], (group I) with a 4-mm tip electrode (group II) in a prospective randomized manner.

Methods: Thirty consecutive patients were randomized to group I or II. For ablation of the RA isthmus 90 second RF pulses were used at sequential sites with a preset temperature of 55°C. Procedural success was defined as noninducibility of AFL and bidirectional isthmus conduction (BIC) block under isoproterenol infusion.

Results: All patients in group I and all but 1 patient in group II underwent successful ablation. A significantly lesser number of RF pulses and a shorter mean fluoroscopy time was found using an 8-mm split-tip electrode [RF pulses 12 ± 3.5 in group I versus 27 ± 9 in group II ($P < 0.0001$), fluoroscopy time 23 ± 13 in group I versus 45 ± 28 min in group II ($P = 0.01$)]. With comparable mean follow-up times [4.3 ± 2.8 in group I versus 4.8 ± 2 months in group II], only 1 patient in group II had an AFL recurrence.

Conclusions: Ablation of type I AFL can be performed using an 8-mm split-tip RF catheter. Requirement of less RF pulses and fluoroscopy time suggest superiority of an 8-mm split-tip electrode over a 4-mm tip electrode.

Introduction

Radiofrequency (RF) ablation of type I atrial flutter (AFL) has a high procedural success ($> 95\%$)¹⁻⁶ and a low recurrence rate ($6 - 9\%$)^{3,5,7} after documentation of bidirectional isthmus conduction (BIC) block. However, there are concerns with temperature-guided ablation using a 4-mm tip RF catheter. These include the necessity of multiple RF pulses with creation of potentially proarrhythmic “skip” lesions, extent of myocardial damage following multiple and prolonged RF pulse delivery, and long fluoroscopy and procedure times. Experimental work suggests that the lesion size is greater with an 8-mm tip RF electrode and when a parallel electrode-tissue orientation is achieved.^{8,9,10} However, to ensure tissue contact and to avoid coagulum formation, long ablation electrodes require better temperature monitoring.¹¹ The available clinical experience with the use of a long tip RF electrode for AFL ablation is mostly observational.^{1,2,4,5,12,13} In the present study a new catheter design, an 8-mm split-tip electrode with 2 integrated thermocouples, allowing independent temperature monitoring (Cerablate[®]plus Flutter, Dr. Osypka GmbH, Grenzach-Wyhlen, Germany), was evaluated in a prospective randomized manner against a 4-mm tip electrode for ablation of type I AFL.

Methods

The clinical characteristics of 30 consecutive patients randomized to undergo ablation of the right atrial isthmus for type I AFL using either an 8-mm split-tip (group I) or a 4-mm tip (group II) RF electrode are summarized in Table 1. The concomitant atrial fibrillation was paroxysmal in 6 and persistent in 9 patients. Informed consent was obtained from every patient. Antiarrhythmic drugs were discontinued at the time of study in 4 patients from group I and in none from group II ($P = \text{NS}$). Electrophysiologic study included documentation of BIC and endocardial activation sequence during AFL.¹

The Cerablate[®]plus Flutter RF catheter consists of two 4-mm electrodes spaced 0.5mm apart such that they virtually form one 8-mm electrode if RF energy is delivered simultaneously through both electrodes (Figure 1). The dual thermocouple located on the inner side of the catheter curve monitors temperature from both electrodes. The feedback control in the RF generator takes both measured temperatures into consideration and the highest of the 2 temperatures “leads” the power delivery to both electrodes. The output is regulated so that power is delivered equally to both electrodes and that none of the 2 temperatures should exceed the target temperature significantly.

Table 1. Baseline Characteristics of 30 Patients Randomized to Radiofrequency Ablation using either an 8-mm Split-tip (group I) or a 4-mm Tip (group II) Ablation Electrode.

	Group I (n = 15)	Group II (n = 15)	P
Age, y	54 ± 7	58 ± 10	NS
Male /Female, n/n	14/1	14/1	NS
Structural heart disease, n (%)	7 (47)	3 (20)	NS
Left atrial size, cm	5 ± 0.2	4.5 ± 0.5	0.001
Left ventricular ejection fraction < 50%, n	1	1	NS
Symptom duration, y	10 ± 11	5.4 ± 3.7	NS
No. of failed antiarrhythmic drugs (median), n	2	2	
Concomitant atrial fibrillation, n (%)	7 (47)	8 (53)	NS

Patients from group I underwent ablation of the right atrial isthmus using an 8-mm split-tip ablation catheter. For patients randomized to group II, the same catheter was used as a 4-mm tip electrode by disconnecting the proximal electrode from energy delivery. Each RF pulse was delivered for 90 seconds with a preset temperature of 55°C, 70 W as the cut off limit for power delivery and in unipolar mode. A HAT300Smart (Dr. Osypka GmbH, Grenzach-Wyhlen, Germany), 500kHz RF generator was used. A linear ablation of either posterior and/or septal right atrial isthmus was performed by delivering RF pulses point-by-point at sequential sites. Temperature, power and impedance curves from the RF generator were displayed in real time and guided optimal orientation of the RF catheter to obtain adequate electrode-tissue contact (Figure 2). Noninducibility of AFL (with 3 atrial extra-stimuli and incremental pacing up to 200 ms) after demonstration of BIC block,¹ the endpoint of procedure was also assessed following isoproterenol infusion (1–3 µg/min).^{6,14} Bidirectional isthmus conduction block was defined by observing reversal in activation sequence of the lateral right atrial wall during proximal coronary sinus pacing and craniocaudal activation of the atrial septum with activation of the proximal coronary sinus after His bundle activation during low lateral right atrial pacing. Fluoroscopy time was calculated as the total fluoroscopy time from first RF pulse to completion of the ablation procedure.

Patients were followed in the arrhythmia clinic and Holter recordings were performed at 8 weeks and subsequently at 3-month intervals. Antiarrhythmic drug therapy was continued after successful RF ablation in patients with concomitant atrial fibrillation (n = 15) and was stopped in patients with isolated AFL (n = 15).⁶

Figure 1. The Cerablate[®] plus Flutter is an 8-mm split-tip steerable radiofrequency ablation and mapping catheter with 2 integrated thermocouples. The thermocouple, either distal or proximal, that records the highest temperature controls the power delivered. The energy is delivered through both electrodes simultaneously. Bipolar electrograms are recorded from the 2 distal 4-mm electrodes.

Figure 2. The value of dual thermocouples, distal (T1) and proximal (T2), in the 8-mm split-tip electrode to guide a maximal tissue-electrode contact. The graph shows the temperature (T1 in blue and T2 in pink color), power (in red color) and impedance (in yellow color) curves obtained during radiofrequency ablation using an 8-mm split-tip Cerablate[®] plus Flutter catheter. Left half of the graph shows that the preset temperature (55°C) is achieved in the distal thermocouple (T1) but not in the proximal thermocouple (T2) suggesting an oblique orientation of the electrode with respect to the ablation site. On repositioning the ablation catheter, as seen on the right half of the graph, the preset temperature (55°C) was reached in both the thermocouples (T1 and T2). This suggests a parallel orientation of the electrode with tissue contact along its entire length.

All data are expressed as mean $\pm$ S.D, median and range. Mean values were compared by ANOVA and χ^2 (or Fisher's exact) test was used for testing homogeneity in contingency tables. Results were considered to be significant at 5% critical level ($P < 0.05$).

Results

Table 2 compares the procedural variables in 2 study groups. Before RF ablation, AFL was not inducible in 10 patients. In the remaining 20 patients, a counterclockwise AFL was predominantly observed.

After RF ablation, noninducibility and BIC block were verified under isoproterenol infusion in all patients, except in 3 patients from group II. In the latter 3 patients, isoproterenol was not used because of sustained AF induced inadvertently earlier during the procedure, which required external cardioversion. However, persistence of BIC block was confirmed at least $\frac{1}{2}$ hour after delivery of the last RF pulse in each of these 3 patients. Before achieving procedural success, a reversal of BIC block under isoproterenol infusion occurred in 4 patients (3 patients in group I and 1 patient in group II) and required additional RF pulses. The acute success rate at the completion of the procedure was 100% for group I and 93% for group II. A significantly fewer number of RF pulses [12 ± 3.5 (median 11) in group I vs 27 ± 9 (median 23) in group II, $P < 0.0001$] were required to achieve success when using an 8-mm split-tip catheter. Also, the mean fluoroscopy time (23 ± 13 min in group I vs 45 ± 28 min in group II, $P = 0.01$) was shorter when ablation was performed using an 8-mm split-tip catheter. However, the mean procedure time remained comparable in both groups. There were no procedure-related complications.

Biophysical parameters recorded during the RF ablation procedure in both groups are presented in Table 3. A preset temperature (55°C) was achieved using both electrode sizes. A higher mean power (group I, 44 ± 15 W vs group II, 26 ± 11 W, $P < 0.0001$) and a lower mean impedance (group I, $72 \pm 4 \Omega$ vs group II, $97 \pm 7 \Omega$, $P < 0.0001$) was noted with the 8-mm split-tip RF catheter, and no audible "pop" or carbonization of the catheter tip occurred. In 2 patients carbonization of the ablation electrode was noted while using a 4-mm tip ablation electrode.

A comparable mean follow-up was available in both groups (group I, 4.3 ± 2.8 and group II, 4.8 ± 2 months, $P = \text{NS}$). Antiarrhythmic drugs were continued in all patients with a concomitant atrial fibrillation, except 1. No patient in group I had an AFL recurrence. One patient in group II had recurrence of AFL at 5 months after RF ablation. Successful re-ablation required 7 RF pulses using an 8-mm split-tip catheter.

Table 2. Results of Electrophysiology Study and Radiofrequency Ablation Procedure Comparing the Use of an 8-mm Split-tip (group I) and a 4-mm tip (group II) Ablation Electrode.

	Group I (n = 15)	Group II (n = 15)	P
Initial rhythm during the study, n (%)			
Incessant AFL	5 (33)	7 (47)	NS
Sinus	10 (67)	8 (53)	
AFL induced, n	5	3	NS
AFL cycle length, ms	232 ± 34	264 ± 25	0.007
Rotation of AFL:			
Documented [counterclockwise/clockwise], n/n	10 [10/0]	10 [9/2]	NS
Not documented, n (%)	5 (33)	5 (33)	
Rhythm during radiofrequency ablation, n (%)			
Coronary sinus pacing	8 (53)	10 (67)	NS
AFL	3 (20)	4 (27)	
Both	4 (27)	1 (6)	
Right atrial isthmus ablated, n (%)			
Posterior	11 (73)	12 (80)	NS
Septal	2 (13.5)	0	
Both	2 (13.5)	3 (20)	
Acute procedural success, n (%)	15 (100)	14 (93)	NS
Radiofrequency pulses/ procedure, n			
Mean	12 ± 3.5	27 ± 9	<0.0001
Median	11	23	
Range	(5 – 22)	(15 – 42)	
Procedure time (min)	162 ± 35	179 ± 48	NS
Fluoroscopy time (min)	23 ± 13	45 ± 28	0.01

Table 3. Biophysical Data Comparing the Use of an 8-mm Split-tip (group I) and a 4-mm Tip (group II) Ablation electrode.

	Group I (n = 15)	Group II (n = 15)	P
Mean power, W	44 ± 15	26 ± 11	<0.0001
Mean impedance, Ω	72 ± 4	97 ± 7	<0.0001
Mean total energy, W-sec	55,780 ± 23,137	51,477 ± 21,768	NS

Discussion

We evaluated in a randomized study the use of an 8-mm split-tip steerable RF ablation catheter incorporating dual thermocouples (Cerablate[®] *plus Flutter*, Dr. Osypka GmbH) for ablation of type I AFL and compared the results to ablation using a 4-mm tip catheter. Ablation of the right atrial isthmus was performed using a 90-second RF pulse delivered point-by-point at sequential sites with a preset temperature of 55°C. Noninducibility of AFL and BIC block under isoproterenol infusion was used to document procedural success. When compared with ablation using a 4-mm tip catheter, an equally high procedural success could be achieved with the 8-mm split-tip catheter. These results compare favorably with the previously reported small nonrandomized experience using long tip ablation catheters (6-, 8- or 10-mm).^{1,2,4,5,12,13} When compared with the 4-mm tip catheter, a higher mean power and a lower mean impedance were recorded using the 8-mm split-tip catheter. This is in accordance with information from experimental studies where a direct relation of electrode surface area to mean power and an inverse relation to mean impedance was shown.⁸

In contrast to the 4-mm electrode, successful right atrial isthmus ablation using the 8-mm split-tip electrode required significantly less RF pulses and shorter mean fluoroscopy time. In studies reporting > 98% acute success, as judged by the demonstration of BIC block, varying number of RF pulses were required: median 6 (9 ± 7) by Poty et al,¹ median 3 (5.8 ± 5.5 , range 1 - 21) by Nakagawa et al,² 8 ± 5 (range, 2 - 43) by Schumacher et al,³ 2.3 ± 0.8 (range, 1 - 4) by Iesaka et al,⁴ median 12 (14 ± 8) by Paydak et al,⁵ and 6 ± 3 by Tai et al.⁷ Although the method of RF ablation, cited in these reports, was anatomical and directed at obtaining a line of BIC block, the technique of delivering sequential RF pulses differed. The sequential delivery of RF applications has been variously described as; “progressively withdrawn with sequential stops”,¹ “a single continuous application”,² “linear drag”,³ “sequential lesions with stepwise withdrawal”,⁵ and “continuous application during pull back of catheter”.⁷ Furthermore, a 4-, 6- or 8-mm tip RF catheter was used.^{1-6,12,13} The ablation parameters were not uniform; energy was delivered in a power mode (30 to 60 W)^{1,2,4,5} or temperature mode (with a high preset temperature, 70°C)^{1,3,7} mode, with differing duration of the individual RF pulse (15 to 120 seconds).^{1-5,7} Unlike the previous studies,^{1-5,7} isoproterenol was used to determine acute procedural success in this study. These differences in methodology may have an important influence on the count of RF pulses required for procedural success and therefore a comparison of the present study with those previously reported is invalid.

Conclusion

Linear ablation of the right atrial isthmus can be performed using an 8-mm split-tip RF catheter with an high success rate comparable to a 4-mm tip RF catheter. However, fewer RF pulses and shorter fluoroscopy time supports preference of an 8-mm split-tip RF catheter over a 4-mm tip RF catheter for ablation of type I AFL.

