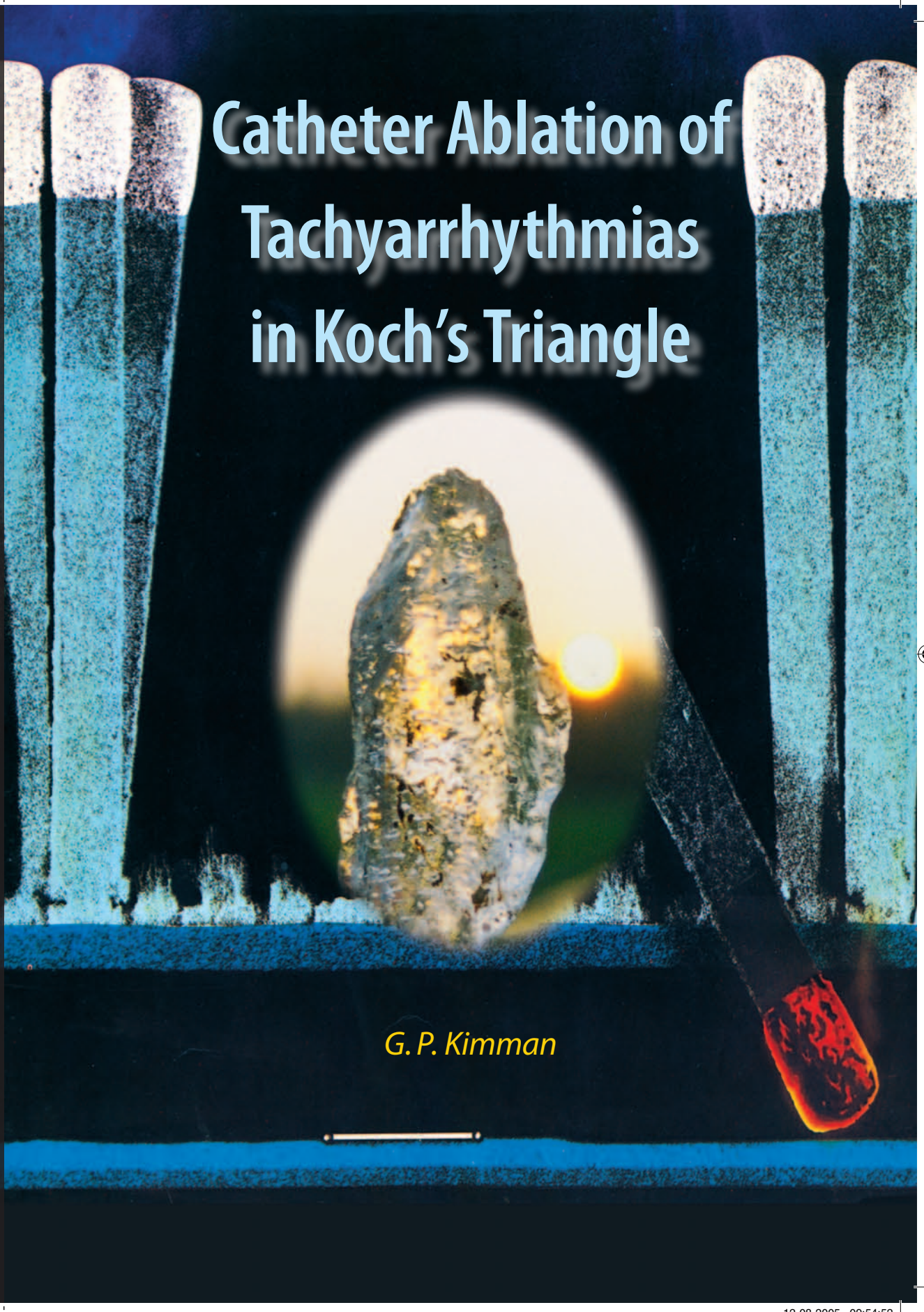
Catheter Ablation of Tachyarrhythmias in Koch's Triangle



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Financial contribution for the production of this thesis is gratefully acknowledged from the following companies:

Guidant Nederland B.V.
Bard Benelux B.V.
Cryocath Technologies Inc.
ELA Medical Nederland B.V.
Medtronic B.V.
St Jude Medical Nederland B.V.
Vitatron

ISBN-10: 90 9019 8709
ISBN-13: 978 90 9019 8705

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Katheterablatie van ritmestoornissen in de driehoek van Koch

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van
rector magnificus

Prof. dr. S. W. J. Lamberts

en volgens besluit van het College voor Promoties

De openbare verdediging zal plaatsvinden op
woensdag 21 september 2005 om 11.45 uur

door

Gerardus Petrus Kimman
geboren te Mierlo

Promotiecommissie

Promotoren:
Prof. dr. L.J.L.M. Jordaens
Prof. dr. N.M. van Hemel

Overige leden:
Prof. dr. D.J.G.M. Duncker
Prof. dr. D. Poldermans
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Het grootse van het aardse bestaan, vraagt om koestering van het kleine;
juist het kwetsbare, kleine maakt het leven groots

Contents

1

The intriguing area of Koch's Triangle: where anatomy and electrophysiology come together. An overview

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Partly to be published in Int J Cardiol 2005

Introduction

Today, the anatomy of the atrioventricular (AV) junction is being investigated for almost 100 years. Wilhelm His was the first one to describe a solitary muscular strand running septally from atrial to ventricular musculatures [1]. However, it was the achievement of Tawara to show in detail that the specialized muscular system responsible for atrioventricular conduction, the bundle of His, arose from a well-dermarcated collection of histologically discrete atrial cells, which he called the "knoten", the compact AV node [2]. He compared the conduction system that sprang from the "knoten" to a tree, with the atrial transitional cells representing the branches, the bundle of His forming the trunk, and the Purkinje fibers, ramifying on either side of the muscular ventricular septum, corresponded to the roots. The atrial transitional cells were approaching the compact node from all sides. He suggested that the boundary between the node and the bundle was the point at which the overall muscular axis entered the insulating tissues of the central fibrous body, easily recognized as an anatomic landmark. This distinction is hardly to make on purely histologic grounds.

The purpose of this review is to address the known architecture and the electrophysiologic mechanisms of the AV node and its direct environment, known as Koch's Triangle. First, the development of the atrioventricular conduction axis is discussed, as well as its anatomical location. Secondly, the electrophysiologic characteristics of this intriguing region is pointed out. In this context, the occurrence of different tachyarrhythmias in the triangle of Koch is described. Finally, the most important pitfalls in the treatment of these arrhythmias are discussed.

Embryology of the atrioventricular conduction

The embryogenesis of the cardiac conduction system is fascinating. The embryologic development of the conduction system is essential in understanding the significance of the transitional cells and the posterior extension of the compact AV node described by Tawara [1]. In the fifth and sixth weeks of development the heart tube loops and balloons to form its atrial and ventricular compartments [3,4]. Subsequent to looping of the ventricular component of the heart tube, a ring of histologically specialized cells that foms the junction between the inlet and outlet parts of the ventricular loop is recognized. Because of their staining reaction to an antibody (GIN 2, Leu 7, HNK-1) derived from the nodose ganglion of the chicken heart, which is a marker for the developing interventricular myocardium, it has been possible to establish that the entire right ventricular myocardium, including its inlet portion, is developed from the distal ventricular component of the primary heart tube. The canal myocardium becomes sequestered as an atrial structure [5-7]. It is visualised that with expansion of the right atrioventricular junction the ring of specialized cells passes from the crest to the ventricular septum to run within the atrial vestibule [8]. At this transition from atrium to ventricle via the atrioventricular musculature, the specialized cells are bordered by the atrioventricular cushion tissues luminally, and by the tissues of the

atrioventricular groove epicardially. This area of transition persists in the septated heart as the penetrating atrioventricular bundle. The downgrowth of the primary atrial septum at the junction of the septum with the posteroinferior atrial wall, brings atrial musculature into contact with the GIN 2 positive cells, forming the AV node, and its caudal extension. Therefore, because the AV node retains its muscular continuity with the ventricular myocardium, it also retains the slow conduction which initially characterizes all of the canal myocardium [9]. The junctions between the cells of the atrioventricular ring and those derived from the atrial septum become the transitional cells. Finally, the original cells of the ring lose their histologic discreteness, and only remnants of the ring are visible in the postnatal heart. While earlier in development the ring can be traced in its course entirely around the developing aortic root, only the end of it is seen as the 'dead-end-tract' [10]. Around the tricuspid valvar orifice they are known as atrioventricular ring tissue, and they can, in malformed hearts, function as a substrate for 'Mahaim' physiology [11,12]. Probably, the anomalous connections, known as accessory pathways, that can exist between a wide variety of structures of the conduction system, are functionally active remnants of these specialized ring cells. Although, accessory atrioventricular connections are common in the human foetus, these are usually severed during postnatal morphogenesis [13]. Thus in normal hearts the penetrating His bundle acts as the only electrical link between the atria and the ventricles. However, if one or more accessory connections persist beyond the initial stages of cardiac development, additional and/or conflicting wavefronts are present, and may permit bidirectional or only antegrade or retrograde conduction (latter referred to as concealed connection) [14].

The anatomic boundaries of the AV node (Koch's Triangle)

The position of the AV node is at the apex of Koch's triangle, where the penetrating bundle extends upward from the ventricular septum, and emerges into the atrial myocardium. When viewed in the anatomic position, the triangle of Koch has its base horizontal and its apex pointing upward [8,15] (Figure 1). On the atrial aspect, the triangle itself is delineated by the tendon of Todaro, a fibrous extension running from the union of the Eustachian and Thebesian valves to insert into the aortic root. The ventricular border is formed by the septal leaflet of the tricuspid valve, which crosses the membranous septum, becoming attached to the aortic root. The right fibrous trigone demarcates the posterior boundary of the root in the left ventricle, and is the rightward end of the fibrous continuity between the aortic leaflet of the mitral valve and the aortic valvar leaflets. The trigone forms together with the membranous septum the central fibrous body. The tendon of Todaro inserts in the atrial aspect of this central fibrous body to mark the apex of Koch's triangle. The base of the triangle is marked by the inferior right atrium around the orifice of the coronary sinus (cavo-tricuspid isthmus), along with the musculature extending to the hinge of the septal leaflet of the tricuspid valve (septal isthmus). Some important anatomic structures can be identified, in relationship with Koch's triangle. Immediately above the mouth of the coronary sinus, positioned posteriorly relative to the apex of the triangle is the oval fossa.

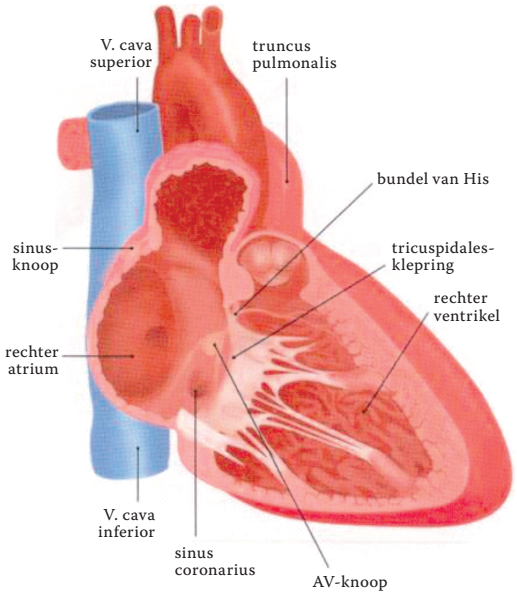


FIGURE 1.
Schematic view of the anatomic position of Koch's triangle

The inferior part (floor) of the fossa is the true atrial septum, and is only a small portion of that part of the atrial wall regarded as the 'septal area'. Because, the tricuspid valve annulus is displaced apically with respect to the mitral valve annulus, a large portion of the inferior limbus fossae ovalis (free border of the septum secundum) separates the right atrium from the left ventricular inflow tract. The anterior part of the limbus fossae ovalis, anterior to the right fibrous trigone (the most anterior part of the central fibrous body) is the right atrial free wall, separating the right atrium from the aortic outflow tract. The region surrounding the orifice of the coronary sinus has direct contact with the tissue of the coronary sulcus (the atrioventricular groove), and is therefore no part of the septum. Therefore, according to the anatomy of the septum, only accessory pathways, classified as 'midseptal' are related to both the atrial and ventricular septum, and are the only true septal pathways [16-19]. As 'anteroseptal' pathways skirt anteriorly along the right fibrous trigone (at the right anterior free wall), they have no septal connections at all. Finally, pathways classified as 'posteroseptal' are located posterior to the central fibrous body, around the mouth of the coronary sinus, and this region is definitely not part of the septum.

Lateral and posterior to the mouth of the coronary sinus is the inferior caval vein, with the musculature between both venous orifices forming the so-called sinus 'septum'. Finally, the terminal crest skirts the orifice of the inferior caval vein and turns toward the triangle of Koch, terminating in an area of musculature located inferiorly relative to the base of the triangle.

The blood supply to the AV node is in approximately 90% of the hearts provided by the ramus septi fibrosi, a branch of the right coronary artery reinforced by branches of the anterior descending artery. The cardiac plexus surrounding the arch of the aorta is responsible for the cardiac innervation. This plexus is formed by sympathic fibers from the upper thoracic spinal cord, and by parasympathic ones (nervus vagus) originating from the me-

dulla. It supplies the sinoatrial node, and its approaches, the atrial septum, the approaches of the AV node, the AV node, and to a lesser degree the AV bundle [20]. Although, the exact distribution of these nerves is still not known, the AV conduction is preferentially sensitive to sympathic adrenergic regulation.

Electrophysiologic characteristics of the AV node and its direct environment

The AV node

The structure of the AV junction makes it likely that nodal architecture as well as cellular morphology contributes to nodal electrophysiology. To understand AV nodal behavior and underlying functional properties is still a challenge. The complexity of rate-induced AV nodal responses, for example the Wenckebach cycles that develop a heart rates slightly faster than those compatible with 1:1 AV conduction, are controlled by 3 main factors: 1. the previous recovery time; 2. a facilitatory factor called facilitation, and 3. a time-and rate-dependent cumulative effect called fatigue [21-25]. The recovery property is reflected by a typical exponential-like increase in A2H2 with decreasing recovery time, and is independent of the basic cycle length, which can be illustrated by a "drawing" a resulting recovery curve [26]. Facilitation refers to the shortening of A2H2 and persistence of conduction at shorter H1A2 than expected from the recovery alone [27]. Facilitation develops within one short cycle length, dissipates within one long cycle length, and increases with the shortening of the inducing cycle. It affects nodal conduction time only in the short coupling range. Fatigue refers to the rate- and time-dependent prolongation in nodal conduction time that develops during fast rates [21,27-29]. These intrinsic nodal properties remain present after autonomic blockade but can be modulated by both cholinergic and adrenergic tone [30-32]. From the resulting recovery curve 2 important AV nodal parameters can be determined. One is the nodal functional refractory period (FRNP; shortest H1H2 reached), which is controlled by the fast pathway, the superior (anterior) aspect of the atrial septum, close to the site of the His bundle (explained later), and is largely cycle-length-dependent. The other one is the effective refractory period (ERPN; the longest A1A2 that results into a blocked beat in the node), which is controlled by the slow pathway, the inferior (superior) septum between the coronary sinus (CS) ostium or inferiorly inside the CS within 1-3 cm of the ostium and the tricuspid annulus (explained later) and is also cycle-length-dependent. In conclusion, the above mentioned basic rules, called recovery, facilitation, fatigue or combined facilitation of fatigue, control intrinsic AV nodal conduction and refractory periods [33].

AVNRT and arrhythmias in the AV node

Cardiac arrhythmias are caused either by abnormal impulse formation or by reentrant excitation. The latter mechanism is responsible for the vast majority of clinical arrhythmias. For a reentry arrhythmia to occur three conditions must be fulfilled: 1. the occurrence of unidirectional block; 2. conduction of the impulse through an alternative pathway around

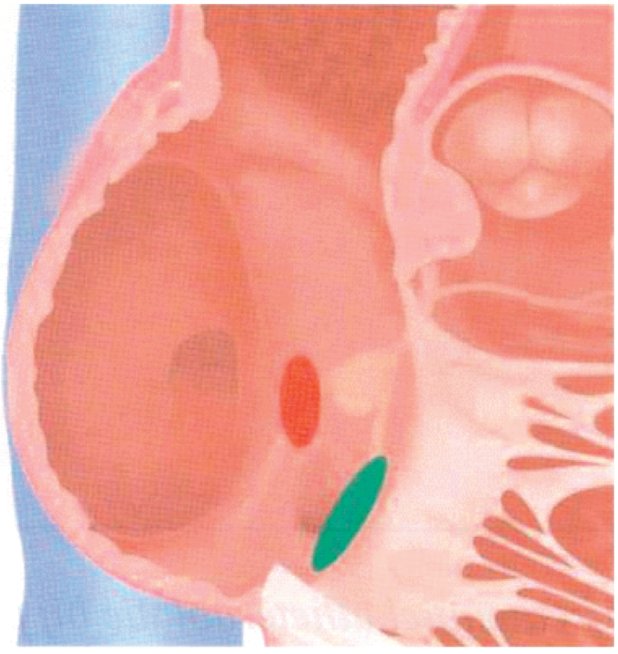


FIGURE 2.
Simplified, schematic view of the "fast" and "slow" pathway in relation to the compact AV node

the block, and 3. retrograde invasion of the zone of block with sufficient delay to allow the fibers proximal to the block to restore their excitability [34]. Heterogenicity in conduction properties and slow conduction and/or a short refractory period will enhance the chance that reentry arrhythmia will originate.

Experimental and clinical studies have revealed different forms of reentry: 1. circuits which are based on macroanatomic pathways (for example atrial flutter type 1); 2. small functionally determined circuits without the involvement of a gross anatomical obstacle; 3. reentry in nonuniform anisotropic tissue, and 4. random reentry of multiple wandering wavelets (Moe's theory of explaining the mechanisms of self-perpetuating atrial fibrillation) [35].

The AV node frequently is the site of reentrant beats and reentry tachycardia. Moe was the first one to demonstrate the presence of two anatomic or functionally distinct AV nodal pathways and hypothesized that dual AV nodal pathways may be the pre-requisite for reciprocal rhythm and paroxysmal nodal tachycardia [36]. Dependent on their conduction time, these pathways were called "slow" or "fast" (FIGURE 2).

The most conclusive evidence of dual AV nodal pathways is not the AH-jump (>50 ms over a 10 ms increase in prematurity) with delivery of increasingly premature atrial beats, eventually followed by an atrial echo or initiation of AVNRT [37-42]. It is the demonstration that, during AVNRT, a ventricular impulse could reach the atrium retrogradely without colliding with the anterograde impulse of the AVNRT [43] and obtaining two ventricular responses from one atrial impulse (44), that confirm the dual pathway physiology concept

in AVNRT. Nowadays, in the clinical setting, the slow and fast pathway refer to specific anatomic sites where the earliest retrograde atrial activation is recorded within the triangle of Koch during AVNRT. If the earliest retrograde atrial activation is registered at the superior (anterior) aspect of the atrial septum, close to the site of the His bundle recording this is considered the fast pathway. Demonstration that the inferior (posterior) septum, between the coronary sinus (CS) ostium or inferiorly inside the CS within 1-3 cm of the ostium, is retrogradely activated first, this is called the slow pathway [45-47]. Untill now it is unclear what the slow pathway really is. Human studies failed to demonstrate a discrete nodal-type structure or bundle. Three possible anatomic substrates are considered [48]:

First, the group of transitional fibers approaching the AV node in the region between the coronary sinus orifice and tricuspid annulus, the so-called posterior atrionodal connections are a likely substrate. They form no discrete bundle but consist of multiple strands with no clear demarcation between the anterior and posterior atrionodal connections. The posterior fibers do not appear to be the normal path of AV conduction, since destruction of these fibers does not destroy the compact AV node or impair AV conduction in the normal heart, in contrast to the anterior fibers [49]. The posterior fibers exhibit nodal-type action potentials. Furthermore, like the compact AV node, these cells lack the gap-junctional protein connexin43, and this may contribute to the slow conduction [50].

Secondly, extensions of nodal-type tissue extending form the posterior end of the AV node for variables lengths posteriorly along the tricuspid annulus, was suggested to represent the substrate of the slow pathway [51,52]. However, this structure was not consistently found in the slow pathway region, and slow pathway could be ablated without any nodal tissue found at the site of the radiofrequency lesion [53].

Third, 3 distinct atrionodal bundles are not consistently described which converge to form a proximal AV bundle [54]. It remains unclear if the lateral atrionodal bundle represents the same structure as the posterior nodal extension.

Also, other different mechanisms of slow pathway conduction are considered. Conduction may be slow in the slow pathway because of a longer conduction path. Considering the conduction speed in atrial tissue, and assuming that the slow pathway consists of "normal" atrial tissue, the pathway should be 12.5 cm long, considering the conduction speed in atrial tissue. This is clearly not the case. If the slow pathway was entirely composed of nodal tissue, the pathway would be 5-15 mm long [55,56]. This is consistent with the assumed length of the slow pathway. Therefore, slow conduction can be entirely explained by the presence of nodal tissue. However, in most studies the presence of compact nodal tissue in the slow pathway region is not demonstrated [53]. Another explanation for slow conduction can be cellular properties. Most of the conduction delay that occurs during normal AV conduction occurs in the transitional zone, where transitional cells are located that have light microscopic properties intermediate between nodal and atrial cells [57]. The cells in the slow pathway region have nodal-type action potential [50]. Cells closest to the tricuspid annulus have action potentials resembling true nodal cells, and cells moving gradually away from the annulus, have more atrial-like characteristics. Although, there is a lack of cells with nodal morphology in the slow pathway region, nodal-type behavior can explain slow conduction. A decreased cell diameter with an increase in intracellular

resistance may also contribute in a small part to the amount of slow conduction [58]. As mentioned earlier, slow conduction can also be the result of missing the gap-junctional protein connexin43 in this region, in comparison with rapidly conducting atrial tissue [50]. Finally, slow conduction can be caused by nonuniform anisotropy [59,60]. Anisotropic conduction is conduction that is perpendicular to muscle fiber orientation. Since cardiac myocytes have fewer side-to-side than end-to-end connections, transverse conduction is slower than longitudinal conduction. If fibrosis develops, with a further decrease in connections, nonuniform anisotropy occurs with even more slowing in conduction. However, these effects are unlikely to play an important role in the slow pathway region.

In conclusion, the substrate of the slow pathway is probably a normal structure, and exists of posterior nodal connections of transitional fibers containing cells with nodal-type action potentials.

Thus, AVNRT is probably a functional abnormality. It is likely that any of the transitional fibers may have appropriate properties of conduction velocity and refractoriness to form a reentrant circuit. To describe the different subforms of AVNRT, terms as slow anterograde-fast retrograde (typical), fast anterograde-slow retrograde(atypical), and slow anterograde-slow retrograde are used [61-63]. However, the definitions of these subforms are ill-defined. Recently, Heidbuchel provided an useful definiton of these 3 subforms, depending especially on the identification of the site of earliest retrograde atrial activation and not on the HA interval during tachycardia [64]. Hereby, slow-fast AVNRT is characterized by: 1. antegrade conduction over a slow pathway with an AH interval >200ms; 2. earliest retrograde atrial activation in the superior septum (fast pathway conduction); 3. H-Ap (interval during pacing at the same cycle length of the tachycardia, immediately after termination of the tachycardia) is <70 ms, and 4. there is generally no evidence for a lower common pathway (LCP). In fast-slow AVNRT: 1. an AH interval <200 ms: 2. earliest retrograde activation at the inferior septum, and 3. the presence of a LCP is essential. Finally, slow-slow AVNRT is defined by: 1. antegrade conduction over a slow pathway with an AH interval >200ms; 2. earliest retrograde atrial activation in the inferior septum or proximal CS; 3. H-Ap usually of >70 ms; and 4. evidence for a significant LCP. The small number of AVNRT that do not fit in any of these categories, is called undetermined.

Cavo-tricuspid dependent atrial flutter

The region between inferior caval vein (IVC) orifice an tricuspid valve orifice, known as cavo-tricuspid isthmus, which is the base of the triangle of Koch, is known for its slow conduction properties. Atrial flutter type 1 (AF1) is an unique arrhythmia, characterized by regular atrial depolarizations at a rate between 250 en 350 beats per minute (BPM) and a saw tooth morphology of the flutter-waves [65,66]. Electrophysiological studies, including activation mapping and entrainment techniques supported that AF1 is based on a right atrial macro-reentrant movement with an excitable gap, where the cavo-tricuspid isthmus is the critical part of the reentry circuit [67,68]. The double potentials recorded along the crista terminalis during AF1 suggest that it forms the posterior barrier of the flutter circuit, whereas the TV annulus forms the anterior barrier [69-71]. Thus, the anatomical barriers provided by the endocardial architecture seems to determine the location of the

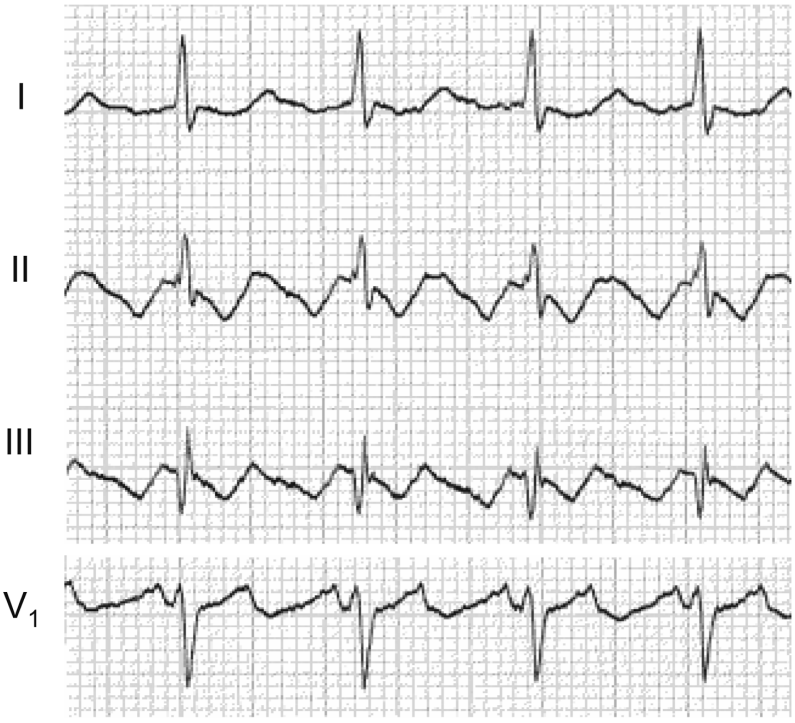


FIGURE 3.
Example of a Class 1C atrial flutter

AFL circuit in the RA. Counter clockwise AF1 is characterized by a broad band of peri-tricuspid activation that enters the isthmus, slows in its medial part, ascends up the septum, reaches the root of the superior caval vein, usually crossing it anteriorly and rarely fushing around it to descend down the free wall [72]. Clockwise AF1 shares the same circuit in the opposite direction.

It is known that atrial fibrillation (AF) is the most frequent, sustained, symptomatic tachyarrhythmia in patients with or without structural heart disease [65,73,74]. The incidence of this tachyarrhythmia increases with age and is twice as common in males as females. It remains a therapeutic challenge and the success rate of maintaining long-term sinus rhythm with pharmacologic therapy alone is less than optimal. Class 1C antiarrhythmic drugs (AAD) have been recommended as first line therapy to prevent AF recurrences in patients with no or minimal heart disease [75]. Amiodarone, a class III AAD, is the key-stone agent to prevent AF recurrences in patients with structural heart disease, and superior to class 1C AAD. Under both classes of AAD 'transformation' of AF to atrial flutter (AFL) is well-known [76,77] (FIGURE 3). Increase in wavelength due to increase in the atrial refractory period in a tachycardia dependent manner , and the unique arrangement and orientation of the atrial muscle fibers between inferior vena caval orifice (IVC) and tricuspid valve annulus (TV) may promote nonuniform anisotropic slow conduction in the cavo-tricuspid isthmus, and therefore promote the conversion of AF in AFL [78,79].

The initiation of AF1 can be achieved by premature extrastimuli [80]. However, termination with an extrastimulus is rare. Trains of rapid pacing are almost always required to terminate AF1 [80,81]. Atrial activation mapping during AF1 is feasible, but was limited by the fact that: 1. access to the left atrium is mostly only obtained form recordings of the coronary sinus, and 2. the anatomy of the right atrium is rather complex [82-84]. Nowadays, more insight in both isthmus and non-isthmus dependent atrial flutter became available with electroanatomic, and non-contact mapping [85,86]. Concealed entrainment can be demonstrated by pacing in the cavo-tricuspid isthmus at a cycle length 20 msec shorter than the atrial flutter cycle length with a post-pacing interval equal to the flutter cycle length.

(Para)Septally located acessory pathways

Common characteristics

Unlike the AV node, conduction over an accessory pathway usually behaves in an all-or-none fashion [87]. Rapid pacing or atrial premature depolarizations almost always either conduct without delay (no change in P-to-delta wave) or block suddenly. Decremental conduction, visible as a prolonged P-delta wave interval is mostly due to intra-atrial conduction delay between the site of stimulation and the bypass tract [88,89]. Intermittent conduction over a bypass tract can be observed. It has to be distinguished from inapparent preexcitation that is due to prolonged intra-atrial conduction, accelerated AV conduction, prolonged conduction over a bypass tract, or any combination of these. Intermittent preexcitation can be caused by: 1. phase-3 and phase-4 block in the accessory pathway [90-92]; 2. AV bypass tracts with long refractory periods and supernormal conduction [93,94], and 3. antegrade or retrograde concealed conduction produced by an atrial premature depolarization (APD) [95,96].

With the absence of preexcitation at long cycle lengths, followed by evidence of preexcitation at short cycle lengths, with the sudden disappearance again of preexcitation at even shorter cycle lengths, it is possible to demonstrate phase-3 and phase-4 block in accessory pathways. Supernormal conduction is demonstrated by the existence of preexcitation at long cycle lengths , followed by block at shorter cycle lengths (but still relatively long), and long bypass refractory periods. At shorter pacing cycle lengths preexcitation occurs again with the same P-to delta interval. Concealed conduction can be demonstrated by the disappearance of preexcitation caused by an APD that is nonconducted over the bypass tract or a ventricular premature depolarization (VPD) influencing antegrade conduction over the bypass tract at subsequent beats. An example is atrial fibrillation with runs of preexcited beats followed by runs of absent preexcitation.

Most accessory pathways permit bidirectional conduction. However, approximately 25 % only conduct in retrograde direction and are referred to as concealed bypass tracts. A minority (less than 5 %) only conducts antegradely [14].

	I	II	III	aVL	aVR	aVF	V1	R/S V1	R/S V2	R/S V3
anteroseptal	pos	pos	pos			pos	Bif/pos	< 1	< 1	< 1
midseptal	pos	pos	Iso/neg	pos		Iso/neg	Iso/neg			
Right posteroseptal		Iso/neg	neg		neg	Iso/neg	neg			
Left posteroseptal		Iso/neg	neg		neg	Iso/neg	Iso/pos			

Tabel 1.
Discrimination of accessory pathways based on delta wave polarity.

Bif = bifasic Neg = negative
Iso = isoelectric Pos = positive

Specific characteristics of Accessory Pathways in Koch's Triangle

Typical electrocardiographic findings in anteroseptal accessory pathways include a positive delta wave in leads I, II, III, aVF, a biphasic or positive delta wave in V1, an R/S ratio <1 from V1 to V2 or V3, and an R/S ratio >1 in III. A midseptal accessory pathway is considered if there is a positive delta wave in I, II, aVL, and an isoelectric or negative delta wave in III, aVF, V1. The surface ECG suggests a right posteroseptal accessory pathway in patients with a negative delta wave in III, aVR, V1, and a isoelectric or negative delta wave in II, aVF. A positive or isoelectric delta wave in V1 indicates a left posteroseptal accessory pathway (Table 1). During incessant long RP-tachycardia a negative P-wave in the inferior leads, and a biphasic P-wave in I, aVL, V1 suggested a posteroseptal origin of the accessory pathway. The final classification can only be made according to the successful ablation site [16-19]. By definition, pathways are classified as anteroseptal if an accessory pathway activation potential as well as a His bundle potential are simultaneous recorded from a catheter placed at the His bundle region. A pathway is classified as midseptal if an accessory pathway potential is recorded through a catheter located in an area bounded anteriorly by the tip electrode of the His bundle catheter and posteriorly by the coronary sinus ostium. Accessory pathways located within the pyramidal space posterior to the septum may be classified as right and left posteroseptal. Right posteroseptal accessory pathways insert along the tricuspid ring in the immediate vicinity of the coronary sinus ostium. Left posteroseptal accessory pathways have an anatomic course close to the terminal portion of the coronary sinus and may be located either at a subepicardial site around the proximal coronary sinus or middle cardiac vein or at a subendocardial site along the posteromedial ventricular aspect of the mitral annulus [97].

Transvenous catheter ablation of arrhythmias in Koch's triangle and their pitfalls

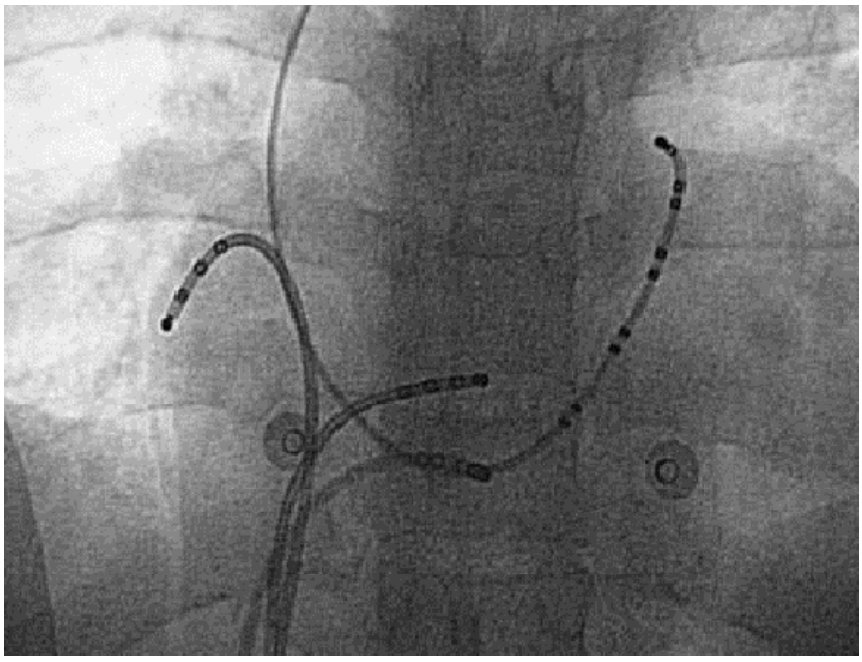
Atrioventricular nodal reentrant tachycardia ablation

Nowadays radiofrequency (RF) catheter ablation has become the therapy of choice to permanently cure AVNRT [98,99]. It is highly effective with a success rate of about 95% and a low recurrence rate [100-104]. The target is slow pathway ablation/modification guided by both anatomical landmarks and intracardiac electrograms. This is achieved by positioning the catheter at the posterior and middle third of the triangle of Koch, anterior to the coronary sinus, just superior to the tricuspid annulus insertion into the inferior interatrial septum [47,100]. Others are searching for slow pathway potentials, though their elimination has not been proven necessary to cure AVNRT. Furthermore, similar potentials can also be recorded in other patients, with or without tachyarrhythmias [105]. The slow pathway is considered to be ablated if dual pathway physiology is completely abolished, and is modified if the slow pathway conduction time is lengthened or echo beats are still inducible, but without sustained arrhythmia. The anterior approach or fast pathway ablation is performed by placing the ablation catheter across the tricuspid annulus to record a His bundle potential. It is thereafter slowly withdrawn until the amplitude of the atrial electrogram exceeds that of the ventricular electrogram with a small or absent His bundle potential [106]. A 30% prolongation of the PR-interval is considered to be a successful ablation [106]. This approach is reserved for highly symptomatic patients in whom the slow pathway ablation is not successful. It can also be the initial approach in patients with preexisting prolonged PR interval at baseline, which seems to be dependent on the slow pathway for antegrade conduction [47]. However, even in these patients slow pathway ablation can be curative with preservation of antegrade AV conduction, further supporting the functional nature of the AV nodal propagation. The endpoint for both slow or fast pathway ablation is noninducibility of AVNRT with or without isoprotenol.