References

1. Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter: further insights into the various types of isthmus block: application to ablation during sinus rhythm. *Circulation* 1996;94:3204-3213.
2. Nakagawa H, Lazzara R, Khastagir T, Beckman K, McClelland JH, Imai S, Pitha JV, Becker AE, Arruda M, Gonzalez MD, Widman LE, Rome M, Neuhauser J, Wang X, Calame J, Goudeau MD, Jackman WM. Role of tricuspid annulus and the eustachian valve/ridge on atrial flutter. Relevance to catheter ablation of the septal isthmus and a new technique for rapid identification of ablation success. *Circulation* 1996;94:407-424.
3. Schumacher B, Pfeiffer D, Tebbenjohanns J, Lewalter T, Jung W, Lüderitz B. Acute and long-term effects of consecutive radiofrequency applications on conduction properties of the subeustachian isthmus in type I atrial flutter. *J Cardiovasc Electrophysiol* 1998;9:152-163.
4. Iesaka Y, Takahashi A, Goya M, Yamane T, Tokunaga T, Amemiya H, Fujiwara H, Nitta J, Nogami A, Aonuma K, Hiroe M, Marumo F, Hiraoka M. High energy radiofrequency catheter ablation for common atrial flutter targeting the isthmus between the inferior vena- cava and tricuspid valve annulus using a super long tip electrode. *Pacing Clin Electrophysiol* 1998;21:401-409.
5. Paydak H, Kall JG, Burke MC, Rubenstein D, Kopp DE, Verdino RJ, Wilber DJ. Atrial fibrillation after radiofrequency ablation of type I atrial flutter. Time to onset, determinants and clinical course. *Circulation* 1998;94:3204-3213.
6. Nabar A, Rodriguez LM, Timmermans C, vd Dool A, Smeets JLRM, Wellens HJJ. Effect of right atrial isthmus ablation on the occurrence of atrial fibrillation: observations in four patient groups having type I atrial flutter with or without associated atrial fibrillation. *Circulation* 1999;11:1441-1445.
7. Tai CT, Chen SA, Chiang CE, Lee SH, Wen ZC, Huang JL, Chen YJ, Yu WC, Feng AN, Lin YJ, Ding YA, Chang MS. Long-term outcome of radiofrequency catheter ablation for typical atrial flutter: risk prediction of recurrent arrhythmias. *J Cardiovasc Electrophysiol* 1998;9:115-121.

8. Langberg JJ, Gallagher M, Strickberger A, Amirana O. Temperature-guided radiofrequency catheter ablation with very large distal electrodes. *Circulation* 1993;88:245-249.
9. Otomo K, Yamanashi WS, Tondo C, Antz M, Bussey J, Pitha JV, Arruda M, Nakagawa H, Wittkampf FHM, Lazzara R, Jackman WM. Why a large tip electrode makes a deeper radiofrequency lesion: Effects of increase in electrode cooling and electrode-tissue interface area. *J Cardiovasc Electrophysiol* 1998;9:47-54.
10. Chugh SS, Chan RC, Johnson SB, Packer DL. Catheter tip orientation affects radiofrequency ablation size in the canine ventricle. *Pacing Clin Electrophysiol* 1999;22:413-420.
11. McRury ID, Panescu D, Mitchell M, Haines D. Nonuniform heating during radiofrequency catheter ablation with long electrodes. Monitoring the edge effect. *Circulation* 1998;96:4057-4064.
12. Phillipon F, Plumb VJ, Epstein A, Kay GN. The risk of atrial fibrillation following radiofrequency catheter ablation of atrial flutter. *Circulation* 1995;92:430-435.
13. Lesh MD, van Hare GF, Epstein LM, Fitzpatrick AP, Scheinman M, Lee RJ, Kwasman A, Grogan HC, Griffin JC. Radiofrequency catheter ablation of atrial arrhythmias. Results and mechanisms. *Circulation* 1994;89:1074-1089.
14. Nabar A, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Isoproterenol to evaluate resumption of conduction following right atrial isthmus ablation in type I atrial flutter. *Circulation* 1999;99:3286-3291.

Isoproterenol to evaluate resumption of conduction after right atrial isthmus ablation in type I atrial flutter

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ABSTRACT

Background: After radiofrequency (RF) ablation of atrial flutter (AFL) the demonstration of bidirectional isthmus conduction (BIC) block is considered the hallmark of a successful procedure. The purpose of our study was to test the persistence of BIC block after isoproterenol administration and to evaluate the importance of this finding with regard to AFL recurrences.

Methods: Radiofrequency ablation of AFL was performed in 44 consecutive patients with type I AFL by a linear ablation of the posterior isthmus ($n = 29$ patients), septal isthmus ($n = 4$ patients), or both right atrial (RA) isthmi ($n = 11$ patients). The procedural end point was complete BIC block and noninducibility of AFL. In case of noninducibility and apparent BIC block, the pacing protocol was repeated under isoproterenol infusion (1 to 3 $\mu\text{g}/\text{min}$).

Results: Reversal of apparent BIC block occurred in 7 (15.9%) of 44 patients. Six patients had bidirectional and 1 had unidirectional resumption of isthmus conduction. Counterclockwise AFL could be reinduced in 4 of these patients. Two to 24 (median, 4) additional RF applications were required to achieve a permanent BIC block. At a mean follow-up of 7.3 ± 7.6 months (range, 2 to 31 months), 2 (4.5%) of 44 patients had AFL recurrences.

Conclusions: Partial linear RF ablation could possibly aggravate the preexisting nonuniform anisotropic conduction in the RA isthmus, resulting in profound conduction slowing and apparent BIC block. Isoproterenol can unmask apparent BIC block, thus providing an opportunity to assess the possibility of reversal of BIC block and completeness of isthmus ablation during the same procedure. The low incidence (4.5%) of AFL recurrences at follow-up suggests that noninducibility and BIC block under isoproterenol infusion may be a better endpoint for successful AFL ablation.

Introduction

Linear ablation of the right atrial (RA) isthmus is an effective and curative therapy for type I atrial flutter (AFL).¹ Presently, complete elimination of bidirectional isthmus conduction (BIC) is accepted as the best marker of long-term success.^{1,2} Atrial flutter recurrences are associated with failure to achieve complete BIC block at conclusion of the ablation procedure.³ Repeat electrophysiologic studies in patients with an AFL recurrence show regression or complete disappearance of isthmus conduction block.² Therefore, certainty of presence of permanent complete BIC block is essential. Use of isoproterenol in evaluating success, defined as noninducibility of AFL and BIC block, after radiofrequency (RF) ablation of AFL has not been reported previously.

Methods

Forty four consecutive patients who underwent RF ablation of type I AFL for multiple symptomatic episodes were included in the study (Table 1). At the time of RF procedure, 31 patients were taking either class IC (n = 22), class III (n = 8), or combination (n = 1) antiarrhythmic drug (AAD) therapy. Fifteen (34%) of the 44 patients taking class IC therapy developed AFL while being treated for atrial fibrillation (AF), the so called class IC atrial flutter.⁴ The ablation procedure was performed with the patient in a postabsorptive state after informed written consent was obtained. Bidirectional isthmus conduction, both anterograde and retrograde, was documented (Figure 1, A and B), and AFL was induced. In every patient, including patients with class IC AFL, the atrial endocardial activation sequence was suggestive of RA macro-reentry. No entrainment studies were performed. The ablation technique involved point-by-point sequential, 90 second RF applications with the temperature preset to 55°C (Osypka HAT 300S) or 70°C (Stockert GmbH EP Shuttle generator) while the ablation catheter was progressively withdrawn across the RA isthmus under fluoroscopic guidance. A second RF application was delivered at a particular RA isthmus site unless a significant reduction in amplitude of the local atrial electrogram (< 25%) was observed. We validated BIC block by pacing alternately from the coronary sinus (CS) and low lateral RA at a 600 or 500 ms constant cycle length⁵. A retrograde isthmus conduction block was defined by an entirely craniocaudal activation of the lateral RA wall during proximal CS (CS7.8) pacing with terminal activation of the Halo1.2 bipoles and prolongation of the CS7.8 - Halo 1.2 interval (Figure 1C). An anterograde isthmus conduction block was defined by caudocranial activation of the lateral RA wall and craniocaudal activation of the atrial septum with

Figure 1. A (Pacing at CS orifice) and B (pacing at low lateral RA) represent pacing in sinus rhythm before ablation. Dual wavefront of RA activation with BIC is seen. C (Pacing at CS orifice) and D (pacing at low lateral RA) show apparent BIC block. Surface ECG lead III is shown. Intracardiac electrograms recorded include His bundle electrograms (HIS), H1.2 to H19.20 denote 10 bipoles of the duodecapolar Halo catheter positioned around the tricuspid annulus and CS1.2 to CS7.8 represent 4 bipoles of the decapolar catheter placed in the CS.

Table 1. Baseline Characteristics of the 44 Patients Studied.

Age, y	55 ± 13
Male/female, n/n	39 / 5
Mean duration of atrial flutter, y	5 ± 5.3
Additional cardiac disease	
Coronary artery disease	7
Tachycardiomyopathy	2
Status after atrial septal defect repair	1
Left atrial size, cm	4.5 ± 0.4
Number of failed AADs, median (range)	2 (1 - 6)

terminal activation of CS7.8 after activation of the His bundle during low lateral RA pacing (Figure 1D). After apparent BIC block and noninducibility of AFL was obtained, the atrial pacing protocol (up to 3 atrial extrastimuli at 3 pacing cycle lengths and incremental atrial pacing) was repeated under isoproterenol infusion (1 to 3 $\mu\text{g}/\text{min}$). In case of reinduction of AFL or resumption of isthmus conduction under isoproterenol infusion, further RF applications were delivered. The procedural endpoint was the demonstration of BIC block and noninducibility of AFL under isoproterenol infusion.

Post-ablation protocol: Twenty-four-hour Holter monitoring was done before discharge. Patients were followed up in the arrhythmia clinic at 8 and 12 weeks and thereafter at 3-month intervals. Holter recordings were performed at 8 and 12 weeks and additionally when symptoms suggested a recurrence. All patients with concomitant AF, including patients with class IC AFL, received AADs after ablation of the RA isthmus. At follow-up, depending on the incidence of AF recurrences, an attempt was made to discontinue AADs.⁶ However, patients with ablation of class IC AFL continued to receive propafenone or flecainide.⁴

Statistical analysis: All data are expressed as mean $\pm$ S.D or median and range.

Results

Electrophysiologic study and RF ablation: Details of the electrophysiological study and RF ablation procedure are summarized in Table 2. The mean AFL cycle length was 250 ± 41 ms, and a counterclockwise rotation AFL was predominantly documented. Radiofrequency applications were delivered during CS pacing ($n = 26$ patients), AFL ($n = 11$ patients), or during both ($n = 7$

Table 2. Results of Electrophysiology Study and RF Ablation in the 44 Patients Studied.

AFL cycle length, ms	250 ± 41
Rotation AFL, n	
Counterclockwise	39
Clockwise	2
Both	3
Rhythm during RFA, n	
CS pacing	26
AFL	11
Both	7
RA isthmus ablated, n	
Posterior	29
Septal	4
Both	11
RF pulses/procedure, median (range)	24 (4 - 43)
Mean fluoroscopy time, min	46 ± 20
Mean procedure time, min	192 ± 51
Mean follow-up duration, mo	7.3 ± 7.6
AFL recurrences, n (%)	2 (4.5)

patients) rhythms. Twenty-nine patients had linear ablation of the posterior isthmus. In 11 patients, additional ablation of the septal isthmus was performed. Ablation of the septal isthmus alone was done in 4 patients. In all patients, noninducibility of AFL and apparent BIC block was demonstrated.

Under isoproterenol infusion, noninducibility of AFL and BIC block persisted in 37 patients. Seven patients (15.9%) showed a reversal of BIC block. In these 7 patients, resumption of BIC under isoproterenol infusion was noted 23 ± 11 minutes after the last RF application that showed apparent BIC block. In 6 patients, resumption of isthmus conduction was bidirectional (Figure 2). In 3 of these patients, a counterclockwise AFL was reinduced, whereas short runs of clockwise AFL were induced in 2 of the other 3 patients. The remaining patient had persistent retrograde isthmus conduction block, but counterclockwise AFL could be induced, which suggests an unidirectional resumption of isthmus conduction (Figure 3). In the 4 patients with re-inducible AFL, the mean AFL cycle length prior to RF ablation was 240 ± 8 ms. The reinduced AFL was sustained but slower, with a mean cycle length of 285 ± 60 ms. Four (median) additional RF applications (range, 2 to 24) were required to obtain complete and permanent BIC block. These additional RF applications were delivered at the same RA isthmi as those resulting in apparent BIC block.

Figure 2. Recordings from the same patient as in Figure 1 obtained during pacing in sinus rhythm after isoproterenol infusion. A (Pacing at CS orifice) shows dual wave fronts of RA activation with resumption of retrograde isthmus conduction. B (Pacing at low lateral RA) also shows dual wave fronts of RA activation. Electrograms in CS9.10 and CS7.8 show double potential, whereas those in other distal CS bipoles (CS5.6, CS3.4 and CS1.2) show single-component atrial electrogram. Proximal components of atrial double potential, in CS9.10 and CS7.8, are earlier than the atrial electrogram in HIS catheter. This suggests resumption of anterograde isthmus conduction through partially ablated RA isthmus with sequential activation of the 2 proximal CS bipoles (CS9.10 and CS7.8). Distal components of atrial electrogram in CS9.10 and CS7.8, as well as atrial electrograms recorded in CS5.6, CS3.4 and CS1.2, follow atrial activation in HIS catheter and are simultaneous. This sequence suggests activation by craniocaudal wave front. Only the proximal 2 bipoles of the CS catheter (CS9.10 and CS7.8) are activated by paced impulse conducting anterogradely through the isthmus, whereas distal CS bipoles (CS5.6, CS3.4 and CS1.2) are activated by craniocaudal wave front. This suggests slow isthmus conduction in anterograde direction with faster conduction of craniocaudal wave front.

Figure 3. Example of unidirectional resumption of isthmus conduction after isoproterenol infusion. Recordings obtained during CS pacing in sinus rhythm. First 2 paced beats (430 ms interval) are last beats of the basic 10-beat drive. Note single wave front of RA activation, implying retrograde isthmus conduction block. Two extrastimuli are delivered at 300 ms and 210 ms. Second extrastimulus initiated a sustained counterclockwise AFL (cycle length, 290 ms), indicating resumption of anterograde isthmus conduction.

Procedural success was achieved in a single session in every patient after a total 24 (median; range, 4 – 43) RF applications. Mean procedure duration was 192 ± 51 minutes with a mean fluoroscopic time of 46 ± 20 minutes.

Follow-up: Follow-up (mean of 7.3 ± 7.6 ; range, 2 to 31 months) was available in all patients. At the time of the last follow-up visit, 29 patients were receiving AADs for AF recurrences. Two patients had an AFL recurrence at 3 and 7 months after the procedure, respectively, in spite of documentation of persistent BIC block under isoproterenol. During a second procedure, both patients were found to have BIC delay, suggesting regression of isthmus block. Both patients underwent a successful repeat ablation and were free of AFL recurrences at the last follow-up 8 and 10 months later, respectively.