Pitfalls in AVNRT

Whom to ablate?

RF catheter ablation is highly effective in definitively curing patients with recurrent AVNRT [100-104]. The recurrence rate is low, and patients can discontinue their antiarrhythmic drugs, eliminating the risk of side-effects and proarrhythmia. Although the complication rate is low, there is a risk of thromboembolic events, bleeding, cardiac perforation, inadvertent right bundle branch block, or even worse, complete AV block [107-109]. Furthermore, ablation procedures are accompanied by a relatively long radiation exposure, especially in the treatment of arrhythmias in the triangle of Koch, because of the risk of catheter dislodgement in this area in close proximity to the compact AV node [101]. Newer imaging systems as the LocaLisa mapping system, RPM or Ensite NavX enable continuous visualization of the ablation catheter in respect to the His bundle, reducing fluoroscopy time significantly [110, 111, 112]. Because of the aforementioned complications and the fact



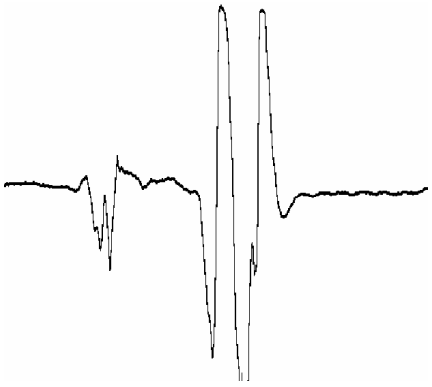


FIGURE 4A.
Anterior-posterior fluoroscopy view of a successful slow pathway ablation site. Shown are a decapolar catheter, positioned in the coronary sinus via the left suclavian vein; a quadripolar catheter positioned in the the right atrial appendage, a quadripolar catheter positoned at the His bundle, and an RF ablation catheter via the right femoral vein.

FIGURE 4B.
Intracardiac electrogram of the successful slow pathway ablation site. Shown is a fragmented atrial signal, no His spike, and an atrial/ventricular ratio < 0.5

that most patients present between late adolescence and age 40, catheter ablation is reserved for symptomatic patients with recurrent AVNRT.

Where to ablate ?

Slow pathway ablation is guided by both anatomical landmarks and intracardiac electrograms [100-104] (FIGURE 4a and 4b). The successful ablation site is mostly located either 5 mm above or below the level of the upper margin of the coronary sinus ostium [113]. Fractionated atrial signals and/or slow pathway potentials can be recorded. A longer atrial potential-slow pathway potential is attended with a higher success, as is an AV ratio of 0.1 to 0.5 [114]. An accelerated junctional rhythm during low energy (10 J) application can

also be used to identify a potentially successful ablation site, reducing the risk of immediately irreversible damage to the compact AV node [115]. Another method is subthreshold stimulation at target sites until termination of AVNRT is achieved or capture occurs [116]. Furthermore, the distance between the ablation target site and the distal end of the AV nodal artery should be >2 mm to avoid any damage to the artery [117]. Also, the distance to the His bundle catheter, or the "drawn His bundle" registered by the LocaLisa system should be >10 mm, again to avoid inadvertent complete AV block [118]. Left-sided ablations for AVNRT have been reported, suggesting that left-sided atrionodal connections may be a critical component of the tachycardia circuit [119-121]. However, the significance of earliest retrograde atrial activation in the CS, which occurs in 8% during AVNRT, as an indication that left-sided ablations may be required is unclear. Successful RF ablation can be performed at standard sites in the triangle of Koch, suggesting that these left-sided atrial inputs are not crucial to the AVNRT reentrant circuit [122].

How to ablate ?

As mentioned before, conventional RF catheter ablation of AVNRT in experienced hands is highly successful with a low complication, and a low recurrence rate [98-105]. Besides the standard 5 catheter (HRA, His, RV, CS, and ablation catheter), a 3 catheter (HRA, His, and ablation catheter), or a single catheter approach can be used, without the necessity of special equipment, such as non-fluroscopic mapping systems [123]. Because the target site is in close proximity of the compact AV node, continuously fluoroscopy during application is necessary to be sure that catheter dislodgement does not occur with the risk of causing and inadvertent complete AV block. This limitation of catheter stability is even further compromised by pain during energy delivery [103,124]. Although non-fluoroscopic equipment and other energy sources are expensive, it can lead to less radiation exposure, and after a learning curve also to shorter procedure times. Furthermore, a better insight in unusual anatomical features is provided. Intracardiac echo could play a role in this respect [125-127]. All together, this may lead to less applications and thus less tissue disruption with less thrombus formation, also being potentially less proarrhythmic [108,109,128].

How do we know that we are successful ?

The final endpoint of catheter ablation in AVNRT is non-inducibility of AVNRT with or without isoprotenol after a 30 minutes waiting period [98-105]. Again, an accelerated junctional rhythm during ablation is a sensitive but not very specific sign of success [117]. This means that if it occurs, the application maybe is successful, but if it doesn't happen it probably is not [47]. Complete slow pathway ablation is achieved if dual pathway physiology is entirely abolished after ablation. However, AVNRT can be cured with only slow pathway modification, characterized by lengthened conduction times or echo beats that are still inducible, but without sustained arrhythmia. Unfortunately, RF catheter ablation of the slow pathway can not be performed on this electrophysiologic basis, because normal AV conduction has to be observed during the whole application. This can only be investigated

after irreversible effect is created. On the other hand, VA block is predictive for long term success after fast pathway ablation [128].

How do we know if complete AV block will occur ?

If transient AV block occurs during or immediately after the application, and the block still persists at the end of the procedure, this is accompanied by a high incidence of permanent AV block requiring a definitive pacemaker implantation [124,129,130]. Also, junctional tachycardia is frequently observed during RF ablation, probably due to thermal injury of the compact AV node and/or the perinodal tissue forming the input of fast and slow pathway into the AV node. A relatively fast rate of this junctional tachycardia with loss of VA conduction is associated with an increased risk of inadvertent AV block with a positive predictive value of 19 % [131]. However, these markers for impending complete AV block do not allow risk stratification before radiofrequency delivery. A useful electrophysiological marker to assess the risk of block before an application is started is the interval between the atrial component of the His bundle electrogram (H) and the atrial signal of the distal mapping (Md) catheter. A short A(H) – A(Md) is associated with a high risk of inadvertent complete AV block [132]. Another method is to perform a pacemapping of the triangle of Koch to recognize patients in whom the anterograde conducting fast pathway is located abnormally far from the anteroseptal region or in whom the anterograde conduction of the fast pathway is absent [133]. On stimulating close to the site where the fast pathway is present, a short stimulus to His (St-H) interval is recorded and, conversely, the greater the distance between the stimulating catheter and the anterograde fast pathway the longer the St-H interval. Also, the distance between the distal end of the AV nodal artery and the ablation target site can be determined. If this is more than 2 mm, the complication of AV block virtually never occurs [117]. Nowadays the LocaLisa system can be used to reduce the risk by 'drawing the His bundle' on the basis of intracardiac His bundle electrograms, from its most distal part (small atrial electrogram with a large ventricular electrogram with a His signal in between) to its most proximal part (large atrial electrogram and small ventricular electrogram with a His signal in between), and to avoid an ablation catheter position within 10 mm of this 'line' [111,118]. However, as this indicates the His bundle and not the compact AV node, displacement of the AV node can not be excluded. Despite these precautions the reported incidence of AV block following RF catheter ablation is between 1 and 2%. As mentioned before, it almost always occur during or shortly after the procedure, but it also can happen even several months later, or even after several years [104,134].

How proarrhythmic is RF catheter ablation of AVNRT ?

Previous studies have suggested that there is an association between atrial flutter and AVNRT. A shared pathway in the low right atrium is possible [104,135,136]. It is already pointed out that slow pathway modification can eliminate AVNRT, while maintaining slow pathway conduction. The late occurrence of atrial flutter is maybe due to damage of this specific area, causing further slowing of conduction and therefore providing a substrate

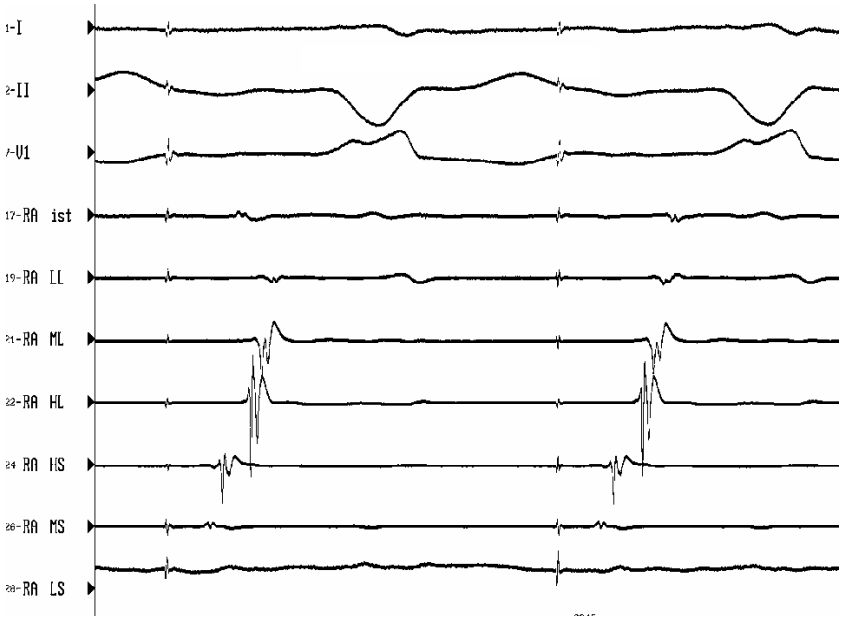


FIGURE 5.
Ablation during coronary sinus pacing in a patient suffering from isthmus dependent atrial flutter. An obvious change in atial activation pattern is seen during the application, suggesting a line of a block

for atrial flutter to occur. On the other hand, slow pathway ablation can interrupt cavo-tricuspid isthmus conduction, curing both AVNRT and isthmus dependent atrial flutter [104]. It is also known that lesions created by radiofrequency energy are inhomogenic [107]. This maybe a source for reentry tachycardia to occur around the created obstacle. However, until now, no studies have directly address to this possible issue. Therefore, no conclusions can be made to this day in this respect.

Cavo-tricuspid dependent atrial flutter ablation

Before RF ablation is started, a standard electrophysiologic study is performed to proof that atrial flutter is cavo-tricuspid dependent. Then, mostly a 8-mm tip electrode ablation catheter is used for temperature controlled sequential point by point RF application between the tricuspid annulus and IVC [137]. RF delivery begins at the right ventricular annulus and is withdrawn towards the IVC after each application, and sometimes already during an application after a pause at each point for 30-45 seconds. The key is to create a complete line of block. Ablation can be performed during SR, pacing from the low lateral right atrium or ostium of the coronary sinus, or during atrial flutter (FIGURE 5). If carried out during pacing, the obvious chance of atrial activation around the isthmus instead of through can not be misunderstood. However, the line between the IVC an TA has to be completed to be successful. Another possibility is to deliver RF energy during atrial flutter on the basis of intracardiac electrograms from the ablation catheter within the isthmus

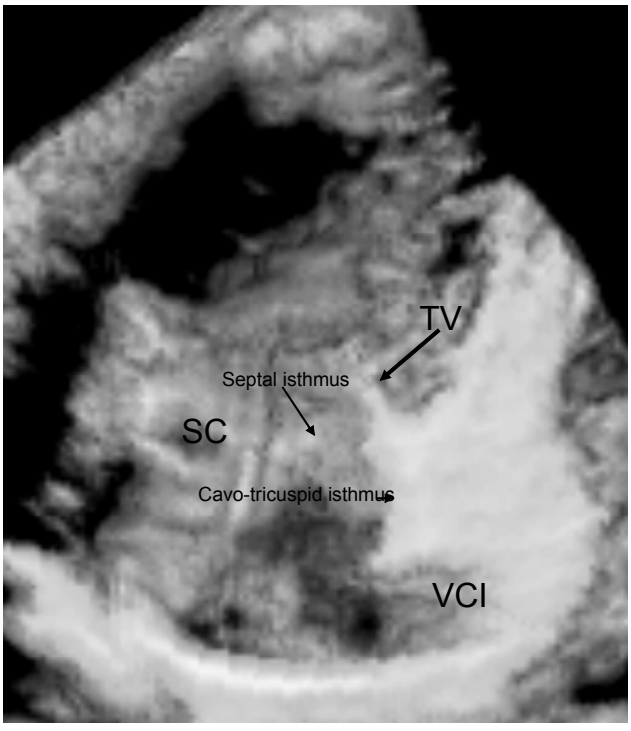


FIGURE 6.
A 3D intracardiac echocardiographic view of the right atrium, showing the tricuspid valve, inferior caval vein, the coronary sinus and the so-called "septal and cavo-tricuspid isthmus"

region coinciding with the center of the surface ECG flutter wave plateau all the way from the TV annulus to the IVC edge [137]. Upon completion of the line of block, widely separated double potentials can be recorded all along the line [83,138-140]. Recently, a functional, rather than anatomic, isthmus is identified, characterized by a preexisting double potential barrier at the cavo-tricuspid isthmus (141). Successful ablation can be achieved by delivering consecutive RF pulses from one anatomic border (always the TA, if applicable) to the blocking double-potential barrier. The endpoint of the ablation, independent of the used method, is bidirectional isthmus block, and not termination of atrial flutter during energy delivery [132,140,142].

Pitfalls in isthmus ablation

Is a complete, linear, transmural line always feasible ?

It can be very difficult to create a linear, transmural line between the tricuspid annulus and the IVC edge. The width of the the isthmus can vary from 1.8-5 cm [143,144]. A longer distance may implicate insufficient reach of the RF catheter to get to the TA. The use of a longer sheath may resolve this problem. The anatomy and in particular the length of the Eustachian crest which in effect forms the posterior boundary of the so-called septal isthmus also varies affecting the functional width of the isthmus [144)] (FIGURE 6). An isthmus

Intracardiac echo with a 9 Mhz US catheter

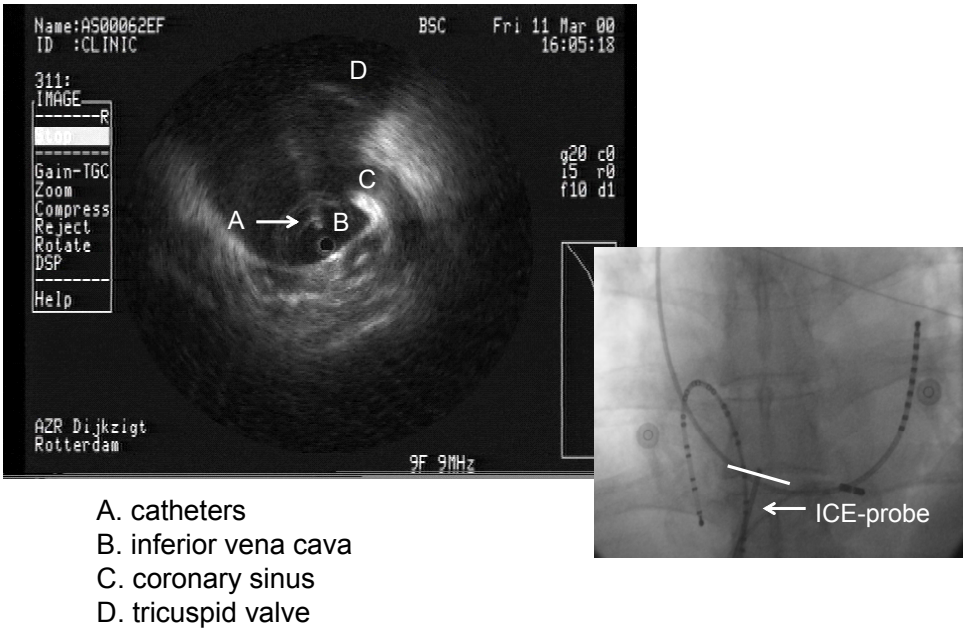


FIGURE 7.
Visualisation of the cavo-tricuspid isthmus during RF ablation by intracardiac echocardiography. The isthmus can be seen, as well as the catheters, the tricuspid valve, and coronary sinus. Inserted is the anterior-posterior fluoroscopy view

area which presents as a deep pouch, can lead to insufficient contact between the ablation catheter and the underlying tissue. Thick pectinate muscles can also cause loss of tissue contact, implicating holes in the ablation line. A more medial approach, the use of a bigger catheter tip or an irrigated tip catheter may solve this problem [145-147]. If the alternative ablation line between the TA and the CS os and the CS os to the IVC is choosen, sedation may be mandatory as the CS os area is very sensitive. Moreover, in about 40 % of the hearts the CS os-IVC area is probably not conducting, because of fibrous tissue. This means that a single ablation line between the TA and the CS os is likely to be sufficient and successful to achieve a bidirectional conduction block in those hearts. Another important issue can be lack of catheter stability, and the difficulty to create a continuous line by this point by point approach which can be difficult to judge by fluoroscopy alone. The use of a longer sheath, the LocaLisa system, intracardiac echocardiography, 3D electroanatomical mapping system, RPM, or Ensite NavX can help to overcome those problems [110-112, 148-150] (FIGURE 7).

How do we know that we are successful ?

As emphasized before, termination of atrial flutter during RF delivery is not a sufficient endpoint [138,141,143]. Mechanical induced termination and/or transient block or conduction

slowing are enough to terminate AF. However, this can be achieved without eliminating or necessarily affecting the substrate. Thus, assessment of complete bidirectional conduction block after termination remains the keystone of a successful ablation procedure. Pacing from one side of the ablation line, time to activation on the opposite side and an atrial activation sequence in the right atrium, showing a 180 degrees change in the direction of activation have been used to demonstrate isthmus block [132,141,151]. However, activation time to the other side of the line by itself is a variable continuum and a specific cutoff is difficult to define. To establish activation sequences and their changes an extensive coverage of the right atrium is necessary, and this is difficult to achieve with duodecapolar catheters, especially on the septal side. The lack of mapping coverage in the immediate surrounding of the ablation line also reduces the specificity of criteria for isthmus block. Occasionally, atrial flutter still is inducible despite apparently complete isthmus block, suggesting that the isthmus is not blocked, or has recovered conduction, or is not a critical part of the circuit [152,153]. To overcome these issues, the use of non-fluoroscopic three-dimensional mapping systems seems very helpful in visualizing the flutter circuit and to demonstrate conduction block [154]. Several studies suggest that morphological changes in bipolar atrial electrograms recorded at sites lateral and adjacent to the target line of block may be used as a unique and robust criterion to validate isthmus conduction block [155,156]. Another criterion that is feasible, is using on-site atrial potential analysis with the recording of parallel, widely spaced double atrial potentials along the ablation line [157]. This analysis seems to be inferior to the classic activation mapping technique, mainly because of the ambiguity of electrogram interpretation along the ablation line. However, when it is combined with the activation mapping technique, it provides additional information regarding isthmus conduction properties in some cases. Therefore, optimally, both methods should be used concomitantly. If with the aforementioned criteria bidirectional isthmus block is not accomplished, locating and ablating residual conduction gaps is necessary. Such residual gaps can be identified by local electrograms with a single or a fractionated potential centered on or spanning the isoelectric interval of adjacent double potentials [83,138-140]. Also, a three-dimensional non-fluoroscopic Localisa mapping system can be very helpful in showing the gaps in the ablation line. Activation mapping is required to show real leakage along the line.

Are there any side effects ?

Although the procedure is well tolerated, a minority of patients require sedation for pain relief during RF delivery [158]. Long fluoroscopy times have been described, although this can be reduced by using earlier mentioned mapping and navigation systems. There is a small risk of creating complete AV block, especially when ablating in the 'septal isthmus' [137]. Using a more lateral approach eliminates this risk. Furthermore, thrombo-embolic complications can occur with the creation of long, linear lines with tissue disruption, requiring anticoagulant therapy during the procedure [159].

Is a hybrid pharmacologic and ablative therapy for the management of symptomatic atrial fibrillation useful ?

Several studies have shown that in patients with atrial fibrillation and the development of a class IC atrial flutter, ablation of the TV-IVC isthmus may reduce the incidence of subsequent episodes of AF while continuing antiarrhythmic drugs [160-165]. This hybrid therapy of combined RF ablation and AAD therapy seems to be more effective in achieving and maintaining SR, in comparison with only pharmacological therapy, or only isthmus ablation. Furthermore, it is also quite common to observe atrial flutter in patients with untreated AF, with periodic transition from one arrhythmia to the other, suggesting a mechanistic and possibly causative relationship between AFL and AF [166]. The mechanism by which atrial arrhythmias trigger AF is uncertain, but rapid atrial rates may increase atrial vulnerability by shortening atrial refractory period or electrical remodelling [80]. Assessment of isthmus conduction is impossible during atrial fibrillation, thus either electrical cardioversion is required, or ablation is aimed at abolishing all local electrical activity. The latter seems to be a reasonable, though unproven option. Patients who suffer mainly from atrial flutter (AF episodes > Afib episodes) seem to benefit the most from this hybrid therapy, with 20-30 % freedom of atrial fibrillation recurrences.

(Para)septally located accessory pathways ablation

First, mapping is performed beginning at the anteroseptal region at the His deflection down to the coronary os and further to the right posterior region [97,167,168]. In patients with manifest ventricular preexcitation during sinus rhythm, the site of earliest ventricular activation is identified, characterized by a short local AV interval, with local ventricular activation preceding the onset of the delta wave on the surface ECG. The earliest retrograde atrial activation is identified during orthodromic circus movement tachycardia and ventricular pacing. If local activation is clearly late, either a transseptal or a retrograde approach is used for the left side. The ability to record an accessory pathway potential can also provide useful information to guide the localization of the accessory fiber along the atrioventricular annulus. However, the finding of such a potential alone does not automatically mean a successful site, as it can be registered in quite a high percentage in unsuccessful sites [169]. Therefore, selection of an optimal ablation site requires proper interpretation of local parameters, as well as adequate and stable catheter tissue contact before and throughout the application. After identification of a prospective ablation site, RF ablation is performed. RF energy normally is switched off after maximally 30 seconds if no effect is observed at that moment. Otherwise, it is continued for a maximum of 60 seconds. Disappearance of accessory pathway conduction within a few seconds almost always indicates a successful ablation. Slow disappearance means a remote spot with a high recurrence rate of conduction.

After a successful application incremental atrial pacing and ventricular pacing as well as single atrial and ventricular extrastimuli are repeated to conclude a successful ablative procedure. Eventually, intravenous adenosine can be administered, during both atrial and ventricular pacing to show complete AV and VA block, respectively. The patients are ob-

served in the electrophysiology laboratory for 30 minutes to make sure that there was no recurrence of accessory pathway conduction.

Pitfalls in (para)septal accessory pathway ablation

Reasons for lengthy and failed ablation attempts?

In 5 -15 % of RF ablation attempts of (para)septal accessory pathways, no success is achieved despite the presence of optimal local electrograms [97,103,167-172]. This tends to occur most often with posteroseptal accessory pathways. Several reasons for this can be mentioned. A more complex geometry of the accessory pathway, a thicker epicardial fat pad, and a course too deep in the epicardial layer to be affected by the RF energy delivered at the endocardial aspect of the atrioventricular annuli can result in failed ablation [173-175]. Other reasons can be: 1. inability to position the ablation catheter at the effective target site; 2. instability of the ablation catheter or inadequate tissue contact at the target site, or both; 3. mapping errors due to an oblique course of the accessory pathway; 4. failure to recognize a posteroseptal accessory pathway as being left-sided instead of right-sided; 5. the failure to recognize abnormal structures such as coronary sinus aneurysms or diverticuli that harbor the culprit pathway; 6. occurrence of a complication; 7. recurrent atrial fibrillation [173]; 8. mechanical block, especially in midseptal position; 9. close proximity to the His bundle.
Several strategies can be used to overcome these problems. The simplest one is the substitution of the operator by a more experienced one. The use of other ablation catheters of varying configurations can also be helpful. Irrigated tip catheters can be used to improve the diameter and depth of the lesion. The rationale behind it is that these catheters can increase the temperature in deep tissue by increasing the current density as impedance rise is prevented by cooling the electrode with saline irrigation.

Furthermore, switching from a retrograde aortic to a transseptal approach, from an inferior to a superior caval vein approach, or the use of a 60-cm guiding sheath all can contribute to a better positioning and increasing stability of the ablation catheter and therefore to a higher success rate. Finally, epicardial instrumentation and ablation is another approach that can be used and appears to be feasible and safe [177].

How to reduce the risk of inadvertent complete heart block ?

Radiofrequency (RF) catheter ablation of accessory atrioventricular (AV) connections in the proximity of His bundle or AV node carries a high risk of developing complete heart block, varying from 0 to 20 % [97,167,168,171,172]. Right bundle branch block has been reported in up to 40-50 % of patients with anteroseptal pathways. Incidentally, during ablation of posteroseptal accessory pathways heart block occurrs, preceded by junctional tachycardia. Therefore, if junctional tachycardia is observed, especially with VA block, careful attention should be paid to normal AV conduction. In pathways where there is concern about the proximity to the AV node, an accessory pathway potential should be sought and distinguished from the His bundle deflection. The optimal ablation site is where the accessory

pathway potential is maximal, and the His deflection is later in timing and considered as far field [97]. To reduce the risk of complete heart block, a small atrial deflection with a larger ventricular deflection is ideal. The presence of preexcitation may mask the occurrence of AV block during RF ablation. To overcome this problem, RF ablation can be carried out during orthodromic circus movement tachycardia so that the integrity of the normal AV conduction system can be closely monitored. Energy delivery is immediately stopped if tachycardia terminates in the antegrade limb, if junctional tachycardia occurs, or if tachycardia does not terminate within 15 seconds. On the other hand, catheter dislodgement at the time of termination of the tachycardia during RF application, carries an increased risk for heart block [178]. Pacing at rates when the accessory pathway is refractory can be of help. Titrating power output with temperature monitoring is also used. Importantly, after a successful ablation, additional applications (insurance or bonus burns) are not indicated and should be avoided.

The rationale for cryoablation

Radiofrequency (RF) energy has become the preferred modality for catheter ablation and has proven to be highly effective in the treatment of atrioventricular nodal reentrant tachycardias (AVNRT), (para)septal accessory pathways, and atrial flutter with a low complication rate [83,138-140,142),(98,104),(97,103,167-172]. Despite this successful approach in definitive treatment of tachyarrhythmias in Koch's triangle, several disadvantages can be expected with RF energy. Lesions created by RF ablation, inevitably involve some degree of tissue disruption with intralesional hemorrhage and ragged edges, not clearly demarcated from the underlying normal myocardium, making it potentially more arrhythmogenic [104,107-109,107,135,136]. High temperature at the subendocardium and endocardium may result in coagulum formation on the electrode, endocardial disruption, steam popping or perforation. Because of the endocardial disruption, this method is accompanied by a high percentage of thrombus formation, which can cause thrombo-embolic events [107-109]. Also bleeding, cardiac perforation with or without tamponade can occur. Furthermore, an increased risk exists of causing a right bundle branch block or inadvertent complete heart block, especially in the treatment of tachyarrhythmias in Koch's triangle, as these arrhythmias are located in close proximity to the compact AV node. Finally, RF ablation can be painfull, especially during energy delivery close to the os of the coronary sinus or the junction of the right atrium and VCI [158,177]. In response to the above limitations, alternative energy sources have been developed, of which cryoablation seems to be very promising.

As cryothermy has the ability to reversibly demonstrate loss of function of tissue with cooling at less negative temperatures ('ice mapping'), prospective ablation sites can be investigated, before a definitive, and irreversible lesion is created [180-183] (Figure 8). Theoretically, this should lead to less applications and abolish the risk for permanent conduction disturbances. The depth of a cryolesion is dependent on colder temperatures, however, lesion area or volume are not significantly associated with cooling rate, temperature, or ablation site [184,185]. In AVNRT, it is the only method to target the slow pathway on EP

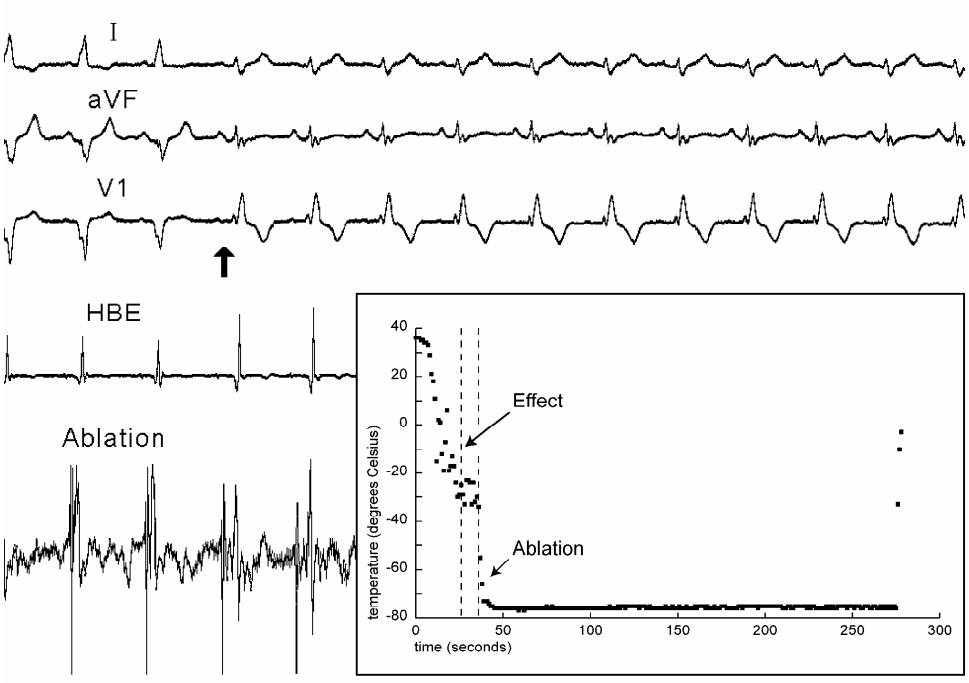


FIGURE 8.
Right posteroseptal accessory pathway. The insert shows the curve of temperature versus time. Shown are leads I, aVF, V1, His bundle electrogram (HBE), and signal from the ablation catheter. Appearance of right bundle branch block (arrow), without intermediate stage of normal ventricular activation, 26 seconds after ice-mapping is started, and a few seconds after –30° C was reached. Ablation is commanded at 36 seconds (which allowed 10 seconds of additional observation of the rhythm), with immediate lowering to –73°C for 4 minutes

basis [180,186-188]. This is possible as during ice mapping, atrial extrastimulus testing can be performed. Disappearance of an AH-jump, termination or non-inducibility of AVNRT is considered to be an identification of abolition or modification of slow pathway conduction, and therefore a potentially successful ablation site. Theoretically, on the basis of these aforementioned characteristics of cryothermy, this should lead to less applications, less tissue damage, and abolish the risk for permanent conduction disturbances. As progressive ice formation at the catheter tip causes adherence to the adjacent tissue, ablation can also safely be performed at otherwise unstable catheter positions, or even during tachycardia, without carrying the risk for catheter dislodgement at termination of the tachycardia. Therefore, cryothermy could be especially useful in ablation of tachyarrhythmias in Koch's triangle to reduce the risk of inadvertent right bundle branch block, or complete AV block [73,189,190]. The more precise delivery of therapy (due to ice mapping and the smaller lesions both in area and volume) with a decrease of tissue damage (less applications), together with the formation of a homogenous fibrosis with a well demarcated border, makes it potentially less proarrhythmic (FIGURE 9). Together with the proven preservation of the extracellular matrix, the incidence of thrombus formation is significantly less than

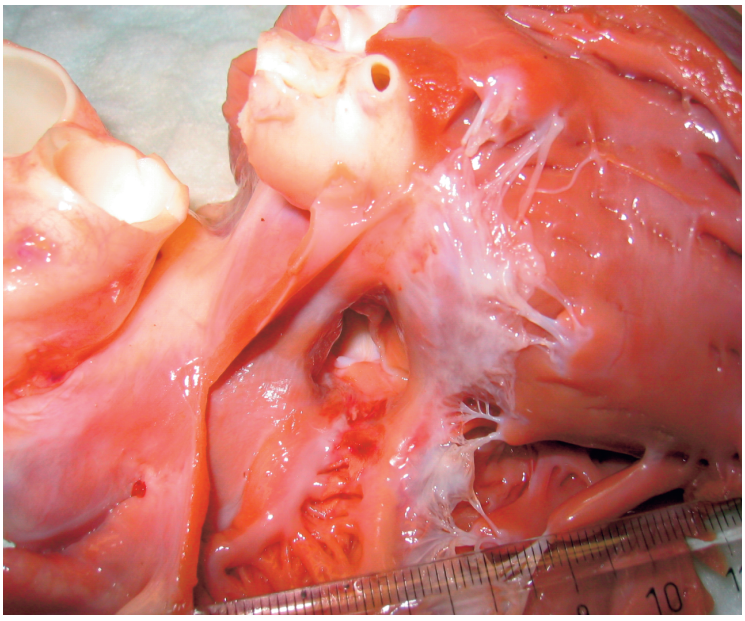


FIGURE 9.
An anatomical section of a pig heart, 4 days after cryoablation. Shown is a well demarcated cryo-lesion on the spot of the AV node

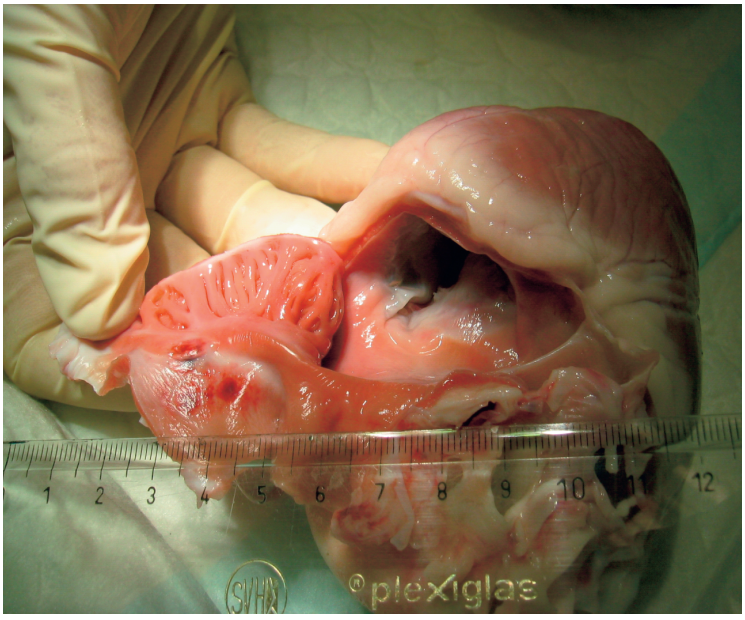


FIGURE 10.
An anatomical section of a pig heart, 4 days after cryoablation. Shown is a lesion in the superior caval vein, with intact vessel wall

with RF energy [185]. This is especially important when linear lesions are made in the left heart, or ablation has to be carried out in pulmonary veins or coronary sinus, which has been shown to be effective and safe [191] (FIGURE 10). Another issue is that cryothermy is painless. This can be of interest during ablation near the os of the coronary sinus, or the border of the right atrium and IVC during cavo-tricuspid isthmus ablation in atrial flutter [158,179,192,193]. Because of these aformentioned advantages of cryothermy, and as experience with cryoablation will grow, there is the potential for it to replace RF for ablation of specific arrhythmic substrates, as tachyarrythmias in Koch's triangle, PV isolation, or to create long linear lesions that are transmural. However, several remarks on have to be made. Until now only a limited number of patients have been treated with cryoablation, and therefore, no definitive conclusions can be made so far. The actual cryocatheters are less steerable than a conventional RF catheter, and this can limit proper catheter positioning. An important question remains if cooling to minus 30 degrees always means maximum effect. In other words, can we always rely on ice mapping in words of safety and/or efficacy, also for intramural or more epicardially located accessory pathways [194,195]? Finally, as tissue temperature rises away from the center, tissue effects that occur late during a cryo-application are expected to be reversible. Although, cryothermy has some advantages in comparison with RF, and as experience with cryoablation will grow, there is the potential for it to replace RF for ablation of specific arrhythmic substrates, as tachyarrythmias in Koch's triangle, PV isolation, or to create long linear lesions that are transmural. However, clinical evaluation is needed.