Discussion

The RA isthmus is a slow conduction zone.⁷ The tricuspid annulus and crista terminalis are the anterior and posterior barriers of the AFL reentrant circuit that are impervious to transversal conduction.⁸ Morphological studies of the RA isthmus by Cabrera et al⁹ revealed a typical oblique orientation of the subendocardial myocardial fibers in 57% of their normal heart specimens, with a narrow zone of intersection of the subendocardial fibers in 79%. Fiber orientation and direction of excitation are important determinants of nonuniform anisotropy¹⁰ and could provide a basis for clinical AFL. The use of class IC or III AADs in 70.5% patients in the present study could have worsened the preexisting nonuniform anisotropy in the RA isthmus.¹¹ Radiofrequency energy application causes focal necrosis, which may not always be transmural considering the variation in thickness of the RA isthmus (3 to 6 mm).⁹ Microscopically, there is a loss of side-to-side connections between groups of fibers and intercellular clefts with shrinkage of contractile elements.¹² Presumably, an incomplete ablation of the RA isthmus aggravates preexisting nonuniform anisotropy and slows the conduction velocity further.¹³ The low effective conduction velocity through the RA isthmus can make it difficult to distinguish between slow conduction and conduction block.^{13,14} The decremental nature of the nonuniform anisotropic conduction is greatest at slower pacing cycle lengths,¹³ as were used (600 and 500 ms) to validate the BIC block. We believe that the initial apparent BIC block noted in 7 patients (15.9%), who showed a reversal of BIC block under isoproterenol infusion, represents profound conduction slowing in the partially ablated isthmus and not failure of impulse conduction. Both class I and III AADs are known to preferentially slow the isthmus conduction, particularly in the setting of nonuniform anisotropy,¹¹ and could have contributed to apparent BIC block in 4 patients who were taking AADs (amiodarone, sotalol, and flecainide) during the study. However, 27 (72.9%) of the 37 patients, who did not show reversal of BIC block were also taking these type of AADs. Recent studies advocate monitoring the amplitude of local electrograms at ablation site and double potentials along the ablation line.^{15,16}

Isoproterenol, via its β adrenergic stimulating action, increases the level of intracellular cyclic AMP.¹⁷ This will decrease the intercellular resistance¹⁸ and increases the rate of rise of the zero phase of the action potential,¹⁹ thereby increasing conduction velocity in the AV node, the atria, and the ventricles.²⁰ Repetition of the post ablation pacing protocol under isoproterenol (1 to 3 $\mu\text{g}/\text{min}$) infusion, at the same or faster pacing cycle lengths as at baseline, resulted in reversal of apparent BIC block in 7 (15.9%) of 44 patients. In 6 patients, there was an evidence to suggest resumption of BIC. In 3 of these 6, a counterclock-

wise AFL was reinduced, and in addition short runs of clockwise AFL were induced in 2 of the remaining 3 patients. The remaining patient had a persistent retrograde isthmus conduction block but an inducible counterclockwise AFL, suggesting an unidirectional resumption of isthmus conduction. These findings imply an improvement in velocity of impulse conduction and an increase in the safety factor for impulse propagation in the incompletely ablated isthmus. In canine myocardial tissue, isoproterenol has been shown to improve the conduction velocity in case of nonuniform anisotropy.²¹ Thus, isoproterenol can unmask an apparent BIC block by improving conduction velocity in the incompletely ablated isthmus.

After a mean follow-up of 7.3 ± 7.6 months (range, 2 to 31 months), 2 (4.5%) of 44 patients had a recurrence of AFL at 3 and 7 months after ablation, respectively. At the last follow-up, 29 patients were receiving AADs for AF recurrences. After demonstration of noninducibility of AFL and BIC block, an AFL recurrence rate of 6 to 9% is reported, with the majority of recurrences occurring within the initial 6 months after ablation.^{2,3} The low AFL recurrence rate in the present study provides evidence that demonstration of noninducibility of AFL and BIC block under isoproterenol infusion may be a better end point after RF ablation of AFL. However, the recurrence of AFL in 2 patients despite documentation of BIC block under isoproterenol indicates a small risk of reversal of BIC block over time.

Study Limitations

Our explanation of profound conduction slowing in the nonuniformly anisotropic RA isthmus after RF ablation as the cause of an apparent BIC block should be proven by detailed mapping of the RA isthmus with recordings from a closely spaced multi-polar catheter²² or by the non-fluoroscopy CARTO™ system.²³ Before isoproterenol is used, pacing close to the line of block may be attempted as another method to detect persistent slow conduction in the incompletely ablated isthmus. However, despite these efforts to validate BIC block, conduction may still persist through deeper (epicardial) fibers surviving below the ablated endocardial region. Currently, this may not be demonstrable, because methods to “check” conduction in this dimension (i.e., depth) with an adequate resolution do not exist for use in a clinical setting. During the procedure, a resumption of isthmus conduction may occur due to an improvement in conduction velocity purely as a function of time rather than isoproterenol. The time course of recovery has been reported to be within 30 minutes and sometimes 1 hour after the last RF application.^{24,25} In the present study, isoproterenol was

used soon after demonstration of an apparent BIC block, and hence this question cannot be adequately addressed. However, the resumption of BIC 23 ± 11 minutes after the last RF application suggests that use of isoproterenol immediately may provide a means to more rapidly end the study.

Conclusions

Partial linear RF ablation could possibly aggravate preexisting nonuniformly anisotropic conduction in the RA isthmus, resulting in profound slowing of conduction and apparent BIC block. Isoproterenol can unmask apparent BIC block by improving conduction in the incompletely ablated isthmus. This provides an opportunity, importantly during the same procedure, to assess an early reversal of BIC block and completeness of isthmus ablation. The low (4.5%) recurrence incidence of AFL reported in the present study suggests that noninducibility and BIC block under isoproterenol infusion may be a better endpoint of successful AFL ablation.

References

1. Poty H, Saoudi N, Aziz AA, Nair M, Letac B. Radiofrequency ablation of type I atrial flutter: prediction of late success by electrophysiological criteria. *Circulation* 1995;92:1389-1392.
2. Schumacher B, Pfeiffer D, Tebbenjohanns J, Lewalter T, Jung W, Lüderitz B. Acute and long-term effects of consecutive radiofrequency applications on conduction properties of the subeustachian isthmus in type I atrial flutter. *J Cardiovasc Electrophysiol* 1998;9:152-163.
3. Tai CT, Chen SA, Chian CE, Lee SH, Wen ZC, Huang JL, Chen YJ, Yu WC, Feng AN, Lin YJ, Ding YA, Chang MS. Long-term outcome of radiofrequency catheter ablation for typical atrial flutter: risk of prediction of recurrent arrhythmias. *J Cardiovasc Electrophysiol* 1998;9:115-121.
4. Nabar A, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Radiofrequency ablation of "class IC atrial flutter" in patients with resistant atrial fibrillation. *Am J Cardiol* 1999; 83:785-787.
5. Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter: further insights into the various types of isthmus block: application to ablation during sinus rhythm. *Circulation* 1996;94:3204-3213.
6. Nabar A, Rodriguez LM, Timmermans C, vd Dool A, Smeets JLRM, Wellens HJJ. Effect of right atrial isthmus ablation on the occurrence of atrial fibrillation: observa-

- tions in four patient groups having type I atrial flutter with or without associated atrial fibrillation. *Circulation* 1999; 99:1441-1445.
7. Olshansky B, Okumura K, Hess P, Waldo AL. Demonstration of an area of slow conduction in human atrial flutter. *J Am Coll Cardiol* 1990;16:1639-1648.
8. Olgin J, Kalman JM, Lesh MD. Conduction barriers in human atrial flutter: correlation of electrophysiology and anatomy. *J Cardiovasc Electrophysiol* 1996;7:1112-1126.
9. Cabrera JA, Sanchez-Quintana D, Ho SY, Medina A, Anderson RH. The architecture of the atrial musculature between the orifice of the inferior caval vein and the tricuspid valve: the anatomy of the isthmus. *J Cardiovasc Electrophysiol* 1998;9:1186-1195.
10. Hocini M, Loh P, Ho SY, Sanchez-Quintana D, Thibault B, de Bakker JM, Janse MJ. Anisotropic conduction in the triangle of Koch of mammalian hearts: electrophysiologic and anatomic correlations. *J Am Coll Cardiol* 1998;31:629-636.
11. Yamashita T, Inoue H, Nozaki A, Kuo TT, Usui M, Sugimoto T. Role of anisotropy in determining the selective action of antiarrhythmics in atrial flutter in dog. *Cardiovasc Res* 1992;26:244-249.
12. Tabuchi T, Okumura K, Matsunaga T, Tsunoda R, Jougasaki M, Yasue H. Linear ablation of the isthmus between the inferior vena cava and tricuspid annulus for the treatment of atrial flutter: a study in the canine atrial flutter model. *Circulation* 1995;92:1312-1319.
13. Spach MS, Daulber PC. Discontinuous anisotropic propagation. In: Rosen MR, Janse MJ, Wit AL, eds. *Cardiac Electrophysiology: A Textbook*. New York, NY: Futura Publishing Co; 1990: 517-534.
14. Dillon SM, Allesie MA, Ursell PC, Wit AL. Influence of anisotropic tissue structures on reentrant circuits in the epicardial border zone of subacute canine infarcts. *Circ Res* 1988; 65:182-206.
15. Azegami K, Satake S, Okishige K, Sasano T, Ohira H, Yamashita K. Monitoring the local electrogram at the ablation site during radiofrequency application for common atrial flutter. *Jpn Circ J* 1998;62:559-564.
16. Shah DC, Haïssaguerre M, Jaïs P, Takahashi A, Hocini M, Clémenty J. High density mapping of activation through an incomplete isthmus ablation line. *Circulation* 1999;99:211-215.
17. Jurevicius J, Fischmeister R. cAMP compartmentalization is responsible for a local activation of cardiac Ca^{+2} channels by beta-adrenergic agonists. *Proc Natl Acad Sci* 1996;43:295-299.
18. Lowenstein WR. Regulation of cell-to-cell communication by phosphorylation. *Bioch Soc Symp* 1985;50:43-58.
19. Matsuda JJ, Lee H, Shibata EF. Enhancement of rabbit cardiac sodium channels by beta-adrenergic stimulation. *Circ Res* 1992;70:199-207.
20. Szekeres L, Papp JG. Effect of adrenergic activators and inhibitors on the electrical activity of the heart. In: Szekeres L, ed. *Adrenergic activators and inhibitors*. Berlin, Germany: Springer Verlag;1980;54(pt 1):597-634.

21. Zuanetti G, Hoyt RH, Corr PB. β -adrenergic mediated influences on microscopic conduction in epicardial regions overlying infarcted myocardium. *Circ Res* 1990;67:284-302.
22. Willems S, Weiss C, Hoffmann M, Meinertz T. Simplified strategy for atrial flutter ablation using single electrode catheter for detection of functional block within the posterior isthmus. *J Am Coll Cardiol* 1998;(suppl 31):807-3.Abstract.
23. Nakagawa H, Jackman WM. Use of a three-dimensional, nonfluoroscopic mapping system for catheter ablation of typical atrial flutter. *Pacing Clin Electrophysiol* 1998;21:1279-1286.
24. Cauchemez B, Haïssaguerre M, Fischer B, Thomas O, Clémenty J, Coumel P. Electrophysiological effects of catheter ablation of the inferior vena cava - tricuspid annulus isthmus in common atrial flutter. *Circulation* 1996;93:284-294.
25. Schwartzman D, Callans DJ, Gottlieb CD, Dillon S, Movsowitz C, Marchlinski FE. Conduction block in the inferior vena caval - tricuspid valve isthmus: association with outcome of radiofrequency ablation of type I atrial flutter. *J Am Coll Cardiol* 1996;28:1519-1531.

Capture and fusion beats during atrial fibrillation and ventricular tachycardia

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ABSTRACT

Two previously unreported observations were made during an electrophysiological study in 2 patients with idiopathic ventricular tachycardia (VT). Patient 1 had an idiopathic left VT while the patient 2 had an idiopathic right ventricular outflow tract VT. Firstly, initiation of idiopathic VT by atrial fibrillation (AF) was repeatedly observed. Secondly, fusion and capture beats were noticed during simultaneous VT and AF. An explanation is given why the latter phenomenon is rarely observed.

Case report

Patient 1

A 50-year old man presented to the out-patient clinic with complaints of episodic palpitations and associated dizziness since 10 years. The 12-lead ECG during sinus rhythm showed a horizontal QRS axis (-30°) and an incomplete right bundle branch block morphology. During arrhythmia, ECG revealed a regular broad QRS tachycardia (QRS width 190 ms), cycle length of 260 ms with right bundle branch block morphology and a north-west QRS axis. Chest x-ray, echocardiography, exercise testing, signal averaged ECG and coronary angiography were normal. A diagnosis of idiopathic ventricular tachycardia (VT) originating from the left ventricle in the apico-septal region was made.¹

An electrophysiological study was performed in a post-absorptive state after obtaining an informed consent. Sotalol was stopped 1 week before the study. The baseline HV interval measured 48 ms. There was no ventriculoatrial conduction

Figure 1. 12-lead ECG with endocardial recordings from Patient 1 during electrophysiologic study showing initiation of the ventricular tachycardia (VT) by atrial fibrillation (AF). HRA: High right atrium, HIS: His bundle, RV: Right ventricle. Note the long (1140 ms) - short (450 ms) RR-cycle length sequence during AF preceding the initiation of VT.

Figure 2. 12-lead ECG from Patient 1, recorded during simultaneous VT and AF. The fifth QRS beat, both from left and from right, represents a fusion beat with different degrees of fusion.

during ventricular pacing. Sustained monomorphic VT, identical to the clinical VT, was easily induced with a single ventricular extrastimulus delivered following ventricular pacing with a basic cycle length of 600 ms. The VT could be terminated by overdrive ventricular pacing. Subsequently, sustained atrial fibrillation (AF) occurred while manipulating the catheter in right atrium and this initiated the same VT once again (Figure 1). Notably, VT initiation during AF was preceded by long followed by a short RR cycle (1140 and 450 ms respectively). Now, both the tachycardias (broad QRS-VT and AF) continued concomitantly. During simultaneous VT and AF, a few narrow QRS beats varying in QRS width with an incomplete right bundle branch morphology were seen, suggesting a fusion beat (Figure 2). Both tachycardias continued incessantly. Intravenous procainamide (500 mg) increased the VT cycle length to 280 ms but did not terminate the VT. The patient developed hemodynamic instability and was cardioverted.

Considering the difficulty in maintaining hemodynamic stability to permit VT mapping, the procedure was terminated. Radiofrequency ablation of the VT was planned at a later date.

Figure 3. 12-lead ECG with endocardial recordings from Patient 2 during electrophysiologic study showing initiation of VT by AF.

Patient 2

This 43-year old woman complained for 1 year of recurrent palpitations lasting few seconds to half an hour, 4 times associated with collapse. Physical examination was normal. The 12-lead ECG in sinus rhythm showed an intermediate QRS axis and incomplete right bundle branch block in lead V1. A regular, broad QRS tachycardia (QRS width 130 ms), with a cycle length of 380 ms, a left bundle branch block pattern and an intermediate axis was documented. Chest x-ray, echocardiography, exercise testing, Holter study and coronary angiography were normal.

During electrophysiologic study, 3 VTs with a left bundle branch block morphology and cycle lengths of 360 ms (vertical axis, R-wave transition between lead V3 and V4), 280 ms (vertical axis, R-wave transition in lead V3)

Figure 4. 12-lead ECG with endocardial recordings from Patient 2 during simultaneous VT and AF showing narrow QRS beats. Panel A, shows a capture beat. Panel B, shows a fusion beat. Note the His bundle electrogram preceding both narrow QRS beats.

and 390 ms (axis $+60^\circ$) were induced by programmed ventricular stimulation. There was 2:1 and 1:1 ventriculoatrial conduction respectively during the first 2 VT morphologies. Sustained AF occurred spontaneously and repeatedly resulted in initiation of the 3rd VT (Figure 3) after a longer RR-interval. In the presence of these simultaneously occurring tachycardias, narrow QRS beats resembling sinus QRS complexes, were intermittently observed. A His bundle electrogram, which during VT was within the QRS complex, was observed to precede the narrow QRS complex confirming a supraventricular capture of the ventricle during AF (Figure 4, Panel A). Additionally, fusion beats with a varying QRS width were noted (Figure 4, Panel B).

Discussion

These cases illustrate two uncommon findings, initiation of VT during AF and the occurrence of fusion and capture beats following atrioventricular (AV) conduction during simultaneous AF and VT.

Firstly, the initiation of VT during AF. Wellens et al., reported that in 16% of patients with a clinically documented VT, the arrhythmia could be initiated during atrial pacing.² Later, in patients with implantable defibrillator, sinus tachycardia, AF and atrial flutter have documented to be the initiating rhythm preceding appropriate shocks in ischemic VT.³ However, initiation of idiopathic VT by AF has not been reported. Atrial fibrillation provides rapid and irregular RR-intervals. Idiopathic left VT, as in patient 1, is probably based on a reentrant mechanism.¹ The mechanism of idiopathic right ventricular outflow tract tachycardia (patient 2), triggered activity versus abnormal automaticity, is still unclear.¹ A long-short RR-interval sequence during AF, as shown in figure 1, could create a unidirectional block and start reentry. In the 2nd patient, idiopathic right VT was induced by incremental atrial pacing and repeatedly by AF. In undiseased hearts with repetitive monomorphic VT, long preceding RR-intervals were found in 77% of cases.⁴ A repeated short-long pattern provided by irregular RR-intervals during AF could lead to a rapid escalation of pause dependent afterdepolarizations above a critical threshold initiating the VT. Lastly, overdrive excitation during AF leading to Ca^{+2} overloading and abnormal automaticity cannot be excluded.⁵

The second unusual observation, occurrence of supraventricular capture of the VT during AF. The ability of a supraventricular impulse to traverse the AV node, His bundle or bundle branches and to reach the ventricle depends upon 1) the antegrade AV nodal refractory period, 2) concealed antegrade conduction in the AV node, 3) the ventricular refractory period during VT, and 4) the ability during VT of retrograde invasion into the bundle branches, bundle of His and the AV node. As shown by Witkamp et al., in patients with AF ventricular pacing may prevent atrial impulses from reaching the ventricle.⁶ This suggest that during ventricular pacing in AF retrograde penetration in the bundle branches, bundle of His or the AV node usually prevents supraventricular impulses from reaching the ventricle. In the 1st patient no ventriculoatrial conduction was found during VT and ventricular pacing, not even at slow ventricular pacing rates. This may indicate inability to retrograde invasion into the conduction system. The fast VT rate with an RR-interval of 260 ms allowed only a small window of excitability in the ventricle by the captured beat. However, in the 2nd patient, 1:1 and 2:1 ventriculoatrial conduction was present during ventricular pacing and VT indicating that antegradely conducted supraventricular impulses may capture the

ventricle in patients having a capacity of ventriculoatrial conduction. Apparently not every beat of the VT penetrated retrogradely in the AV conduction system. Therefore, to be able to have capture and fusion beats during AF and VT several conditions have to be fulfilled: 1) no constant retrograde invasion into the AV conduction system, 2) a sufficiently short antegrade AV nodal refractory period limiting "concealed" AV nodal conduction and 3) a ventricular rate during VT allowing the ventricle to be excitable when the supraventricular impulse arrives in the ventricle. This explains why the phenomenon of capture and fusion beats during AF and VT is seen so rarely.

References

1. Wellens HJJ, Rodriguez LM, Smeets JLRM. Ventricular tachycardia in structurally normal hearts. In Zipes DP, Jalife J, eds: *Cardiac Electrophysiology. From Cell to Bedside*. 2nd edn. W.B.Saunders, Philadelphia, 1995:780-787.
2. Wellens HJJ, Bär FW, Farré J, Ross DL, Wiener I, Vanagt EJ. Initiation and termination of ventricular tachycardia by supraventricular stimuli. Incidence and electrophysiologic determinants as observed during programmed stimulation of the heart. *Am J Cardiol* 1980;46:576-582.
3. Marchlinski FE, Schwartzman D, Gottlieb CD, Gonzalez-Zuelgaray J, Callans DJ. Electrical events associated with arrhythmia initiation and stimulation techniques for arrhythmia prevention. In Zipes DP, Jalife J, eds: *Cardiac Electrophysiology. From Cell to Bedside*. 2nd edn. W.B.Saunders, Philadelphia, 1995, 863-877.
4. Zimmerman M, Maisonblanche P, Cauchemez B, Leclercq JF, Coumel P. Determinants of the spontaneous ectopic activity in repetitive monomorphic idiopathic ventricular tachycardia. *J Am Coll Cardiol* 1986;7:1219-1227.
5. Vassale M. Overdrive suppression and overdrive excitation. In Rosen MR, Janse MJ, Wit AL, eds: *Cardiac Electrophysiology: A Textbook*. Futura, Mount Kisco, NY, 1990;175-190.
6. Witkamp FHM, De Jongste NJL, Lie KI, Meijler FL. Effect of right ventricular pacing on ventricular rhythm during atrial fibrillation. *J Am Coll Cardiol* 1988;11:539-545.

Summary

In recent years, radiofrequency (RF) ablation of atrial flutter (AFL) and atrial fibrillation (AF) has been continuously evolving. The challenges presented include; location of the optimal target tissue, amount of target tissue requiring destruction to effect a cure, methodology and the clinical subset likely to benefit maximally. In the nineties, advances in methods of RF ablation of AFL have lead to a significant improvement in the procedural results and long-term freedom from recurrences. On going work, both in the clinical and experimental setting, provides optimism regarding the use of catheter based therapy to treat AF at least palliatively, if not definitively in every patient with AF. The present thesis has discussed some of the advances as regards current status of catheter ablation of AFL and AF.

AF is the most common arrhythmia seen in clinical practice which is sustained by multiple reentrant wavelets based on anatomic and/or functional barriers. Because of its associated morbidity and mortality, this arrhythmia is currently the focus of extensive clinical and experimental research. Multiple treatment options, both pharmacological and non-pharmacological, are being explored and as yet no single therapy is universally accepted. For the control of AF recurrences; new class III antiarrhythmic drugs (AAD) such as ibutilide and azimilide, refinements in techniques and indications for RF ablation, use of the implantable atrial defibrillator, and single- or multi-site atrial pacing are the various approaches that are currently under investigation. As no single therapeutic intervention is ideal, a combination of modalities might achieve the most optimal effect.

AFL is a macro-reentrant arrhythmia most often contained within the right atrium (RA). The isthmus of atrial tissue bordered by the inferior vena cava and tricuspid annulus forms a critical zone of slow conduction and is crucial for maintenance of reentry. In contrast to RF ablation of AF, a majority of the recent studies report a procedural success $\geq 95\%$ after ablation of type I AFL and an AFL recurrence rate of $< 10\%$. Therefore, RF ablation of type I AFL is curative and well-established, and can be recommended as the treatment of first choice.

When AADs are used intravenously or orally for AF, conversion rates between 35% and 80% are reported for restoration of sinus rhythm. However, the recurrence rate within first 6 months of achieving sinus rhythm is disappointingly high ($\approx 50 - 60\%$). Class IC agents (propafenone and flecainide) are recommended for patients with AF and no or minimal structural heart disease. Clinical and experimental studies in the human atrium have shown that in most instances AF is

an initiating arrhythmia for AFL. Although the exact incidence is not clear, the possibility of “transformation” of AF to AFL under the effects of AAD (both class I and III) is well-known. We define “**class IC atrial flutter**” as a new AFL developing in patients receiving class IC AADs for recurrent episodes of AF. The hypothesis of our study presented in **Chapter II** was, that successful RF ablation of the RA isthmus in patients with resistant AF who develop AFL while receiving class IC AAD therapy could favorably modify the “natural” course of AF. Fourteen patients (53.7 ± 13.9 years, 12 males) with daily recurrences of therapy resistant (median, 3 AADs) AF, paroxysmal ($n = 8$) or chronic persistent ($n = 6$), who developed class IC AFL (cycle length = 230 ± 28 ms) while on propafenone ($n = 9$) or flecainide ($n = 5$) therapy for a median duration of 3 months, underwent RF ablation of AFL by the anatomical approach. RF ablation was successful [AFL noninducible and bidirectional isthmus conduction (BIC) block] in 12 patients, partially successful [AFL non inducible but no BIC block] in 1 patient and failed [operated Ebstein’s anomaly] in 1 patient. All, but 1 patient continued to take class IC AAD. At a mean follow-up of 4 months (range 2 to 13 months) following successful RF ablation ($n = 13$, including 1 partial success), 9 patients were symptom free and 2 patients have had a few (1 and 4 each), short-lasting AF recurrences. Thus 11 of 13 (85%) patients improved clinically after RF ablation. The last two patients underwent successful repeat RF ablation for AFL recurrence but later had AF recurrences, albeit less frequent. RF ablation of the RA isthmus results in clinical improvement, at least short-term, in 85% of patients and provides an alternative management strategy for a subset of patients with therapy-resistant AF.

AFL and AF often coexist in the same patient. However, little attention is given to a previous history of AF in patients undergoing RF ablation for type I AFL. Further, it is not known whether elimination of AFL can modify the clinical behaviour of AF in patients who experience both these arrhythmias. Should we accept patients with documented AF for AFL ablation?

The goal of the study described in **Chapter III** was to test the hypothesis that the occurrence of AF, in at least some patients with coexisting type I AFL, is based on macro-reentry around the tricuspid valve orifice including the RA isthmus. This was done by evaluating AF recurrences following successful ablation of AFL. Eighty-two consecutive patients with type I AFL, with or without concomitant AF, underwent RF ablation of the RA isthmus by an anatomical approach. The results were analyzed in 4 groups of patients: group 1 (only AFL; 29 patients), group 2 (AFL > AF; 22 patients), group 3 (AF > AFL; 15 patients) and group 4 (class IC AFL; 16 patients). In all groups, RF ablation of type I AFL was performed with a high ($\geq 93\%$) procedural success rate. In group 1, only 2 (8%) patients had AF after (18 ± 14 months) AFL ablation. These figures were

38% (20 ± 14 months) and 86% (13 ± 8 months) in groups 2 and 3, respectively. Group 4 patients (4 ± 2 months) had a 73% freedom of AF recurrences in continuation with a class IC agent. We conclude that the low incidence of new AF during long-term follow-up after RF ablation of type I AFL makes it unlikely that RF lesions promote the development of AF. The impact of isthmus ablation on AF recurrences differs according to the clinically predominant atrial arrhythmia and suggests a possible role of the RA isthmus in the occurrence of AF in some patients. Ablation of class IC AFL in patients with therapy-resistant AF is a novel approach to management of this patient subset. Careful classification of AF patients plays a role in the selection of the site of ablation therapy.

The concept of “hybrid” therapy is that in a given patient with AF, a combination of therapeutic modalities may be useful by achieving a synergistic effect. “Organized” pattern of AF may facilitate the effects of non-pharmacological therapies, such as ablation, defibrillation and pacing. The usefulness of the “hybrid” approach (presented in Chapter II), for patients with AF who develop AFL during AAD (class IC) therapy will depend upon the improvement with regard to control of AF recurrences at long-term. A standard 12-lead ECG remains the cornerstone for clinical recognition of AFL. The aim of the study included as **Chapter IV** was 1) to describe the ECG and electrophysiologic characteristics of the so called class IC AFL and 2) to report long-term success following RA isthmus ablation, in relation to their ECG pattern during AFL. The 12-lead ECG findings during electrophysiological study, acute results of RA isthmus ablation, and long-term outcome as to AF recurrences were examined in 24 consecutive AF patients (54 ± 12 years, 19 males) who were diagnosed as developing AFL while taking propafenone ($n = 12$) or flecainide ($n = 12$). On retrospective analysis, ECG was considered suggestive of typical AFL in 13 patients (54%). The ECG was classified as atypical AFL ($n = 8$) or coarse AF ($n = 3$) in the remaining patients. On electrophysiological study, the RA isthmus conduction time was slower in lateromedial than in mediolateral direction (104 ± 32 ms versus 75 ± 34 ms, $P = 0.023$). During the study, a counterclockwise (CCW) AFL was documented in 7 out of 7 and 4 out of 5 patients having typical and atypical AFL respectively. Acute success of ablation was similar in patients with typical (92%) and atypical (100%) AFL. At long-term follow-up (13 ± 6 ; range, 6 - 26 months), continuation of AAD therapy resulted in better control of AF recurrences, in patients with typical (11 out of 13) than atypical (4 out of 8) AFL. Coarse AF ($n = 3$) persisted despite ablating the RA isthmus. At follow-up, the latter 3 patients continued to have frequent recurrences of AF. This study showed that, in patients with class IC AFL, electrocardiographically both typical and atypical AFL morphologies are seen. The AFL circuit was always located in RA and the isthmus was crucial for maintaining reentry. The best long-term

control of AF using the “hybrid” approach was obtained in patients with an AFL ECG pattern of typical AFL. Patients developing coarse AF are no candidates for this strategy.

Unfortunately, transformation to class IC AFL cannot be predicted. Furthermore, the exact incidence of AFL in patients with AF receiving IC AAD therapy and the AF subset most likely to develop this transformation needs to be defined. More data are needed regarding dose and duration of class IC therapy resulting in class IC AFL, and the risk of proarrhythmia (1:1 atrioventricular conduction during AFL) when given to ambulatory patients. Until a larger, prospective and controlled long-term experience regarding the efficacy and safety is available; this strategy, although beneficial to suppress the frequent and unpleasant symptoms of AF, cannot be regarded as established and widely applicable to all patients with AF.