Conclusion

Koch's triangle is a fascinating area. In the previous chapters an overview is given from the embryology of the atrioventricular conduction axis which already exists in the fith and sixth week of the development of the heart, to the anatomy and electrophysiologic characteristics of these region with the development of different tachyarrhythmias and their cure with transvenous catheter ablation. Although it has been a source for intensive research, a lot of questions on anatomy and physiology of this region are still unresolved. This introduction intended to provide a state-of-the-art in todays knowledge about Koch's triangle.

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2

Visualisation of Intra-cardiac Structures and Radiofrequency Lesions Using Intracardiac Echocardiography

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Eur J Echocardiography 2003;4:17–22

Aims: Fluoroscopy does not allow identification specific anatomical landmarks during electrophysiological studies. Intra-cardiac echocardiography permits visualization of these structures with excellent accuracy, but the optimal method has not been fully described. The aim of this study was to assess the capability of intra-cardiac echocardiography for the visualization of such structures using two different approaches. We also assessed its capability for the evaluation of radio frequency lesions 20 min after catheter ablation of the cavo-tricuspid isthmus.

Methods: Intra-cardiac echocardiography was performed using a 9 MHz rotating transducer in eight consecutive patients (age range: 37–76 years) after radio frequency ablation of the cavo-tricuspid isthmus. The ultrasound catheter was inserted through the femoral vein into the superior vena cava and was pulled back to the inferior vena cava. The echo catheter was then reinserted through the subclavian vein and advanced into the right ventricular apex and was pulled back from the right ventricular to the superior vena cava. Qualitative evaluation and intracardiac measurements were performed off-line.

Results: The fossa ovalis, the tricuspid valve, and the terminal crest were visible in all patients regardless of the method of introduction of the echo catheter. Left-sided structures were less accurately seen by intra-cardiac echocardiography. The horizontal diameter of the fossa ovalis was 8·9 ± 1·8 mm. The cavo-tricuspid isthmus was visible using the femoral approach in three patients. The isthmus could be visualized in all patients, and in three patients together with the ostium of the coronary sinus, using the subclavian approach. radio frequency lesions were not visible 20 min after ablation. Additionally, both the left and right ventricles could be seen using the subclavian approach.

Conclusions: The subclavian approach is feasible, safe and superior to visualize the isthmus. Twenty minutes after radio frequency ablation of the cavo-tricuspid isthmus radio frequency lesions are not visible using intra-cardiac echocardiography.

Keywords: intracardiac echocardiography; ablation; isthmus; flutter.

Introduction

Arial flutter is a frequent arrhythmia due to re-entry around the large vascular structures in the right atrium [1,2]. Radio frequency (RF) catheter ablation is an effective method in management of atrial flutter [3]. However, a considerable proportion of the cases is unsuccessful and a substantial number of patients have recurrences [3]. One possible explanation for the unsuccessful procedures and recurrences is related to anatomical variations of the cavo-tricuspid isthmus. Furthermore, radio frequency lesions can be inadequate, allowing slow conduction through the cavo-tricuspid isthmus. Fluoroscopy does not allow identification of important anatomic landmarks during electrophysiological studies. Improved imaging techniques such as intra-cardiac echocardiography may have a role to improve success rate of radio frequency ablations by guiding these procedures [4,5]. Although intracardiac echocardiography allows guiding of electrophysiological procedures by visualizing important structures, there are controversial data available about its capability to assess the radio frequency lesions after ablation [6-8]. The aim of the present study was to test two different approaches for visualization of anatomical structures and radio frequency lesions. We compared the capability of intracardiac echocardiography imaging using two different entry sites such as the femoral vein (inferior approach) and the subclavian vein (superior approach). Furthermore, we assessed radio frequency lesions in the cavotricuspid isthmus region 20 min after radio frequency ablation of the cavo-tricuspid isthmus.

Methods

Study Patients

Eight consecutive patients who underwent radio frequency ablation of typical atrial flutter were included in this study. The mean age of the patients was 56 ± 11·1 years (range: 37–76). Three patients were women.

Electrophysiological Procedure

Standard electrophysiological studies were performed under intravenous sedation with 5–10 mg diazepam. After a subclavian venipuncture, a 5 F decapolar diagnostic catheter (Supreme CS, DAIG Corp. St. Jude Medical Inc, Minnesota, MN, U.S.A.) was inserted into the coronary sinus through a short vascular sheath. In one patient there subclavian venous access could not been achieved. A steerable 20-pole Orbiter catheter (Bard, U.S.A.) was positioned around the tricuspid annulus. 5000 IU of heparin was administered intravenously. A Cosio radio frequency mapping/ablation catheter (Medtronic, U.S.A.) was used for mapping the critical isthmus between the inferior vena cava and the posterior tricuspid annulus. All patients underwent an anatomically guided catheter-based ablation with creation a line of lesions from the posterior part of the tricuspid annulus to the inferior vena cava. Successful ablation was assessed by demonstration a bi-directional block using conventional pacing techniques.

FIGURE 1.
The ultrasaound transducer, showing a distal sonolucent sheath, which houses the rotating echotransducer

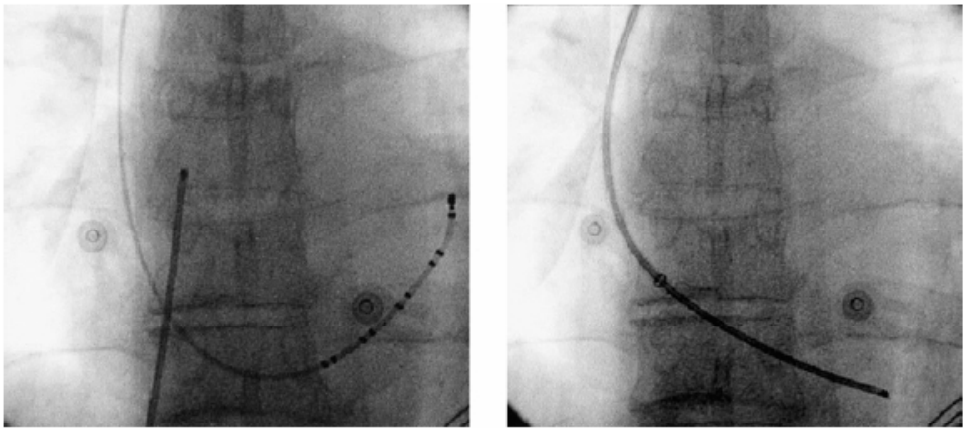

FIGURE 2.
AP fluoroscopy view of the intra-cardiac echocardiography transducer introduced into the heart. Left panel: subclavian approach

Intra-cardiac Echocardiography Imaging

The mechanical intravascular ultrasound and intracardiac echocardiography system ClearView (Cardio- Vascular Imaging Systems Inc, Fremont, CA) was used with a 8F sheath-based intra-cardiac echocardiography imaging catheter that incorporated a 9 MHz bevelled single-element transducer rotating at 1800 rpm (model 9900, EP Technologies, Boston Scientific Corp., San Jose, CA, U.S.A.). These catheters are equipped with an 1-cm long sonolucent distal sheath, which has a lumen housing the imaging transducer (FIGURE 1). This sheath prevents direct contact of the imaging core with the cardiac wall. The intra-cardiac echocardiography catheter is filled with 3–5 cc sterile water and then connected to an ultrasound console (model I5007, Boston Scientific Corp., San Jose, CA, U.S.A.). This catheter obtains cross-sectional images in a plane, which is perpendicular to its long axis. The images are displayed on a monitor and recorded on videotape. The position of the catheter is checked in three fluoroscopy views (AP, LAO, RAO). The ultrasound catheter is initially inserted through the femoral vein into the superior vena cava and is pulled back to the inferior vena cava inferior vena cava. The multipolar electrode catheter was removed

from the coronary sinus, and the short vascular sheath was exchanged for an 8F and 60 cm long straight vascular sheath. The echo catheter is then reinserted through this sheath into the right ventricular apex and pulled back from the right ventricle to the superior vena cava during recording of two-dimensional images (FIGURE 2). Qualitative analysis and intra-cardiac measurements are performed off-line. Data are reported as mean_standard deviation.

Results

Clinical characteristics of the patients are shown in TABLE 1. Radio frequency catheter ablation of the flutter circuit was successful in all cases. The mean number of radio frequency applications was 19 ± 4·2. The procedure and fluoroscopy times were 203 ± 91·6 min and 55 ± 34·4 min, respectively. The results regarding visualization of anatomically important structures and radio frequency lesions are shown in TABLE 2. The fossa ovalis, the tricuspid valve, the terminal crest were visible in all cases regardless the way of introduction of the echo catheter (FIGURE 3). The size of the fossa ovalis was 8·9 ± 1·8 mm. Left-sided structures such as the mitral valve, aortic valve and the aorta were less visible but were not different using the two approaches. The cavotricuspid isthmus was poorly visible (three patients/37%) using the femoral approach (FIGURE 4). The isthmus could be visualized in all patients using the subclavian approach (eight patients/100%). In addition, in three

Table 1. Demographic and echocardiography data of the patients

No. of patients (*n*)	8
Age (years)	56 ± 11·1
Gender (M/F)	5/3
Other/underlying cardiac disease	
Other SVT (*n*)	1
Hypertension (*n*)	3
Afib (*n*)	4
VHD (*n*)	4
Cardiac dimensions	
LA (mm)	42·5 ± 7·3
LV EDD (mm)	55·6 ± 7·5
LV ESD (mm)	34·5 ± 9·8
IVS (mm)	10·1 ± 3·7

n=number of patients, M=male, F=female.
SVT=supraventricular tachycardia; Afib=atrial fibrillation; VHD=valvular heart disease; LA=left atrium; LV EDD=end-diastolic diameter of left ventricle; LV ESD=end-systolic diameter of left ventricle; IVS=intra-ventricular septum.

Table 2 Comparison of visualisation of intracardiac structures

Pt. no.	Ao	AoV	TV	MV	PV	PA	CS	isthmus	FO	Size: FO (mm)
Femoral approach										
1.	–	–	+	–	–	–	–	–	+	7·7
2.	+	–	+	+	–	+	–	+	+	7·2
3.	+	–	+	–	+	–	–	–	+	12·1
4.	+	–	+	+	–	–	–	+	+	10·9
5.	+	–	+	–	–	–	–	+	+	7·2
6.	+	–	+	–	–	–	–	–	+	7·4
7.	+	+	+	–	–	+	–	–	+	10
8.	+	+	+	–	–	+	–	–	+	9·1

Pt. no.	LV, RV	Ao	AoV	TV	MV	PV	PA	CS	isthmus	FO
Subclavian approach										
1.	+	–	+	+	–	–	–	–	+	–
2.	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
3.	+	+	+	+	–	–	–	+	+	+
4.	+	+	–	+	+	–	–	+	+	+
5.	+	+	–	+	–	–	–	–	+	+
6.	+	+	–	+	–	–	–	–	+	+
7.	+	+	+	+	+	–	+	+	+	+
8.	+	+	+	+	+	–	+	–	+	+

Ao=Aorta; AoV=Aortic valve; TV=tricuspid valve; Mv=mitral valve; PV=pulmonary veins; PA=pulmonary artery; CS=coronary sinus; FO=oval fossa; LV=left ventricle; RV=right ventricle.

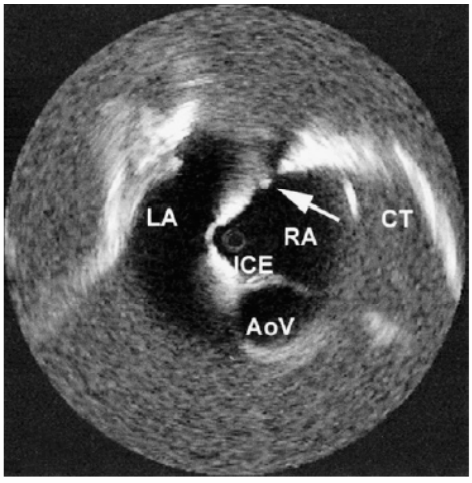

Figure 3. Visualization of electrophysiologically important structures obtained by the femoral approach. The crista terminalis, the aortic valve, and the fossa ovalis are visible together with the left atrium. The arrow shows the cross-section of a diagnostic catheter. LA=left atrium, RA=right atrium, AoV=aortic valve, CT=crista terminalis, ICE=central artefact of the intra-cardiac echo transducer.

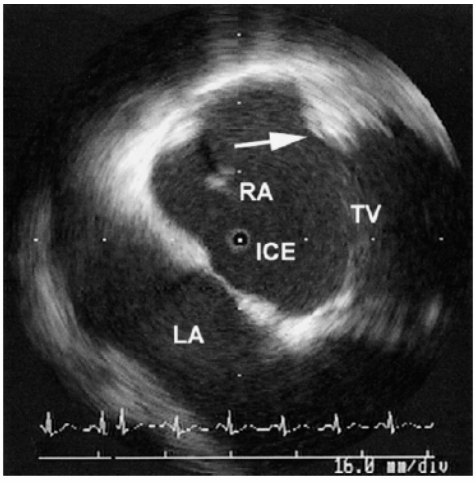

Figure 4. Visualization of the cavo-tricuspid isthmus using the femoral approach. The isthmus can be seen above the tricuspid valve (arrow). RA=right atrium, LA=left atrium, TV=tricuspid valve, ICE=central artefact of the intra-cardiac echo transducer

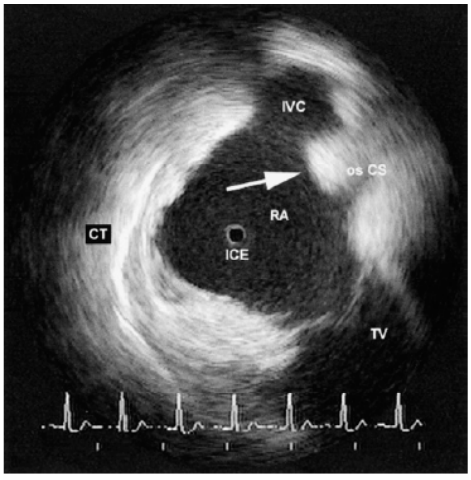

Figure 5. The isthmus is optimally visualized using the subclavian approach (arrow). The ostium of the coronary sinus is also visible. CT=crista terminalis, RA=right atrium, IVC=inferior vena cava, TV=tricuspid valve, os CS=ostium of the coronary sinus, ICE=central artefact of the intra-cardiac echo transducer.

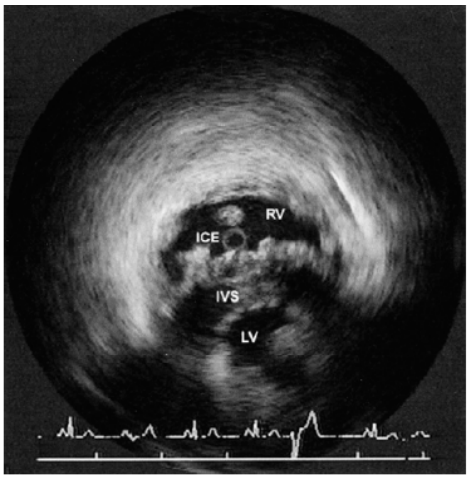

Figure 6. The left and right ventricles are exclusively visualized by the subclavian approach. RV=right ventricle, LV=left ventricle, IVS=intraventricular septum, ICE=central artefact of the intra-cardiac echo transducer.

patients the ostium of the coronary sinus was visible (three patients/37%) (Figure 5). Both the left and right ventricles could be seen using the subclavian approach, and were not visualized by the femoral approach (Figure 6). Radio frequency lesions and more particularly craters were not observed 20 min after ablation. There were no observable differences between the ablated region and other cardiac walls (Figures 4 and 5). The echodensity of the wall was not different from adjacent regions. There were no complications related to radio frequency ablation and/or intra-cardiac echocardiography catheterization.

Discussion

The main findings of our study are that, the isthmus is better visualized using the subclavian approach rather than by the femoral approach using a non-steerable catheter. The radio frequency lesions are not visible using this technique 20 min after the procedure.

The Role of Intra-cardiac Echocardiography in Ablation of Atrial Flutter

Radio frequency catheter ablation is an option in management of atrial flutter [3]. The aim of the procedure to create a lesion over the isthmus, the region between the inferior vena cava and the posterior region of the tricuspid valve interrupting the re-entry circuit.

Although the procedure has a success rate over 90%, approximately 10% of the patients have recurrences necessitating a second procedure. Obviously, these procedures add significant radiation exposure and a risk of other complications [3]. Intra-cardiac ultrasound can visualize intra-cardiac structures [9-11]. Occasionally, atrial malformations can be de-

tected in the region of interest. Dimensions of the isthmus can be measured and the alignation and correct apposition to the tissue of the catheters can be judged [12]. According to our results, pulling back the intra-cardiac echocardiography catheter from the right ventricle through the tricuspid valve after left subclavian venipuncture provides a better image than a pullback from the superior vena cava to inferior vena cava on this important region. Therefore visualization of important anatomical structures and observation anatomical variations is more appropriate with a superior approach.

Ablation Lesion Assessment

It was hypothesized that tissue changes may be detected using intra-cardiac echocardiography. Crater formation and increased echodensity was reported immediately after radio frequency ablation [7]. Despite these early and promising reports we could not observe any changes in the ablated region after linear ablation. We did not see craters 20 min after radio frequency ablation. Possible explanation for this finding is related to the timing of our examinations, as we assessed the lesions 20 min after radio frequency ablation to exclude temporary changes.

Future Clinical Applications

The ostium of the coronary sinus could be optimally visualized in some patients during subclavian insertion of the intra-cardiac echocardiography catheter. Similar images could not be obtained using the femoral approach and this non-steerable ultrasound system. Novel, steerable catheters are also available[13]; however, these catheters substantially increase the cost of the procedure. Regardless this issue, intra-cardiac echocardiography seems to be a feasible guiding tool for cannulation the ostium of the coronary sinus if necessary during electrophysiology and multisite pacing procedures.

For visualization of radio frequency lesion further developments such as tissue characterization are necessary.

In conclusion, the subclavian approach is a feasible technique to perform intra-cardiac echocardiography and using a non-steerable echocardiography probe it is more appropriate to visualize the inferior vena cavatricuspid annulus isthmus than the conventional femoral approach. Radio frequency lesions cannot be identified 20 min after creation using this 9 MHz fixed frequency intracardiac ultrasound probe in the absence of baseline pre-ablation intra-cardiac imaging.

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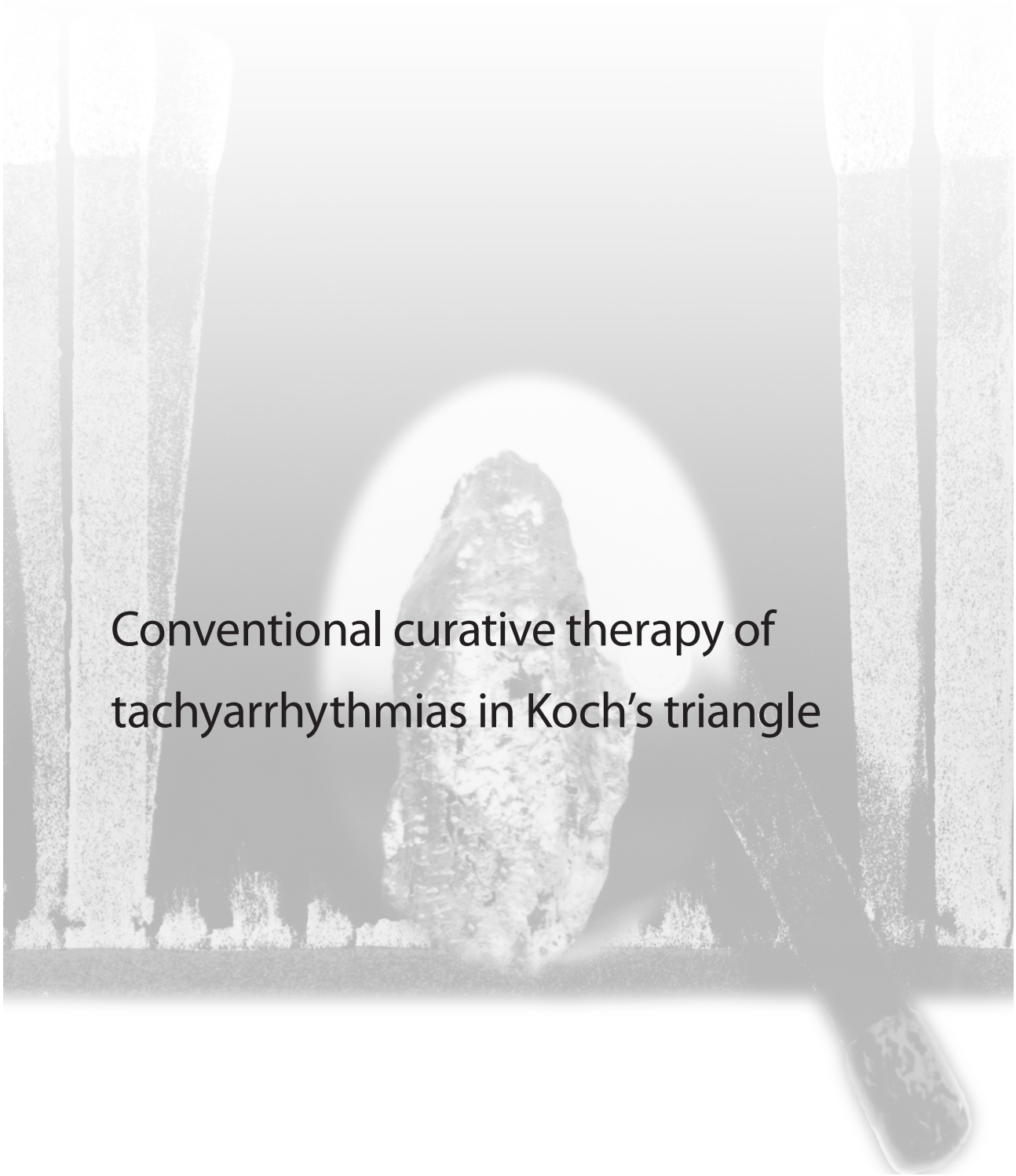

Conventional curative therapy of tachyarrhythmias in Koch's triangle

3

Comparison of late results of surgical or radiofrequency catheter modification of the atrioventricular node for atrioventricular nodal reentrant tachycardia

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Eur Heart J 1999;20:527-534

Abstract

Aims Although arrhythmia surgery and radiofrequency catheter ablation to cure atrioventricular nodal reentrant tachycardia differ in technical concept, the late results of both methods, in terms of elimination of the arrhythmogenic substrate and procedure-related new and different arrhythmias, have never been compared. This constituted the purpose of this prospective follow-up study.

Methods and Results Between 1988 and 1992, 26 patients were surgically treated using perinodal dissection or 'skeletonization', and from 1991 up to 1995, 120 patients underwent radiofrequency modification of the atrioventricular node for atrioventricular nodal reentrant tachycardia. The acute success rates of surgery and radiofrequency catheter ablation were 96% and 92%, respectively. Late recurrence rate in the surgical and radiofrequency catheter ablation groups was 12% and 17%, respectively. Mean follow-up was 53 months in the surgical group and 28 months in the radiofrequency catheter ablation group. The final success rate after repeat intervention was 100% in the surgical group and 98% in the radiofrequency catheter ablation group. Comparison of the initial and recent series of radiofrequency catheter ablated patients showed an increased initial success rate with fewer applications. In the radiofrequency catheter ablation group, a second- or third-degree block developed in three patients (2%), requiring permanent pacing, whereas in the surgical group no complete atrioventricular block was observed. Inappropriate sinus tachycardia needing drug treatment was observed in 13 patients (11%), mostly after fast pathway ablation, but was never observed after surgery. New and different supraventricular tachyarrhythmias arose in 27% of the patients in the surgical group and in 11% of the radiofrequency catheter ablation group, but did not clearly differ.

Conclusion This one-institutional follow-up study demonstrated comparable initial and late success rates as well as incidence of new and different supraventricular arrhythmias following arrhythmia surgery and radiofrequency catheter ablation for atrioventricular nodal reentrant tachycardia. Today radiofrequency catheter ablation has replaced arrhythmia surgery for various reasons, but the late arrhythmic side-effects warrant refinement of technique.

Keywords: Atrioventricular nodal reentrant tachycardia, arrhythmia surgery, radiofrequency catheter ablation, supraventricular tachyarrhythmia.

Introduction

Initially, surgical modification of the atrioventricular node was the only method to interrupt atrioventricular nodal reentrant tachycardia. Both cryosurgery for modification of the perinodal tissues along the perimeter of the triangle of Koch [1,2] and 'skeletonization', a dissection technique to interrupt all atrial inputs of the atrioventricular node except the 'deep' left atrial input [3], resulted in successful cure of the tachycardia while preserving atrioventricular conduction. For several reasons radiofrequency catheter ablation is today's treatment of choice for abolishment of recurrent atrioventricular nodal reentrant tachycardia [4-8]. While the early results of surgical and radiofrequency catheter atrioventricular nodal modification show a high immediate success rate and a low complication rate [4-8], the late clinical outcome and arrhythmic side-effects of these interventions have rarely been reported [9-14]. The purpose of this prospective one-institutional study was to compare these effects of both interventions in order to examine our therapeutic progress.

Patients and Methods

Between 1988 and 1992, 26 patients atrioventricular nodal reentrant tachycardia underwent operative perinodal dissection, and from 1991 to 1995, 120 patients were treated with radiofrequency catheter ablation (Table 1). In the surgical group, one patient had mild mitral valve stenosis. In the radiofrequency catheter ablated group there were three patients with associated coronary artery disease, three patients suffered from chronic obstructive pulmonary disease, one patient had a surgically corrected ventricular septal defect, and another patient a concomitant non-sustained ventricular tachycardia unassociated with structural heart disease.

Table 1 Demographic and electrophysiological data before ablation

Preablation data	RF catheter ablation			Surgery (mean ± SD)
	Fast pathway (mean ± SD)	Slow pathway (mean ± SD)	Slow and fast pathway (mean ± SD)	
n	40	47	33	26
Male/Female	12/28	12/35	10/23	6/20
Age (years)	45 ± 17·5	42 ± 15·5	44 ± 10·9	47 ± 14·3
Duration of symptoms (years)	14·6 ± 12·0	12·9 ± 11·4	13·9 ± 10·8	14·5 ± 14·5
Typical AVNRT	38 (95%)	41 (87%)	32 (97%)	23 (89%)
Atypical AVNRT	2 (5%)	6 (13%)	1 (3%)	3 (11%)
PR interval (ms)	154 ± 21·5	152 ± 30·4	151 ± 16·9	159 ± 17·6
AH interval (ms)	73 ± 18·1	73 ± 26·9	70 ± 14·7	77 ± 18·3
Jump in AH interval present	17 (43%)	23 (49%)	16 (48%)	10 (38%)
Jump in AH interval (ms)	122 ± 53·3	103 ± 61·1	98 ± 40·4	121 ± 63·0
ERP AV (ms)	258 ± 49·4	238 ± 52·4	269 ± 50·7	300 ± 25·5
ERP VA (ms)	259 ± 54·0	237 ± 40·2	280 ± 104·1	271 ± 43·1
AVNRT cycle length (ms)	332 ± 49·8	326 ± 59·9	341 ± 75·2	313 ± 50·0
Preexistent paroxysmal type 1 AFlut	1	1	1	0

Electrophysiological testing before intervention

The electrophysiological study was performed in the post-absorbative state. If necessary, the patients were sedated with diazepam, fentanyl or a combination of these drugs. Prior to the study, antiarrhythmic drugs were discontinued for at least five half-lives. For recording of intracardiac electrocardiograms and performing programmed electrical stimulation, diagnostic catheters were positioned high in the right atrium, in the His bundle region, the coronary sinus and the right ventricular apex. Standard criteria were used to establish the diagnosis of dual atrioventricular nodal pathways and typical and atypical atrioventricular nodal reentrant tachycardia [15,16]. If atrioventricular nodal reentrant tachycardia could not be induced by programmed electrical stimulation with different paced heart rates, using up to three extrastimuli, isoprenaline (titrated to increase heart rate by >20%) or atropine were administered intravenously (maximum dose of 2 mg). This procedure was repeated if atrioventricular nodal reentrant tachycardia recurred after a previously successful procedure.

Surgical atrioventricular node modification ('skeletonization')

Using normothermic cardiopulmonary bypass, the atrioventricular node region was exposed through a right atriotomy along the tricuspid annulus, extending to the atrial membranous septum [1]. The tendon of Todaro was identified. The inferior medial right atrial wall was incised along the septal segment of the tricuspid annulus below the atrial membranous septum. Dissection of the right atrial wall was completed and extended inferiorly towards the coronary sinus orifice and superiorly where a plane of cleavage was identified between the right atrial wall and the intermediate atrioventricular node, to meet the anterior septal incision. The septal atrial wall was divided and deflected posteriorly to expose the atrioventricular node. The intermediate atrioventricular node was identified by its oblique, pale myocardial fibres and dissected from surrounding tissue to separate superficial and posterior atrial inputs while deep inputs were left intact. Atrioventricular nodal conduction was monitored during the operation. The end-point of the procedure was the non-inducibility of atrioventricular nodal reentrant tachycardia during electrophysiological testing, prior to closure of the atrium. Inducibility of no more than one nodal echo beat was accepted.

Radiofrequency atrioventricular node modification

A quadripolar Steerocath or Tracfinder catheter (EP Technologies), or a quadripolar 4 mm tip catheter (Cordis-Webster) with deflectable curves were used. Radiofrequency energy pulses of 7 to 50 Watt at a frequency of 500 kHz were delivered by a custom-made available electrosurgical device by delivering current between the distal electrode and a cutaneous, indifferent, dispersive pad positioned on the patient's back.

Selective fast pathway ablation

During a fast pathway ablation procedure, the ablation catheter was positioned across the tricuspid annulus to record a His bundle potential during sinus rhythm and thereafter slowly withdrawn until the amplitude of the atrial electrogram exceeded the ventricular electrogram and the His bundle potential was small or hardly visible [11]. Radiofrequency

application was initially delivered at this target site. After each application of radiofrequency energy, electrophysiological induction of the tachycardia was attempted and when still inducible, the above procedure was repeated in an attempt to reach a better position or better tissue contact as described above. Ablation was considered immediately successful when atrioventricular nodal reentrant tachycardia was no longer inducible or when a 30% prolongation of the PR interval or an inadvertent second- or third-degree atrioventricular block occurred. Atrial pacing at a cycle length of 500 ms was started at the onset of the accelerated atrioventricular junctional rhythm, thereby permitting continuous monitoring of atrioventricular conduction.

Selective slow pathway ablation

The site of slow pathway ablation was established by positioning the ablation catheter septally, just across the tricuspid valve posterior to the atrioventricular node immediately posterior, anterior or at the level of the ostium of the coronary sinus. That area was examined for the presence of slow pathway potentials thought to be presented by double potentials in the bipolar atrial electrocardiogram of the ablation catheter. When these signals could not be located within a time frame of 20 min, a more aspecific ablation of the posterior perinodal atrium was performed. Radiofrequency energy was applied between the tricuspid valve and the os of the coronary sinus, whereas the amount was titrated to inducibility of atrioventricular nodal reentrant tachycardia [5,15,16] The end-point of slow pathway ablation was non-inducibility of atrioventricular nodal reentrant tachycardia with preserved atrioventricular nodal conduction.

Combined slow and fast pathway ablation

If initially a slow pathway approach was chosen and ablation was not successful after more than an arbitrary 20 radiofrequency applications, the previously described fast pathway ablation approach was applied during the same procedure. Conversely, if fast pathway ablation was unsuccessful, slow pathway ablation was carried out, again during the same session. The end-point of this approach was based on the previously mentioned end-points for fast and slow pathway ablation.

Patient follow-up

All patients were followed for at least 1 year in our outpatient clinic or by the referringcardiologist. If a patient experienced symptoms of palpitations, a 24-h Holter recording or a self-activating ambulatory single channel ECG recording and exercise testing were performed. An electrophysiological study was scheduled if recurrence of atrioventricular nodal reentrant tachycardia could not be confirmed while symptoms remained present. When the diagnosis of atrioventricular nodal reentrant tachycardia was established, a second ablation procedure was carried out.

Statistical analysis

Data are expressed as mean+SD. Chi-square and Student's t-test were used for statistical comparison whenever appropriate. For censored data the logrank test was used. A two-tailed P value <0·05 was considered significant.

Results

One hundred and thirty-four of the 146 patients (92%) had typical atrioventricular nodal reentrant tachycardia, and in 12 patients (8%) it was atypical. There were no significant differences in electrophysiological baseline characteristics between the surgical and various ablation groups (Table 1). Fast pathway ablation significantly increased the PR and AH intervals ($P<0{\cdot}05$) compared with the values observed after slow pathway ablation and surgery (Table 2).

Surgical atrioventricular node modification

In 25 of 26 patients (96%), immediate success was achieved (Table 2). In 10 patients (38%), transient complete atrioventricular block was observed, but atrioventricular conduction normalized in all patients within a few minutes, except for two patients (8%) in whom a first degree atrioventricular block persisted (Table 3). One patient had a pneumothorax, and in one patient an occlusion of the left anterior descending coronary artery occurred, associated with an anterior myocardial infarction. Three of the 25 immediately successful surgical patients experienced recurrences of atrioventricular nodal reentrant tachycardia (Table 3). In two of these patients atrioventricular nodal reentrant tachycardia recurred in the early 7 months after surgery, in one patient a recurrence was documented 3 years after surgery. Two of the latter three patients had a subsequently successful radiofrequency catheter ablation, one patient underwent three successive radiofrequency catheter ablation sessions because of repetitive recurrences of atrioventricular nodal reentrant tachycardia. In this patient, the tachycardia did not reoccur during a mean follow-up of 17 months. The patient with an immediately unsuccessful first procedure had a successful second operation. New and different supraventricular tachycardias arose in seven patients (Table 3). Two patients underwent radiofrequency catheter ablation of the His bundle and pacemaker implantation since these arrhythmias (type 1 atrial flutter and atrial fibrillation) became drug refractory.

Table 2 Electrophysiological data shortly after ablation

Postablation data	RF catheter ablation			Surgery (mean ± SD)
	Fast pathway (mean ± SD)	Slow pathway (mean ± SD)	Slow and fast pathway (mean ± SD)	
n	40	47	33	26
Immediate success rate (%)	90	98	82	96
Ablation time (min)	76 ± 47·6	44 ± 34·4	84 ± 47·2	n.a.
Number of applications	14 ± 17	13 ± 15	25 ± 28	n.a.
PR interval (ms)	199 ± 49·0*	158 ± 27·7	183 ± 41·8	161 ± 34·0
AH interval (ms)	121 ± 43·6*	79 ± 25·6	101 ± 48·9	76 ± 21·5
Jump in AH interval present	9 (23%)	8 (17%)	2 (6%)	4 (15%)
Jump in AH interval (ms)	126 ± 60·4	103 ± 39·9	110 ± 56·6	120 ± 42·4
ERP-AV (ms)	248 ± 58·9 n=17	232 ± 82·3 n=27	246 ± 65·7 n=20	309 ± 61·3 n=17
ERP-VA (ms)	310 ± 119·9 n=7	226 ± 59·1 n=17	261 ± 85·8 n=10	264 ± 45·0 n=9
VA block present	13 (33%)	5 (11%)	7 (21%)	8 (31%)

ERP=effective refractory period; n.a.=not applicable; *$P<0{\cdot}05$.

Radiofrequency atrioventricular node modification

Selective fast pathway ablation

Immediate success was obtained in 36 of 40 patients (90%) treated with this technique (TABLE 2). One patient developed complete atrioventricular block requiring pacemaker implantation (TABLE 3). Immediately after catheter ablation, eight patients suffered from inappropriate sinus tachycardia and required a beta-blocking agent for 2 weeks to 3 months. Atrioventricular nodal reentrant tachycardia recurred in three patients (8%) with an immediately successful ablation (TABLE 3). They were successfully treated with a second fast pathway catheter ablation procedure. Two of the four patients with an unsuccessful first attempt had no recurrence of atrioventricular nodal reentrant tachycardia after a second ablation session. One patient required a third and one a fourth session. Eventually, all were free of atrioventricular nodal reentrant tachycardia. Table 3 displays the onset of late new supraventricular tachycardias.

Selective slow pathway ablation

Forty-six of 47 patients (98%) had an immediately successful slow pathway ablation (TABLE 2). One patient developed complete atrioventricular block requiring pacemaker implantation (TABLE 3). Four patients had inappropriate sinus tachycardia and received a betablocking agent for 2 to 8 weeks. Nine of 46 patients with an immediately successful ablation suffered from recurrences of atrioventricular nodal reentrant tachycardia and required a

Table 3 Clinical data at late follow-up

Follow-up data	RF Catheter ablation			Surgery
	Fast pathway	Slow pathway	Slow and fast pathway	
n	40	47	33	26
Late recurrence	3 (8%)	9 (20%)	6 (22%)	3 (12%)
Mean follow-up (months)	33	26	25	53
Persisting 1st degree AV block	19	4	13	2
Persisting 2nd degree AV block	0	0	1	0
Persisting 3rd degree AV block	1	1	0	0
Pacemaker implantation	1	2*	1	2†
Inappropriate sinus tachycardia	8	4	1	0
New supraventricular tachyarrhythmias				
type 1 atrial flutter	0	0	1	2
chronic atrial fibrillation	1	3	1	3
atrial tachycardia	4	0	1	1
paroxysms of type 1 AFlut/AF	2	1	0	1

AF=atrial fibrillation; AFlut=atrial flutter.
*=His bundle ablation+pacemaker implantation in one patient.
†=His bundle ablation+pacemaker implantation in two patients.

second attempt (seven patients) or a third session (two patients) (Table 3). Eventually, all were successfully controlled. The patient with an unsuccessful first ablation was controlled after two successive repeat catheter ablations. Table 3 displays the onset of new supraventricular tachycardias.

Combined slow and fast pathway ablation

After unsuccessful fast or pathway ablation, 33 patients underwent additional slow pathway ablation or vice versa during the same session. Immediate success was reached in 27 of 33 patients (82%) (Table 2). Symptomatic second-degree atrioventricular block was seen in one patient requiring pacemaker implantation (Table 3). After an immediately successful procedure, six patients had recurrences of atrioventricular nodal reentrant tachycardia (Table 3). Successful slow and fast pathway ablation was performed again in four of them. The two remaining patients were treated with a repeat slow pathway ablation, of which only one was successful. Two of the six patients with an immediately unsuccessful ablation refused a second ablation attempt and were treated with antiarrhythmic drugs. Three patients were successfully treated in a second ablation session and one needed a third procedure. Table 3 displays the onset of new supraventricular tachycardia. Recurrences of atrioventricular nodal reentrant tachycardia after an immediately successful radiofrequency modification of the atrioventricular node, emerged most frequently (73%) in the early months (maximum 7 months) after ablation, although one recurrence was documented after 25 months. Time of recurrence was not associated with the applied method of atrioventricular node modification. Considering all radiofrequency catheter procedures, the following complications were observed. Three patients suffered from a pneumothorax due to a subclavian vein puncture, two developed pericarditis and one had an ischaemic cerebral infarction 2 h after the procedure, despite adequate intravenous heparinization. The latter patient fully recovered with conventional drug therapy.

Discussion

Immediate results

From a historical perspective this study provides a unique opportunity to compare the early and late results of a relatively large series of surgically treated patients with those of radiofrequency catheter ablated patients. It should be noticed that surgery was practised only briefly and was quickly overtaken by radiofrequency catheter ablation. There was no statistical difference in patient characteristics between either group regarding clinical presentation and failure of drugs, although during the years the indication for radiofrequency catheter ablation has extended because of the easier approach. Despite differences in technical approach, the immediate success rates of surgery (96%) and radiofrequency catheter ablation (92%) are well comparable, and agree closely with the results of earlier studies in which radiofrequency catheter atrioventricular node modification was exclusively applied [4-8], although our immediate success rate of radiofrequency catheter ablation is slightly lower. However, the immediate success rate of the 40 recently treated patients was 95%,

in comparison with 89% of the 80 first treated patients (P=0·26). The mean number of applications also differed significantly between the 80 first treated patients and the 40 recently treated patients, namely 16 and seven respectively (P<0·05). Opposite to surgery, radiofrequency catheter modification of the atrioventricular node caused complete atrioventricular block in two patients (2%) and a second-degree atrioventricular block in one patient (1%), requiring pacemaker implantation. One of these patients underwent catheter modification of the slow pathway in an area anatomically distant from the His bundle, an approach which is assumed to be related to a low risk for complete atrioventricular block [13,14,24,28-30]. Other studies describe a higher incidence of atrioventricular block, specifically complicating fast pathway ablation, varying from 3·5% in experienced investigators up to 21% in inexperienced operators [4,6,9,13,14,17,24,26-30]. Therefore, one may question whether the atrioventricular node can functionally or even anatomically be regarded as a distinct structure, as suggested by earlier experimental data [37,38]. Persistent inappropriate sinus tachycardia requiring treatment with a beta-blocking agent, was observed in 13 patients (11%), and occurred mostly after fast pathway ablation. This observation is in agreement with previously reported incidence of inappropriate sinus tachycardia after catheter atrioventricular node modification [31-33] but was never found to be complicating the surgical procedure [1-3,9-11].

Late results and new arrhythmias

After an immediately successful surgical or radiofrequency catheter modification of the atrioventricular node, atrioventricular nodal reentrant tachycardia recurred in three (12%) and 18 (17%) patients, respectively. Most recurrences (73%) occurred in the early months (maximum 7 months) after the intervention, but recurrence after 3 years was also documented in the surgical group, and after 2 years in the radiofrequency catheter ablated group. In comparison with earlier studies, the recurrence rate in the radiofrequency catheter ablation group was high [4-8,12,13,15,16,18,23-25]. However, the recurrence rate of the 40 recently treated patients was 8%, in comparison with 21% in the 80 first treated patients (P=0·07), and in agreement with these studies. The final outcome after repeat interventions was also very comparable between both approaches, namely 100% in the surgical group and 98% in the radiofrequency ablation group. These results are in agreement with earlier studies [9,10,12,13,17-25]. Both procedures for atrioventricular node modification were associated with the onset of new and different supraventricular tachycardia, including paroxysmal and chronic atrial flutter, atrial tachycardia and atrial fibrillation. The incidence was 27% in the surgical and 11% in the radiofrequency catheter ablation group. Despite a difference in follow-up interval, the incidence of these new arrhythmias did not differ in either group (log rank test: P=0·2).

Ventricular tachyarrhythmias were never observed. Previous studies have suggested a causal relationship between type 1 atrial flutter and atrioventricular nodal reentrant tachycardia, because of a possibly shared pathway in the lower right atrium [34,35]. In our study, two out of three patients with preexistent paroxysmal type 1 atrial flutter had no recurrence of either atrioventricular nodal reentrant tachycardia or atrial flutter after successful radiofrequency catheter ablation of only the atrioventricular node, supporting the

aforementioned hypothesis. On the other hand, in a few other patients, both surgery and radiofrequency catheter ablation were able to eliminate atrioventricular nodal reentrant tachycardia, but type 1 atrial flutter arose afterwards or persisted in one patient (TABLE 3). This can be explained by an inter-patient difference in size of the critical area in the perinodal atrium to allow the initiation of atrial flutter and atrioventricular nodal reentrant tachycardia. Furthermore, successful cure of atrioventricular nodal reentrant tachycardia can be achieved with discrete lesions that interrupt the zone of slow conduction in the low right atrium. However, such lesions are not sufficient to cure type 1 atrial flutter [34]. This latter assumption is supported by the observation that atrioventricular node modification can be successful, while maintaining slow pathway conduction [5-7,24]. The late occurrence of atrial flutter in these patients can probably be ascribed to the damage produced to this specific area, which instead of generating conduction block may have caused further slowing of conduction, thereby providing a substrate for type 1 atrial flutter to emerge. Because the patients in whom atrial fibrillation became manifest had either mitral valve disease or dilated atria, it is more likely that the mechanism of this arrhythmia can be attributed to an ongoing atrial disease, rather than being procedure-related [36]. Patients with atrial tachycardia after successful atrioventricular nodal reentrant tachycardia treatment did not show underlying heart disease, and therefore it is postulated that this arrhythmia is caused by unfavourable effects on radiofrequency energy on cardiac node innervation and/or atrial tissue. More data on late follow-up is required to support this hypothesis.

Limitation of the study

The results of both interventions represent the outcome of a 'learning curve' by our centre. Additionally, training facilities must also be taken into account. This explains the initially large number of applications as well as the initially high recurrence rate. Furthermore, the time of follow-up for patients who underwent radiofrequency catheter ablation was shorter than for the surgically treated patients, but it was at least 1 year for all patients. Because most recurrences of atrioventricular nodal reentrant tachycardia can be expected to occur within the first months after the procedure, the results of both procedures appear valid, although during late follow-up recurrences of atrioventricular nodal reentrant tachycardia were registered in both the radiofrequency and surgical group, even after 25 months and 3 years, respectively, which also contributed to the high recurrence rate. Electrophysiological follow-up studies were performed only in patients with symptoms suggesting recurrent atrioventricular nodal reentrant tachycardia. However, it has been reported that atrioventricular nodal reentrant tachycardia was only inducible at follow-up electrophysiological study in patients who had a clinical recurrence of atrioventricular nodal reentrant tachycardia [8].

Conclusion

Radiofrequency catheter ablation has become today's choice for elimination of recurrent atrioventricular nodal reentrant tachycardia because this intervention avoids thoracotomy and reduces hospitalization. Despite differences in methodology, initial and late results of both interventions were very comparable in this one-institutional study. The percutaneous approach has therefore rightly replaced arrhythmia surgery, but its late arrhythmic side-effects warrant refinement of the technique.

The authors wish to thank Mrs Gerda van der Kuijl for preparation of the manuscript.

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Surgery or radiofrequency catheter ablation for atrioventricular nodal reentrant tachycardia – the impossible choice

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Eur Heart J 1999;20:480-481

Direct surgical techniques employed to ablate an arrhythmogenic substrate have been proved very useful in the treatment of many supraventricular arrhythmias, including atrioventricular nodal reentrant tachycardia[1-3]. Development of these techniques has paralleled the evolution of our understanding of electrophysiology and created the conditions for the study and use of new forms of treatment, such as radiofrequency catheter ablation. Today, radiofrequency catheter ablation has become the treatment of choice for atrioventricular nodal reentrant tachycardia and no single argument can be used to defend a direct surgical approach. Nevertheless, recognition of the contribution of surgery to the development of actual catheter ablative techniques is mandatory. The paper by Kimman *et al.*[4] in this issue is probably the best possible tribute to atrioventricular nodal reentrant tachycardia surgery. It demonstrates that, in selected, highly motivated centres, surgery was at least as effective as radiofrequency catheter ablation techniques. Due to its technical difficulties, very few centres around the world were prepared in the past to use direct surgery for the treatment of this arrhythmia. Also, the need of a median sternotomy was a strong limitation for its widespread use and many thought that this treatment was too aggressive for a benign arrhythmia. They were probably right, but these pioneers accelerated the arrival of what we think of as the 'golden age' of arrhythmology. It is impressive to see how complicated the surgical techniques used to be with complete 'skeletonization' of the atrioventricular node, and how the placement of a radiofrequency lesion in the slow atrioventricular nodal pathway can be accomplished easily today. The former required a long hospitalization, general anaesthesia, a slow recovery, and left permanent marks of the intervention procedure. Radiofrequency catheter ablation can be done on an outpatient basis, using local anaesthesia, recovery is almost immediate and no scars will remain. These facts have expanded indications of radiofrequency catheter ablation to almost all patients with the arrhythmia. In the vast majority of cases there is no objective reason to initiate or continue pharmacological treatment and today it is probably unethical to propose a direct surgical approach. Universal use of radiofrequency catheter ablation has also produced an expected, undesired effect. Surgeons are no longer interested in a direct surgical approach to reentrant supraventricular tachycardias. They are no longer trained in this technique, they are unfamiliar with it and they are not motivated to carry it out. In most centres in the world, it will be impossible to find a surgeon prepared to perform such an intervention. This brings the discussion on the hypothetical choice between surgery or catheter ablation to an impossible position. Surgery is no longer an option for atrioventricular nodal reentrant tachycardia. The paper by Kimman *et al.*[4] raises the question of complications using one or other technique, in particular the occurrence of complete atrioventricular block and the development of new and different supraventricular tachyarrhythmias after the procedure. These issues will still need to be refined in years to come. Many invasive electrophysiologists probably think it will be very difficult to do better, just as did surgeons some years ago. Let us see whether in years from now training in catheter ablation will have been surpassed by safer and more effective approaches, developed, for instance, by molecular biologists. Until then we will have to accept that we were lucky to live in the silver but not yet the golden age of arrhythmology.

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Hybrid pharmacologic and ablative therapy for the management of symptomatic atrial fibrillation

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Neth Heart J 2002;10:8-12

Abstract

Background Hybrid therapy for atrial fibrillation Class 1c and class III antiarrhythmic drugs (AAD) can convert atrial fibrillation (AF) into an isthmus-dependent atrial flutter (AFL) in more than 10 % of the patients. Hybrid pharmacologic and ablative therapy offers a safe and effective means of achieving and maintaining sinus rhythm. We evaluated the efficacy of this hybrid approach for the management of paroxysmal or persistent AF.

Methods Eighteen patients with symptomatic AF treated with AAD and typical counterclockwise/clockwise AFL underwent radiofrequency (RF) ablation of AFL with an anatomical approach.

Results RF ablation was successful in all patients. All but 1 patient continued AAD. Four patients (22%) had recurrences of AFL. Two of them also had a recurrence of AF. Another three patients had recurrences of AFonly, and finally, one patient developed an atrial tachycardia more than 1 year after the procedure. In conclusion, 11 patients (61%) did not experience recurrences of AF/AFL after tricuspid valve annulus (TV) – inferior caval vein (IVC) isthmus ablation with continuing of antiarrhythmic drugs.

Conclusion Hybrid pharmacologic and ablative therapy is a safe and effective treatment for the management of patients with symptomatic AF.

Keywords Hybrid therapy, atrial fibrillation

Introduction

Atrial fibrillation (AF) is the most frequent, sustained, symptomatic tachyarrhythmia in patients with or without stuctural heart disease [1-3]. The incidence of this tachyarrhythmia increases with age and is twice as common in males as females [4,5]. It remains a therapeutic challenge and the success rate of maintaining long-term sinus rhythm with pharmacologic therapy alone is less than optimal [6,7]. Under class 1c, but also class III antiarrhythmic drugs (AAD), which are the first line agents to prevent AF recurrences, 'transformation' of AF to atrial flutter (AFL) is well-known [8-11]. Increase in wavelength due to increase in the atrial refractory period in a tachycardia dependent manner , and the unique arrangement and orientation of the atrial muscle fibers between inferior vena caval orifice (IVC) and tricuspid valve annulus (TV) may promote nonuniform anisotropic slow conduction in the so-called 'isthmus', and therefore promote the conversion of AF in AFL [12-14]. Nowadays, 'isthmus dependent AFL' can be succesfully treated by radiofrequency catheter (RF) ablation of the aforementioned region between the IVC and TV annulus. A bidirectional isthmus block is accompanied by a high success rate and a low recurrence rate of AFL. Recent studies demonstrated that maintenance of AAD after successful AFL ablation, continuously modifies the atrial substrate to prevent fractionation in atrial activation leading to recurrence of AF [10,11,15-18]. This hybrid therapy for AF offered a safe and effective means of achieving and maintaining sinus rhythm (SR). In this present study the first results of this hybrid approach for management of AF in the Thoraxcentre Rotterdam are evaluated.

Methods

Patient Population

Eighteen patients with symptomatic paroxysmal or persistent AF treated with antiarrhythmic drug therapy who had subsequent conversion to AFL by 12-lead ECG were included. The 12-lead ECG recorded during clinical AFL episode was classified with regard to the morphology of the flutter waves. Typical counter-clockwise or clockwise AFL was defined using standard surface ECG characteristics [1].

Electrophysiologic study and Radiofrequency catheter ablation

All patients underwent electrophysiologic study with a standard decapolar catheter (DAIG Corp.) placed in the coronary sinus (CS), a steerable 20-pole Orbitercatheter (Bard), positioned around the tricuspid annulus. A Cosio ablation catheter (Medtronic) was used for mapping and ablation. When a patient had sustained AFL, mapping of the atrial activation sequence was carried out. Concealed entrainment of the tachycardia was attempted by pacing with the ablation catheter from the anatomic isthmus at 20 or 40 ms below the atrial cycle length. Concealed entrainment was defined as fulfillment of all the following criteria: 1. postpacing interval equaling tachycardia cycle length ± 10 ms; 2. identical intracardiac atrial activation pattern during pacing from the isthmus as during tachycardia;

3. stimulus to surface flutter wave interval equaling electrogram to surface flutter wave interval ± 10 ms [10,19]. If a patient was in SR, bidirectional isthmus conduction was evaluated at pacing cycle lengths of 600 and 400 ms [20]. No attempt was made tot induce AFL, because of the risk of inducing sustained AF.

All patients underwent anatomically guided catheter-based ablation with creation of linear lesions in the TV annulus-IVC isthmus and/or the TV annulus-CS-IVC isthmus. Succesful ablation was assessed by demonstrating bidirectional block with pacing at two different cycle lengths (600 and 400 ms) [21-23].

Follow-Up

After the procedure all patients were advised to continue treatment with AAD. Patients were followed for recurrences via outpatient clinics, contacts with primary physicians, and Holter recordings were requested when symptoms suggested an arrhythmia recurrence. Patients having a recurrence of AFL underwent re-ablation. After isthmus ablation, patients having no AF recurrences, or symptomatic but short-lasting AF recurrences were considered to be well-controlled. Patients with frequent or symptomatic recurrences of AF were considered as inadequately controlled.

Statistical analysis

Data are presented as mean ± SD and were compared using a two-tailed Student's *t*-test. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

All eighteen patients were classified as typical counterclockwise/clockwise AFL on documented standard surface ECG. Demographic characteristics are shown in Table 1. There were 13 men, and the mean age was 59.5 years (SD ± 9). In all patients at least one AAD had failed. At the time of the procedure 13 patients were on class III AAD and 4 patients were on Class IC AAD. One patient was taking only verapamil. Six patients (33%) had daily, weekly or monthly episodes of paroxysmal AF/AFL (i.e. self terminating AF/AFL, lasting <24 hours per episode), and 12 patients experienced one or more episodes of persistent AF/AFL (sustained AF/AFL lasting 24 to 72 hours, requiring direct current (DC) cardioversion in the six months before ablation). Twelve patients had structural cardiovascular disease: 3 with mitral valve replacement, 2 with coronary artery disease, 2 with both aortic valve replacement and coronary artery bypass grafting (CABG), 1 with hypertension, and 4 with sick sinus syndrome with prior pacemaker implantation.

TABLE 1.
Demographic characteristics

age (years) ± SD	59.5 ± 9
male/female (n/n)	13/5
structural heart disease (n)	
• none	5
valvular disease	3
• coronary artery disease	2
• valvular and coronary artery disease	2
• hypertension	1
• sick sinus syndrome	4
• amiodarone/class IC AAD (n/n)	13/4
• verapamil (n)	1

AAD = antiarrhythmic drug

TABLE 2.
Electrophysiologic Study Results

• Number	18
• Counterclockwise/clockwise AFL (n/n)	17/1
• RFA during SR/AFL (n/n)	10/7
• RFA during AF (n)	1
• Site(s) ablated(n)	
TV-IVC	9
subsequently TV-CS and CS-IVC	9
• Success (n)	
BICB	17
unkown	1

AFL = atrial flutter, AF = atrial fibrillation, RFA = radiofrequency ablation,
SR = sinus rhythm, TV = tricuspid valve, IVC = inferior caval vein,
CS = coronary sinus, BICB = bidirectional isthmus conduction block

Electrophysiologic characteristics and Radiofrequency ablation (TABLE 2)

At the time of the EP study seven patients (39%) were in AFL. Intracardiac mapping and entrainment pacing revealed 6 of these patients to have typical counterclockwise (craniocaudal along the right free wall) and one patient typical clockwise (caudocranial along the right free wall) flutter circuits traversing through the TV-IVC isthmus. In these patients RF ablation was performed during AFL. Eleven patients were in SR. Bidirectional conduction isthmus conduction was present in all of them, and ablation was performed during sinus rhythm. However, in one of these patients AF was induced during manipulation of the ablation catheter. After unsuccessful external DC cardiovision, it was decided to ablate this patient during AF.

Linear ablation of the TV-IVC isthmus was carried out under anatomic and electrogram guidance. This created a complete line of block in 9 patients. The other nine patients subsequently underwent RF ablation of the TV-CS and CS-IVC isthmus with finally bidirectional isthmus conduction block in eight. In 1 patient this could not be demonstrated,

TABLE 3.
Follow-up results after successful RFA of AFL

• Number	18
• Follow-up duration (months) ± SD	8.1 ± 5.9
• AAD after RFA (n)	17
• AFL recurrence (n)	2
• AF recurrence (n)	3
• AF/AFL recurrence (n)	2
• AT occurrence (n)	1
• Repeat RFA of AFL (n)	2
• Hisablation and PM-implantation (n)	1

Abbreviations as in Tables 1 and 2.
AT = atrial tachycardia, PM = pacemaker

because of persisting AF during the procedure, despite repeated external electric cardioversions. After the procedure SR was restored spontanously, In the end, 17 (94%) patients were considered to be succesfully ablated. One patient with severe systolic left ventricular dysfunction and a history of malignant ventricular arrhythmia developed complete AV block during the procedure, requiring dual chamber ICD implantation. In one patient an arteriovenous fistula was diagnosed, and corrected surgically. All patients were advised to continue antiarrhythmic drug therapy.

Follow-Up (TABLE 3)

During a mean follow-up of 8.1 months, ± 5.9, in total 4 patients had recurrences of AFL and two of them also had recurrences of AF. One patient had a recurrence after only 1 day, developed AF the next day, and underwent His ablation with pacemaker implantation. Two other patients had recurrences of AFL within 1 month, and in one patient AFL recurred after three months with a recurrence of AF als well. Two patients underwent reablation for AFL. One of them was in AFL at the time of reablation and entrainment mapping clearly showed an isthmus dependency. This patient was cardioverted to obtain a more stable catheter position during ablation. In both patients restoration of bidirectional isthmus conduction could be demonstrated and reablation of the so-called gaps in the line was performed. Bidirectional block was achieved again in both patients. However, during follow-up one of them experienced recurrent AFL with demonstration of restoration of isthmus conduction. He underwent a third ablation. In the end, both patients were free of recurrences. Three patients only experienced recurrences of AF. One patient had two episodes of AF, after two days and 15 months, respectively. Another patient developed AF two months after ablation. This patient was the one ablated during AF, and a diagnostic EP study was performed. During this procedure bidirectional isthmus block was confirmed . The third patient experienced an episode of AF after his antiarrhythmic drug was interrupted accidentally, but after reinitiation no recurrence of AF has been observed in a 6 months follow-up. Finally, one patient developed atrial tachycardia 1 year after ablation. FIGURE 1 shows the overall event free survival.

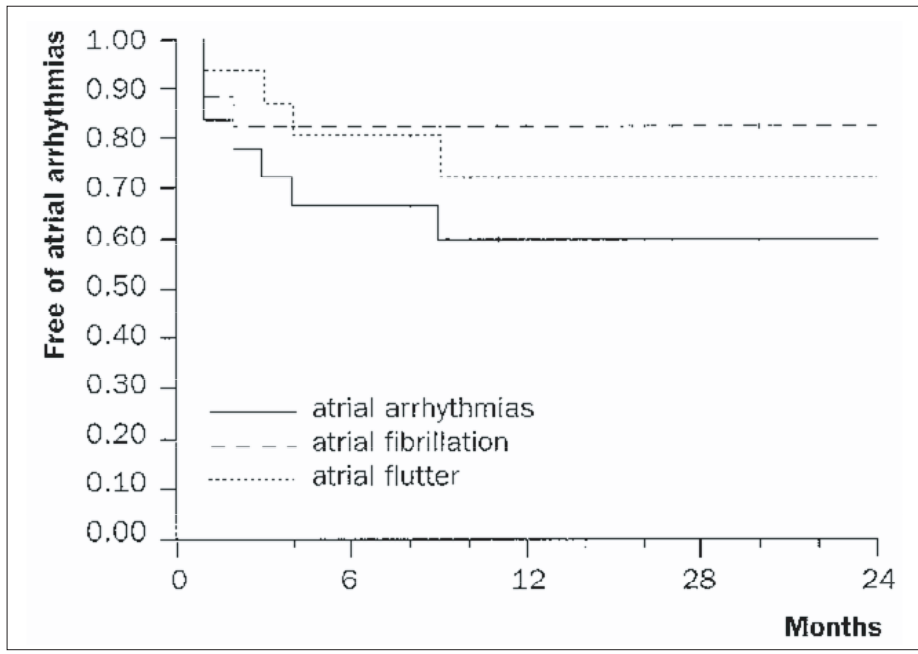

FIGURE 1.
Event-free survival of patients after successful isthmus ablation

In conclusion, of the 18 patients who underwent ablation for typical AFL, 14 (78%) patients were free of AF with continuing AAD, including the patient who was free of AF after reinitiation of his AAD. If both AF and AFL were considered, 11 (61%) patients were free of recurrences.

Discussion

The potential for AAD to convert AF to AFL in up to 10 % or more of patients is well documented in previous reports. The AAD most commonly associated with occurrence of AFL include class 1C drugs, and class III drugs [8-11]. These drugs increase the wavelength by increasing the atrial refractory period and leading to organization along the trabeculated right atrium. This, togetheter with the distinct tissue-specific anisotropic conduction properties along the trabeculated right atrium and the anatomic barriers favor conversion of AF to AFL [12-14]. Several studies showed that in these patients, ablation of the TV-IVC isthmus may reduce the incidence of subsequent episodes of AF while continuing antiarrhythmic drugs [10,11,15-18]. This hybrid therapy of combined RF ablation for and AAD therapy seems to be more effective in achieving and maintaining sinus rhythm, in comparison with only pharmacologic therapy, or only isthmus ablation [18]. Furthermore, atrial flutter in patients with untreated AF is quite common, with periodic transition from

one arrhythmia to the other, suggesting a mechanistic and possible causative relationship between AFL and AF [24]. This was also seen in our patients treated with verapamil. In this patient, ablation of AFL could have reduced recurrences of AF by eleiminating a potential trigger for AF. The mechanism by which atrial arrhythmias trigger AF is uncertain, but rapid atrial rates may increase atrial vulnerability by shortening atrial refractory period or electrical remodelling [25,26].

In the present study four patients had recurrences of AFL. In all four patients, the morphology of the flutter waves on the 12-lead ECGs during AFL was similar before and after ablation. Two of them underwent a reablation. In both patients the first ablation was performed during SR after demonstration of bidirectional isthmus conduction. However, in both patients AFL was not induced before the first ablation, because of the risk of inducing AF. Therefore, a non-isthmus dependent AFL could be an explanation, although entrainment mapping of AFL during reablation clearly showed isthmus dependency in one patient. Again, the other patient underwent reablation during sinus rhythm, without inducing AF. Data from initial studies, using the demonstration of complete isthmus block as an endpoint, had comparable outcome with a recurrence rate between 9-16% [27,28].

In total five patients (27%) had recurrences of AF (including two patients with recurrent AFL, as well), although one patient only had a recurrence of AF after accidentially stopping his AAD. This patient did not experience recurrent AF in six months after reinitiation of pharmacological therapy. These patients were considered to be inadequately controlled. So finally, 14 patients (78%) were free of recurrences of AF with continuing AAD, and were considered well controlled. This is comparable with earlier studies and again illustrates that continuing of antiarrhythmic agents is important for a favourable outcome [10,11,15-18].

One patient developed an atrial tachycardia one year after ablation, and the morphology of the P wave suggested a focus in the low septal region of the right atrium. Possibly, this can be a late proarrhythmic effect of the ablation, as suggested in an earlier study after slow pathway ablation for AVNRT [29].

Study Limitations

In 11 patients, RF ablation was performed during SR. In these patients no attempt was done to induce AFL, because of the risk for inducing sustained AF. In the absence of entrainment studies, determining of an isthmus dependent AFL is limited. Therefore, a non-isthmus-dependent AFL could be an explanation for recurrences of AFL. However, in one of the two patients who underwent reablation, an isthmus-dependent AFL could clearly be demonstrated.

Therapeutic success in this study was determined by symptomatic recurrences on routine surveillance. Asymptomatic recurrences could go undetected, however all patients were highly symptomatic prior ablation. One patient was only treated with verapamil. It is quite common to observe AFL in patients not treated with IC/III AAD, or with untreated AF. Therefore, this patient did not receive hybrid pharmocological and ablative therapy,

and should be excluded. However, this patient is still free of recurrent AF/AFL, and illustrates that with the ablation of AFL a possible potential trigger for AF is eliminated. Finally, in the present study there was only a short follow-up period.

Conclusions

Both class 1C and class III AAD are able to convert AF into an isthmus dependent AFL. Linear isthmus ablation with creating bidirectional conduction block, in combination with continuing of AAD can be an effective therapy in achieving and maintaining SR. This hybrid approach offers a substantial improvement in the management in a subset of patients with AF.

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5

Ten years follow-up after Radiofrequency catheter ablation for Atrioventricular Nodal Reentrant Tachycardia in the early days.

Forever cured, or a source for new arrhythmias?

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Abstract

Background Radiofrequency (RF) catheter ablation is highly effective with a low complication rate. However, lesions created by RF energy are irreversible, inhomogenous, and therefore potentially proarrhythmic.

Objectives The aim of this study was to focus on the magnitude and importance of long-term proarrhythmic effects of RF energy.

Methods and results Between 1991 and 1995, 120 patients underwent RF ablation for AVNRT. Of these patients, data were collected by contacting patients and/or fill out a questionnaire. Medical files were screened for recurrent, documented arrhythmias, medical treatment, and repeated EP study. Referring cardiologists were asked about recurrences of tachyarrhythmias. Fourteen patients (11%) were lost to follow up. During a mean follow-up of ten years, six patients died. In total 29 pts (24%) suffered from new arrhythmias, 6 from type 1 atrial flutter, 6 from atrial tachycardia, 9 from atrial fibrillation, and finally 16 pts from symptomatic PAC's, needing medical treatment, or a combination of these arrhythmias. Seven patients underwent pacemaker implantation, 4 after developing procedural AV conduction disturbances, 2 after His ablation for permanent atrial fibrillation, and 1 patient for sick sinus syndrome. Another 2 patients developed late AV block, respectively 7 and 9 years after ablation, also requiring pacemaker therapy.

Conclusion During long term follow-up after RF ablation for AVNRT, a significant number of patients (24%) suffered from new arrhythmias or late AV block. This study provides a new insight in the magnitude and importance of a possible proarrhythmic effect of RF energy, and supports the search and use of new energy sources.

Keywords: atrioventricular nodal reentrant tachycardia; radiofrequency; catheter ablation; proarrhythmia; long-term follow-up

List of abbreviations:

AF	atrial fibrillation
AFL	atrial flutter
AT	atrial tachycardia
AVNRT	atrioventricular nodal reentrant tachycardia
PAC	premature atrial contraction
PM	pacemaker
RF	radiofrequency

Introduction

Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common regular small QRS-complex tachycardia. Nowadays, transvenous radiofrequency (RF) catheter ablation is the treatment of choice for treatment of patients with recurrent AVNRT and in most cases should be considered as first line therapy [1,2]. Although it is accompanied by a high success rate and a low complication rate, RF is not the optimal energy source. Lesions created by hyperthermia cause some degree of tissue disruption or "carbonisation" of the targeted tissue that increases the risk for perforation and thromboembolism [3,4]. It is difficult to obtain stable lines of block, and it is neccessary to have reliable tissue contact. Furthermore, the inhomogeneous lesions, produced by RF, appear proarrhythmic [5].

Until now no study has focussed on a possible long-term proarrhythmic effect of RF energy. This study can provide a deeper understanding of the magnitude and importance of this adverse effect and eventually will enhance the search and use of new energy sources for the treatment of both supraventricular and ventricular arrhythmias.

Hypothesis

It is postulated that RF catheter ablation is associated with new supraventricular arrhythmias during long term follow up due to proarrhythmic effects of this therapy.

Study Design

A retrospective, single centre study.