Clinical experience using a long tip electrode for RF catheter ablation of type I AFL is largely observational. Therefore, in **Chapter V** we compared a new RF catheter design with an 8-mm split-tip electrode having integrated thermocouples [Cerablate[®]plus Flutter, Dr Osypka GmbH], (group I) with a 4-mm tip electrode (group II) in a prospective randomized manner. Thirty consecutive patients were randomized to group I or II. For ablation of the RA isthmus 90 second RF pulses were used at sequential sites with a preset temperature of 55°C. All patients in group I and all but 1 patient in group II underwent successful ablation. A significantly lesser number of RF pulses and a shorter mean fluoroscopy time was found using an 8-mm split-tip electrode [RF pulses 12 ± 3.5 in group I versus 27 ± 9 in group II ($P < 0.0001$), fluoroscopy time 23 ± 13 in group I versus 45 ± 28 min in group II ($P = 0.01$)]. With comparable mean follow-up times [4.3 ± 2.8 in group I versus 4.8 ± 2 months in group II], only 1 patient in group II had an AFL recurrence. Our conclusions were, that ablation of type I AFL can be performed using an 8-mm split-tip RF catheter. Requirement of less RF pulses and fluoroscopy time suggest superiority of an 8-mm split-tip electrode over a 4-mm tip electrode.

After RF ablation of AFL the demonstration of BIC block is considered the hallmark of a successful procedure. The purpose of our study presented in **Chapter VI** was to test the persistence of BIC block after isoproterenol administration and to evaluate the importance of this finding with regard to AFL recurrences. RF ablation of AFL was performed in 44 consecutive patients with type I AFL by a linear ablation of the posterior isthmus ($n = 29$ patients), septal isthmus ($n = 4$ patients), or both RA isthmi ($n = 11$ patients). The procedural end point was complete BIC block and noninducibility of AFL. In case of noninducibility and apparent BIC block, the pacing protocol was repeated under isoproterenol infusion (1 to 3 $\mu\text{g}/\text{min}$). Reversal of apparent BIC block occurred in 7 (15.9%)

of 44 patients. Six patients had bidirectional and 1 had unidirectional resumption of isthmus conduction. CCW-AFL could be reinduced in 4 of these patients. Two to 24 (median, 4) additional RF applications were required to achieve a permanent BIC block. At a mean follow-up of 7.3 ± 7.6 months (range, 2 to 31 months), 2 (4.5%) of 44 patients had AFL recurrences. Partial linear RF ablation could possibly aggravate the preexisting nonuniform anisotropic conduction in the RA isthmus, resulting in profound conduction slowing and apparent BIC block. Isoproterenol can unmask apparent BIC block, thus providing an opportunity to assess the possibility of reversal of BIC block and completeness of isthmus ablation during the same procedure. The low incidence (4.5%) of AFL recurrences at follow-up suggests that noninducibility and BIC block under isoproterenol infusion may be a better endpoint for successful AFL ablation.

Two interesting observations made in 2 patients with idiopathic left and right ventricular outflow tract ventricular tachycardias (VT), during the presence of simultaneous AF and VT are the subject of **Chapter VII**. AF repeatedly initiated the VT. The possible role of irregular RR-intervals, with reference to the known mechanism of idiopathic VT viz reentry (left VT) and triggered activity versus abnormal automaticity (right ventricular outflow tract VT), are discussed. Also, capture and fusion beats were observed during the dual tachycardias. The conditions that have to be fulfilled by the AV conduction system to permit a supraventricular capture of the ventricle when both tachycardias are incessantly present are discussed.

Samenvatting

De laatste jaren hebben nieuwe ontwikkelingen plaats gevonden op het gebied van radiofrequentie catheter ablatie (RF-ablatie) van boezemflutter en boezemfibrilleren. Belangrijke vragen hierbij zijn onder meer: waar is de plaats in het atrium waar RF-ablatie een optimaal resultaat heeft; hoeveel atriaal weefsel moet geableerd worden om de ritmestoornis onder controle te brengen; wat is de beste methodologie en welke categorie patiënten heeft er het meeste baat bij? In de negentiger jaren hebben nieuwe methodes voor RF-ablatie van boezemfibrilleren en boezemflutter geleid tot een belangrijke verbetering van het directe succespercentage en de resultaten op langere termijn. In dit proefschrift worden een aantal van deze nieuwe ontwikkelingen besproken.

Boezemfibrilleren is de meest frequent voorkomende ritmestoornis bij de mens en is gebaseerd op multiële re-entry golven op basis van anatomische en/of functionele barrières in de boezem. Vanwege de morbiditeit zoals pompfalen en thrombo-embolieën en ook de toename in mortaliteit van deze ritmestoornis vindt veel klinisch en experimenteel onderzoek plaats. Zo zijn zowel farmacologische als niet-farmacologische behandelingsmogelijkheden onderzocht. Het is daarbij duidelijk geworden dat er geen uniform succesvolle behandeling bestaat. Voor de behandeling van recidiverend boezemfibrilleren zijn momenteel de volgende nieuwe behandelwijzen in onderzoek: farmacologische therapieën met nieuwe klasse III anti-aritmica zoals ibutilide en azimilide; en niet-farmacologische therapieën zoals RF-ablatie van paroxysmaal en chronisch boezemfibrilleren, implantatie van een boezemdefibrillator en atriale stimulatie op een of meerdere plaatsen. Aangezien deze therapeutische interventies afzonderlijk niet altijd tot een succesvolle behandeling leiden, zal het meest optimale effect vaak alleen met een combinatie van therapieën bereikt kunnen worden.

De boezemflutter is een ritmestoornis die het gevolg is van een macroreentry circuit dat meestal in het rechter atrium gelokaliseerd is. Een essentieel onderdeel van het circuit is de isthmus van atriaal weefsel dat begrensd wordt door de vena cava inferior en de tricuspidaal annulus. Dit is een zone met trage geleiding en speelt een cruciale rol bij het in stand houden van reentry. RF ablatie van deze zone geeft bij boezemflutter een direct succes $\geq 95\%$ met een recidiefpercentage $< 10\%$. Derhalve is de RF-ablatie van de boezemflutter een curatieve therapie en kan dan ook aanbevolen worden als behandeling van eerste keuze bij patiënten met recidiverende aanvallen van boezemflutter. Bij intraveneuze of orale toediening van anti-aritmica bij boezemfibrilleren wordt bij 35% tot 80% van de patiënten herstel van sinusritme waargenomen. Het recidiefpercentage van

boezemfibrilleren in de 6 maanden daarna ligt echter hoog (50 - 60%). Klasse I anti-aritmica (propafenon en flecaïnide) worden aanbevolen voor patiënten met boezemfibrilleren zonder of met minimale structurele hartafwijkingen. Bij klinisch en experimenteel onderzoek bij de mens is aangetoond dat de boezemflutter in de meeste gevallen door boezemfibrilleren geïnitieerd wordt. Hoewel de exacte incidentie ervan niet duidelijk is, is het een bekend feit dat boezemfibrilleren onder invloed van anti-arrhythmica (zowel klasse I als III) tot boezemflutter kan “transformeren”. Wij spreken van “*klasse IC boezemflutter*” als de boezemflutter optreedt bij patiënten die met klasse IC anti-arrhythmica behandeld worden voor recidiverende episodes van boezemfibrilleren. De in **Hoofdstuk II** weergegeven hypothese luidde dan ook dat een geslaagde RF-ablatie van de RA-isthmus het “natuurlijk” verloop van boezemfibrilleren in gunstige zin kan modificeren bij patiënten met boezemfibrilleren bij wie zich boezemflutter ontwikkelt tijdens een behandeling met klasse IC antiarrhythmica. Veertien patiënten ($53,7 \pm 13,9$ jaar, 12 mannen) met dagelijks aanvallen van therapie-resistent boezemfibrilleren, paroxysmaal ($n = 8$) of chronisch ($n = 6$), bij wie zich een klasse IC boezemflutter (cyclus lengte = 230 ± 28 ms) ontwikkelde tijdens een behandeling met propafenon ($n = 9$) of flecaïnide ($n = 5$), ondergingen RF-ablatie van hun boezemflutter. RF-ablatie had bij 12 patiënten succes [boezemflutter niet-induceerbaar en bidirectioneel isthmus geleidingsblok]. Bij 1 patiënt was er gedeeltelijk [boezemflutter niet-induceerbaar maar geen bidirectioneel isthmus geleidingsblok] en bij 1 patiënt geen succes [een patiënt met een geopereerde anomalie van Ebstein]. Bij op één na alle patiënten werd de toediening van klasse IC anti-arrhythmica voortgezet. Bij een gemiddelde follow-up van 4 maanden (2 tot 13 maanden) na een succesvolle RF-ablatie ($n = 13$, 1 gedeeltelijk succes inbegrepen) waren 9 patiënten vrij van hun ritmestoornis en hadden 2 patiënten enkele kortdurende recidieven van boezemfibrilleren. Van de 13 patiënten waren er dus 11 (85%) klinisch verbeterd na RF-ablatie. De twee patiënten met kortdurende recidieven ondergingen met succes een tweede RF-ablatie van de rechter atrium-isthmus. Dus bij 85% van dit soort patiënten was er sprake van klinische verbetering, in ieder geval op de korte termijn, en is er dus een nieuwe behandelingsmogelijkheid voor een bepaalde categorie patiënten met therapieresistent boezemfibrilleren.

Boezemflutter en boezemfibrilleren komen vaak samen voor bij één patiënt. Er wordt echter weinig aandacht geschonken aan het optreden van boezemfibrilleren bij patiënten die RF-ablatie ondergaan voor een boezemflutter. Voorts is het niet bekend of ablatie van de boezemflutter een modificerend effect heeft op de hoeveelheid aanvallen van boezemfibrilleren bij patiënten met een combinatie van deze ritmestoornissen. De vraag is dus of wij patiënten voor boezemflutter-ablatie moeten accepteren bij wie ook boezemfibrilleren is geregistreerd.

In **Hoofdstuk III** werd de hypothese getest dat boezemfibrilleren zou kunnen optreden bij patiënten met boezemflutter, op basis van macro-reentry rond de tricuspidaal annulus met inbegrip van de rechter atrium-isthmus. Deze hypothese werd getest door het optreden van recidieven van boezemfibrilleren na een met succes uitgevoerde boezemflutter-ablatie te evalueren. Tweeëntachtig opeenvolgende patiënten met boezemflutter, al of niet met gedocumenteerde aanvallen van boezemfibrilleren, ondergingen RF-ablatie van de rechter boezem-isthmus. De resultaten werden in 4 groepen van patiënten geanalyseerd: groep 1 (uitsluitend documentatie van boezemflutter; 29 patiënten), groep 2 (meer aanvallen van boezemflutter dan boezemfibrilleren; 22 patiënten), groep 3 (meer aanvallen van boezemfibrilleren dan boezemflutter; 15 patiënten) en groep 4 (klasse IC boezemflutter; 16 patiënten). In alle groepen had RF-ablatie van de boezemflutter een hoog ($\geq 93\%$) succespercentage. In groep 1 ontstond bij slechts 2 patiënten (8%) boezemfibrilleren na 18 ± 14 maanden. In beide gevallen na hartchirurgie. In de groepen 2 en 3, bedroegen deze cijfers respectievelijk 38% (20 ± 14 maanden) en 86% (13 ± 8 maanden). Bij de patiënten van groep 4 bleef 73% (4 ± 2 maanden) vrij van boezemfibrilleren-recidieven bij verdere toediening van een klasse IC anti-aritmicum. De conclusie is dat, gezien de lage incidentie van nieuwe boezemfibrilleer-episoden tijdens een lange-termijn follow-up na RF-ablatie van patiënten met alleen boezemflutter, het onwaarschijnlijk is dat RF-laesies het ontstaan van boezemfibrilleren bevorderen. Het effect van isthmus-ablatie ten aanzien van het recidiveren van boezemfibrilleren is afhankelijk of het boezemfibrilleren of de boezemflutter de meest voorkomende ritme- stoornis is. Ablatie van de klasse IC boezemflutter bij patiënten met therapie-resistent boezemfibrilleren is een nieuwe benadering in de behandeling van deze patiënten. Een zorgvuldige classificatie van patiënten met boezemfibrilleren speelt dus een rol bij de beslissing een isthmus ablatie al of niet uit te voeren.

Het concept van een “hybride” therapie berust op de gedachte dat een combinatie van farmacologische en niet-farmacologische therapeutische maatregelen bij de patiënt met boezemfibrilleren bruikbaar kan zijn. Een voorbeeld van de “hybride” benadering (zie ook Hoofdstuk II) is het uitvoeren van een isthmus ablatie bij patiënten met boezemfibrilleren bij wie zich tijdens een therapie met klasse IC anti-arrhythmica een boezemflutter ontwikkelt. De in **Hoofdstuk IV** beschreven studieopzet was om uit te zoeken of bepaalde ECG bevindingen tijdens de klasse IC boezemflutter van voorspellende waarde waren ten aanzien van het lange-termijn effect van rechter boezem-isthmus-ablatie. Daarnaast werden ook de electrofysiologische karakteristieken van de klasse IC boezemflutter bestudeerd. Dit onderzoek werd verricht bij 24 opeenvolgende patiënten (54 ± 12 jaar, 19 mannen) met boezemfibrilleren die boezemflutter ontwikkelden

tijdens een behandeling met propafenon ($n = 12$) en flecaïnide ($n = 12$). Bij retrospectieve ECG analyse werd bij 13 patiënten een klassieke boezemflutter gevonden. Bij de overige patiënten werd het ECG als atypische boezemflutter ($n = 8$) of grofslagig boezemfibrilleren ($n = 3$) geclassificeerd. Bij elektrofysiologisch onderzoek bleek de geleidingstijd van de rechter boezem-isthmus in lateromediale richting langer te zijn dan in mediolaterale richting (104 ± 32 ms versus 75 ± 34 ms, $P = 0,023$). Tijdens de studie werd er een 'counterclockwise' boezemflutter gevonden bij 7 van de 7 en 4 van de 5 patiënten met respectievelijk een typische en een atypische boezemflutter. Het onmiddellijke succes was bij patiënten met een typische (92%) en atypische (100%) boezemflutter ongeveer gelijk. Bij lange-termijn follow-up (13 ± 6 ; uitersten: 6 - 26 maanden) bleek dat continueren van de anti-aritmische therapie een gunstiger effect op het optreden van boezemfibrilleren recidieven had bij patiënten met een typische (11 van de 13) boezemflutter dan bij patiënten met een atypische (4 van de 8) boezemflutter. Grofslagig boezemfibrilleren bleef bestaan ($n = 3$) ondanks ablatie van de rechter boezem-isthmus. Bij follow-up bleek dat bij deze laatste 3 patiënten het boezemfibrilleren frequent recideerde. Deze studie heeft dus aangetoond dat er bij klasse IC boezemflutter electrocardiografisch zowel typische als atypische flutter morfologieën gezien worden. Het flutter circuit was altijd in het RA gelokaliseerd en de isthmus speelde een cruciale rol bij het in stand houden van de reentry. Met de "hybride" benadering werd boezemfibrilleren op lange termijn het beste onder controle gehouden bij patiënten met een ECG-patroon van een typische boezemflutter. Patiënten bij wie grofslagig boezemfibrilleren ontstaat na klasse IC antiarrhythmica komen niet in aanmerking voor rechter boezem-isthmus ablatie.