Patients and Methods

Between 1991 and 1995, 120 patients underwent RF ablation/modification of the AV node for AVNRT in the Antonius Hospital Nieuwegein [6]. After an electrophysiological study was performed to confirm the diagnosis of AVNRT (Table 1), a quadripolar Steerocath or Tracfinder catheter (EP Technologies) or a quadripolar 4 mm tip catheter (Cordis-Webster) with deflectable curves were used for ablation. Radiofrequency pulses of 7 to 50 Watt at a frequency of 500 kHz were delivered by a custom-made available electrosurgical device by delivering current between the distal electrode and a cutaneous, indifferent dispersive pad positioned on the patient's back. A selective fast pathway, or selective slow pathway was carried out, using both intracardiac electrograms as anatomical landmarks. Which approach was used, depended on the operator's own insight and experience. If the initial fast or a slow pathway ablation was not successful after more than an arbitrary number of 20 applications, the other approach was applied during the same procedure. A fast pathway ablation was considered immediately successful when AVNRT was no longer inducible

Table 1.
Demographic and electrophysiological data before ablation.

Preablation data	Fast pathway	Slow pathway	Slow and fast pathway
Number of patients (n)	40	47	33
Male/female (n)	12/28	12/35	10/23
Age (years)	45 ± 17.5	42 ± 15.5	44 ± 10.9
Duration of symptoms (years) ± SD	14.6 ± 12.0	12.9 ± 11.4	13.9 ± 10.8
Typical AVNRT (n)	38	41	32
Atypical AVNRT (n)	2	6	1
PR interval (ms) ± SD	154 ± 21.5	152 ± 30.4	151 ± 16.9
AH interval (ms) ± SD	73 ± 18.1	73 ± 26.9	70 ± 14.7
Jump in AH interval present (n)	17 (43%)	23 (49%)	16 (48%)
Jump in AH interval (ms) ± SD	122 ± 53.3	103 ± 61.1	98 ± 40.4
AVNRT cycle length (ms) ± SD	332 ± 49.8	326 ± 59.9	341 ± 75.2
Preexistent paroxysmal type 1 AFlut (n)	2	1	1
Preexistent ATach (n)			1
Preexistent AFib		2	

AFib = atrial fibrillation; AFlut = atrial flutter; ATach = atrial tachycardia; n = number of patients;

or when a 30% prolongation of the PR interval or an inadvertent second- or complete AV block occurred. The end-point of a slow pathway ablation was non-inducibility of AVNRT with preserved AV nodal conduction. The slow pathway was considered to be ablated if dual pathway physiology was completely abolished, and was modified if the slow pathway conduction time was lengthened or echo beats were still inducible, but without sustained arrhythmia.

Patients follow-up

All the aboved mentioned patients were included in this long term follow-up study. If possible, all patients were contacted either by telephone or letter, and asked to answer to or fill out a questionnaire. Furthermore, all medical dossiers were screened for recurrent, documented arrhythmias, medical treatment, and/or repeated EP study. Referring cadiologists were asked about recurrent, documented arrhythmias, and to send, if available, electrocardiograms of these arrhythmias.

Table 2.
Electrophysiological data immediate after ablation

Postablation data	Fast pathway	Slow pathway	Slow and Fast pathway
Number of patients (n)	40	47	33
Initial succces (%)	90	98	82
Ablation time (min)	76 ± 47.6	44 ± 34.4	84 ± 47.2
Number of applications (n) ± SD	14 ± 17	13 ± 15	25 ± 28
PR interval (ms) ± SD	199 ± 49.0	158 ± 27.7	183 ± 41.8
AH interval (ms) ± SD	121 ± 43.6	79 ± 25.6	101 ± 48.9
Jump in AH interval present (n)	9 (23%)	8 (17%)	2 (6%)
Jump in AH interval (ms) ± SD	126 ± 60.4	103 ± 39.9	110 ± 56.6
VA block (n)	13 (33%)	5 (11%)	7 (21%)

N = number of patients; min = minutes; SD = standard deviation

Statistical analysis

Data will be expressed as mean ± SD. Chi-square and Student's t-test will be used for statistical comparison whenever appropriate. For censored data the log-rank test will be used. A two tailed p value < 0.05 will be considered significant.

Results

There were no significant differences in baseline characteristics between the various ablation groups (Table 1) Patients were divided into the fast pathway group after a selective fast pathway ablation, in the slow pathway group after a selective slow pathway ablation, and in the slow and fast pathway group after a slow and fast pathway approach during the same procedure. Two patients in the fast pathway group, and 1 patient in both the slow, and slow and fast pathway group were also suffering from type 1 atrial flutter (AFL). Another patient in the slow and fast pathway group had experienced paroxysms of an atrial tachycardia (AT), and in 2 patients in the slow pathway group, atrial fibrillation (AF) was registered before ablation.

Of 9 patients in the fast pathway group, 8 patients in the slow pathway, and 2 patients in the slow and fast pathway group, an AH jump was still present during electrophysiological study shortly after ablation, suggesting persisting slow pathway conduction (Table 2). However, in not all patients these data were available. The final success rates after 1 or more ablation procedures was 100 % in both groups with a selective fast or slow pathway ablation, and 91 % in the slow and fast pathway group, respectively (Table 3).

TABLE 3.
Success rates of RF catheter ablation

	Fast pathway	Slow pathway	Slow and fast pathway
Number of patients (n)	40	47	33
Initial success (%)	90	98	82
Pts with recurrent AVNRT (n)	3	9	6
Final success after 1 or more repeated RF ablations (%)	100	100	91

n = number of patients

TABLE 4.
Late clinical outcome after RF ablation for AtrioVentricular Nodal Reentrant Tachycardia (AVNRT) in the period 1991-1995

Follow-up data (120 pts)	Fast pathway	Slow pathway	Slow and Fast pathway
Number of patients (n)	40	47	33
Follow-up < 3 years	6	4	4
Mean follow-up (years ± SD)	10.1 ± 3.3	9.3 ± 3	9 ± 2.9
Total number of pts with new arrhythmias:	10	14	5
Type 1 atrial flutter	4	1	1
Atrial tachycardia	3	1	2
Atrial fibrillation Structural heart disease	3 0	5 2	1 0
Type 1 Aflut/AF Structural heartdisease	3 0	0 0	1 0
Type 1 Aflut/AF/AT Structrural heartdisease	1 0	0 0	1 0
Medical therapy for symptomatic PAC's	5	7	4
Late AV block	1		1
Pacemaker therapy	4*	3°	2"
Death	2˘	4ˆ	0

*1 pt procedural complete AV bock; 1 pt 10 years later for Sick Sinus Syndrome; 1 pt 5 years later His ablation and PM implantation
°2 pts procedural complete AV block (1 after 4 ablations); 1 pt 1 year later His ablation and PM implantation
"1 pt procedural complete AV block
˘2 pts sudden cardiac death
ˆ1 pt myocardial infarction and cardiogenic shock; 1 pt lung cancer
AF = atrial fibrillation; AFlut = atrial flutter; AT = atrial tachycardia; n= number of patients; PAC = premature atrial contraction; SD = standard deviation

The mean follow-up was 10.1 ± 3.3 years in the fast, 9.3 ± 3 in the slow, and 9 ± 2.9 in the slow and fast pathway group, which was comparable (Table 4). In 6 patients in the fast, 4 in the slow, and 4 in the slow and fast pathway group the follow-up was less than 3 years, and were either lost to follow-up (11 patients) or died (3 patients). In total 6 patients died, 2 in the fast and 4 in the slow pathway group. Both patients in the fast pathway group died suddenly. In one of these 2 patients a wide QRS complex tachycardia was registered before ablation, but not inducible during the procedure, and was considered as aberrant conduction. The second patient suffered from acute myocarditis. One patient in the slow pathway group died of myocardial infarction with cardiogenic shock, and one patient of lung cancer. In the other 2 patients the cause of death remained unknown. Ten patients (25%) in the fast pathway group experienced new arrhythmias. In 4 patients a type 1 AFL was registered, in 3 an AT, and in 3 patients atrial fibrillation (AF), or a combination of these arrhythmias. Namely, of the 4 patients with type 1 AFl, 2 patients also experienced episodes of AF, and in 1 patient both AF and AT was registered besides AFL. In none of these patients structural heart disease was diagnosed. Five patients also had symptomatic premature atrial contractions (PAC's), and needed drug therapy. In the slow pathway group 14 patients (30%) sufferered from new arrhythmias, 1 patient with type 1 AFL, 1 with AT, and 5 with AF, of which 2 had structural heart disease. Seven patients were medically treated for symptomatic PAC's. In the slow and fast pathway group a total of 5 patients (15%) experienced new arrhythmias. Type 1 AFL was seen in 1 patient, AT in 2, and AF in 1. One patient had both AFL and AF, and another one AFL and AT. No patients were known for structural heart disease. Four patients had drug therapy for symptomatic PAC's. As is shown in Table 5, there seems to be a tendency for the occurrence of arrhythmias if more RF energy was applied, although, as was valid for all 3 groups, the difference was not statistically significant between patients with or without new arrhythmias.

In none of the patients with pre-existent type I AFL, AT, or AF a recurrent arrhythmia was registered after ablation.

Two patients developed late AV block, 1 in the fast pathway, and 1 in the slow and fast pathway group, respectively 7 years after the last ablation at the age of 36 and 9 years after the last ablation at the age of 59 years. The patient in the fast pathway group had a transient complete AV block during her second procedure, lasting less than 10 seconds. In the other patient no transient second or complete procedural AV block was seen. Additionally, 7 patients underwent pacemaker implantation, of which 4 had a second degree or complete AV block during the procedure. In 2 other patients with permanent AF, His-ablation and pacemaker implantation was carried out. Finally, in 1 patient with a sick sinus syndrome a pacemaker implantation was performed.

TABLE 5.
Differences in used ablation energy

	Fast pathway		*Slow pathway*		*Slow and fast pathway*	
	New arrhythmias	No new arrhythmias	New arrhythmias	No new arrhythmias	New arrhythmias	No new arrhythmias
Total number of patients with completed follow up (n)	10	24	13	30	5	24
Data available	9	22	12	29	5	24
Mean ablation energy (joule) ± SD	17676 ± 28041	10682 ± 12242	26501 ± 24696	13182 ± 11622	18872 ± 14810	26945 ± 20185
Median ablation energy	7840	4575	25370	9260	20520	23480

n = number of patients; SD = standard deviation

Student's t-test new and no new arrhythmias:
Fast pathway group: P = 0.5
Slow pathway group: P = 0.1
Slow and fast pathway group: P = 0.3
Total group: P = 0.3

Discussion

Treatment nowadays and in the past

In the past the first line treatment for symptomatic patients with recurrent AVNRT was drug therapy. If this was unsuccessful, surgical modification of the AV node was the only method to permanently eliminate AVNRT. Both cryosurgery and "skeletonization" resulted in successful cure of the tachycardia with preservation of AV conduction [7,8]. Although highly successful, it was a major intervention for a non life-treatening arrhythmia, which only could be performed in specialized centres by a few well trained cardiac surgeons. Long term proarrhythmic effects of surgery have been scarcely reported and were limited to recurrences of AVNRT, occurrence of other supraventricular tachycardias and the induction of non-sustained ventricular tachycardia with standard EP study, which is a non-specific finding in this patient population [9]. A case report documented spontaneous ventricular tachycardia and inducible type 1 AFL nine years after successful surgery for the Wolff-Parkinson-White syndrome, which was considered a remote, unwanted effect of arrhythmia surgery that can be applicable for other, non-pharmalogical interventions for arrhythmias [9,10].

Nowadays RF catheter ablation has become the first line therapy for patients with recurrent AVNRT [1,2]. It has proved to be highly successful and safe with a low recurrence

and complication rate, as was also seen in this patient population [6]. During long term follow up, sporadic recurrences of AVNRT were registered, even 3 years after the procedure. These observations led to the conclusion that patients, who underwent a successful RF ablation for AVNRT, were definitively cured. However, until now no study has focussed on the very long term follow-up (>3 years) after RF ablation, and the occurrence of new (tachy)arrhythmias.

New (tachy)arrhythmias and their mechanisms

In this study, 29 (24%) patients suffered from new (tachy)arrhythmias, most frequently symptomatic PAC's, needing drug therapy. It is possible that these PAC's were already existing prior to ablation, being a trigger for AVNRT to occur, and therefore patients were not aware of them before treatment. However, after successful ablation, patients became conscious of these PAC's. Another possibility is that these PAC's were the result of the lesions created by RF energy.

Previous studies have suggested a causal relationship between type 1 AFL and AVNRT, because of a possible shared pathway in the low right atrium [6,11,12]. In this patient population, 4 patients with preexisting type 1 AFL had no recurrence of either AVNRT or AFL after successful RF ablation of only the AV node, supporting the aforementioned hypothesis. On the other hand, in 6 other patients type 1 AFL arose after successful ablation for AVNRT. It is known that successful cure of AVNRT can be achieved with discrete lesions that only modify, and not completely interrupt the zone of slow conduction in the low right atrium. Such lesions are not sufficient to cure type 1 AFL. The damage that is produced to this specific area, which instead of generating conduction block, may cause further slowing of conduction, can provide a substrate for type 1AFL to occur. However, 4 patients suffered from AFL after fast pathway ablation, which can not directly be explained by the aforementioned theory. The inter-patient difference in size of the critical area in the perinodal atrium to allow the initiation of AFL, or an abnormally located antegrade fast pathway, located in the posteroseptal region, which exists in about 3% of patients presenting with AVNRT, [13] can support the reason for this observation. Eight other patients developed AF, of which 2 had either mitral valve disease or an enlarged atrium. In these cases it is more likely that AF is the result of an ongoing atrial disease rather than being procedure-related. The other 6 patients were not known for structural heart disease at the time of the occurrence of AF. The mean age of these patients at the time of occurrence of AF was 60.1 ± 19.8 years. The prevalence of AF in this patient population during a 10 years follow-up is in agreement with the Framingham Heart Study, which showed a biennial prevalence of AF ranged from 6.2 and 3.8 cases per 1000 in men and women aged 55-64 years [14]. Interestingly, 4 (3 in the fast pathway group) patients also suffered from type 1 AFL. Atrial flutter in patients with untreated AF is quite common, with periodic transition from one arrhythmia to the other, suggesting a mechanistic and possible causative relationship between AFL and AF [15]. Six patients with AT after successful RF ablation did not show underlying heart disease. In 3 of these patients a 12 leads surface ECG during tachycardia supported an origin from the AV node region. Therefore, it seemes likely that this arrhythmia is caused by unfavourable effects of RF energy on the atrial tissue in this area.

To support the hypothesis of a possible proarrhythmic effect of RF energy, table 5 showed that the more energy was used, the likelihood of developing new arrhythmias seemed to increase. A possible explanation for this observation could be that it is necessary to have sufficient damaged atrial tissue for a new atrial arrhythmia to occur. However, in the slow and fast pathway group this effect was not seen. Maybe this can partly be explained by the fact that only a few patients in this group developed a new (tachy)arrhythmia. Another reason could be that both the slow and fast pathway region had been ablated, causing probably a more "homogeneous" damage to this region, making it less likely for a (micro)reentry arrhythmia to occur. On the other hand, it is known that RF lesions are characterized by intralesion hemorrhage and ragged edges less clearly demarcated from the underlying normal myocardium [5]. This can cause nonuniform anisotropy, which may be responsible for slow conduction and/or unidirectional block that allows (micro)reentry tachycardia to occur. In this context, the results shown in table 5, can also support the hypothesis that these characteristics of RF are causing new arrhythmias, and not the amount of applied RF energy.

Late complete AV block

In total 9 patients underwent a pacemaker implantation. Two of them developed late AV block, 7 years after fast pathway and 9 years after slow and fast pathway ablation, respectively. It remains unclear if this can be the result of damage to the AV node region by the earlier RF ablation, although the occurrence of a late AV block at the early age of 36 years after fast pathway ablation is very suggestive for a causal relation.

Limitations

The results of this study can be related to the technique used in this particular centre in the early years of RF therapy. Although, the technique has been refined, the amount of RF energy which is applied in this study is comparable with the amount of energy used in current practice. This, together with the known characteristic of this energy source of creating, inhomogeneous lesions, the results in this study may also be valid today. It therefore would be interesting to study patients, ablated after 1995 until now, to show if indeed the outcome will be comparable. In 14 patients (11%) follow-up was less than 3 years, of which 3 died in this period. These patients also could have suffered from both recurrent AVNRT and new arrhythmias. However, most recurrences as well as new arrhythmia emerged in the first 2 years after the procedure. Furthermore, it seems highly unlikely that these missing patients had been treated for recurrent tachycardia, without informing the intervention centre. To support the theory of any proarhythmic effect of RF energy, all patients with new arrhythmias should undergo a repeated EP study, to map these new arrhythmias and compare this to the localisation of the earlier applications. Determining the exact localisation of an earlier ablation, however, is impossible. This observational study only can make it plausible that at least some new arrhythmias, as AT and AFL, are the result of a proarrhythmic effect of RF energy. Finally, as this is an observational study, a matched control study is missing.

Conclusion

Radiofrequency catheter ablation is highly successful for elimination of AVNRT with a low complication rate. Although, it is difficult to prove a direct relation, new supraventricular arrhythmias and late AV block, can be the result of the earlier RF ablation. These data provide a new insight on the magnitude and importance of a possible proarrhythmic effect of RF energy, and support research into and use of alternative energy sources.

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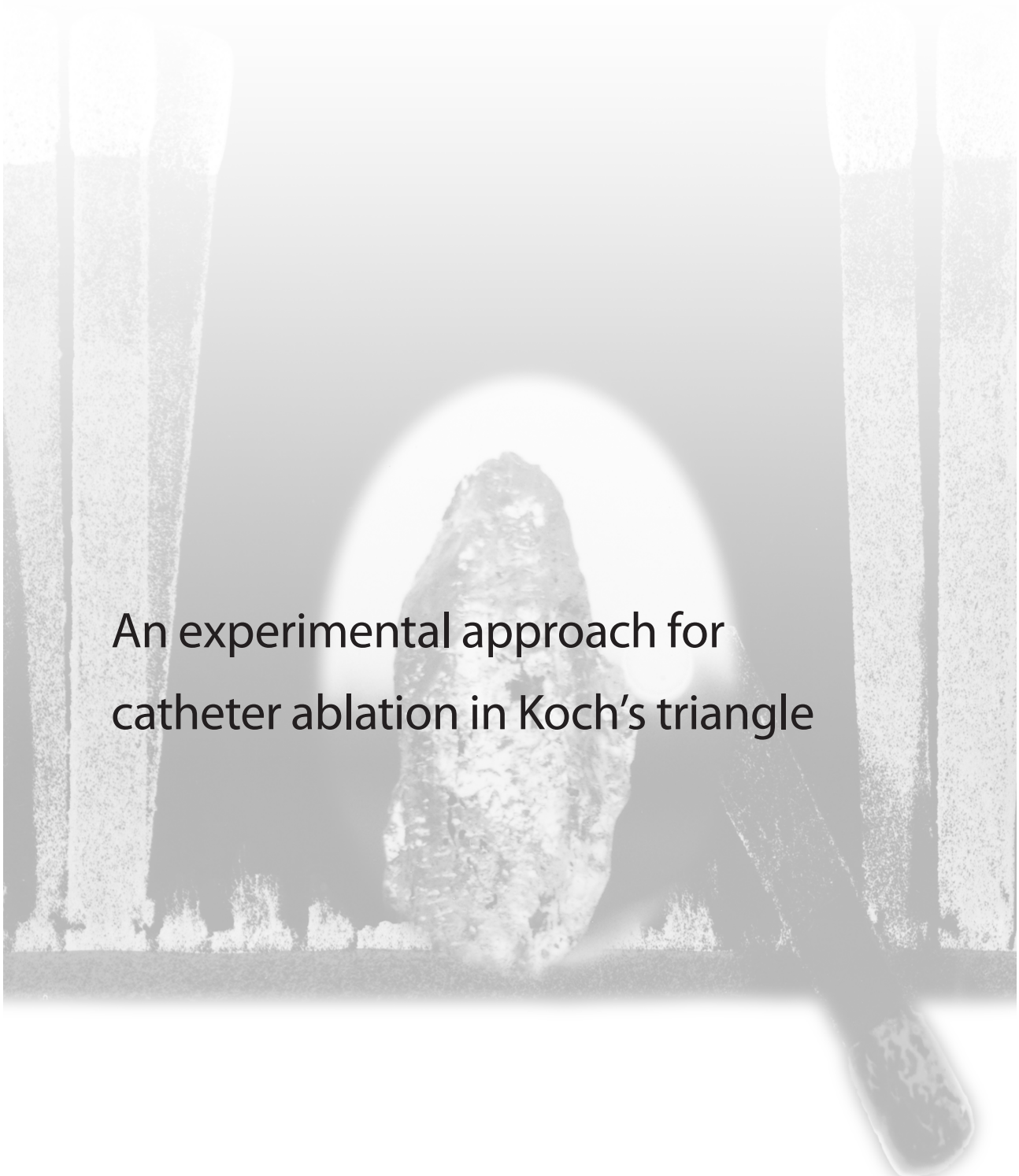

An experimental approach for catheter ablation in Koch's triangle

6 Transvenous Cryothermal Catheter Ablation of a Right Anteroseptal Accessory Pathway

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J Cardiovasc Electrophysiol 2001;12:1415-1417

Abstract

Transvenous Cryothermal Catheter Ablation In patients with Wolff-Parkinson-White syndrome, right anteroseptal accessory pathways are uncommon and run from the atrium to the ventricle in close anatomic proximity to the normal AV conduction system. Radiofrequency catheter ablation is the first-line therapy for elimination of these accessory pathways. Although the initial success rate is high, there is a potential risk of inadvertent development of complete heart block, and the recurrence rate is relatively high. The capability of cryothermal energy to create reversible lesions (ice mapping) at less severe temperatures provides a potential benefit in ablation of pathways located in a complex anatomic area, such as the mid-septum and anteroseptum.

Keywords: arrhythmia, catheter ablation, cryosurgery, Wolff-Parkinson-White syndrome

Introduction

Catheter ablation currently is the first-choice therapy for paroxysmal supraventricular tachycardia, including that involving accessory AV pathways. "Septal" accessory pathways are the least common. Anteroseptal pathways account for 4% to 8% of all accessory bundles [1-6]. Despite this low incidence, the close proximity to the AV node and His bundle poses an increased risk of right bundle branch block or inadvertent complete AV block during catheter ablation [1-6]. This, together with a relatively high recurrence rate [1-6], makes this site a challenge, as mechanical block also often occurs during procedures. Currently, radiofrequency current is the main energy source for ablation. However, other methods are being investigated. A useful property of cryothermal energy is its ability to reversibly demonstrate loss of function of tissue with cooling (ice mapping) at less severe temperatures, thereby demonstrating the suitability of prospective ablation sites without inducing permanent injury [7-9]. Furthermore, once the catheter tip temperature is reduced to 0°C, progressive ice formation at the catheter tip causes adherence to the adjacent tissue (cryoadherence), thus allowing safe ablation during tachycardia without the risk of dislodgement after termination of the tachycardia [7-9]. These properties of cryothermal energy are potential assets for ablation of "delicate" accessory pathways. In this case report, transvenous cryothermal catheter ablation of a right anteroseptal accessory pathway is described.

Case Report

A 16-year-old boy was referred because of recurrent shortlasting episodes of palpitations. Twelve-lead surface ECG showed a positive delta wave in leads I, II, aVL, and aVF, and biphasic in lead III, suggesting a right anteroseptal accessory pathway. The decision was made to perform an electrophysiologic study and to use cryothermal catheter ablation, because of the location of the accessory pathway with the risk of inadvertent complete heart block.

Methods

A standard electrophysiologic study was performed with the patient in the sedated, postabsorptive state. Sotalol therapy was discontinued for five drug half-lives. Two quadripolar catheters and one bipolar catheter were inserted via the right femoral vein and advanced to the high right atrium, Hisbundle position, and right ventricular apex. A decapolar catheter was inserted in the coronary sinus via the left subclavian vein. An orthodromic circus movement tachycardia could easily be induced. The earliest retrograde atrial activation during both tachycardia and ventricular premature beats was seen in the His-bundle region. Single premature ventricular stimuli during tachycardia at the time the His bundle was refractory could reset retrograde atrial activation and tachycardia. This confirmed the presence of an accessory pathway, right anteroseptally. To allow more precise mapping, the

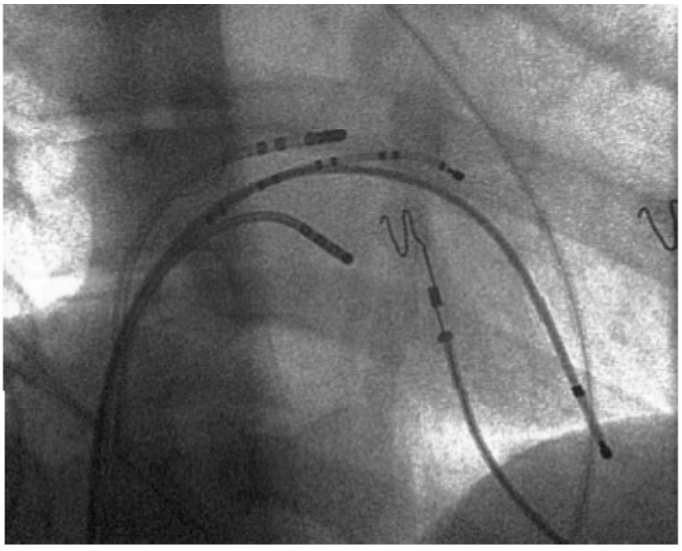

Figure 1. *Right anterior oblique view during procedure with the Freezor cryocatheter positioned anterosuperiorly from the His-bundle catheter. The decapolar catheter is replaced over the His-bundle region to allow more precise mapping.*

decapolar catheter was positioned over the His-bundle region. After the diagnostic study, the high right atrium catheter was replaced by a 7-French Freezor cryocatheter (Cryocath Technologies Inc., Kirkland, Quebec, Canada).

Cryoablation System

The cryocatheter is a 7-French steerable catheter with four electrodes at its distal end: the distal cooling 4-mm tip electrode and three proximal ring electrodes. The catheter has a hollow shaft with a closed electrode tip into which the refrigerant fluid (nitrous oxide) is delivered under pressure from a control console. Within the tip, a phase change occurs (liquid to gas), and the resultant gas is removed under vacuum. This transformation causes cooling of the tip to temperatures as low as –70°C. The gas is conducted away from the tip through the vacuum return lumen and is collected in the console [7].

Ice Mapping and Cryoablation

In this patient with manifest ventricular preexcitation during sinus rhythm, the site of earliest ventricular activation was identified. It was characterized by a short local AV interval, with local activation preceding the onset of the delta wave on the surface ECG. Slightly

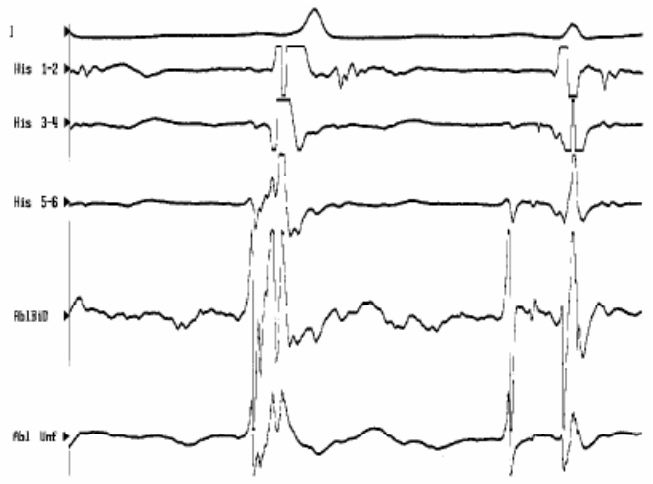

Figure 2. *Disappearance of ventricular preexcitation during ice mapping. After sudden loss of ventricular preexcitation, a His-bundle potential is recorded from the ablation catheter. Because of cryoadherence, atrial and ventricular pacing with extrastimulus testing could be performed to assess normal AV conduction. At this site of successful ice mapping, a permanent lesion is produced by cryoablation without development of complete heart block.*

anterosuperiorly from the His-bundle region, the earliest retrograde atrial activation was identified during orthodromic circus movement tachycardia and ventricular pacing. There was concordance with the earliest site of retrograde atrial activation and earliest site of ventricular activation. After identification of a first prospective ablation site, ice mapping was performed by cooling to –30°C for a maximum of 80 seconds. As the ice mapping had no effect, it was discontinued. At the second site investigated (FIGURE 1), local activation preceded the onset of the delta wave by 43 msec. During ice mapping, there was a sudden loss of ventricular preexcitation with a clear His-bundle potential recorded on the cryoablation catheter after 30 seconds (FIGURE 2). Because of catheter adherence, incremental atrial pacing (with the distal electrode of the quadripolar catheter placed in the coronary sinus) and ventricular extrastimulus testing were performed, which showed preserved normal AV conduction and decremental concentric VA conduction, respectively. At this site of successful ice mapping, cryoablation was performed by cooling to –70°C for a 4-minute period to create a permanent lesion. After cryothermy was terminated, the tissue rewarmed passively (FIGURE 3). Incremental atrial pacing and ventricular pacing as well as single atrial and ventricular extrastimuli were repeated to conclude a successful ablative procedure. During an intravenous bolus of adenosine 12 mg, complete AV block occurred. The patient was observed in the electrophysiology laboratory for 30 minutes to ensure there was no recurrence of accessory pathway conduction. The next day, 12-lead ECG showed sinus rhythm with a PR interval of 160 msec, with no ventricular preexcitation or right bundle branch block. After 3 months, the patient is free of palpitations, and 12 lead-ECG shows no delta waves.

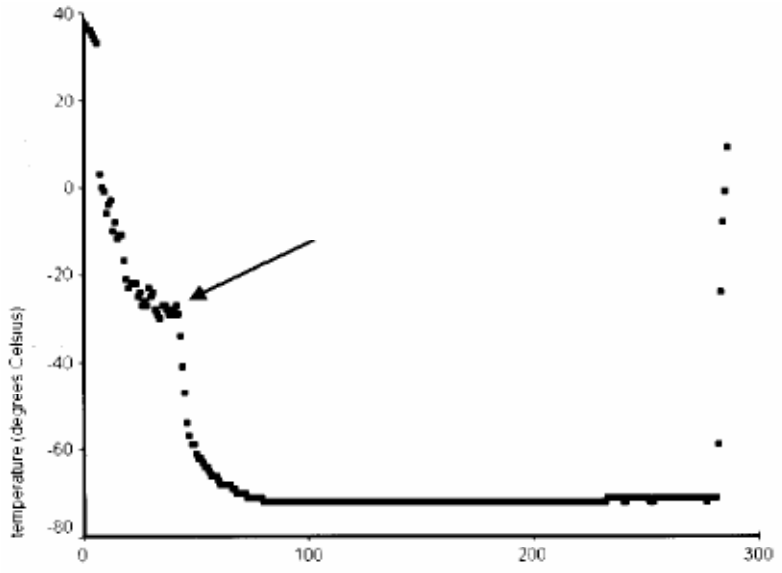

Figure 3. *Temperature versus time. At 30 seconds (ice mapping), preexcitation disappears. It was decided to freeze to −80°C. When the freezing is switched off, temperature rises immediately.*

Discussion

Pathways classified as anteroseptal have no septal connection at all, as they skirt along the central fibrous body of the right fibrous trigone, i.e., at the right anterior free wall [10]. These accessory pathways are in close proximity to the normal conduction system. Although radiofrequency catheter ablation of these pathways has a high success rate, inadvertent complete heart block or right bundle branch block may occur. Also, a recurrence rate up to 15% and mechanical block have been reported [1-6].

Unlike radiofrequency ablation, cryothermal energy creates a lesion that initially is reversible. This so-called ice mapping allows demonstration of functionality of tissues before the formation of a permanent destructive lesion [7-9]. Furthermore, the formation of ice at the catheter tip causes adherence of the catheter to adjacent tissue (cryoadherence), allowing atrial and ventricular pacing without dislodgment of the cryocatheter.These advantages of cryothermal energy makes it a potential unique new technique to create lesions adjacent to sensitive structures such as the compact AV node. Results in this field with the earlier generation of catheters were promising, given that it was not possible to cool to temperatures <60° with the AZ-20 refrigerant fluid that was used for this trial [9].

To the best of our knowledge, this is the first report of successful transvenous cryocatheter ablation of a right anteroseptal accessory pathway. It was demonstrated clearly that during ice mapping and cryoadherence, the delta wave disappeared with preserved normal AV conduction, despite the registration of a His-bundle potential from the abla-

tion catheter after loss of preexcitation. Consequently, cryoablation could be performed without the risk of development of inadvertent complete heart block.

It remains to be determined whether cryoablation also will be successful in left-sided procedures, considering the warming effects in that region. The sensitivity of cryoablation to blood pool warming while delivering epicardial linear cryoablation lesions was previously demonstrated [11].

In conclusion, transvenous cryothermal catheter ablation seems to be an effective new technique with unique features as ice mapping and cryoadherence, which make it especially useful in ablation of "delicate" accessory pathways or the slow pathway in AV reentrant tachycardia.

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7

Comparison of Radiofrequency versus Cryothermy Catheter Ablation of Septal Accessory Pathways

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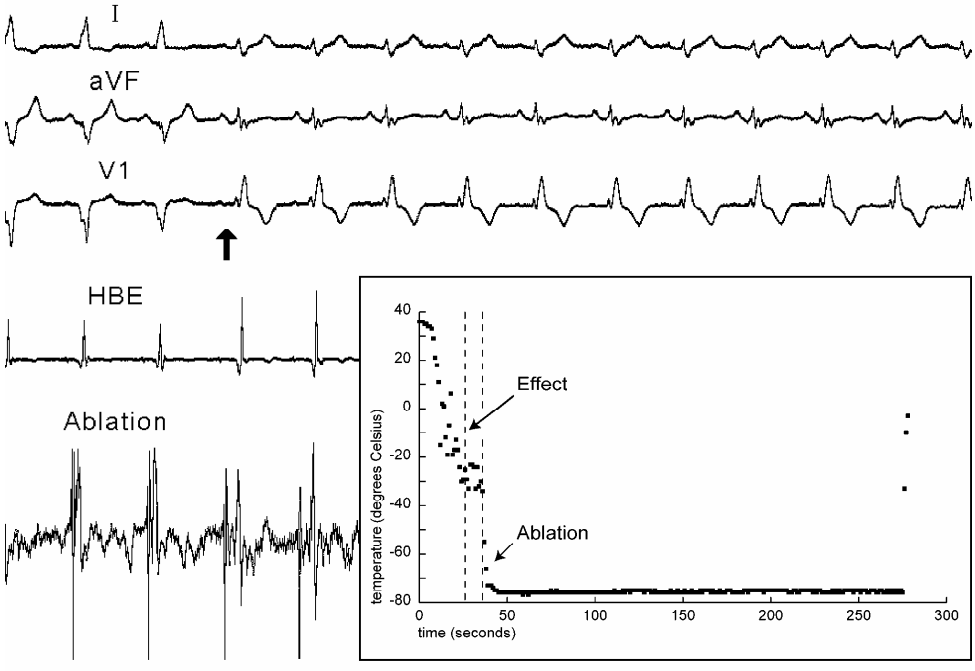
Heart 2003;89:1091-1092

Introduction

Approximately 30 % of all accessory pathways are located in the 'septal' area. As these pathways are in close proximity to the atrioventricular node, there is an increased risk of right bundle branch block or inadvertent complete AV block during catheter ablation [1]. Lesions created by radiofrequency (RF) energy, inevitably involve some degree of tissue disruption, and are irreversible.