Transformatie van boezemfibrilleren naar klasse IC boezemflutter is helaas niet te voorspellen. Ook is de exacte incidentie hiervan niet bekend. Meer gegevens zijn nodig over dosering en duur van de klasse IC-behandeling die een dergelijke transformatie tot gevolg hebben. Ook zal bekeken moeten worden of en hoe vaak een klasse IC behandeling bij patiënten met boezemfibrilleren leidt tot pro-arrhythmieën zoals 1 op 1 atrioventriculaire geleiding.

De klinische ervaring met een lange-tip elektrode voor RF-ablatie van boezemflutter is beperkt. In **Hoofdstuk V** wordt een prospectief, gerandomiseerd onderzoek beschreven van een nieuw ontworpen RF-catheter met een 8 mm split-tip-elektrode met geïntegreerde thermokoppels [Cerablate[®] plus Flutter, Dr Osypka GmbH] (groep I) in vergelijking met een 4 mm tip-elektrode (groep II). Er werden 30 patiënten onderzocht en ingedeeld in groep I of II. Voor ablatie van de rechter boezem-isthmus werden RF-pulsen van 90 seconden gebruikt met een vooraf ingestelde temperatuur van 55°C . Bij alle patiënten uit groep I en op één na alle patiënten uit groep II werd de ablatie met succes uitgevoerd. Bij

gebruik van een 8 mm tip-elektrode werden een significant lager aantal RF-pulsen gebruikt en een kortere gemiddelde fluoroscopietijd gevonden [RF pulsen $12 \pm 3,5$ in groep I versus 27 ± 9 in groep II ($P < 0,0001$), fluoroscopietijd 23 ± 13 min. in groep I versus 45 ± 28 min. in groep II ($P = 0,01$)]. Bij een vergelijkbare gemiddelde follow-up-tijd [$4,3 \pm 2,8$ maanden in groep I versus $4,8 \pm 2$ maanden in groep II] trad bij slechts één patiënt (uit groep II) een recidief van boezemflutter op. Onze conclusie luidt dat gezien het feit dat er minder RF-pulsen en minder fluoroscopietijd nodig zijn, een 8 mm split-tip elektrode effectiever is dan een 4 mm elektrode.

Als er na RF-ablatie van boezemflutter een bidirectioneel isthmus-blok aangetoond wordt, dan wordt dat beschouwd als bewijs van een met succes uitgevoerde procedure. De in **Hoofdstuk VI** beschreven studie had als doel om na te gaan of blijvende afwezigheid van dat blok na toediening van isoproterenol van belang was om het lange termijn succes te voorspellen. Er werd bij 44 opeenvolgende patiënten met een boezemflutter een RF-ablatie uitgevoerd door middel van een lineaire ablatie van de posterior isthmus ($n = 29$ patiënten), de septale isthmus ($n = 4$ patiënten), of beide rechter boezem-isthmi ($n = 11$ patiënten). Het eindpunt van de procedure was een volledig bidirectioneel isthmus blok en de onmogelijkheid om boezemflutter te induceren. Bij niet-induceerbaarheid en een kennelijk bidirectioneel isthmus-blok werd het stimulatieprotocol herhaald maar nu onder een isoproterenol-infusie (1 tot 3 $\mu\text{g}/\text{min}$). Bij 7 (15,9%) van de 44 patiënten verdween het bidirectioneel isthmus-blok. Bij 6 patiënten kwam bidirectionele en bij 1 patiënt unidirectionele isthmusgeleiding terug. Bij 4 van deze patiënten kon toen opnieuw een boezemflutter geïnduceerd worden. Er waren 2 tot 24 (mediaan: 4) extra RF-applicaties nodig om een blijvend bidirectioneel isthmus-blok te bereiken. Bij een gemiddelde follow-up van $7,3 \pm 7,6$ maanden (uitersten: 2 en 31 maanden) trad er bij 2 (4,5%) van de 44 patiënten een recidief van de boezemflutter op. Partiële lineaire RF-ablatie heeft de preëxistente non-uniforme anisotrope geleiding in de rechter atrium-isthmus mogelijk verergerd, hetgeen resulteerde in een ernstige geleidingsvertraging en een ogenschijnlijk bidirectioneel isthmus-blok. Met isoproterenol kan dit ontmaskerd worden, waarna tijdens dezelfde procedure door herhaalde RF ablatie een volledig bidirectioneel isthmus blok kan worden bereikt. De lage incidentie (4,5%) van boezemflutter recidieven bij de follow-up duidt erop dat niet-induceerbaarheid en een bidirectioneel isthmus-blok onder isoproterenol-infusie een goed eindpunt is voor een succesvolle boezemflutter-ablatie.

Twee interessante waarnemingen bij 2 patiënten met respectievelijk een idiopathische linker en een idiopathische rechter kamertachycardie vormen de inhoud van **Hoofdstuk VII**. Bij beide patiënten was er sprake van gelijktijdig

optreden van de kamertachycardie en boezemfibrilleren. De kamertachycardie werd herhaaldelijk door het boezemfibrilleren geïnitieerd. Het mechanisme hiervan, met name de rol van het wisselende R-R interval tijdens boezemfibrilleren, wordt besproken. Tijdens het gelijktijdig bestaan van de twee tachycardiën werden capture en fusion beats waargenomen. Er wordt aangegeven aan welke voorwaarden het AV-geleidingssysteem moet voldoen wil supraventriculaire capture van de ventrikel mogelijk zijn tijdens deze situatie.

सारंश

नब्ज (हृदय की धड़कन) तेज़ होने के कई कारण हैं। इन कारणोंमें शामिल हैं, एट्रियल फ़िब्रिलेशन (atrial fibrillation, AF) और एट्रियल फ्लटर (atrial flutter, AFL)। पिछले कुछ सालोंमें, इन दोनों ही कारणोंकी रेडिओफ्रिक्वेन्सी अब्लेशन (radiofrequency ablation, RFA) चिकित्सा पद्धती में निरंतर प्रगती हो रही है। फिर भी, इस उपचार पद्धती से संबंधित कई प्रश्न अभी भी अनुत्तरित हैं, जैसे कि: हृदय का वह कौन सा भाग इस चिकित्सा पद्धती के लिए सही लक्ष्य होगा, इस लक्ष्य को अब्लेट करने की कौनसी विधि सर्वोत्तम मानी जा सकती है, तथा AFL और AF के किन मरीजोंको इस चिकित्सा पद्धती का सबसे अधिक लाभ होगा? इस विषय को लेकर आयुर्विज्ञान में जो प्रगती हो रही है, उससे ऐसा प्रतीत होता है कि, आने वाले वर्षोंमें RFA चिकित्सा पद्धती से AF के कुछ मरीजोंको काफी हद तक लाभ पहुँच सकता है। यही प्रस्तुत प्रबंध का विषय है।

AF, यह नब्ज के तेज़ होने का एक आम कारण भी है। ऐसा माना जाता है कि, हृदय में इसका उत्पन्न होना, एट्रिया (atria) के भीतर, एक ही समय, अनेक तरंगोंके घुमते रहने पर (random reentry of multiple wavelets) निर्भर है। AF के कारण, शरीरमें अन्य दुष्परिणाम संभव हैं। इसलिए, इन दिनों, इस विषय को लेकर काफी शोधकार्य हो रहा है। नयी उपचार पद्धतियों में संमिलित है: नयी वर्ग 3 अंटीअरिदमिक् औषधियाँ (antiarrhythmic drugs, AAD) जैसे कि आयबुटिलाइड (ibutilide) और अज़िमिलाइड (azimilide), RFA चिकित्सा के नये तरीके, हृदय में लगाया जाने वाला एट्रियल डिफ़िब्रिलेटर उपकरण (implantable atrial defibrillator) तथा एक- अथवा अनेक- स्थानों से एट्रियल पेसिंग (single- or multi-site atrial pacing)। क्योंकि, इनमेंसे कोईभी एक उपचार पद्धती, AF के सभी तरह के मरीजोंके लिए योग्य नहीं है, यह संभव है कि, एकसे अधिक पद्धतियोंका प्रयोग करना उचित होगा।

AFL दाहिने एट्रियम (right atrium) में एक बड़े तरंग (macro-reentrant wave) के घुमते रहने से उत्पन्न होता है। दाहिने एट्रियम के इस्थमस् (isthmus) की सीमाएँ, इन्फ़ीरियर विना कावा (inferior vena cava) एवं ट्रायकस्पिड अंन्युलस (tricuspid annulus) द्वारा बनती हैं। इन्ही सीमाओं के मध्य, AFL के इस बड़े तरंग की गती धीमी होती है, तथा इस पर AFL का जारी रहना निर्भर है। RFA चिकित्सा पद्धती द्वारा, AFL को रोकने के लिए इसी जगह (इस्थमस्) को अब्लेट किया जाता है। प्रकार 1 AFL (type I AFL) के RFA की सफलता का दर ९५% से भी अधिक है, एवं AFL के पुनः उत्पन्न होनेकी संभावना १०% से भी कम है। AF के RFA के मुकाबले में, AFL के RFA की सफलता का दर बहुत अधिक है। अतः केवल AFL से परेशान मरीजोंके लिए RFA चिकित्सा पद्धती का प्रयोग निःसंदेह किया जाना चाहिए।

३५% से ८०% AF के मरीजोंकी धड़कन को दवाईयोंके इलाज से पुनः ठीक किया जा सकता है। परंतु, इस विषय में निराशाजनक बात यह है कि, ६ मास के अंदर, लगभग ५०% से ६०% मरीजोंमें, दवाईयाँ लेने के बावजूद, पुनः AF का दौरा पड़ सकता है। AF के औषधी इलाज में, वर्ग 1 सी संमिलित (class IC) AADs {जैसे कि प्रोपाफ़ेनॉन, (propafenone) और फ्लेकनाईड (flecainide)} को प्राधान्य दिया गया है। वर्ग 2 सी संमिलित AADs से उपचार के दौरान, कई बार, AF का AFL में परिवर्तन देखा गया है। परंतु, इस बात की निश्चित संभावना कितनी है, यह अभी स्पष्ट नहीं है। हमने, इस परिवर्तित नये AFL को पहचानने के लिए, वर्ग 2 सी AFL (class IC atrial flutter), इस नई परिभाषा को अपनाया है।

इस प्रबंधक के द्वितीय अध्याय में, हमने, दवाईयों के बावजूद AF से पीड़ित उन १४ मरीजों की (उम्र: 53.6 ± 9.3 वर्ष, १२ पुरुष) जानकारी प्रस्तुत की है, जिन में, वर्ग १ सी संमिलित औषधों का प्रयोग करते हुए (प्रोपाफिनॉन = ९ मरीज, फ्लेकनाईड = ५ मरीज), AF का AFL में "परिवर्तन" पाया गया। AFL को पहचानने के बाद (वर्ग १ सी AFL की गति = 230 ± 22 मि.से), RFA पद्धति का उपयोग किया गया। देखना यह था कि, क्या AFL के RFA के पश्चात वर्ग १ सी दवाईयाँ लेते रहने पर, इन मरीजों को AF की परेशानी से राहत मिल सकती है? RFA चिकित्सा १२ मरीजों में पूरी तरह सफल रही, एक और मरीज में आंशिक रूप से (अधिकतर) सफल रही, किंतु बचे हुए एक मरीज में यह चिकित्सा असफल मानी गयी। RFA चिकित्सा के उपरांत, १ मरीज को छोड़कर, बाकी सभी मरीज वर्ग १ सी AAD ले रहे थे। औसतन ४ माह के पश्चात, जिन १३ मरीजों में RFA चिकित्सा कामयाब रही, उनमें से ९ मरीज, AF तथा AFL के प्राकृतिक परिणामों से पूरी तरह मुक्त थे। दो और मरीजों को, सिर्फ कुछ बार (१ और ४) AF के दौर पड़े। परिणाम स्वरूप, इस मिश्र चिकित्सा प्रणाली का लाभ, इनमें से ८५% मरीजों को पहुँच पाया। शेष दो मरीजों को, AFL के सफल अब्लेशन के बावजूद, AFL का फिर से दौर पड़ा। इसे फिर एक बार सफलतापूर्वक अब्लेट किया गया। तब भी, इन दोनों ही मरीजों को बार-बार AF के दौरे, हालाँकी, पहले से कम दर में पड़ रहे थे। इस अनुभव के पश्चात हम इस निष्कर्ष पर पहुँचे कि, चाहे थोड़े समय के लिए ही सही, इस नवीन चिकित्सा प्रणाली का प्रयोग करने से ८५% AF से पीड़ित मरीजों को निश्चित रूप से लाभ होगा।

प्रायः, AF तथा AFL, यह जलद नाड़ी के दोनों विकार एक ही मरीज में दिखायी देते हैं। इस तरह के मरीजों में, AFL का अब्लेशन करने से, क्या हो रहे AF के दौरों पर कुछ असर पड़ेगा? इस प्रश्न की बारिकी से समीक्षा नहीं हुई है। इस प्रश्न का उत्तर पाने से यह भी निश्चित किया जा सकता है कि, क्या AFL और AF दोनों से ही पीड़ित मरीजों में, AFL अब्लेशन का प्रयोग करना उचित होगा?