As cryothermy energy has the ability to reversibly demonstrate loss of function of tissue with cooling ('ice mapping') at less negative temperatures, and progressive ice formation at the catheter tip causes adherence to the adjacent tissue, this ablation method potentially has advantages over RF for safe ablation of septal accessory pathways [2-4]. In this retrospective study we compare transvenous RF with cryoablation in patients with septal accessory pathways.

FIGURE 1.
Right posteroseptal accessory pathway. The insert shows the curve of temperature versus time. Shown are leads I, aVF, V1, His bundle electrogram (HBE), and signal from the ablation catheter. Appearance of right bundle branch block (arrow), without intermediate stage of normal ventricular activation, 26 seconds after ice-mapping is started, and a few seconds after –30° C was reached. Ablation is commanded at 36 seconds (which allowed 10 seconds of additional observation of the rhythm), with immediate lowering to –73°C for 4 minutes.



Methods

Between January 2000 and October 2001, fifteen patients were treated with RF, and the next consecutive 9 patients with cryoablation for septally located accessory pathways. The final classification of the accessory pathways was made according to the successful ablation site on fluoroscopy.

A standard EP study was performed and after confirmation of the presence of an accessory pathway, a transvenous RF or cryoablation was carried out.

Mapping was performed beginning at the anteroseptal region at the His deflection down to the coronary os and further to the right posterior region. For both energy forms standard techniques were used to identify prospective ablation sites. For cryoenergy procedures, initially ice mapping was done by cooling to –30° C for a maximum of 80 seconds, using a 7F cryocatheter (Freezor, curve 3, Cryocath Technologies Inc). Because of the catheter adherence, incremental atrial pacing and ventricular extrastimulus testing was used, to show preserved normal AV conduction and decremental concentric VA conduction, respectively. If there was a sudden loss of ventricular preexcitation, or sudden termination of the tachycardia, cryoablation was performed by cooling to –70° C for a 4 minutes period, to create a permanent lesion (Figure 1). The pacing protocol as well as single atrial and ventricular extrastimuli were repeated to conclude a successful ablative procedure immediately, and after a 30 minutes waiting period. Eight weeks after discharge, the patients were seen at the outpatient clinic. Continuous variables were expressed as means ± standard deviation. Non-parametric data were compared using a Mann-Whitney test. The level of significance was set at $P < 0.05$.

Results

The localisations of accessory pathways in the RF and cryogroup were left posteroseptal in 6 versus 1, right posteroseptal 7 versus 2, midseptal 1 versus 2, and anteroseptal 1 versus 2 patients respectively. Success at the end of the procedure was achieved in 12 patients (80%) in the RF group, and in 6 (67%) in the cryogroup. One patient in the RF, and the remaining 3 patients in the cryogroup had temporary success during and after several applications. The not successfully ablated pathways were located left (1) and right (2) posteroseptally in the RF group, and left posteroseptally (1), right posteroseptally (1), and midseptally (1) patient in the cryogroup.

In the RF group a median number of 9 (range: 1-34) applications were applied, versus 2 (range: 1-21) in the cryogroup. Procedure and fluoroscopy times were comparable. In both groups 1 patient developed right bundle branch block. These blocks remained present after one day. It was incomplete for the cryothermy patient, and disappeared at the first ambulatory control after 6 weeks. One patient in the cryogroup had a temporary inadvertent complete heart block, 30 seconds after icemapping. It resolved spontaneously, and was probably mechanically induced. One patient in the RF group had a cardiac tamponade, and needed pericardiac drainage. After successful procedures, no late recurrences were ob-

served in the RF group. Six weeks after ablation, one patient in the cryogroup experienced recurrent palpitations, although no tachycardia was documented. She is asymptomatic on sotalol. In 2 out of 3 patients with a failed first ablation attempt in the RF group a successful redo was performed. Redo with cryoenergy failed in two patients, and was successful in one. However, one of the two failing patients had intermittent preexcitation. No cross over from cryoablation to RF was performed to have a more reliable comparison between both techniques. If we include the redo procedures, RF was successful in all, versus 7/9 complete successes (78%) in the cryogroup, with one additional intermittent preexcitation.

Discussion

RF ablation of septally located accessory pathways is associated with a higher percentage of failures and recurrences in comparison with other localizations, and inadvertent complete heart block or new right bundle branch block may occur [1]. The rationale for attempting cryoablation in these sites is double: enhancing safety with ice mapping of prospective ablation sites, and improving efficacy [2-4].

This retrospective study compared RF with cryoablation for septally located accessory pathways. The primary, acute success rates are for both treatment modalities were comparable. The median number of applications tended to be lower for cryo than for RF energy, and this might decrease tissue damage, which can be both harmful and proarrhythmogenic on the long term. The procedure and fluoroscopy times remained equal for both study groups, although in the cryogroup fluoroscopy time tended to be shorter, certainly when considering only successful procedures. This is an important asset, and could be due to the fact that continuous fluoroscopy is not necessary during cryoenergy application.

After performing a redo with the same energy, 100% success was achieved with RF, and this was not reached with cryothermy, although the difference was not significant. The first explanation could that cryoablation was only carried out if ice mapping was successful, that means, effective with preservation of normal AV conduction. This cautious approach leads to less applications [4]. It is possible that during ice mapping, intramural or more epicardially located accessory pathways were not reached at all, as the cooling was not deep enough to have any effect (while theoretically, it could have been the right spot). However, cooling to temperatures less than –30°C can create irreversible lesions, and therefore also inadvertent complete AV block [2,4].

Secondly, lesions created by cryothermy are probably different in size and certainly in composition from lesions created by radiofrequency catheters. This could mean that a more precise mapping, or a larger catheter tip, or further cooling, is neccessary to achieve the same effect. Third, an important explanation for a failing attempt is inadequate mapping. As the same operators performed both RF and cryoablation an operator effect can be excluded.

Finally, as this is a new technique, a learning curve exists [5]. The cryocatheter is not yet as steerable as a conventional RF catheter, and this could have limited proper positioning of the cryoablation catheter, especially for left sided posteroseptal sites.

This analysis certainly is facing several limitations, including its retrospective character and the small patient number. We could easily foresee a similar, prospective trial, but we realize that this study can not be repeated, as the environment in ablation is changing very fast. New mapping technologies have a serious impact on procedure duration and fluoroscopy time. Future trials have to be done with such technology. Furthermore, the three (or four) different subgroups pose different specific problems, which can not be addressed in a small trial.

Conclusion

In conclusion, transvenous cryothermy catheter ablation seems to be an effective new technique with unique features as ice mapping and cryoadherence, making it especially useful in ablation of 'delicate' accessory pathways or slow pathways in atrioventricular nodal reentrant tachycardia.

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Letter To The Editor

A Cool Ablation

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J Cardiovasc Electrophysiol 2002;13:839

To the Editor:

Recently, cryothermal energy can be used for transvenous catheter ablation. As cryothermal energy has the ability to reversibly demonstrate loss of function of tissue with cooling (ice mapping) at less negative temperatures (minus 30 degrees Celsius), and progressive ice formation at the catheter tip causes adherence to the adjacent tissue (cryoadherence) [1-3], this energy form provides a potential benefit in ablation of "delicate" accessory pathways in close proximity to the AV node [4]. In a recent issue of the *Journal*, Idris et al. reported about a cryoablation of a right anteroseptal accessory pathway (AP) [5]. They described a slowly disappearance of preexcitation after approximately 18 seconds of cooling down to –75 degrees Celsius. Their explanation was that the gradual buildup of the "iceball" coincided with this gradual loss of preexcitation due to progressive slowing anterogradely over the AP prior to block. This finding led to the conclusion that in contrast to the sudden loss of preexcitation seen during radiofrequency ablation, cryoablation may be associated with gradual loss of preexcitation.

Despite this interesting observation made by the authors, a few issues should be mentioned. The authors did not reported if ice mapping at the successful ablation site was performed prior to cryoablation. It would be very interesting to know if also during ice mapping a gradually loss of preexcitation was recorded, after how many seconds this occurred, and at which temperature. In this context also the time to reach minus 30 degrees Celsius should be mentioned, because that is indeed the moment the catheter adheres to the endocardial surface to produce a lesion (1),although it is still unknown if this cooling is always deep enough to achieve maximal effect. If, in our experience, during ice mapping, the time to reach minus 30 degrees Celsius took longer than 40 seconds, a successful cryoablation at this site was unlikely, even if preexcitation subsequently disappeared. Therefore, the role of the temperature-time constanceuring ice mapping seems important to predict a successful ablation site (Theuns et al., submitted to JCE [6]). An explanation for this observation is probably a poor wall contact of the ablation catheter, or an suboptimal (remote) ablation site. Also a gradually loss of preexcitation during cryoablation usually indicated an unsuccessful ablation, with a high incidence of gradually reappearance of preexcitation, sometimes more than 30 minutes after the application. The same effect can sometimes been seen after radiofrequency catheter ablation, especially in posteroseptal accessory pathways. Because the time to reach minus 75 degrees during cryoablation was almost always achieved within three seconds a gradual buildup of the "iceball" seems no to be the explanation of this phenomenon, rather a suboptimal target position, or intramural/ epicardially located accessory pathway.

Therefore, a successful ablation of an accessory pathway with cryothermal energy is characterize by a high temperature-time constant during ice mapping with sudden disappearance of preexcitation. In this respect, there is no real difference with radiofrequency ablation.

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Ice mapping during cryothermal ablation of accessory pathways in WPW: the role of the temperature time constant

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Europace 2004;6:116-122

Abstract

Aim Cryothermal energy has the ability reversibly to demonstrate loss of function with cooling, ice mapping, at less deep temperatures. The purpose of this study was to investigate the time course of the temperature during ice mapping of accessory pathways.

Methods and results Thirteen patients with the Wolff-Parkinson-White (WPW) syndrome underwent cryoablation. After identification of a prospective ablation site, ice mapping was performed by cooling the tip to a minimum of –30°C. Successful ice mapping was defined by loss of accessory pathway (AP) conduction. A total of 104 ice maps were analyzed. Successful ice mapping was demonstrated in 17 attempts. There was no significant difference in mapping temperature between successful and unsuccessful ice mapping (–29.4 ± 3.2° C vs –30.4 ± 1:7° C). The temperature time constant t during successful ice mapping was significantly shorter compared with unsuccessful ice mapping (7.0 ± 1:1 s vs 10.1 ± 1:3 s; P <0.0001). The response time (RT) to mapping temperature of -30 (C was significantly prolonged in unsuccessful ice mapping attempts (35.8 ± 4:5 s vs 53.5 ± 11.0 s; P <0.0001). Significant correlations were found between successful ice mapping and the temperature time constant, and between RT and the temperature time constant (P<0:001).

Conclusion The ability to identify prospective ablation sites by ice mapping was demonstrated. Successful ice mapping attempts were characterized by a short temperature time constant and a short response time to mapping temperature with a sudden disappearance of pathway conduction.

Keywords: ablation; accessory pathway; arrhythmia; mapping; cryothermal energy

Introduction

Radiofrequency (RF) catheter ablation is a very effective and well-recognized treatment for abnormal pathway conduction [1,2]. However, RF energy has several limitations [3-5]. Success of RF application at a specific site cannot be predicted prior to energy delivery. Lesions created by RF energy, inevitably involve some tissue disruption which is irreversible. In contrast to RF energy, cryothermal energy has the ability to demonstrate reversible loss of function of tissue during progressive lowering of the temperature (ice mapping) [6-8]. Therefore, this property of cryothermy has the potential to predict a successful ablation site, without causing irreversible damage.

The aim of the present study was to investigate whether the time course of temperature during ice mapping of the AP in patients with Wolff-Parkinson-White (WPW) syndrome would predict a successful outcome.

Methods

Study population

The study population consisted of 13 patients who were treated with cryothermal ablation of accessory pathways in the WPW syndrome, confirmed by 12-lead ECG and electrophysiological study. Antiarrhythmic drug therapy was discontinued for a duration of 5 half-lives prior to the study. All patients underwent a standard electrophysiological study in the sedated, postabsorptive state.

Electrophysiological study

Two quadripolar diagnostic catheters and one bipolar diagnostic catheter were inserted via the right femoral vein and advanced to the high right atrium, His bundle position, and the right ventricular apex under fluoroscopic control. A decapolar diagnostic catheter was positioned into the coronary sinus via the left subclavian vein. The earliest retrograde atrial activation during ventricular extrastimulus testing and tachycardia was registered to assess the location of the accessory pathway. The location of the accessory pathways was described using the new nomenclature [9]. In case of tachycardia, single ventricular premature stimuli were applied at the time the His bundle was refractory to reset retrograde atrial activation and tachycardia. This confirmed the involvement of an accessory pathway. After the diagnostic study, the high right atrial catheter was replaced with a 7F Freezor cryothermal ablation catheter (Cryocath Technologies Inc, Kirkland, Quebec, Canada). Right-sided accessory pathways were mapped and ablated using the cryothermal ablation catheter positioned from the inferior vena cava. In case of left-sided accessory pathways, mapping and ablation were performed using either the retrograde aortic approach or a transseptal approach as previously described [10].

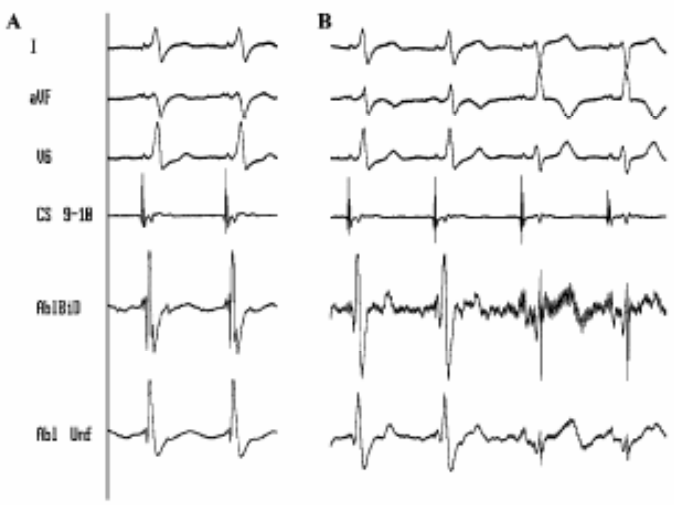

Figure 1 Loss of ventricular preexcitation during ice mapping of a right inferoparaseptal accessory pathway. Shown from top to bottom are recordings from the proximal coronary sinus (CS 9-10), distal bipolar ablation (AblBiD), and distal unfiltered ablation (Abl Unf); and ECG leads, I, aVF, and V6. Left panel (A) shows the recordings at the onset of ice mapping. In the right panel (B), a transient lesion is produced by cryothermy. At this site of successful ice mapping a permanent block will be created.

Cryoablation system

The cryothermal ablation catheter is a 7F steerable catheter with a 4-mm-tip electrode at its distal end and 3 proximal ring electrodes. Temperature is recorded at the distal tip by using an integrated thermocouple. A refrigerant fluid (nitrous oxide) is delivered under pressure through an inner lumen from the console into the hollow tip of the catheter. Within the tip, a liquid-to-gas phase change occurs which causes cooling of the tip to temperatures as low as –70 °C. The resultant gas is removed from the tip under vacuum and is collected in the console.

Ice mapping procedure

One of the potential advantages of cryothermal technology is the ability to demonstrate reversible loss of function of tissue with cooling which is called ''ice mapping''. Further, the progressive ice formation at the catheter tip during cooling causes adherence to the adjacent tissue (cryoadherence) which can prevent dislodgment of the catheter. In patients with manifest ventricular preexcitation during simus rhythm, the site of earliest ventricular activation was identified, characterized by a short local AV interval with local ventricular activation preceding the onset of the delta wave on the surface ECG. The earliest retrograde atrial activation was identified during orthodromic circus movement

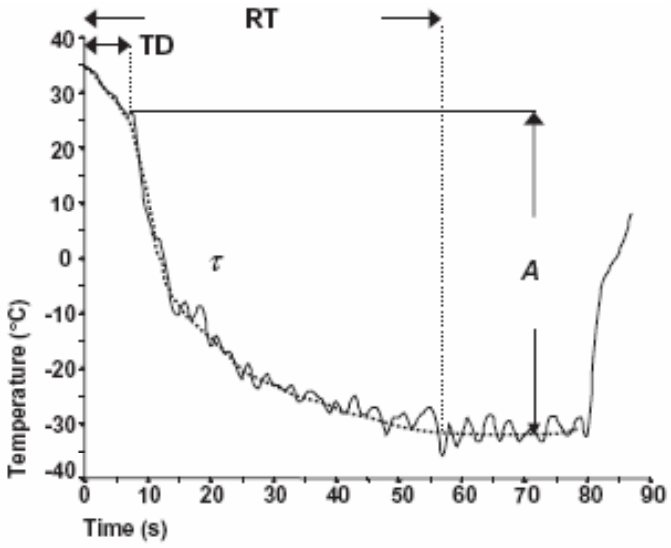

Figure 2 Features of the exponential model used to describe the temperature response during ice mapping. *A*, asymptotic value; RT, response time; τ, time constant; TD, time delay.

tachycardia and/or ventricular pacing. After identification of a prospective ablation site, ice mapping was performed by cooling to a minimum of –30 °C, for a maximum time of 80 s. Successful ice mapping was defined if loss of accessory pathway conduction properties was demonstrated (FIGURE 1). In case of successful ice mapping, cryoablation was immediately carried out by cooling to –70 °C for a duration of 4 min, creating a permanent lesion. If ineffective results were obtained after 80 s, ice mapping was discontinued to allow rewarming of the catheter tip. The catheter was relocated to an adjacent site and ice mapping was repeated.

During ablation, ventricular pacing was performed to confirm loss of accessory pathway conduction. Ablation was defined as successful by atrial and ventricular incremental pacing and extrastimulus testing, if both antegrade and retrograde accessory pathway conductions were completely abolished.

Data analysis

The entire dataset was reviewed from digitally stored files using time-logged parameters. Ice mapping sections were selected and submitted to detailed analysis of the time course of the temperature during ice mapping.

To facilitate comparisons, the time course of the temperature was described in terms of an exponential function that was fitted to the data by using a non-linear-regression technique. The computation of best fit parameters was chosen to minimize the sum of the squared differences between the fitted function and the observed response.

Table 1 Characteristics of the patients and ice mapping attempts at −30 °C

Patient no.	Gender	Age (years)	Site of AP	No. of maps at −30 °C	Average τT unsuccessful	Average τT successful
1	M	16	RSPS	3	11.33	6.49
2	F	44	LP	1	NA	6.84
3	M	18	RS	4	12.51	6.91
4	M	22	LIPS	30	9.54	7.26
5	F	42	LP	11	8.78	6.87
6	M	32	LP	3	9.30	8.55
7	M	17	RIPS	9	9.69	6.59
8	F	50	RIPS	3	10.99	NA
9	F	15	RIPS	2	10.66	6.73
10	F	26	RA	20	10.42	NA
11	F	53	RIPS	3	10.50	4.38
12	M	45	RSPS	9	11.02	7.85
13	M	43	LP	6	10.24	7.33

M = male; F = female; LIPS = left inferoparaseptal; LP = left posterior; RA = right anterior; RIPS = right inferoparaseptal; RS = right septal; RSPS = right superoparaseptal; τT = temperature time constant; NA = not available.

Temperature

The mathematical model for the temperature response during ice mapping consisted of an exponential term (FIGURE 2). The exponential term began after a time delay
$T(t) = T(b) - A\,(1 - e^{-(t-TD)/\tau})$ where T(b) is the temperature baseline value, A is the asymptotic value for the exponential term, τ is the time constant, and TD is the time delay. The relevant amplitude of the exponential term was set to the value of the steady level of mapping temperature.

The response time (RT) of temperature was calculated as the interval between the onset of ice mapping and onset of steady-state of mapping temperature.

Flow and pressure

The flow and pressure response had a similar but not identical appearance to temperature. The monoexponential models were described as
$Fl(t) = Fl(b) + A\,(1 - e^{-t/\tau})$
$P(t) = P(b) + A\,(1 - e^{-t/\tau})$
where Fl(b) and P(b) are the baseline values of flow and pressure.

Statistical analysis

Continuous variables are summarized as mean ± standard deviation. The level of significance was set at $P < 0{:}05$. Non-parametric data were compared using Wilcoxon signed-rank test. Correlations between continuous variables were assessed using the Pearson correlation test. Binary logistic regression analysis was used to test the correlation between successful ice mapping, the different time constants and RT. Statistical analysis was made with SPSS (Statistical Package for Social Sciences, version 9.0) for Windows.

Results

Thirteen patients (mean age 33 ± 14 years, 7 men) were treated with cryothermal ablation for accessory pathway conduction (TABLE 1). At baseline, ventricular preexcitation

with antegrade accessory pathway conduction was seen in all patients. Five patients had a left-sided AP and 8 patients had a right-sided AP. For the 5 left-sided APs, a transseptal approach was used in 4 patients and a retrograde approach in 1 patient.

Ice mapping of accessory pathway

A total of 104 ice maps were analyzed. An average of 8 ice maps (range 2-19) per patient with a mean duration of 72 ± 14 s were attempted. Successful ice mapping of the accessory pathway was demonstrated in 17 maps at a tip temperature of –30 °C.

There was no significant difference in mapping temperatures between successful ice mapping and unsuccessful ice mapping (–29.4 ± 3.2 °C vs –30.4 ± 1.7 °C). In 11 ice maps, a sudden loss of accessory pathway conduction was demonstrated. In the remaining 6 maps, a gradual disappearance of accessory pathway conduction was registered. No differences in electrogram characteristics were demonstrated in maps with sudden or gradual loss of accessory pathway conduction. The temperature time constant τ during all successful ice maps was significantly shorter compared with unsuccessful ice maps (7.0 ± 1:1 s vs 10.1 ± 1:3 s; $P < 0.0001$). The RT to mapping temperature of –30 °C was significantly prolonged in unsuccessful ice mapping attempts compared with successful attempts (35.8 ± 4:5 s vs 53.5 ± 11:0 s; $P < 0.0001$). Subanalysis of the temperature time constant and RT between ice maps with sudden or gradual disappearance of accessory pathway conduction demonstrated a significantly shorter time constant and RT in ice maps with sudden loss of pathway conduction ($P < 0.01$). In Figure 3, examples with a prolonged and a short temperature time constant are displayed.

Successful ice mapping was not significantly different between left-sided and right-sided accessory pathways. The temperature time constant τ during successful ice mapping was not significantly different between left-sided and right-sided accessory pathways (7.4 ± 0.7 s vs 6.5 ±1.1 s).

The correlation between the temperature measurements is shown in Table 2. There were significant correlations between successful ice mapping and the temperature time constant as well as RT ($P < 0.001$). The correlation between RT and the temperature time constant was significant ($r = 0.98$; $P < 0.001$).

There were no significant correlations between successful ice mapping and the flow time constant as well as the pressure time constant. The correlation between the flow time constant and the pressure time constant was significant ($P < 0.001$).

The correlations between the temperature time constant and the pressure time constant as well as the flow time constant were significant ($P < 0.01$).

Cryothermal ablation

Success at the end of the procedure was achieved in 9 patients (69%). The not successfully ablated pathways were located right anterior (n = 1), right inferoparaseptal (n = 1), left inferoparaseptal (n = 1) and left posterior (n = 1). Patients with a successful cryoablation demonstrated during ice mapping a sudden disappearance of pathway conduction compared with patients with an unsuccessful ablation. The time interval between the onset of ice mapping and the disappearance of accessory pathway conduction was significantly

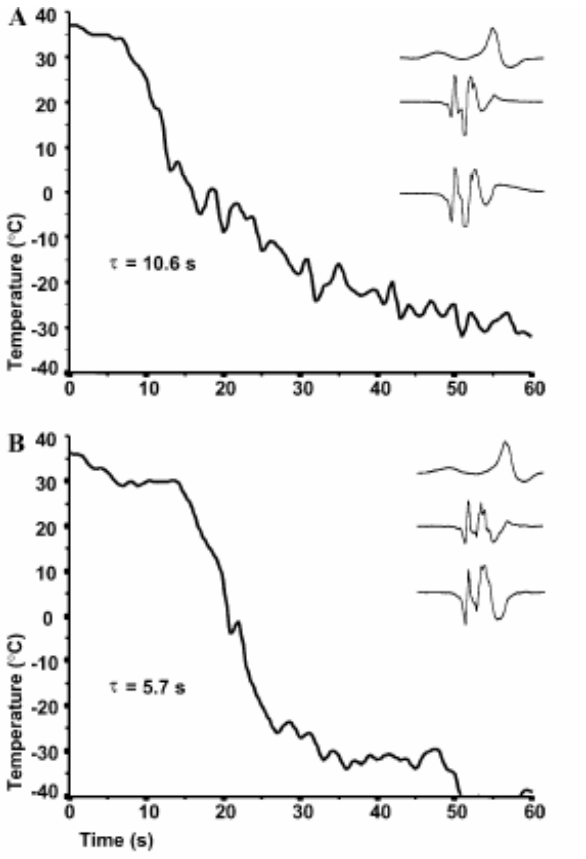

Figure 3 The time course of tip temperature during ice mapping. The upper panel shows an ice mapping attempt with a long time constant, and the lower panel shows an ice mapping attempt with a short time constant. The bipolar electrograms recorded by the cryoablation catheter at the onset of ice mapping are displayed for both attempts.

shorter in successfully ablated pathways compared with unsuccessfully ablated pathways (21.8 ± 9.7 s vs 44.5 ± 0:7 s; P < 0.05). In 6 ice mapping attempts, the disappearance of accessory pathway conduction was gradual. In none of these sites could a successful cryoablation be performed.

Complications

Two patients developed right bundle branch block. This block remained present after 1 day, but disappeared at the first follow-up after 6 weeks. One patient had temporary, inadvertent, complete heart block, 30 s after ice mapping. It resolved spontaneously and was probably a mechanically induced block.

Table 2 Correlation between temperature variables during ice mapping

	τ Temp	RT	Success	τ Flow
RT	$r = 0.98$			
	$P < 0.001$			
Success	$r = 0.69$	$r = 0.72$		
	$P < 0.001$	$P < 0.001$		
τ Flow	$r = 0.30$	$r = 0.20$	$r = 0.01$	
	$P < 0.01$	$P < 0.05$	NS	
τ Pressure	$r = 0.31$	$r = 0.24$	$r = 0.03$	$r = 0.87$
	$P < 0.01$	$P < 0.05$	NS	$P < 0.001$

RT = response time; τ = time constant; Temp = temperature.

Discussion

This report describes the first results of cryomapping during percutaneous catheter cryothermal ablation of accessory pathways in WPW. The use of cryothermal energy for accessory pathway ablation was initially described in cryosurgical reports [11-13]. Cryothermal energy has several advantages over radiofrequency energy. In contrast to radiofrequency energy, cryothermy causes tissue destruction with preservation of the underlying tissue architecture which decreases the risk of thromboembolism and tissue perforation [4]. The potential benefit of cryothermal energy is the ability reversibly to demonstrate loss of electrophysiological properties of tissue before the creation of a permanent lesion [6,8]. Furthermore, the formation of ice during cooling causes adherence of the catheter to the adjacent tissue (cryoadherence) allowing atrial and ventricular pacing without catheter dislodgment.

The results of this study confirm the concept of ice mapping. The use of cryothermal energy to demonstrate reversible loss of function has been described in the surgical literature [11]. Differences in mapping temperature with reversible effect between surgical mapping and our mapping are explained by differences in the warming effect of the blood pool circulating around the catheter tip. In this study, a minimum temperature of –29.4 °C ± 3:2 °C was reached during ice mapping. This mapping temperature is in agreement with experimental animal data on ice mapping of the atrioventricular node which demonstrated only irreversible lesions created by cooling to temperatures lower than –30 °C [6,14].

The course of the temperature during ice mapping can be described by the temperature time constant. The time constant is reflected in the time interval between the onset of ice mapping and the steady-state mapping temperature of –30 °C. In this study, sudden disappearance of accessory pathway conduction was demonstrated during ice mapping attempts with a short temperature time constant. The response time to steady-state map-

ping temperature of –30 °C in those attempts was less than 40 s. The temperature time constant is dependent on several factors.

First, the efficiency of cooling during cryothermal energy delivery can be affected by poor electrode contact with the endocardium. A significant "thermal sink" can be created when a major part of the electrode is in contact with the bloodstream. This warming effect will result in a prolonged response time to reach the mapping temperature. A loss of freezing power was not reflected in the flow time constant and the pressure time constant, although significant correlations between the temperature time constant and the pressure time constant as well as the flow time constant were found. This means that a higher pressure to maintain delivery of the refrigerant fluid is necessary to reach the mapping temperature when electrode contact with endocardium is poor. Secondly, the warming effects of the blood pool in regions with a high blood flow can have effects on the outcome [4]. However, our results did not demonstrate a difference in temperature time constant between left- and right-sided located accessory pathways. The temperature time constant is an indication of the electrode contact with the endocardium. This time constant is reflected in the response time to steady-state mapping temperature of –30 °C. During this time interval, the electrophysiological properties of accessory pathway conduction can be modified.

In our study, there was a significant difference in time intervals with respect to the disappearance of accessory pathway conduction. In successfully ablated patients, the disappearance of pathway conduction conduction during ice mapping was sudden. This observation is in agreement with the sudden loss of preexcitation as seen during radiofrequency ablation. In the unsuccessfully ablated pathways, there was a gradual loss of preexcitation during mapping. This observation was not related to mapping temperature. Possible explanations for this observation are a suboptimal (remote) ablation site or intramurally/epicardially located pathways. Some data suggest that the volume of the lesion is smaller with cryothermy compared with radiofrequency energy [15]. Other data suggested a comparable size for both energy forms [6], but the lesion size will be clearly dependent on the catheter tip.

From results in previous studies and the data in our study, the following characteristics of the temperature curve during ice mapping can be described. First, the temperature time constant is an indication for the electrode contact with the endocardium. The temperature time constant is reflected in the response time to steady-state mapping temperature of –30 °C. Good electrode contact with the endocardium is indicated by a short response time to steady-state mapping temperature. Arbitrarily, a cut-off value of 40 s as maximum for the response time was chosen, which was based on observations during our study. The second point is that during this interval of 40 s, the electrophysiological properties of the accessory pathway conduction have to be modified. A sudden modification of the electrophysiological properties within this interval is an indication of being at the right prospective ablation site.

Therefore, successful cryoablation could be predicted by both a short temperature time constant and a short response time to mapping temperature combined with a sudden loss of accessory pathway conduction.

Study limitations

The number of mapping attempts per patient varied considerably and also reflected our learning curve. The results are likely to improve as the experience with this novel technique increases. Repeated ice mapping, with different time constants at the same spot should be performed to prove our point. However, fluoroscopic visualization of the catheter tip has several limitations. With better imaging techniques, a series of ice mapping attempts at the same spot could be performed to determine the temperature time constant during these attempts and to analyze the concept of ice mapping in a different way.

Conclusion

Ice mapping allows accurate localization of accessory pathways before creating a permanent lesion. This technique provides a potential benefit in the ablation of ''delicate'' accessory pathways in close proximity of the AV node. The time course of the temperature during ice mapping can be used clinically to predict a successful ablation site. Therefore, successful ablation of an accessory pathway with cryothermal energy is characterized by reaching the mapping temperature of –30 °C within 40 s combined with sudden disappearance of pathway conduction.

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10

An 'atypical' case of 'typical' AVNRT?

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Pacing Clinical Electrophsiol 2003;26:630-631

Keywords: AV nodal tachycardia, multiple pathways

Case presentation:

A 62-year old man developed syncope during bicycle training. At arrival of the ambulance his rhythm was ventricular fibrillation which was terminated by 360J DC shocks. He had no history of any significant cardiac or non-cardiac disease and did not take any medication. Echocardiography showed a slightly diminished left ventricular function with an estimated left ventricular ejection fraction of 45%. During exercise testing sustained fast monomorphic ventricular tachycardia (VT) started and terminated spontaneously. During electrophysiology (EP) testing a fast monomorphic VT, cycle length (CL) 202 ms, was easily and reproducibly induced with programmed ventricular stimulation. Its morphology was identical to the one observed during exercise testing. Besides the VT, a regular narrow complex tachycardia was easily and repeatedly induced with ventricular programmed stimulation during electrophysiological testing (Figure 1). The patient recognized this tachycardia as the source of palpitations during exercise training for at least two decades. Programmed atrial stimulation revealed more than one sudden AH "jump" (>50 ms) with echo cycles. Intravenous administration of 12 mg adenosine resulted in VA dissociation during ventricular pacing at a CL 500 ms. Retrograde conduction was midline and decremental during programmed ventricular stimulation. The above mentioned findings supported the diagnosis of AV nodal reentrant tachycardia (AVNRT). Several additional findings were noted. Without obvious alteration of CL, there was a significant change in the retrograde as well as in the anterograde activation times. The earliest retrograde activation was observed in the posteroseptal region. This phenomenon was associated with a noticeable alteration on the surface ECG. When the retrograde activation was faster there was no observable retrograde P-wave on the surface ECG. The longer retrograde activation time was associated with a negative deflection at the end of the QRS in leads II, III and aVF. The initial decrease in retrograde activation time was always followed by an increased antero-

Figure 1
Alternation of anterograde and retrograde conduction times during slow-fast AV nodal tachycardia, associated with changes on the surface ECG (explanation in text).

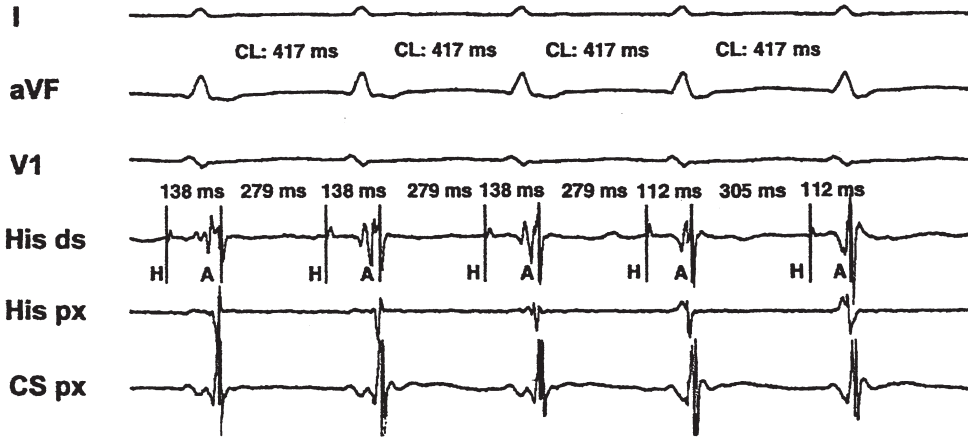
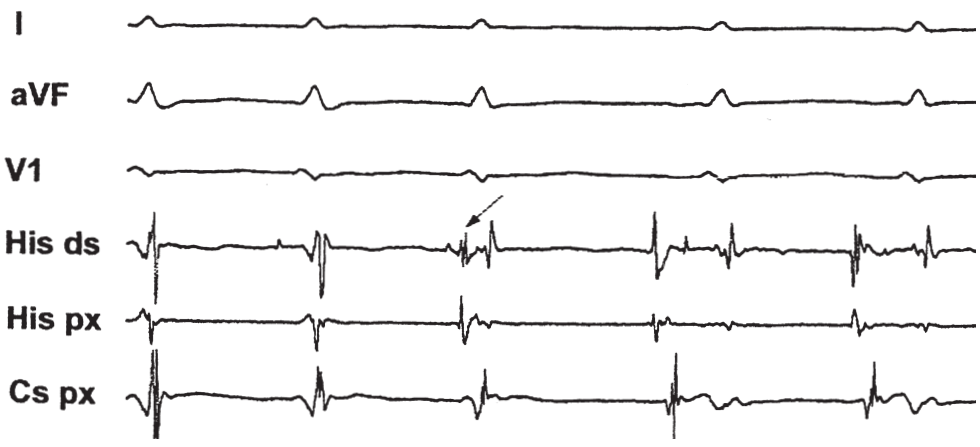


FIGURE 2
Termination of the AVNRT with simultaneous induction of an atrial tachycardia.



grade activation time (FIGURE 1). The slow-fast AVNRT merged into an atrial tachycardia with slower rate (FIGURE 2). Furthermore, atrial flutter and atrial fibrillation with fast ventricular response could be easily and repeatedly induced as well.

***Questions*:** What is the mechanism of the alternation of anterograde and retrograde times during AVNRT?

Commentary:

When a PAC initiates typical AVNRT, the fast pathway is refractory and anterograde conduction occurs over the slow pathway allowing reentry. Alternating CL during AVNRT is usually an indication of multiple slow AV nodal pathways [1]. In the present case, alternation of the RR intervals could not be seen because the compensatory changes in anterograde and retrograde activation times. In the present case there was an initial change in the AA interval before the HH interval. Thus the HA actually shortens before the AH prolongs substantively. This suggests the presence of multiple fast/retrograde AV nodal pathways. The corresponding change in the anterograde conduction can theoretically be a result of a rate dependent delay due to prematurity of the retrograde impulse. Another possible explanation is the presence of a second anterograde pathway as suggested by the basic EP study. In this case the faster retrograde conduction may "switch" the anterograde conduction over the other slow pathway having different conduction properties (conducting slower and having shorter refractory period).

In order to cure AV nodal tachycardia and to prevent fast AV nodal conduction in the event of other atrial arrhythmias we elected to ablate the fast pathway, using cryothermy. By

using ice-mapping, safe ablation of pathways at locations associated with high incidence of inadvertent AV block can be performed [2,3]. After cryo-ablation the PR interval remained prolonged and the tachycardia was no longer inducible. A dual chamber implantable cardioverter defibrillator was then implanted, allowing optimization of the AV delay.

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11

CRAVT: A prospective, randomized study comparing transvenous Cryothermal and Radiofrequency Ablation in AtrioVentricular nodal reentrant Tachycardia.

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Eur Heart J 2004;25:2232-7

Abstract

Background. Transvenous catheter ablation of atrioventricular nodal re-entrant tachycardia (AVNRT) with radiofrequency (RF) is effective and safe, but carries a 1-3% incidence of early and potentially late heart block. Cryothermy can create transient effects, and identify potentially successful ablation sites and decrease the risk for permanent heart block.

Methods. In this prospective, randomized trial 102 patients with recurrent narrow QRS-complex tachycardia suggestive of AVNRT were randomized to either RF or cryoablation before a diagnostic study .

Results. In 63 patients with AVNRT, 33 were randomized to RF and 30 to cryoablation. Procedural success was achieved respectively in 30 (91%) patients in the RF and 28 (93%) in the cryoablation group. The median number of cryothermal applications was significantly lower than the number of RF applications (2 versus 7, $p < 0.005$). No accelerated junctional rhythm was seen with cryothermy, while it was present in 31/33 RF patients. Both fluoroscopy and procedural times were comparable. The radiological position of the successful site in relation to anatomical landmarks was slightly different ($p<0.05$). No cryothermy related complications were observed, and no permanent AV conduction disturbances occurred. During a mean follow up of 13±7 months long-term clinical success was seen in one additional patient in each group. In the same period, 3 patients in both groups experienced recurrent AVNRT.

Conclusion. Cryoablation is as effective and safe as RF for AVNRT. Significantly fewer applications are necessary, with comparable procedure times. This makes cryothermy useful for the treatment of tachyarrhythmias near the compact AV node.

Introduction

Catheter-based radiofrequency (RF) energy has become the preferred modality for tachyarrhythmia ablation and has proven to be highly effective in the treatment of atrioventricular nodal re-entrant tachycardias (AVNRT), accessory pathway tachycardias, atrial flutter, focal atrial fibrillation, and ventricular tachycardias. However, lesions created by RF energy inevitably involve some degree of tissue disruption, are irreversible and thrombogenic [1-3]. During ablation of the slow pathway in AVNRT, and of (para)septally located accessory pathways, there is an increased risk of right bundle branch block or inadvertent complete AV-block, as these pathways run in close proximity to the atrioventricular node [4-10]. Applications should be delivered during sinus rhythm and not during tachycardia, because of the risk of catheter dislodgement at termination of the tachycardia.

Because freezing (cryothermy) has the ability to reversibly demonstrate loss of function of tissue with cooling at less negative temperatures (ice mapping), and because progressive ice formation at the catheter tip causes adherence to the adjacent tissue, this ablation method potentially has advantages over RF ablation for safe ablation, even during tachycardia [11]. Therefore, cryothermy could be especially useful in AVNRT and (para)septally located accessory pathways, to reduce the risk of inadvertent right bundle branch block, or complete AV-block [12-14]. The purpose of this prospective, randomized, single centre study was to compare cryothermal and RF ablation in AVNRT. We hypothesized that cryoablation is as effective as RF, that it is a safe method, and in comparison with RF ablation less applications will be necessary, with no occurrence of complete AV-block or thrombo-embolic complications.

Methods

Consecutive patients with recurrent narrow QRS-complex tachycardia, suggestive for AVNRT were enrolled. All patients signed informed consent and were randomized by an independent institution (Cardialysis) to either cryothermal or RF ablation before the baseline electrophysiological study. All antiarrhythmic drugs were discontinued for a duration of 5 half-lives. A standard electrophysiological study was performed. One bipolar catheter and two quadripolar catheters were inserted into the right femoral vein and advanced to the high right atrium, His bundle position, and right ventricular apex, respectively. A decapolar catheter was positioned in the coronary sinus via the left subclavian vein. A detailed measurement of the AV junction in relation to radiological hallmarks was made on the CAAS II system (delineation of the His bundle, and its relation and distance to the os of the coronary sinus). Images of this position were stored in three radiological views: anteroposterior (AP), right anterior oblique (RAO 30), left anterior oblique (LAO 30). Incremental atrial and ventricular pacing and extra stimulus testing were performed, with determination of the anterograde and retrograde effective refractory periods (ERP) of the AV node, as well as the Wenckebach point, and the stable 2:1 AV-block interval. Diagnosis of dual AV nodal pathways (AH-jump) and AVNRT was made on the basis of standard

diagnostic criteria. If sustained tachycardia could not be induced, isoproterenol and eventually atropine were infused to facilitate tachycardia.

Ablation

The target in both ablation techniques was slow pathway ablation guided by a combination of intracardiac electrogram criteria and anatomical landmarks [15].

Catheter positioning and handling was performed during continuous fluoroscopy. The target position was labelled in the 3 mentioned radiological planes, with the His bundle and coronary sinus catheter as references. The endpoint was non-inducibility of AVNRT. For RF ablation, a 7Fr 40-60 mm curve, 4 mm tip catheter (Conductr, Medtronic, Minneapolis, USA) was used with a conventional electrosurgical generator (Atakr II, Medtronic, Minneapolis, USA) as a source of radiofrequency energy. Each application was started with power set at 10 W; if AV conduction was preserved, the power was increased up to 40 W until a maximum of 65°C was reached. Fluoroscopy was used throughout each application. For cryoablation, a 7 Fr 53 mm curve, 4 mm tip catheter (Freezor 3, Cryocath Technologies, Montréal, Canada) was used, and a CCT2 CryoConsole (Cryocath Technologies, Montréal, Canada). Initially, ice mapping was performed by cooling to minus 30° C for a maximum of 60 seconds. Fluoroscopy was applied until a stable temperature of minus 30° C was reached. During these 60 seconds, atrial extra stimulus testing was performed. Disappearance of an AH-jump, termination or non-inducibility of AVNRT was considered to be an identification of a potentially successful ablation site, and ablation was subsequently performed by cooling to minus 75° C for a 4 minutes period to create a permanent lesion (Figure 1). If there was no clear AH-jump, and AVNRT was difficult to induce at baseline, prolongation of the anterograde AV refractory period during atrial extra stimulus testing during ice mapping was used to identify a target site.

In both the cryothermy and RF group, inducibilty of AVNRT was tested after each application, and if non-inducible, repeated after a 30-minute waiting period. Conduction and ERP-intervals were measured again. Procedure time was measured from the moment of arrival of the patient at the EP lab until the end of the treatment, including the 30 minutes waiting period.

Follow-up

After ablation, all patients received an event recorder for 3 months to transmit an ECG during symptoms and were seen at the out patient clinic. One year after the procedure all patients were approached by telephone and asked about recurrent palpitations.

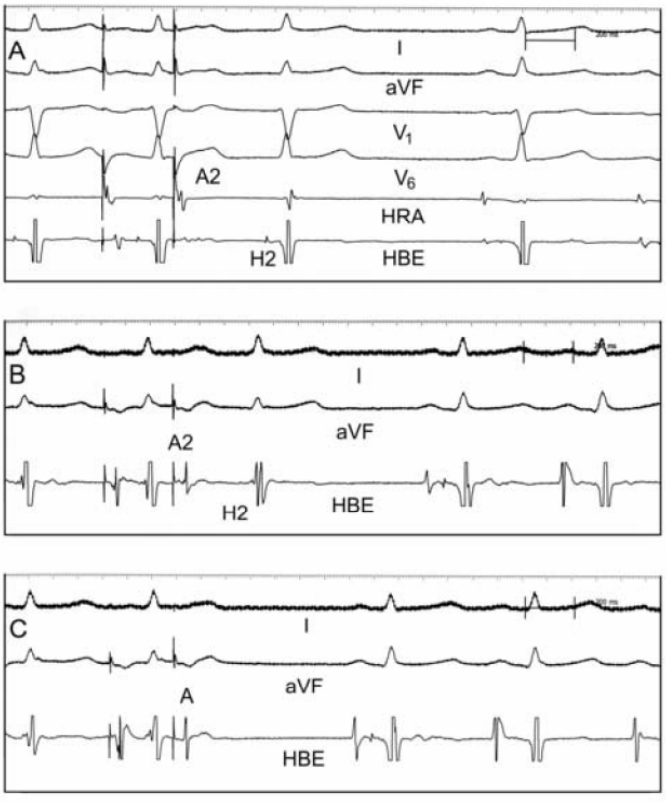

Figure 1.
Programmed electrical stimulation in the high right atrium (HRA) at baseline (A) and after ice mapping was started (B and C). In A, conduction of the extra stimulus A2 is conducted over the slow pathway (A2H2 interval 360 ms). When ice mapping is started A2H2 is conducting over a faster path, 240 ms in B, and AV conduction is blocked in panel C. This sign that the fast pathway is preserved can be used to start ablation

Statistical analysis

Continuous variables were expressed as mean ± standard deviation. Non-parametric data were compared using the Mann-Whitney U test. The level of significance was set at $P < 0.05$.

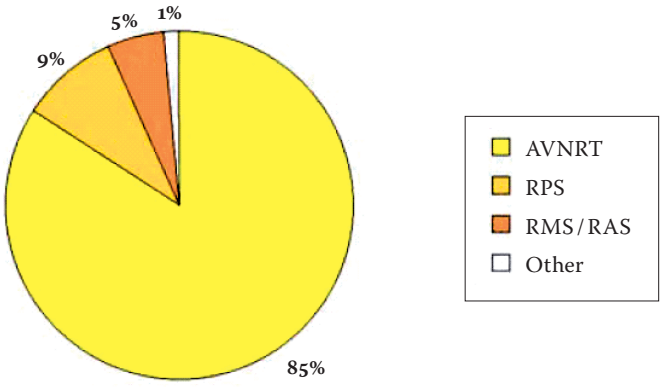

FIGURE 2.
Diagnosis after baseline electrophysiological study in patients included in the trial and in whom the arrhythmia was located in Koch's triangle. Atrioventricular nodal re-entrant tachycardia (AVNRT), right posteroseptal pathways (RPS); right midseptal and anteroseptal pathways (RMS / RAS). Other: focal tachycardia.

Results

A total of 102 patients were enrolled in this study. After baseline study, AVNRT was diagnosed in 63 patients (FIGURE 2). Of the remaining 39 patients, 12 had a (para)septally located accessory pathway, and 13 patients suffered from other circus movement tachycardias. Atrial flutter was the target arrhythmia in 3 patients; in another 3 patients it was a focal atrial tachycardia, and in 8 patients arrhythmias were non-inducible. Of the 63 patients with AVNRT, 33 were randomized to RF and 30 to cryoablation before baseline EP study (TABLE 1). There were 10 men and 23 women in the RF group with a mean age of 44 years. The cryothermy group consisted of 14 men and 16 women with a mean age of 52 years. Successful ablation was achieved in 30 (91%) patients in the RF and 28 (93%) in the cryothermy group, respectively (TABLE 1). The median number of ice maps (applications until –30°C) was 5. The median number of applications in the cryothermy group was significantly lower than in the RF group, namely 2 versus 7 ($p < 0.005$). The median fluoroscopy time was 35.2 minutes in RF and 29.2 minutes in the cryothermy group and were not significantly different. The procedure times were also comparable with both techniques, namely 144 minutes in the RF and 142.5 minutes in the cryothermy group. Furthermore, there were no differences in electrophysiological characteristics before and after the procedure in both groups (TABLE 2). One patient in the RF group had a pericardial effusion (due to the right ventricular lead positioning), which resolved after drainage. No other procedural complications were seen. In one patient in the RF group a temporary PR prolongation was registered for the duration of a few beats. In the cryothermy group, 2 patients had temporary complete AV-block, lasting 10 and 13.4 seconds, while this was

Table 1.
Result of radiofrequency (RF) and cryoablation in AVNRT

	RF ablation	Cryoablation
Number of patients (N)	33	30
Male/female (N/N)	10/23	14/16
Procedural success (N;%)	30 (91%)	28 (93%)
Ice maps (median, N)	-	5(2-42)
Fluoroscopy time (median, min)	35.2	29.2
Procedural time (median, min)	144	142.5
Applications (median,N)	7(1-31)	2 (1-13)*
Complications	0	0

* = $P < 0.05$

Table 2.
Conduction intervals and refractory periods before and after ablation

	Radiofrequency		Cryothermy	
	Before	After	Before	After
PR interval (ms)	160±33	157±24	158±21	157±24
AH interval (ms)	91±25	91±19	83±21	88±21
HV interval (ms)	42±12	41±7	42±8	41±7
ERP_{AVN} (ms)	279±67	270±69	248±52	263±44
Wenckebach (ms)	356±71	359±64	340±73	332±66
2:1 AV block (ms)	306±45	312±47	301±45	295±51
ERP_{VA} (m s)	274±80	256±70	262±49	251±57
VA block (ms)	331±84	318±63	318±70	306±54

ERP: effective refractory period; AVN: atrioventricular node (antegrade); VA: atrioventricular node (retrograde)

not observed during cryomapping (Figure 3). Transient AV-block was observed during icemapping in 2 patients, and 2:1 block in one during mapping while in AVNRT. No permanent AV conduction disturbances were seen. During RF applications, a fast junctional rhythm was observed in all but 2 patients in the successful application; it was never seen during cryothermy. The radiological position of the ablation tip at the successful site was different between both approaches in the RAO 30° angle. The median distance in systole between ablation tip and the vertical perpendicular line from the His bundle distal tip

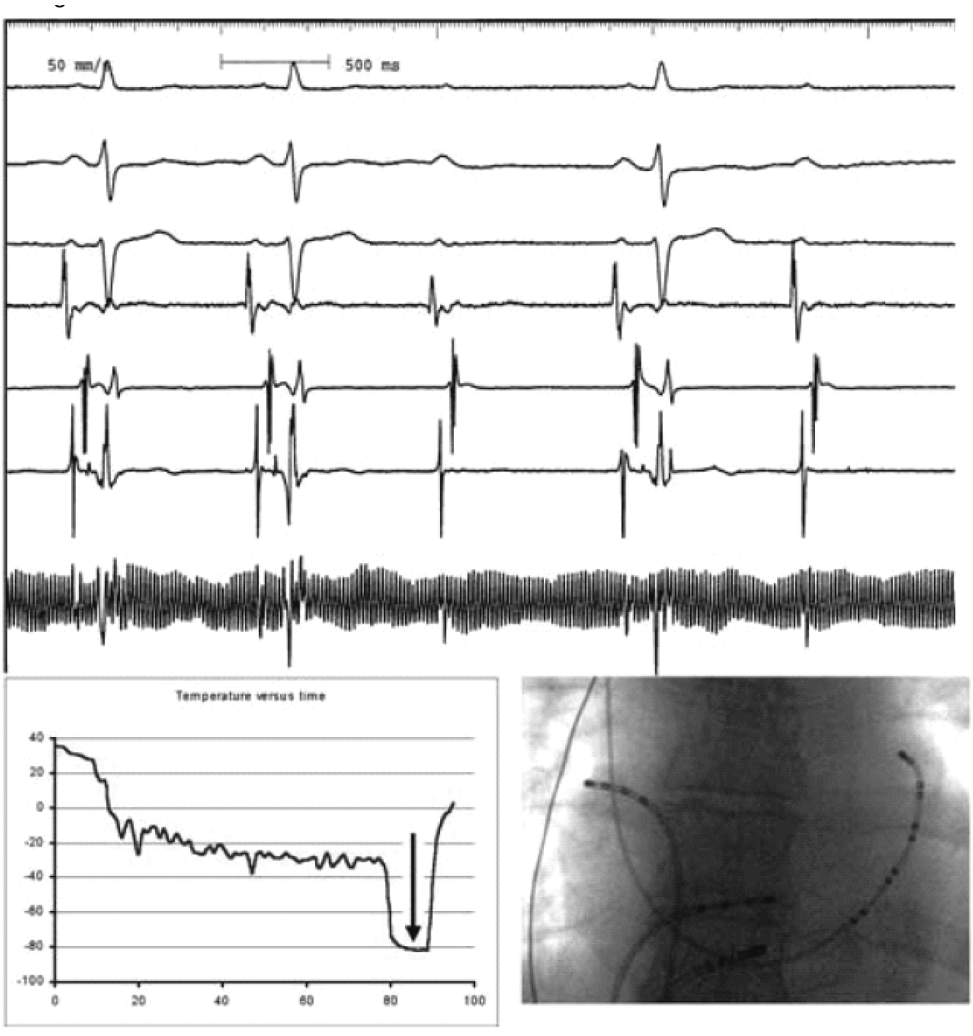

FIGURE 3.

Onset of temporary complete AV block with cryoablation (leads I, aVF, V1, HRA, proximal CS, His and ablation signal). During ice mapping (–30°) AVNRT could no longer be induced and normal AV conduction was present. However, after 7 seconds of cryoablation (-80°) heart block was seen. Freezing was discontinued. This temporary AV block lasted for 17 seconds. Inserted is the temperature-time curve of the cryoconsole, and the position of the ablation and his catheter in anteroposterior view. The arrow points to the moment that the block starts.

Table 2.
Follow-up of patients treated with radiofrequency (RF) or cryoablation in AVNRT

	RF ablation	Cryoablation
Number of patients (N)	33	30
Duration of follow up (months)	12.9 (1-22)	11.7 (1-22)
Long-term success after		
failed 1st procedure (N)	1	1
Acute success (N;%)	31 (94%)	29 (97%)
Recurrence of AVNRT (N)	3	3

electrode was 12.7 mm for RF and 4.5 mm for cryothermy ($p<0.05$). The distance with the coronary sinus os in horizontal axis also showed a similar difference ($p<0.05$). During a mean follow-up of 12.9 ± 6.3 months in the RF and 11.7± 7.0 in the cryothermy group, long-term clinical success was seen in 2 patients (one in each group) after a failed procedure (Table 3). In the same period 3 patients in each group experienced recurrent AVNRT. One patient of the RF group had recurrent palpitations due to atrial fibrillation.

Discussion

AVNRT is the most common regular narrow QRS complex tachycardia in humans. Nowadays, RF catheter ablation is the treatment of choice in patients with recurrent episodes of AVNRT. Although RF ablation is highly successful, the success rate is not 100% and a risk of an inadvertent RBBB or complete AV-block still exists [4-10]. Because cryothermal energy has the ability to create temporary lesions (ice mapping), prospective ablation sites can be investigated, before a definitive, and irreversible lesion is created [11-14]. Theoretically, this should lead to less applications and abolish the risk for permanent conduction disturbances. On the other hand, it still remains to be proven that cryothermy is as effective as RF both during the procedure and in long-term follow-up. In this study, the acute success rate of both cryoablation and RF ablation was comparable. There was no difference in the median number of ice maps in the cryothermy group in comparison with the number of applications in the RF group. However, the number of real applications in the cryothermy group was significantly lower than the number of applications in the RF group. This can be explained by the characteristics of cryoenergy. Ice mapping provides a tool to investigate prospective ablation sites. In both techniques these sites are initially chosen by the same kind of intracardiac electrograms and anatomical landmarks. However, if during ice mapping, AVNRT is still inducible and/or an AH jump is stil present, ice mapping

is terminated and no ablation will be carried out. So, no irreversible lesions are created. On the contrary, with RF, ablation is immediately performed on the grounds of the same markers, almost immediately causing irreversible tissue damage. This more precise delivery of therapy with cryothermy results in less tissue damage (less applications), together with the formation of homogenous fibrosis with a well demarcated border [16]. This makes cryothermy, in contrast to RF, potentially less proarrhythmic. Earlier studies with RF in AVNRT suggested at least a relationship with the late occurrence of atrial flutter [15,17-18]. No persisting conduction disturbances were observed in either group, and no thromboembolic complications occurred. During long-term follow up a comparable number of patients in both groups had recurrent AVNRT.

Observations with cryothermy

At this time the cryocatheter is not as manoeuvrable as a conventional RF catheter, and this could limit the proper positioning of the cryoablation catheter. A question that still remains is whether cooling to minus 30 degrees always implies that the observed effect is maximal. In other words, is it possible that this is not cold enough to cause an effect, while theoretically it could be the right spot? Indirect evidence is the observation that while complete AV-block was observed in one case a few seconds after cryoablation was started, this conduction delay was not present during ice mapping. Full recovery of AV conduction occurred within a few seconds of termination of cryoablation. This is in-line with an observation that most conduction damage recovers very quickly after freezing [20]. Furthermore, during an earlier study with cryoablation, we observed that, especially in left posteroseptally located accessory pathways, ice mapping did not always interrupt or modify pre-excitation, while cryoablation at the same spot could still be successful [14]. An explanation for this observation could be a deeper or even epicardially located accessory pathway. On the other hand, as tissue temperature rises away from the centre, tissue effects that occur late during a cryo-application are expected to be reversible. This could mean that more precise mapping is necessary, or that delivery of more energy, e.g. with larger tips, is necessary. At this moment no definitive conclusion can be made, and more experimental studies are needed to provide an answer to these observations. The fact that we did find a slight radiological difference underscores the importance of cryomapping.

Fluoroscopy

Finally, because of cryoadherence of the cryocatheter, an important asset could be a diminished fluoroscopy time. In this study there was only a tendency in favour of cryothermy. The relatively long fluoroscopy time can be explained by the fact that ablation was carried out in the "old fashioned" way by continuous fluoroscopy, and not directed by a navigation system, such as LocaLisa [21]. Furthermore, catheter handling during ablation was mostly done by less experienced physicians, with the senior electrophysiologist operating

the EP lab. Indeed, a learning curve was seen, as fluoroscopy time was decreasing during the course of the study.

Conclusion

This study showed that, in AVNRT, cryothermy is as effective and safe as RF – both acutely and chronically. Procedures are comparable in length, and results remain similar during long-term follow-up. No persisting conduction disturbances or thromboembolic complications occurred. The lower number of applications also makes it attractive for other sites in the heart, as less collateral damage will occur. It is the only method potentially targeting the slow pathway on an electrophysiological basis, offering a way to avoid the fast pathway. The fact that no accelerated junctional rhythm is seen with cryothermy is another argument to believe that this energy form is safer [22]. There is a potential for cryothermy to replace RF, or to be used as an alternative for ablation of (para)septal circus movement tachycardia and also for pulmonary vein isolation, to create lesions that are deeper and transmural, without the danger of creating pulmonary vein stenosis [23]. With the reversibility, it is an excellent teaching tool.

Acknowledgements

We thank G.A. van Es, Cardialysis, Rotterdam, for the randomization and support. Cryocath provided an educational grant for this study.

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12

One-year follow-up in a prospective, randomized study comparing radiofrequency and cryoablation of arrhythmias in Koch's triangle

Clinical symptoms and event recording

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Abstract

Background To rely solely on clinical symptoms of recurrent palpitations to evaluate the success of interventional procedures can be misleading. This study was designed to assess the efficacy of event recording in evaluating long-term success in patients treated for atrioventricular nodal reentrant tachycardia (AVNRT) or right posteroseptally located accessory pathways (RPS) either by radiofrequency (RF) or cryoablation (CA).

Methods Sixty-three patients with AVNRT and 8 with a RPS were randomized. Patients were encouraged to activate an event recorder in case of recurrent palpitations for the first three months. One year after the procedure patients were asked specific arrhythmia related questions.

Results Thirty-six patients underwent RF and 35 CA. Acute success was finally achieved in 34 (94%) patients in the RF and 33 (94%) in the CA group. Assessment of long-term success demonstrated a similar proportion of palpitations in the RF and CA groups: 11 (31%) versus 17 (49%). Only twelve patients activated the event recorder, 4 patients in RF, including one patient with chest pain, and 8 in the CA group. Analysis of recordings revealed recurrent AVNRT or CMT in 4 patients (1 RF and 3 CA), atrial fibrillation in 1 RF patient, and sinus tachycardia in 6 (1 RF and 5 with CA). Additionally, a complete 12 lead ECG of a recurrent arrhythmia was made in 3 RF and 2 CA patients (in hospital, or after the event recording). A total of 7 patients underwent a second procedure (4 RF, 3 CA). Without the event recorder 7 patients would have been misclassified for recurrent arrhythmia.

Conclusion Event recording enhances the sensitivity of detecting arrhythmia recurrences in evaluating therapy efficacy, and should be considered in every interventional follow-up study. Analysis of recordings showed that cryoablation is as effective as RF in the treatment of AVNRT and RPS at long-term follow-up.

Keywords: atrioventricular repentant tachycardia; accessory pathway; radiofrequency catheter ablation; cryoablation; event recording; long-term follow-up

Introduction

Radiofrequency (RF) catheter ablation has become the first line therapy for patients with recurrent atrioventricular nodal reentrant (AVNRT) and circus movement tachycardia (CMT) [1-4]. Although it is highly successful, lesions created by RF energy are inhomogeneous, irreversible, thrombogenic and potentially proarrhythmic [4-7]. Cryoablation (CA) creates homogeneous and smaller lesions and is less thrombogenic [8]. Together with the specificic tools of ice mapping and cryoadherence, this therapy has proven to be especially useful in AVNRT and (para) septally located accessory pathways to reduce the risk of inadvertent AV block [9-14]. After interventional procedures, the follow-up is important to assess long-term success of the procedure. A follow-up based solely on clinical symptoms has a potential risk of misleading results [15-19]. The purpose of this study was to evaluate long-term success of patients treated either with RF of CA by using an event recorder and a specific questionnaire conducted at 1 year.

Methods

As described earlier, all consecutive patients with a recurrent tachyarrhythmia, suggestive of AVNRT or a CMT with the use of a right posteroseptally located accessory pathway, were randomized by an independent institution (Cardialysis) to either RF or CA before baseline electrophysiological (EP) study [10]. The diagnosis of both dual AV nodal pathways, AVNRT and CMT was made on the basis of standard diagnostic criteria. The earliest retrograde atrial activation during both tachycardia and ventricular premature beats was registered. Single premature atrial and ventricular stimuli were applied during tachycardia at the time the His bundle was refractory to assess if tachycardia could be reset. This confirmed the presence or absence of an accessory pathway. In patients with manifest preexcitation the site that recorded the earliest ventricular activation was identified. If sustained tachycardia could not be induced, isoproterenol was used. In the case of an accessory pathway, the final classification was made according to the successful ablation site.

Ablation

For AVNRT, the target in both ablation techniques was slow pathway ablation guided by a combination of intracardiac electrogram criteria and anatomical landmarks. The endpoint was non-inducibility of AVNRT with or without isopreterenol after a 30 minutes waiting period. For CMT, mapping was performed beginning at the anteroseptal region at the His deflection down to the coronary os and further to the right posterior region. In patients with manifest ventricular preexcitation during sinus rhythm, the site of earliest ventricular activation was identified, characterized by a short local AV interval, with local ventricular activation preceding the onset of the delta wave on the surface ECG. The earliest retrograde atrial activation was identified during orthodromic circus movement

Table 1.
Results of radiofrequency (RF) and cryoablation in AVNRT/RPS

	RF ablation AVNRT	Cryoablation AVNRT	RF ablation RPS	Cryoablation RPS
Number of patients	33	30	3	5
Male/female (N/N)	10/23	14/16	3/0	4/1
Procedural success (N;%)	30 (91%)	28 (93%)	3 (100%)	4 (80 %)
Ice maps (median,N;SD)	-	5 (2-42)	-	6 (2-23)
Applications (median,N;SD)	7 (1-31)	2 (1-13)	1.5 (1-2)	3 (1-8)
complications	0	0	1*	1°

AVNRT = atrioventricular nodal reentrant tachycardia; N = number of patients; RPS = right posteroseptal pathway; SD = standard deviation
* = pneumothorax after subclavian puncture
° = tamponade caused by RV catheter (Medtronic, 6416, temporary transvenous, active fixation)

tachycardia and ventricular pacing. A successful ablation was defined as a sudden loss of ventricular preexcitaton, a sudden loss of VA conduction or change from an eccentric to a concentric VA conduction, or sudden termination of the tachycardia during an application. Patients were also observed for 30 minutes, and a repeated EP study was performed to confirm loss of accessory pathway conduction. Specific differences in both ablation techniques for either AVNRT or CMT were described before.

Follow-up

After hospital discharge, all patients received an event recorder for at least 3 months and were encouraged to activate it in case of recurrent palpitations. They all visited the outpatient clinic approximately 3 months after the procedure, and thereafter were send to their referring cardiologist. One year after the procedure all patients were approached by telephone or written letter and asked to answer specific questions related to their symptoms, recurrences, and repeated ablation.

Statistical analysis

Continuous variables were expressed a mean ± standard deviation. Non-parametric data were compared using the Mann-Whitney U test. The level of significance was set at $p < 0.05$.

Table 2.
One-years follow-up of patients ablated for AVNRT/RPS

	RF ablation AVNRT	Cryoablation AVNRT	RF ablation RPS	Cryoablation RPS
Number of patients (N)	33	30	3	5
Long term success after failed 1st procedure (N)	1	1		
Acute success (N;%)	31 (94%)	29 (97%)	3 (100%)	4 (80%)
Recurrence of palpitations (N;%)	10 (30%)	13 (43%)	1 (33%)	4 (80%)
ER activated (N;%)	3 (9%)	6 (20%)	1 (33%)	2 (40%)
Documented arrhythmias with ER: • AVNRT or CMT(N) • Afib (N) • ST (N)	 1 1 1	 2 4		 1 1
Clinically documented recurrence (N)	3	2		
Redo procedure (N)	4	2		1

Afib = atrial fibrillation; AVNRT = atrioventricular nodal reentrant tachycardia;
CMT = circus movement tachycardia; ER = event recorder; N = number of patients;
RPS = right posteroseptal pathway; ST = sinustachycardia

Results

In 63 patients the diagnosis of AVNRT was made. Of these patients, 33 were randomized to RF and 30 to CA. In 8 other patients, a right posteroseptally located accessory pathways was diagnosed, in which 3 were randomized to RF and 5 to CA, respectively (Table 1). Procedural success in AVNRT was achieved in 30 (91%) patients in the RF and 28 (93%) in the CA group.

Radiofrequency ablation for CMT was successful for all 3 patients in the RF group, and in 4 out of 5 patients in the CA group. For patients with AVNRT the number of ice maps was 5, and 6 with CMT, respectively. The median number of applications was 5 for RF, versus 2 ($p<0.002$) for CA for the total group. The median number of applications in the treatment of AVNRT was also significantly lower ($p<0.05$) in the CA group than in the RF group, namely 2 versus 7. In the CMT group 2 complications occurred, one pneumothorax after a subclavian puncture, and one tamponade caused by the RV catheter (a Medtronic, 6416, temporary transvenous, active fixation lead), which was used as reference catheter

for the LocaLisa system. During a follow-up of 1 year, long-term success was seen in 2 patients treated for AVNRT (one in each group) after a failed procedure (Table 2). Therefore, the acute success rate in patients with AVNRT was 31 (94%) in the RF, and 29 (97%) in the CA group.

Recurrent palpitations occurred in 10 patients treated for AVNRT with RF, and in 13 patients after CA, as assessed by the questionnaire. Nine of these patients activated an event recorder, 3 treated with RF, and 6 with CA, respectively. The documented arrhythmia in the RF group was recurrent AVNRT in 1 patient, atrial fibrillation in 1, and sinus tachycardia in 1. In the CA group recurrent AVNRT was seen in 2 patients. In 4 other patients sinus tachycardia was registered. In patients who underwent ablation for CMT, the questionnaire revealed that 5 patients had recurrent palpitations, namely 1 in the RF group and 4 in the CA group. Of these patients, 3 activated an event recorder, once with a recurrence of CMT, 1 with sinus tachycardia, and 1 with chest pain. In 5 other patients recurrent tachycardia was documented in hospital, or after the period with event recording. In conclusion, 32 (45%) patients experienced recurrent palpitations. In only 9 of these 32 patients recurrent AVNRT/CMT was confirmed. Without the event recorder 7 patients would potentially have been misclassified for a recurrence of the treated arrhythmia. A total number of 7 patients underwent repeated ablation (6 with AVNRT, 1 with CMT); this was in 4 cases after RF, and 3 treated with CA. Two are scheduled for a new procedure.