अध्याय ३ इस प्रश्न को लेकर है कि, वे मरीज जो AF के साथ-साथ प्रकार १ AFL का अनुभव करते हैं, क्या उनमें AF की तरंगें इस्थमस् (दाहिने एट्रियम में) पर निर्भर हैं? हमने, इस प्रश्न का उत्तर पाने के लिए, AFL (प्रकार १) के सफल अब्लेशन के बाद हो रहे AF के दर को परखा। परिणाम का विश्लेषण करते हुए, ८२ मरीजों को निम्नलिखित ४ वर्गों में बाँटा गया:-

वर्ग १ : केवल AFL से परेशान (२५ मरीज),

वर्ग २ : अधिक AFL और कम AF (२२ मरीज),

वर्ग ३ : अधिक AF और कम AFL (१५ मरीज) एवं

वर्ग ४ : वर्ग १ सी AFL (१६ मरीज)।

AFL के अब्लेशन की सफलता सभी वर्गों में उत्तम थी ($\geq ९३\%$)। अब्लेशन के उपरांत, वर्ग १ में केवल २ मरीजों को (८%, १८ ± १४ माह के भीतर) नये AF का अनुभव हुआ। वर्ग २ तथा ३ में क्रमशः ३८% (२० ± १४ माह के भीतर) और ८६% (१३ ± ८ माह के भीतर) मरीजों को अब्लेशन के बाद AF के दौरे पड़ रहे थे। AFL अब्लेशन के बाद, वर्ग ४ में संमिलित ७३% (४ ± २ माह के भीतर) मरीजों को AF से दोबारा शिकायत नहीं रही। इन परिणामों से ऐसा प्रतीत होता है कि, AFL अब्लेशन के कारण नवीन AF उत्पन्न होने की संभावना नहीं के बराबर है। प्रथमतः AFL तथा AF का साथ-साथ अनुभव करने वाले मरीजों में, AFL के अब्लेशन के बाद, AF के दौरों का दर कम होता है। परंतु, यह दर किस हद तक कम होगा, यह बात अब्लेशन से पहले इन मरीजों में AFL तथा AF अनुभव करने का प्रमाण क्या था, इस बात पर निर्भर है। अर्थात्, प्राकृतिक परिणामों में अधिक लाभ, प्रायः AF के दौरे कम होने वाले वर्ग (वर्ग २, $AFL > AF$) में ज्यादा है। इस जानकारी से ऐसा लगता है कि, AFL तथा AF का साथ-साथ अनुभव करने वाले मरीजों में, AF के तरंगों के कायम रहने में इस्थमस् का संभाग महत्वपूर्ण है। वर्ग १ सी AFL का अब्लेशन से इलाज, यह AF की चिकित्सा पद्धति में एक नया कदम माना जाना

चाहिए। हृदय की विशिष्ट जगह को अब्लेशन द्वारा सफलतापूर्वक इलाज का लक्ष्य बनाने के लिए AF के मरिजों का योग्य चयन करना जरूरी है।

इलाज के एक से अधिक पद्धतियों का प्रयोग करने पर, AF पर अधिक नियंत्रण पाया जा सकता है। इस इलाज पद्धती को हायब्रिड (hybrid या संकरित) चिकित्सा प्रणाली भी कह सकते हैं। अगर AF की तरंगें “नियंत्रित” (organized AF) रूप में हो तो, अब्लेशन, डिफिब्रिलेशन अथवा पेसिंग यह उपचार पद्धतियों का बेहतरीन प्रयोग किया जा सकता है। अध्याय दो में AF के इलाज के लिए योग्य, एक नयी और सफल चिकित्सा प्रणाली का विवरण किया गया है। इस तरह से इलाज करना तब ठीक होगा, जब कि, अब्लेशन चिकित्सा के उपरांत AF के दौरों पर लंबे समय के लिए नियंत्रण किया जा सके। यह बात स्पष्ट है कि, इलेक्ट्रोकार्डिओग्राम (electrocardiogram, ECG) यह AFL को जाँचने का उत्तम तरीका है। अध्याय ४ इन सवालियों को लेकर था कि : १) वर्ग १ सी AFL के ECG तथा इलेक्ट्रोफिजियोलॉजी (electrophysiology) जाँच के परिणाम क्या थे? तथा २) क्या वर्ग १ सी AFL अब्लेशन चिकित्सा प्रणाली, AF के दौरों पर लंबे समय के लिए नियंत्रण पा सकती है? इस विषय में हमने २४ मरीजों की (उम्र: 58 ± 9.2 वर्ष, १९ पुरुष) समीक्षा की। इन मरीजों में, वर्ग १ सी संमिलित AAD लेते हुए (प्रोपाफिनॉन = १२ मरीज, फ्लेकनाइड = १२ मरीज), AF का एक नये AFL में परिवर्तन देखा गया। ECG को फिर से जाँचने पर यह दिखायी दिया कि, AFL १३ मरीजों में टिपिकल (typical AFL, आम तरह का) तथा ८ मरीजों में एटिपिकल (atypical AFL, भिन्न तरह का) था। शेष ३ मरीजों में कोर्स (coarse) AF तरह का था। इस्थमस में चलन की गती (isthmus conduction time) बाहर से अंदर की दिशा में (lateromedial direction), इसके विरुद्ध दिशा से (mediolateral direction), कम (धीमी) थी (90.8 ± 3.2 मि. से मुकाबले 65 ± 3.8 मि. से, $p = 0.023$)। शायद इसीलिए, अधिकांश वर्ग १ सी AFL काँउटर क्लॉकवाइज (counterclockwise, घड़ी के विरुद्ध) दिशा में थे। सभी टिपिकल AFL तथा ५ में से ४ एटिपिकल AFL काँउटर क्लॉकवाइज थे। इन दोनों ही तरह के AFL में, अब्लेशन की सफलता उत्तम और एक सी थी (टिपिकल AFL ९२% तथा एटिपिकल AFL १००%)। अब्लेशन के बाद, लंबे समय तक (93 ± 6 , ६ - २६ महीनों तक) इन मरीजों की नियमित रूप से जाँच की गई। इस जाँच के दौरान यह देखा गया कि, टिपिकल (93 में से 99 मरीज) या एटिपिकल (8 में से 8 मरीज) वर्ग १ सी AFL को अब्लेट करने के बाद, AAD के पुनः प्रयोग से AF के दौरों पर कुछ मरीजों में ज्यादा अच्छा काबू किया जा सकता है। परंतु कोर्स AF के तीनों ही मरीजों में, AF पर काबू पाना पहले जितना ही कठिन रहा। संक्षेप में, वर्ग १ सी AFL, ECG रूप में, टिपिकल अथवा एटिपिकल हो सकता है। यह दोनों ही तरह के AFL के तरंगों का पथ (macro-reentrant circuit) दाहिने एट्रियम में स्थित है तथा इस्थमस पर निर्भर है। हायब्रिड इलाज पद्धती का प्रयोग करने से, टिपिकल प्रकार के वर्ग १ सी AFL के मरीजों में, लंबे समय तक AF के दौरों पर काबू पाया जा सकता है। यदि इन मरीजों में ECG पर कोर्स AF पहचानी जाय, तो हायब्रिड इलाज पद्धती का अवलंब नहीं करना चाहिए।

वर्ग १ सी AAD लेते हुए, AF के किन मरीजों में और कितने हद तक AFL में परिवर्तन देखा जाएगा, यह बात निश्चित नहीं है। ऊसी तरह, इस परिवर्तन को देखने से पहले, वर्ग १ सी दवाई का किस मात्रा में और कितने दिनों तक उपयोग करना जरूरी है, यह भी पूरी तरह मालूम नहीं है। यह भी जानना जरूरी है कि, क्या वर्ग १ सी AAD लेते हुए मरीजों को नब्ज की कोई अन्य समस्या उत्पन्न हो सकती है? इन प्रश्नों को मध्यनजर रखते हुए, यह स्पष्ट होना जरूरी है कि, इस इलाज प्रणाली का निश्चित लाभ, मरीजों की अधिक संख्या में तथा काफी लंबे समय के बाद कितना है?

अक्सर, AFL (प्रकार १) के RFA के लिए, ४ मि. मि लंबाई के इलेक्ट्रोड टिप कॅथेटर (electrode tip catheter) का प्रयोग होता है। ८ मि. मि. इलेक्ट्रोड टिप कॅथेटर के उपयोग से AFL का अब्लेशन इस विषय पर विधीपूर्वक अध्ययन नहीं हुआ है। इस प्रबंध के ५ वे अध्याय में, ३० मरीजों में, प्रकार १

AFL अब्लेशन के दौरान, ८ मि.मि विभाजित-टिप इलेक्ट्रोड कॅथेटर (सेराब्लेट प्लस फ्लटर, वर्ग-१) के उपयोग की तुलना ४ मि. मि इलेक्ट्रोड कॅथेटर (वर्ग २) से की गयी। AFL अब्लेशन के दौरान, इस्थमस् में, एक के पिछे एक रेडिओफ्रिक्वेन्सी पल्सेस (RF pulses) देने से अब्लेशन की रेखा बनती है। एक RF पल्सकी, हमारी, व्याख्या थी; ५५°C तापमान को लेकर, ९० सेकंद के लिए, RF energy का उपयोग। अब्लेशन चिकित्सा, वर्ग १ के सभी तथा वर्ग २ के अधिकतर (१५ में से १४ मरीज) मरीजों में सफल रही। ८ मि.मि विभाजित-टिप इलेक्ट्रोड का उपयोग करने से कम RF पल्सेस (वर्ग १ : 9.2 ± 3.5 मुकाबले वर्ग २ : 2.6 ± 1.9 ; $p < 0.0009$) और कम फ्लुरोस्कोपी समय (fluoroscopy time, वर्ग १ : 23 ± 9.3 मिनट मुकाबले वर्ग २ : 8.5 ± 2.2 मिनट; $p = 0.09$) का प्रयोग करना पड़ा। लगभग उतने ही समय के उपरांत (वर्ग १ : 8.3 ± 2.2 महीने मुकाबले वर्ग २ : 8.2 ± 2.2 महीने), केवल १ मरीज (वर्ग २) को दोबारा AFL का दौरा पड़ा। इन परिणामों से यह बात स्पष्ट है कि, AFL अब्लेशन के लिए ८ मि.मि विभाजित-टिप इलेक्ट्रोड का प्रयोग श्रेष्ठ है।

सफल AFL अब्लेशन के लिए, इस्थमस् में अब्लेशन की रेखा बनाना जरूरी है। ऐसा करने पर, इस्थमस् में, दोनों ही दिशाओं में, तरंगों का कंडक्शन (conduction, चलन) बंद होता है। इसे बायडायरेक्शनल कंडक्शन ब्लॉक (bidirectional conduction block, BIC block) कहते हैं। यही, AFL के अब्लेशन चिकित्सा का सर्वोत्तम ध्येय माना जाता है, क्योंकि ऐसा करने पर दोबारा AFL निर्माण होने की संभावना बहुत ही कम है। इसी कारण, BIC ब्लॉक का लंबे समय के लिए बने रहना जरूरी है। अध्याय ६ में हमने इस बात की परीक्षा की, क्या प्रथमतः BIC ब्लॉक साध्य होने के पश्चात, आयसोप्रोटेरेनॉल (isoproterenol) का उपयोग करने से BIC ब्लॉक कायम रहता है? और क्या, इस तरह BIC ब्लॉक कायम रहने से, आगे चलकर AFL के दोबारा होने की संभावना और भी कम हो सकती है? इस विषय को जाँचते हुए, AFL के ४४ मरीजों में; पोस्टेरियर (posterior, २९ मरीज), सेप्टल (septal, ४ मरीज) तथा दोनों ही (११ मरीज) इस्थमस् का अब्लेशन किया गया। अब्लेशन के उपरांत, इन सभी मरीजों में, AFL उत्पन्न नहीं किया जा सका, तथा BIC ब्लॉक सिद्ध था। इसके बाद आयसोप्रोटेरेनॉल (१ - ३ माइक्रोग्राम/मि.) का उपयोग किया गया। इस पर यह देखा गया कि, ४४ में से ७ मरीजों में इस्थमस् में कंडक्शन फिर शुरू हुआ (reversal of BIC block); ६ मरीजों में इस्थमस् के दोनों दिशाओं में तथा १ मरीज में सिर्फ एक दिशा में शुरू हुआ। ७ में से ४ मरीजों में, फिर एक बार, AFL उत्पन्न हुआ। BIC ब्लॉक को फिरसे हासिल करने के लिए, अतिरिक्त २ - से - २४ (मिडियन- ४) RF पल्सेस का उपयोग करना पड़ा। इसके बाद, इन सभी मरीजों की औसतन 6.3 ± 6.5 महीनों तक (१ - ३१ महीने) नियमित जाँच हुई। इस समय में, २ मरीजों को (४.५%) दोबारा AFL का दौरा हुआ। सारांश में, यह हो सकता है कि, अब्लेशन के उपरांत इस्थमस् में नॉनयुनिफॉर्म अँनआयसोट्रोपिक कंडक्शन (non-uniform anisotropic conduction) अधिक हो रहा हो। इस कारण, इस्थमस् में हो रहे बहुत ही धीमे कंडक्शन को (slow conduction), हमने, कंडक्शन का पूरी तरह बंद होना समझा। आयसोप्रोटेरेनॉल का उपयोग करने से, इस्थमस् के कंडक्शन में दोबारा शुरूवात हुई, जिसे पहचान लिया गया। इस्थमस् में कंडक्शन ब्लॉक, AFL को रोकने के लिए जरूरी है। RFA विधी के बाद आयसोप्रोटेरेनॉल का प्रयोग, BIC block को निश्चित करने के लिए जरूरी है। इस अध्ययन में, दोबारा AFL के दौरों का दर बहुत कम था, और यह बात आयसोप्रोटेरेनॉल के उपयोग को और भी महत्व देती है।

अध्याय ७ में, दो अभ्यासनीय अनुभवों का विस्तार से वर्णन किया गया है, और इस विषय की विस्तार से चर्चा की गयी है। यह अनुभव, आयडियोपथिक वेन्ट्रिक्युलर टैकिकार्डिया (idiopathic ventricular tachycardia) से पीड़ित दो मरीजों के साथ हुआ। पहला अनुभव यह था कि, दोनों ही मरीजों में इलेक्ट्रोफिजिओलॉजी परीक्षा के दौरान, वेन्ट्रिक्युलर टैकिकार्डिया की शुरूवात AF के कारण हुई। दूसरा, हृदय में वेन्ट्रिक्युलर टैकिकार्डिया और AF के साथ-साथ होने के दौरान कॅप्चर और फ्यूजन बीट्स (capture and fusion beats) देखे गये। यह दोनों ही बातें बहुत कम देखने में आती हैं, इसलिए रोचक भी हैं।

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List of Publications

Original Articles

1. **Nabar A**, Bhatia SJ, Abraham P, Mistry FP. Total and segmental colonic transit time in non-ulcer dyspepsia. *Indian J Gastroenterol* 1995;14:131-133.
2. Naik AM, **Nabar AA**, Lokhandwala YY, Kulkarni HL, Deshpande JR, Sivaraman A. Is hemorrhagic myocardial infarction more common with streptokinase? *Ind Heart J* 1997;49:387-390.
3. Ranjan A, Lokhandwala YY, Vora AM, Naik AM, **Nabar AA**. Scope and efficacy of complex radiofrequency ablation. *Ind Heart J* 1998;50:193-198.
4. Dalvi B, **Nabar A**, Goyal V, Naik A, Kulkarni H, Ramakanthan R. Transcatheter closure of patent ductus arteriosus in children weighing < 10 kg with Gianturco coils using the balloon occlusion technique. *Cathet Cardiovasc Diagn* 1998;44:303-308.
5. **Nabar A**, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Radio-frequency ablation of "class IC atrial flutter" in patients with resistant atrial fibrillation. *Am J Cardiol* 1999;83:785-787.
6. **Nabar A**, Rodriguez LM, Timmermans C, vd Dool A, Smeets JLRM, Wellens HJJ. Effect of right atrial isthmus ablation on the occurrence of atrial fibrillation : Observations in four patient groups having type I atrial flutter with or without associated atrial fibrillation. *Circulation* 1999; 99:1441-1445.
7. **Nabar A**, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Isoproterenol to evaluate resumption of conduction following right atrial isthmus ablation in type I atrial flutter. *Circulation* 1999;99: 3286-3291.
8. Timmermans C, **Nabar A**, Rodriguez LM, Ayers G, Wellens HJJ. Use of sedation during cardioversion with the implantable atrial defibrillator. *Circulation* 1999; 100:1499-1501.
9. Lokhandwala YY, Vora AM, Naik AM, **Nabar A**, Kavthale, S. Dual morphology of idiopathic ventricular tachycardia. *J Cardiovasc Electrophysiol* 1999;10:1326-1334.
10. Rodriguez LM, **Nabar A**, Timmermans C, Wellens HJJ. Should we prefer a long tip electrode to perform radiofrequency ablation of type I atrial flutter? Results of a prospective randomized study comparing an 8-mm split-tip versus a 4-mm tip ablation catheter. *Am J Cardiol* 2000; In Press.
11. **Nabar A**, Rodriguez LM, Timmermans C, van Mechelen R, Wellens HJJ. Electrocardiographic and electrophysiological findings and their importance on long-term outcome after right atrial isthmus ablation. (*submitted for publication*)

Case Reports

1. Jadhav MN, **Nabar A**, Lokhandwala Y. Electrocardiographic Diagnosis. *J of Applied Medicine*, June 1992.
2. Vora A, Kerkar P, Kulkarni H, **Nabar A**, Dalvi B. Percutaneous balloon mitral valvuloplasty by the retrograde (Babic) technique in a patient with inferior vena cava stenosis (letter to editor). *Cathet Cardiovasc Diagn* 1995;36:291-292.
3. Fulwani M, **Nabar A**, Lokhandwala YY. Blade-balloon atrial septostomy in primary pulmonary hypertension - a case report. *Ind Heart J* 1997;49:185-186.
4. Naik AM, Lokhandwala YY, **Nabar AA**, Dalvi BV. Catastrophic WPW syndrome in a 13 month child- cure by radiofrequency ablation. *Indian Pediatrics* 1997;34:931-937.
5. Naik AM, **Nabar A**, Dalvi BV. Double outlet left atrium: a case report. *Ind Heart J* 1997;49:418-420.
6. Gupta A, **Nabar A**, Lokhandwala YY. Hemorrhage resulting in isolated myocardial infarction without coronary atherosclerosis in a young lady. *Ind Heart J* 1997;49:450-451 (Letter to editor)
7. **Nabar A**, Vora A, Lokhandwala Y. Emergence of bidirectional accessory pathway conduction in adulthood. *J Cardiovasc Electrophysiol* 1998;9:648-651.
8. **Nabar A**, Rodriguez LM, Timmermans C, Kattenbeck K, Wellens HJJ. Capture and fusion beats during atrial fibrillation and ventricular tachycardia. (*submitted for publication*)

Dissertation

Nabar A, Patel KC. Total and segmental colonic transit time in non-ulcer dyspepsia. Dissertation accepted by University of Bombay for the award of MD (General Medicine), 1993.

Abstracts

1. **Nabar A**, Shah A, Karnad D, Doiphode S, Tilve GH. Effect of stopping the use of gentamicin on the sensitivity of gram negative respiratory pathogens to amikacin and gentamicin. Presented at the Xth National Conference of Respiratory diseases (*Abstract issue*) 1990.
2. Narula D, Kerkar P, Vora A, Gupta S, Banker D, **Nabar A**, Shah C, Kulkarni H. Balloon dilatation of modified Blalock-Taussig shunts. *Ind Heart J* 1994;46:220.
3. Vajifdar B, Shah C, Vora A, Kerkar P, Lokhandwala Y, Dalvi B, **Nabar A**, Banker D. Three years follow-up after percutaneous balloon pulmonary valvuloplasty. *Ind Heart J* 1994;46:226.

4. Sathe S, Vora A, Kerkar P, Lokhandwala Y, Narula D, **Nabar A**, Banker D, Kulkarni H. Radiofrequency catheter ablation for tachyarrhythmias: an initial experience. *Ind Heart J* 1994;46:226.
5. Kale P, Vora A, Kerkar P, Banker D, Kulkarni H, Gupta S, **Nabar A**, Dalvi B. Percutaneous mitral valvuloplasty in juvenile mitral stenosis: intermediate term follow-up. *Ind Heart J* 1994;46:226.
6. Gupta S, Gupta S, Pandit RB, Kerkar P, **Nabar A**, Kulkarni H, Shah C, Narula D. Magnesium and acute myocardial infarction. *Ind Heart J* 1994;46:263.
7. **Nabar A**, Bhatia SJ, Abraham P, Shah P, Mistry FP. Colonic transit time in non-ulcer dyspepsia. World Congress of Gastroenterology, Los Angeles, California, USA. (*Abstract issue*, page 1109); 1994.
8. **Nabar A**, Dalvi B, Lokhandwala Y, Vajifdar B, Goyal V, Shah P, Iyer R, Kulkarni H. Congenital anomalies of the coronary arteries - diagnosis by color Doppler echocardiography. *Ind Heart J* 1995;47:570.
9. Dalvi B, Vora A, Ramakanthan R, Bandekar V, Narula D, **Nabar A**, Shah P, Kulkarni H. Non-coronary use of stents. *Ind Heart J* 1995;47:570.
10. **Nabar A**, Iyer R, Vora A, Narula D, Banker D, Dalvi B, Kulkarni H. Aneurysms of the sinus of Valsalva. *Ind Heart J* 1995;47:570.
11. **Nabar A**, Vora A, Kerkar P, Lokhandwala Y, Dalvi B, Narula D, Kulkarni H. Transcatheter retrieval of therapeutic occlusion devices. *Ind Heart J* 1995;47:570.
12. Vora A, Sathe S, Lokhandwala Y, **Nabar A**, Narula D, Vajifdar B, Goyal V, Dalvi B, Kulkarni H. Radiofrequency ablation of accessory pathways. *Ind Heart J* 1995;47:582.
13. **Nabar A**, Dalvi B, Tendolkar A, Simha P, Shah C, Vajifdar B, Kulkarni H. Fontan circulation: a color Doppler echocardiography study. *Ind Heart J* 1995;47:583.
14. Shah P, Dalvi B, Vora A, **Nabar A**, Goyal V, Iyer R, Kulkarni H. Pulmonary venous wedge: does it correlate with pulmonary artery pressure? *Ind Heart J* 1995;47:595.
15. Dalvi B, **Nabar A**, Vora A, Banker D, Vajifdar B, Kulkarni H. Color Doppler echocardiography in evaluation of Sideris buttoned device. *Ind Heart J* 1995;47:603.
16. Shah P, Narula D, **Nabar A**, Goyal V, Vora A, Iyer R, Dalvi B. Echocardiography guided balloon atrial septostomy. *Ind Heart J* 1995;47:604.
17. Goyal V, Lokhandwala Y, Kerkar P, Banker D, Shah C, **Nabar A**, Dalvi B. Validation of echocardiography in the determination of pulmonary artery anatomy and size in cyanotic congenital heart disease. *Ind Heart J* 1995;47:619.
18. Sathe S, Lokhandwala Y, Vora A, Iyer R, Narula D, **Nabar A**, Vajifdar B, Kulkarni H. Electrophysiologic properties of the AV node after radiofrequency catheter ablation of slow pathway for AV nodal reentrant tachycardia. *Ind Heart J* 1995;47:621.
19. Vora A, **Nabar A**, Narula D, Lokhandwala Y, Banker D, Sathe S, Shah C, Iyer R. Radiofrequency catheter ablation for idiopathic ventricular tachycardia. *Ind Heart J* 1995;48:649.
20. **Nabar A**, Narula D, Rodriguez C, Soren D, Vora A, Lokhandwala Y, Dalvi B, Kulkarni H, Ghosh K, Mohanty D. Is there a prethrombotic state in left atrial blood

in rheumatic mitral stenosis? *Ind Heart J* 1996;48:552 finalist for the *Prof DP Basu memorial award* at the 48th Annual conference of the Cardiological Society of India.

21. **Nabar A**, Fulwani M, Naik A, Ranjan A, Charantimath M, Shah P, Dalvi B. Diagnosis of total anomalous pulmonary venous drainage by color Doppler echocardiography. *Ind Heart J* 1996;48:538.
22. Kerkar P, Goyal V, **Nabar A**, Jijina F, Pathare A, Naik A, Dalvi B. Hemolysis following PDA coil closure by coil embolization. *Ind Heart J* 1996;48:541.
23. Fulwani M, Narula D, Kulkarni H, Kerkar P, **Nabar A**, Vajifdar B, Dalvi B. Balloon pulmonary valvotomy in Tetralogy of Fallot: initial results. *Ind Heart J* 1996;48:542.
24. Kulkarni H, Iyer R, Narula D, Lokhandwala Y, Goyal V, Shah C, **Nabar A**. Radiofrequency ablation of atypical AV nodal reentrant tachycardia. *Ind Heart J* 1996;48:494.
25. Goyal V, Nair N, Goyal Vinay, Patel R, **Nabar A**, Kulkarni H, Dalvi B. Radionuclide lung studies following coil embolization of patent ductus arteriosus. *Ind Heart J* 1996;48:494.
26. Ghosh K, Mohanty D, Shetty S, Phillips C, Soren D, Bharucha K, **Nabar A**, Kulkarni H. Is there a prethrombotic state in left atrial blood in rheumatic mitral stenosis. At the 14th International Conference on Thrombosis, Montpellier, France. 1996.
27. **Nabar A**, Ranjan A, Vora A, Lokhandwala Y. Radiofrequency ablation - spectrum and efficacy. At the 4th Conference of the Indian College of Cardiology, (*Abstract issue*) 1997.
28. Ranjan A, **Nabar A**, Vora A, Lokhandwala YY. Complex radiofrequency ablation. Presented at the 4th Conference of the Indian College of Cardiology, (*Abstract issue*) 1997.
29. Lokhandwala Y, **Nabar A**, Iyer R. New observations during radiofrequency ablation for idiopathic ventricular tachycardia. *Pacing Clin Electrophysiol* 1997;20(Part II):2317.
30. Kerkar P, Goyal V, Khan A, Naik A, **Nabar A**, Garasia M, Ramakanthan R, Dalvi B. Transcatheter closure of patent ductus arteriosus in children weighing < 10kg with Gianturco coils using temporary balloon occlusion technique. *Ind Heart J* 1997;49:597.
31. Gupta A, Shah P, Ranjan A, Vajifdar B, **Nabar A**, Lokhandwala Y, Kulkarni H. Simple new electrocardiographic signs to differentiate between right coronary and left circumflex artery occlusion in inferior wall infarction. *Ind Heart J* 1997;49:602.
32. Shah P, Vajifdar B, Fulwani M, **Nabar A**, Vora A, Lokhandwala Y, Kerkar P. Age at onset and gender distribution of atrioventricular nodal tachycardia and atrioventricular reentrant tachycardia. *Ind Heart J* 1997;49:609.
33. Kavthale S, Shah P, Naik A, Goyal V, **Nabar A**, Vora A, Kerkar P. Intra-arterial blood pressure changes during atrioventricular nodal tachycardia and atrioventricular reentrant tachycardia. *Ind Heart J* 1997;49:609.

34. Vora A, Fulwani M, Naik A, Iyer R, **Nabar A**, Kulkarni H. Intermediate term follow-up after radiofrequency ablation of accessory pathways. *Ind Heart J* 1997;49:610.
35. Iyer R, Vajifdar B, **Nabar A**, Goyal V, Dalvi B, Kulkarni H. Differences in velocity and gradients recorded by four different frequency Doppler transducers. *Ind Heart J* 1997;49:613.
36. Fulwani M, Gupta A, Iyer R, **Nabar A**, Lokhandwala Y, Kerkar P, Kulkarni H. Can sinus rhythm be restored in patients with chronic atrial fibrillation after balloon mitral valvotomy. *Ind Heart J* 1997;49:620.
37. Goyal Vinay, Nair N, Goyal V, **Nabar A**, Patel R, Dalvi B. Use of radionuclide lung scintigraphy for assessment of pulmonary perfusion in patients with coil closure of patent ductus arteriosus. *Ind Heart J* 1997;49:620.
38. **Nabar A**, Fulwani M, Vajifdar B, Deshpande J, Sivaraman A, Dalvi B. Echocardiographic assessment of coronary artery anatomy in transposition of great arteries. *Ind Heart J* 1997;49:652.
39. Iyer R, Goyal VG, **Nabar AA**, Lokhandwala YY. Is there a change in AV Wenckebach after ablation of slow pathway for AVNRT dependent upon presence of demonstrable duality. *Pacing Clin Electrophysiol* 1997;20:2345.
40. **Nabar A**, Rodriguez LM, Timmermans C, vd Dool Adri, Smeets JLRM, Wellens HJJ. Radiofrequency ablation of "class IC atrial flutter" in patients with resistant atrial fibrillation. *Circulation* 1998;98:2976. At the 71st Annual Scientific Sessions of the American Heart Association, Dallas, Texas, USA. 1998.
41. **Nabar A**, Rodriguez LM, Timmermans C, vd Dool A, Smeets JLRM, Wellens HJJ. Effect of right atrial isthmus ablation on the occurrence of atrial fibrillation : Observations in four patient groups having type I atrial flutter with or without associated atrial fibrillation. *J Am Coll Cardiol* 1999;33:117A. At the 48th Annual Scientific Sessions of the American College of Cardiology, New Orleans, Louisiana, USA. 1999.
42. Rodriguez LM, Timmermans C, Donker D, Smeets J, **Nabar A**, Kattenbeck K, Wellens HJJ. In contrast to the right atrium the right ventricle does not show electrical remodelling during atrial fibrillation. *Pacing and Clin Electrophysiol* 1999;22:794. At the 20th Annual Scientific Sessions of the North American Society of Pacing and Electrophysiology, Toronto, Canada. 1999.
43. **Nabar A**, Rodriguez LM, Timmermans C, Smeets JLRM, Wellens HJJ. Isoproterenol to evaluate resumption of conduction following right atrial isthmus ablation in type I atrial flutter. *Eur J Cardiol* 1999;20:99. At the 21st Annual Scientific Sessions of the European Society of Cardiology, Barcelona, Spain. 1999.
44. **Nabar A**, Rodriguez LM, Timmermans C, Wellens HJJ. Electrocardiographic patterns of flutter wave in "class IC atrial flutter". *Eur J Cardiol* 1999;20:100. At the 21st Annual Scientific Sessions of the European Society of Cardiology, Barcelona, Spain. 1999.
45. **Nabar A**, Rodriguez LM, Timmermans C, Wellens HJJ. Electrophysiology of "class IC atrial flutter". *Eur J Cardiol* 1999;20:99. At the 21st Annual Scientific Sessions of the European Society of Cardiology, Barcelona, Spain. 1999.

46. Timmermans C, Masset S, Rodriguez LM, Ayers G, Lambert H, **Nabar A**, Wellens HJJ. Comparison of a new 2-lead system with a 3-lead system for atrial defibrillation. *Eur J Cardiol* 1999;20:108. At the 21st Annual Scientific Sessions of the European Society of Cardiology, Barcelona, Spain. 1999.
47. Rodriguez LM, **Nabar A**, Timmermans C, Wellens HJJ. Should we prefer a long tip electrode to perform radiofrequency ablation of type I atrial flutter? Results of a prospective randomized study comparing a 8-mm split-tip versus a 4-mm tip ablation catheter. *Circulation* 1999 (In Press). At the 72nd Annual Scientific Sessions of the American Heart Association, Atlanta, Georgia, USA. 1999.