Discussion

RF ablation for AVNRT and (para)septally located accessory pathways is accompanied by an increased risk of inadvertent RBBB or complete AV-block [1-4, 20-22]. Because cryothermy has the ability to create temporary lesions (ice mapping), prospective ablation sides can be investigated, before a definitive, and irreversible lesions is created [9-14]. In this study it was confirmed that cryoablation is as effective as RF ablation in the treatment of these arrhythmias, as is in agreement with other studies [9-14]. It was also shown that in patients treated for AVNRT, this can lead to less applications and abolish the risk for AV conduction disturbances [9-12]. In patients treated for right posteroseptally located accessory pathways this could not be confirmed in our study, merely by the fact that the group consisted of only 8 patients. As is valid for all interventional studies, an adequate follow-up is important to assess long-term success of the procedure. To rely solely on clinical symptoms of recurrent palpitations has a potential risk of misleading results [15-19]. For example, in studies of catheter ablation for atrial fibrillation (AF), success is defined as absence of symptoms or less symptoms after treatment [17-19]. However, it is well-known that approximately up to 50% of the episodes of AF are not experienced as such by the patients, and therefore success rates can be overestimated. On the other hand, as is shown in this study, not all recurrent palpitations are by definition recurrences of the treated arrhythmia. Seventeen patients (49%) treated with cryoablation complained about recurrent palpitations in comparison with 11 patients (31%) treated with RF, as was assessed by a questionnaire after one year. However, only 8 patients in the cryo group and 4 in the

RF group activated the event recorder, because of recognizable palpitations. Probably, in patients who did not acitivate the event recorder, the palpitations were not identical in comparison with preablation, or were too short lasting. By the event recorder, a recurrence of the treated arrhythmia could be registered in 7 patients. In one patient in the RF group atrial fibrillation was documented. Sinus tachycardia was seen in 1 patient in the RF, and 5 patients in the cryo group. The presence of sinus tachycardia, especially after cryoablation of the slow pathway ablation, as was seen in 4 patients, is remarkable. It has been associated with inadvertent damage to the fast pathway [23]. The reason for this observation can be a more anterior position of the ablation catheter, due to the smaller lesions created by cryothermy, or an abnormally located antegrade fast pathway, located in the posteroseptal region, which exists in about 3% of patients presenting with AVNRT [24]. Without the event recorder, 7 patients (2 in the RF group, and 5 in the CA group) would have been misclassified for a recurrence of the treated arrhythmia.

Conclusions

Our data demonstrate that event recording and not specific arrhythmia related questionnaire enhances the sensitivity of detecting arrhythmia recurrences. This has implications for the interpretation and design of clinical trials in the evaluation of treatment efficacy. Based on event recording, CA is as effective as RF for arrhythmias in Koch's triangle during long-term follow-up.

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Summary, conclusion, and future perspectives

Koch's triangle is an intruiging area. On the atrial aspect, the triangular area itself is delineated by the tendon of Todaro, which inserts in the atrial aspect of the central fibrous body to mark the apex of Koch´s triangle. The ventricular border is formed by the septal leaflet of the tricuspid valve. The base of the triangle is marked by the inferior right atrium around the orifice of the coronary sinus (cavo-tricuspid isthmus), along with the musculature extending to the hinge of the septal leaflet of the tricuspid valve, i.e. septal isthmus. The anatomy and electrophysiological chararteristics of this region provide a substrate for different arrhythmias to develop. **Chapter 1** is devoted to address to all these different aspects. In the first part an overview is given of the known embryology of the atrioventricular conduction axis and its direct environment, as well as the anatomy and electrophysiological characteristics of this region. Until now a lot of questions on its anatomy and physiology still exist, despite intensive research. As already mentioned, different arrhythmias can develop, which can be cured with transvenous radiofrequency (RF) catheter ablation, although some pitfalls still remain present.

Fluoroscopy does not allow delineation of important anatomic landmarks during electrophysiological studies. Imaging techniques such as intra-cardiac echocardiography can improve the success rate of RF ablations by guiding catheter positioning. In **Chapter 2** it was shown that intra-cardiac echocardiography, using a non-steerable 2D probe, was able to visualize various atrial structures. RF lesions could not be identified 20 minutes after catheter ablation of the cavo-tricuspid isthmus.

In the past, surgical modification of the atrioventricular node was the only method to eliminate atrioventricular nodal reentrant tachycardia (AVNRT). Both cryosurgery for modification of the perinodal tissues along the perimeter of the triangle of Koch and 'skeletonization', a dissection technique to interrupt all atrial inputs of the atrioventricular node except the 'deep' left atrial input, resulted in successful cure of the tachycardia while preserving atrioventricular conduction. Nowadays, transvenous catheter ablation is the first-line therapy for patients with recurrent AVNRT. **Chapter 3** described that both surgery, and RF catheter ablation in the early days, were effective and safe in the elimination of recurrent AVNRT. During mid-term follow-up, sporadic recurrences of AVNRT were registered, even 3 years after the procedure. These observations led to the conclusion that patients, who underwent successful surgery or RF ablation for AVNRT, were definitively cured.

The region between the inferior caval vein orifice and tricuspid valve orifice, known as cavo-tricuspid isthmus, forms the base of Koch's triangle, and is known for its slow conduction properties. Both class 1C and class III anti-arrhythmic drugs (AAD) are able to convert atrial fibrillation (AF) into a isthmus dependent atrial flutter (AFL). **Chapter 4** presents a study in which is shown that a linear isthmus RF ablation, in combination with the continuation of AAD is associated with a high success rate of achieving and maintaining sinus rhythm in patients with AF who developed an isthmus dependent AFL under AAD therapy .

Although, RF ablation is highly effective in the treatment of both supraventricular and ventricular tachyarrhythmias with a low complication and recurrence rate, RF is not the optimal energy source. Lesions created by RF energy are irreversible, cause some degree of

tissue disruption or "carbonisation" of the targeted tissue that increases the risk for perforation and thromboembolism. The lesions are inhomogeneous, and therefore potentially proarrhythmic. Indeed, new tachyarrhythmias, after RF ablation for AVNRT, were already seen during mid-term follow-up in **Chapter 3**. **Chapter 5** focussed on the magnitude and importance of this adverse effect on the long-term. This study demonstrated an obvious risk of developing new supraventricular arrhythmias, such as symptomatic atrial premature beats, type 1 AFL, atrial tachycardia and AF, but also late AV block after RF ablation. These data and known characteristics of RF energy support the research for and the use of new energy sources and other ablative techniques.

Furthermore, during RF ablation of AVNRT and (para)septally located accessory pathways there is an increased risk of right bundle branch block or inadvertent complete AV block, as these pathways run in close proximity to the compact AV node. Applications should be delivered during sinus rhythm and not during tachycardia, because of the risk of both instable endocardial tissue contact during and catheter dislodgement at termination of the tachycardia. As cryothermy has the ability to reversibly demonstrate loss or change of function of tissue at less negative temperature (ice mapping), potential ablation sites can be investigated, before a definitive and irreversible lesion is created. As progressive ice formation at the catheter tip causes adherence to the adjacent tissue, ablation can also safely be performed at otherwise unstable catheter positions, or even during tachycardia. Therefore, cryothermy could be especially useful in ablation of tachyarrhythmias in Koch's triangle, to reduce the risk of AV conduction disturbances.

Chapter 6 demonstrates that cryoablation could be performed effectively and safe in a patient with a right anteroseptally located accessory pathway. As a result of this, a retrospective study was performed, in which RF was compared with cryoablation in the treatment of (para)septally located accessory pathways **(Chapter 7)**. The rationale for attempting cryoablation in these sites was, besides enhancing safety, also improving efficacy, as it is known that RF ablation of septally located accessory pathways is associated with a higher percentage of failures, and recurrences. The acute success rates for both treatment modalities were comparable, as were procedure and fluoroscopy times. The number of applications tended to be lower with cryoablation. After performing a redo with the same energy, the final success rate of RF tended to be higher. The reasons of this difference remain unclear, because of the small number of patients under study. In **Chapter 8** some characteristics of cryoablation are discussed, referring to an observation made by other investigators, that a successful cryoablation could be accompanied by a slowly disappearance of preexcitation, in contrast to RF ablation [1]. However, in our experience, as tissue temperature rises away from the center of the ablation site, tissue effects that occur late during a cryo-application are expected to be reversible, and indicate a suboptimal (remote) ablation site, and/or poor wall contact. In this context, successful ice mapping attempts were characterized by a short temperature time constant and a short response time to mapping with a sudden loss of pathway conduction, as is described in detail in **Chapter 9**.

In **Chapter 10** it was shown that a successful cryoablation of the fast pathway could be performed without the occurrence of second degree or complete heart block, in a difficult

case of AVNRT. Subsequently, in **Chapter 11** a prospective, randomized single centre study is presented to compare RF and cryoablation in AVNRT. Both success and recurrence rates were comparable, and no persisting conduction disturbances or thromboembolic complications were observed in both methods. Again a lower number of applications was seen with cryoablation. It was illustrated that cryoablation provided a method to targeting the slow pathway solely on an electrophysiological basis, offering a way to avoid the fast pathway, even if this latter is located in an anatomically different site. To investigate if cryoablation was also successful during long-term follow-up, the study described in **Chapter 12** was carried out. As it is known that it can be misleading to rely solely on clinical symptoms of recurrent palpitations, the efficacy of event recording in evaluating long-term success in patients treated for AVNRT and right posteroseptally located accessory pathways was also assessed. It was demonstrated that long-term follow-up in these treated arrhythmias was comparable between RF and cryoablation, and that event recording enhanced the sensitivity of detecting arrhythmia recurrences in evaluating therapy efficacy. Therefore, it should be considered in every interventional study.

Conclusions

Transvenous RF catheter ablation has become first line therapy for patients with arrhythmias in Koch's triangle. Although it is highly successful with a low recurrence and complication rate, several pitfalls remain present. To overcome these issues, new techniques are needed like cryothermy with or without intracardiac visualization of anatomical landmarks. Despite the fact that cryothermy possesses the properties of ice mapping and cryoadherence, the technique still has to develop and improve.

Future perspectives

Today's limitations in cryoablation and suggested solutions

Several remarks on cryothermy have to be made. In AVNRT, several studies have shown that the acute procedural success rate of cryoablation was comparable with RF [2-5], although in others the success rate was lower than one would expect from RF ablation [6,7]. For atrioventricular reentry tachycardia (AVRT) and pulmonary vein isolation the success rates tend to be lower than for RF, although the endpoints in AF ablation studies are not that clear and differ from one study to another [7-11]. However, comparable success rates are achieved in atrial flutter ablation [11,12]. The same conflicting results are obtained for the rates of arrhythmia recurrences and procedure times [2-7]. As this is a new technique and energy source, a learning curve exists and this could have been translated into initially lower procedural success rates, and longer procedure times. Probably, the latter is mainly due to the longer duration of energy application in cryoablation. Larger prospective, randomized studies are necessary to prove the same efficacy and safety of cryoablation, in comparison with RF.

Lesions created by cryothermy are different in size and certainly in composition from lesions created by RF catheters. Cryoadherence during ablation results in fixation of the catheter, and not passively sliding along a larger area, as under RF [5]. This can mean that a more precise mapping, a larger catheter tip to create lesions of greater area, or colder temperatures to achieve deeper lesions, are necessary to obtain a similar effect. The current cryocatheters are composed of an outer shaft maintained under constant vacuum and an inner injection tube through which liquid nitric oxide is injected. This is the cause of more stiffness than that of a conventional RF catheter, limiting proper catheter positioning. New developments in catheter designs can maybe overcome these problems.

An crucial question remains if cooling to minus 30 degrees always means that the predicted effect is maximal: this has important consequences for safety and/or efficacy [14]. It is possible that during ice mapping, intramural or more epicardially located accessory pathways are not reached at all, while theoretically, it can be the right spot, as the cooling is not deep enough to have any effect. This also depends on differences in regional microcirculation, as is valid for RF [15]. This is a clear limitation of the concept of ice mapping. Also the observation that complete AV block can occur after cryoablation is started, while this conduction delay is not present during ice mapping [3,6], is an evidence that ice mapping can be an unreliable diagnostic method. Fortunately, until today, no permanent AV block has been reported after interrupting with either ice mapping or cryoablation [2-5,7-9]. On the other hand, it is known from experimental animal studies that cooling to temperatures less than –30°C can create irreversible lesions [16]. More experimental data can provide important information for the arrhythmia expert about the ideal ice mapping temperature and duration.

Finally, as is mentioned earlier, tissue temperature rises away from the center, and therefore, tissue effects that occur late during a cryothermy application are assumed to be reversible. Probably, this can be considered as an 'ice mapping' effect, and indicates a suboptimal (remote) position.

In conclusion, there is the potential for cryothermy to replace RF for ablation of specific arrhythmic substrates, although several issues still have to overcome.

Besides the use of new energy sources, additional imaging techniques have to be developed to improve efficacy and safety of percutaneous ablation procedures and to reduce radiation exposure for both patients and investigators, especially in more compex arrhythmias and anatomy. For many years both mono- or biplane intermittent fluoroscopy has been used to visualize these cardiac target structures. However, by nature, fluoroscopy is only two-dimensional, and underrepresents the complex cardiac anatomy, which has a potential important role in arrhythmia genesis. The implementation of several non-invasive 3D imaging modalities, such as 3D spiral computer tomography (CT), 3D magnetic resonance imaging (MRI) and intracardiac echocardiography (ICE) can provide more detailed knowledge of the individual 3D cardiac anatomy. Integration of pre-procedural 3D imaging techniques is nowadays already possible for all 3D electrophysiologic mapping systems. However, real-time 3D imaging still has to develop, and will further improve treatment. Also, the use of new navigation systems can contribute to optimizing catheter ablation. The magnetic

navigation system is a new platform technology allowing remote-controlled navigation of an ablation catheter. In conjunction with a motor drive unit, it has already shown to be successful in completely remote-controlled mapping and ablation of arrhythmias [17]. The catheter control system is another navigation system, consisting of a remotely placed workstation, a robotically controlled catheter manipulator, and an input device, that allows the investigator to steer the catheter in three dimensions.

What will the future bring? Maybe, a real-time 3D imaging, integrated with a 3D electrophysiologic mapping system, performing a catheter ablation with the use of a new energy source, carried out with a completely remote-controlled navigation system by an investigator sitting at his office/home behind his computer, is not that far away. On the other hand, what will become of the patient, who has to undergo all this, and who is losing personal contact with his treating physician. And, last but not least, who has to pay for all these expensive new techniques, especially in an area where insurance companies are determining what is, or is not permitted.

Samenvatting, conclusies, en toekomstperspectieven

De driehoek van Koch is een intrigerend gebied. Aan de atriale zijde wordt de driehoek begrensd door de 'tendon of Todaro', die insereert in het atriale gedeelte van het centraal fibreuze lichaam om zo de top van de driehoek van Koch aan te geven. De ventriculaire zijde wordt gevormd door het septale blad van de tricuspidalis klep. De basis van de driehoek wordt afgegrensd door het basale rechter atrium rondom de uitmonding van de sinus coronarius (cavale-tricuspidale isthmus), tesamen met de musculatuur die reikt tot aan het ophangapparaat van het septale blad van de tricuspidalis klep (septale isthmus). Door de anatomie en de electrofysiologische eigenschappen van deze regio kunnen verschillende aritmieën ontstaan. In **hoofdstuk 1** worden deze verschillende aspecten besproken. Het eerste deel geeft een overzicht van de embryologie van het atrioventriculaire (AV) geleidingssysteem en haar directe omgeving, maar ook van de anatomie en de electrofysiologische karakteristieken van dit gebied. Ondanks intensief onderzoek, bestaan hierover nog vele vragen. Zoals al eerder vermeld, kunnen verschillende aritmieën zich ontwikkelen, die kunnen worden behandeld met radiofrequente (RF) katheterablatie. Echter, bij deze behandelmethode zijn nog steeds "adders onder het gras aanwezig".

Met behulp van röntgendoorlichting is het niet mogelijk om tijdens electrofysiologische onderzoeken belangrijke, anatomische structuren af te grenzen. Nieuwe afbeeldingstechnieken, zoals intracardiale echocardiografie, kunnen het succespercentage van RF ablaties verhogen door het beter sturen van de ablatiekatheter. **Hoofdstuk 2** laat zien dat het mogelijk was om met intracardiale echocardiografie, met gebruikmaking van een niet-stuurbare twee-dimensionele scoop, verschillende atriale structuren af te beelden. Echter, 20 minuten na een RF ablatie van de cavale-tricuspidale isthmus, konden geen RF letsels worden waargenomen.

In het verleden was chirurgische modificatie van de AV knoop de enige methode om AV nodale reentry tachycadieën (AVNRT) definitief te behandelen. De chirurgische behandeling bestond uit dissectie van het omgevende weefsel van de AV-knoop, waarbij diverse methoden beschreven zijn. Tegenwoordig, is transveneuze katheterablatie de eerste keuze bij de behandeling van patiënten met herhaalde aanvallen van AVNRT. **Hoofdstuk 3** beschrijft dat zowel chirurgie als RF katheter- ablatie succesvol en veilig waren voor de behandeling van AVNRT. Gedurende een middellange follow-up werden sporadisch recidieven gezien, soms zelfs pas 3 jaar na de procedure. Dit leidde tot de conclusie dat patiënten, die een succesvolle chirurgische ingreep danwel RF katheterablatie hadden ondergaan, definitief waren genezen.

De regio tussen de vena cava inferior en de tricuspidalis klep, de cavale-tricuspidale isthmus, vormt de basis van de driehoek van Koch, en staat bekend om zijn trage geleidingseigenschappen. Zowel klasse 1C als klasse III antiarrhythmica zijn in staat om atrium fibrilleren (AF) te 'organiseren', en om te zetten in een isthmus-afhankelijke atriale flutter (AFL). In **hoofdstuk 4** wordt een studie gepresenteerd, waaruit blijkt dat een lineaire isthmusablatie, in combinatie met het continueren van antiarrhythmica, gepaard gaat met een hoog succespercentage om sinusritme te verkrijgen en te behouden bij deze patiënten.

Alhoewel RF ablatie zeer effectief is in de behandeling van supraventriculaire en ventriculaire ritmestoornissen, en geassocieerd is met een laag aantal complicaties en recidie-

ven, is het niet de optimale energiebron. De letsels, die door RF worden gecreëerd zijn onherstelbaar, ontwrichten de onderliggende weefselstructuur, met als gevolg een verhoogd risico op perforatie en thrombo-emboliën. Door het inhomogene karakter van de letsels, zijn ze potentieel aritmogeen. Inderdaad werden al nieuwe ritmestoornissen waargenomen tijdens de middellange follow-up in **hoofdstuk 3**. In **hoofdstuk 5** wordt aandacht geschonken aan de grootte en belang van dit nadelig effect op de lange termijn. De beschreven studie demonstreerde dat na RF ablatie van AVNRT, er niet alleen een risico bestaat om nieuwe ritmestoornissen te ontwikkelen, zoals symptomatische premature atriale contracties (PAC's), AFL type 1, atriale tachycardie (AT) en AF, maar ook voor het verkrijgen van een laat compleet AV-blok. Deze gegevens en karakteristieken van RF energie ondersteunen de zoektocht naar nieuwe energiebronnen en alternatieve ablatietechnieken.

Bovendien, bestaat tijdens RF ablatie van AVNRT en (para) septale extraverbindingen een risico op het ontwikkelen van een ongewenst rechter bundeltak blok, of een compleet AV-blok, doordat het substraat van deze ritmestoornissen dichtbij het normale geleidingssysteem is gelegen. Applicaties moeten tijdens sinusritme worden afgegeven om een stabiele katheterpositie te verkrijgen en te houden, omdat anders een kans bestaat dat de katheter disloceert op het moment dat de ritmestoornis termineert. Cryothermie heeft de eigenschap om tijdelijk een verandering in geleidingskarakteristieken aan te tonen door het weefsel minder diep te koelen (ice mapping). Hierdoor kunnen toekomstige ablatieplaatsen worden onderzocht, voordat een definitief en onherstelbaar letsel wordt veroorzaakt. Door de ijsvorming aan de kathetertip plakt deze aan het aangrenzende weefsel (cryoadherence), en zodoende kan een ablatie ook veilig worden uitgevoerd tijdens een onstabiele katheter positie of een ritmestoornis. Door deze eigenschappen van cryothermie, lijkt deze energiebron met name geschikt voor ablatie van ritmestoornissen in de driehoek van Koch, om zo het risico op AV geleidingsproblemen te verminderen.

Hoofdstuk 6 laat zien dat cryoablatie succesvol en veilig kon worden uitgevoerd bij een rechts anteroseptaal gelegen extraverbinding. Vervolgens werd een retrospectieve studie verricht, waarbij RF met cryoablatie werd vergeleken bij patiënten met een (para)septaal gelegen extraverbinding **(hoofdstuk 7)**. Het idee om dat juist bij deze patënten te doen, was om de veiligheid en effectiviteit van de behandeling te verhogen, omdat RF ablatie van deze extraverbindingen gepaard gaat met een lager succespercentage en een hoger aantal recidieven. Het acute succes bleek voor beide behandelingen vergelijkbaar. Dit gold ook voor de doorlichtings- en proceduretijden. Er was een trend zichtbaar voor een minder aantal benodigde applicaties met cryoenergie. Na het verrichten van een hernieuwde ablatie, neigde RF naar een uiteindelijk hoger succespercentage.

In **hoofdstuk 8** worden enkele karakteristieken van cryoablatie besproken naar aanleiding van een observatie dat een succesvolle cryoablatie gepaard kan gaan met het langzaam verdwijnen van de preexcitatie in het kader van de behandeling van het WPW-syndroom **[1]**. Uit onze ervaring blijkt, dat de weefseltemperatuur hoger wordt naarmate de afstand tot het centrum van de ablatieplaats toeneemt, en dat effecten die laat tijdens een cryoapplicatie optreden meestal reversibel zijn. Dit betekent een suboptimale ablatieplaats, en/of een slecht weefselcontact. In dit verband blijken succesvolle "ice mapping" pogingen gepaard te gaan met een korte temperatuur/tijdsconstante en een korte respons-

tijd met het plotseling verdwijnen van de delta-golf. Dit wordt in detail beschreven in **hoofdstuk 9**.

In **hoofdstuk 10** wordt aangetoond dat een succesvolle cryoablatie van het snelle geleidende pad kon worden uitgevoerd bij een atypische casus van AVNRT waarbij de suggestie werd gewekt van de aanwezigheid van meerdere snel teruggeleidende paden. Dit kon veilig worden gedaan zonder dat een tweedegraads of totaal AV blok ontstond. Als gevolg hiervan, wordt in **hoofdstuk 11** een prospectieve, gerandomiseerde studie gepresenteerd, waarin RF met cryoablatie wordt vergeleken bij patiënten met AVNRT. Voor beide behandelmethoden gold dat zowel het succes als recidief percentages vergelijkbaar waren en er geen blijvende AV geleidingsproblemen of thrombo-embolische complicaties optraden. Opnieuw werd een lager aantal applicaties gevonden bij cryoablatie. Illustratief was dat cryoablatie kon worden uitgevoerd puur op basis van de electrofysiologische eigenschappen van het langzaam geleidende pad, zelfs als deze op een afwijkende anatomische positie was gelegen. Zodoende kon een ongewenste ablatie van het snelle geleidende pad worden vermeden. Om aan te tonen dat cryoablatie ook op de lange termijn succesvol is, is de studie, zoals beschreven in **hoofdstuk 12** uitgevoerd. Het is bekend dat het misleidend kan zijn om alleen op de klachten van een patient af te gaan om te weten of er recidieven zijn. Derhalve werd de effectiviteit van een transtelefonische ECG registratie geëvalueerd om het succes op de lange termijn te beoordelen van patiënten die geableerd waren voor een AVNRT of een rechts posteroseptaal gelegen extraverbinding. Er kon worden aangetoond dat de langetermijns follow-up van RF en cryoablatie in deze patiëntengroepen vergelijkbaar was. Bovendien bleek een transtelefonische ECG registratie de sensitiviteit voor het vastleggen van recidieven te verhogen. Derhalve moet een dergelijke follow-up bij iedere interventie studie worden overwogen.

Conclusies

Transveneuze RF katheter ablatie is de eerstelijns behandeling van patiënten met ritmestoornissen in de driehoek van Koch. Alhoewel dit gepaard gaat met een hoog succespercentage en een laag aantal recidieven en complicaties, blijven sommige valkuilen tijdens deze behandeling bestaan. Om deze te overwinnen zijn nieuwe technieken, zoals cryoenergie nodig, met of zonder intracardiale visualisatie van anatomische structuren. Ondanks het feit dat cryoenergie eigenschappen bezit als "ice mapping" en "cryoadherence", zal deze techniek zich nog verder moeten ontwikkelen en verbeteren.

Toekomstperspectieven

De huidige beperkingen van cryoablatie en mogelijke oplossingen

Ten aanzien van cryoenergie kunnen een aantal kanttekeningen worden geplaatst. In de behandeling van AVNRT laten sommige studies zien dat de resultaten vergelijkbaar zijn met RF [2-5], terwijl in andere studies het succespercentage lager uitviel [6-7]. Voor atrioventriculaire reëntry tachycadieën (AVRT) en pulmonaal venen isolatie geldt dat het succes

hiervan lager lijkt te zijn dan met RF, alhoewel de eindpunten in AF studies niet duidelijk zijn en per studie verschillen [7-11]. Bij de behandeling van AFL echter zijn de succespercentages weer wel vergelijkbaar [11,12]. Ook als men kijkt naar het optreden van het aantal recidieven en de proceduretijden, blijken er tegengestelde resultaten te bestaan [2-7]. Gezien het feit dat het hier een nieuwe techniek en energiebron betreft, bestaat er een leercurve, en deze kan zich vertalen in een lager procedure gerelateerd succes, en langere proceduretijden. Waarschijnlijk wordt dit laatste echter voornamelijk veroorzaakt door de langer duur van een enkele cryoapplicatie. Grote, gerandomiseerde studies zijn noodzakelijk om te kunnen aantonen dat cryoablatie net zo effectief en veilig is als RF.

De letsels die door cryoenergie worden veroorzaakt zijn verschillend in omvang en zeker qua karakter, in vergelijking met RF. Door het plakken van de katheter aan het weefsel tijdens een cryoablatie, beweegt deze zich niet passief langs het oppervlakte, in tegenstelling tot RF energie [5]. Dit kan betekenen dat een nog nauwkeuriger in kaart brengen van de oorsprong van de ritmestoornis, een grotere tip van de katheter om grotere letsels te kunnen maken, of het nog dieper koelen van het weefsel om diepere letsels te veroorzaken, noodzakelijk zijn om eenzelfde effect te bereiken als met RF. De huidige cryokatheters bestaan uit een buitenste holle schacht, die onder continue vacuüm staat, en een binnenste injectie schacht waardoor vloeibare stikstof word geïnjecteerd. Hierdoor zijn deze katheters stijver dan een RF katheter, wat het positioneren van de katheter kan bemoeilijken. Nieuwe ontwikkelingen in kathetervormgeving kunnen deze problemen wellicht verhelpen.

Een cruciale vraag blijft of het koelen tot minus 30 graden Celsius altijd betekent dat het voorspelde effect maximaal is: dit heeft namelijk belangrijke consequenties voor de veiligheid en/of effectiviteit van "ice mapping" [14]. Het is mogelijk dat tijdens "ice mapping", intramuraal of epicardiaal gelegen extraverbindingen niet worden bereikt, terwijl theoretisch gezien, het wel de juiste plek is. De koeling blijkt dan echter niet diep genoeg om enig effect te sorteren. Ook verschillen in de microcirculatie kunnen hiertoe bijdragen, zoals dat ook geldt voor RF [15]. Dit is een duidelijke tekortkoming van het concept van "ice mapping". Een ander bewijs hiervoor is dat een totaal AV blok tijdens cryoablatie kan ontstaan, terwijl dit niet wordt waargenomen tijdens "ice mapping" [3,6]. Gelukkig is, tot op heden, geen melding gemaakt van een blijvend totaal AV blok, indien de "ice mapping" of cryoablatie direct wordt gestaakt [2-5,7-9]. Aan de andere kant, hebben dierenexperimenten aangetoond dat het koelen tot temperaturen lager dan 30 graden Celsius, onherstelbare letsels kunnen veroorzaken [16]. Meer experimentele studies kunnen bijdragen tot een dieper inzicht in de optimale "ice mapping" temperatuur en duur hiervan.

Tot slot, is al eerder vermeld dat de weefseltemperatuur hoger wordt naarmate de afstand tot het centrum van de ablatieplaats toeneemt, met als gevolg dat effecten die laat optreden tijdens een applicaties vaak reversibel zijn. Dit kan als een "ice mapping"-effect van de omgeving worden beschouwd, en geeft een suboptimale ablatieplaats weer.

Concluderend, heeft cryoenergie de potentie in zich om de plaats van RF over te nemen bij de behandeling van specifieke aritmogene substraten. Hiervoor zullen nog een aantal problemen moeten worden overwonnen.

Naast het gebruik van nieuwe energiebronnen zullen ook additionele afbeeldingstechnieken moeten worden ontwikkeld om de veiligheid en effectiviteit van de ablaties te verbeteren en de doorlichtingstijd voor zowel de patiënt als de behandelaar te verminderen, met name bij complexe ritmestoornissen en anatomie. Al vele jaren is röntgendoorlichting gebruikt om specifieke cardiale structuren in beeld te brengen. Röntgendoorlichting geeft slechts een tweedimensioneel beeld en schiet derhalve tekort bij de complexe cardiale anatomie, die een belangrijke rol kan spelen bij het ontstaan van ritmestoornissen. Het implementeren van niet-invasieve 3D afbeeldingstechnieken, zoals 3D spiraal computer tomografie (CT), 3D MRI, en intracardiale echocardiografie (ICE) kunnen bijdragen tot een betere kennis van de 3D cardiale anatomie van het individu. De integratie van pre-procedurele 3D afbeeldingstechnieken is tegenwoordig al mogelijk voor 3D electrofysiologische mapping systemen. Echter, een continue 3D afbeelding is nog in de ontwikkelingsfase, en zal zeker bijdragen tot een betere behandeling. Het gebruik van nieuwe navigatiesystemen kan de behandeling ook verder verbeteren. Het magnetisch navigatiesysteem is een nieuwe techniek, waarbij met een afstandsbediening de ablatiekatheter kan worden bewogen. Dit heeft al geleid tot volledig op afstand uitgevoerde ablaties van ritmestoornissen. Het controle systeem van de katheter is een ander navigatiesysteem, dat bestaat uit een op afstand geplaatst werkstation, een robotisch katheter manipulator, en een invoerinstrument, waardoor de behandelaar in staat is om de katheter in drie dimensies te bewegen.

Wat zal de toekomst nog meer brengen? Misschien is een continue 3D afbeelding, geïntegreerd met een 3D electrofysiologisch mapping systeem om de ritmestoornis nauwkeurig in kaart te brengen, met het verrichten van een katheterablatie met behulp van een nieuwe energiebron, uitgevoerd met een volledig op afstand bediend navigatiesysteem door een behandelaar al zittend achter zijn computer op zijn kamer of thuis, niet meer zo ver verwijderd. Aan de ander kant moet men zich afvragen hoe de patiënt zich moet voelen, die dit allemaal moet ondergaan, en het contact met zijn behandelaar lijkt kwijt te raken. En als laatste, maar zeker niet als minste, blijft de vraag wie dit allemaal moet gaan betalen, zeker in een tijd waarin de Zorgverzekeraars bepalen wat wel en niet is toegestaan.

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Dankwoord

Bij het tot stand brengen van een proefschrift hoort een dankwoord te worden uitgesproken. Iedereen die mij een beetje kent, weet ook dat dit voor mij geen gemakkelijke opgave is. Dat wil niet zeggen dat ik niemand dank verschuldigd ben, integendeel, maar om dit vervolgens op papier vast te leggen is een moeizame onderneming. Eén of meerdere personen zullen worden vergeten, die zich vervolgens al dan niet gepasseerd voelen. Bovendien weten zij waar ik veel aan te danken heb dit toch al. Tot slot zit niemand te wachten op een tenenkrommende loftuiging mijnerzijds. Het is zoals Theo Maassen (cabaretier) in een afscheidstoespraak voor een goede collega verwoordde: "Chapeau, chapeau, chapeau, wa bende gij toch sympathiek", om vervolgens in dezelfde speech te eindigen met: "eigenlijk zoude ze oe hier ter plekke kapot moete schiete". Desalniettemin zal ik hieronder toch een welgemeende poging doen, en ik verexcuseer me bij voorbaat al voor de personen die ik niet vermeld.

Prof. dr. N.M. van Hemel, beste Norbert, mijn promotor. Jij bent degene die mij voor het eerst wegwijs heeft gemaakt in de wereld van de klinische electrofysiologie. Met de grote hoeveelheid uitgedraaid papier welke ik in het begin na de procedures heb moeten uitpluizen, zou menig stulpje kunnen worden behangen. Jouw kritische blik, volhardendheid, en enthousiasme, heb ik altijd zeer gewaardeerd. Als ik maar een gedeelte hiervan ooit zelf zal kunnen bezitten, dan ben ik al een tevreden cardioloog/electrofysioloog. Gelukkig heb je de taak van promoter, na wat beslommeringen, alsnog op je willen nemen en je weet dat dit voor mij veel betekent.

Prof. dr. L.J.L.M. Jordaens, beste Luc, mijn promotor. Samen met Dominic Theuns zijn wij in het Rotterdamse in 1998 begonnen met de klinische electrofysiologie. Velen hebben gedacht dat dit een onhaalbare kaart was, en ik moet zeggen dat ik mijzelf ook weleens heb afgevraagd of wij ooit een eigen volwaardige afdeling zouden worden met een eigen EFO-lab. Door met name jouw onvoorwaardelijke gedrevenheid, is dit toch voor elkaar gekomen. Dat sommigen, door de soms onnavolgbare ideëen, de weg volledig dreigden kwijt te raken, nam jij op de koop toe. In ieder geval staat de klinische electrofysiologie in het Erasmus MC als een "Belgisch" huis. Verder ben jij voor mij meer dan alleen maar een collega. Ik mis nog weleens de gezellige afzakkertjes en de prachtige anecdotes, waarin jijzelf menigmaal de hoofdrol speelde.

Dr. P.F.H.M. van Dessel, beste Pascal. Jij hebt mede bijgedragen tot mijn toetreden in het St. Antonius Ziekenhuis te Nieuwegein. Ook bij het tot stand komen van enkele artikelen, maar ook dit proefschrift, is jouw steun van belang geweest. Niet alleen op computergebied geldt dat voor jou geen berg te hoog is. Het is voor mij een plezierige gedachte, dat onze wegen zich in het AMC wederom gaan kruisen.

Dr. E.R. Jessurun, beste Emile. De klinische vaardigheden van de katheterablaties heb ik van jou geleerd. Het is geen publiek geheim dat de omgang met je soms wat moeizaam kan zijn en een gesprek gepaard kan gaan met een langdurige "asystolie". Je (in)stelling: "better is the enemy of good enough", is juist, echter dit weet je helaas pas achteraf.

Dr. A.H.L.C. van Kaam, beste Anton, Tony macaroni, mijn beste vriend en paranimf, iemand waarop ik altijd kan terugvallen. Je verwoordt het in je eigen proefschrift al zelf, maar alleen trek je de verkeerde conclusies. Het gaat er niet om of ik, als cardioloog, zo uitgekookt (en rijk) ben, maar meer of jij, als neonatoloog, zo naïef (en arm) bent. Het blijft ongelofelijk, dat een geboren regelneef als jij, voor je eigen promotie alles zelf hebt gedaan tegen een "hongerloontje". Dat neemt niet weg dat ik, mede door jouw drang om altijd het naadje van de kous te willen weten, niet alleen wetenschappelijk, maar ook persoonlijk meer open sta voor de meningen en gevoelens van anderen. Het heeft deze oppervlakkige man in ieder geval meer diepgang gegeven.

Dr. D.A.M.J. Theuns, beste Dominic, "shockrocker" en paranimf. In het Erasmus MC dachten ze in het begin dat wij broers waren, omdat voor hen een zachte G, tesamen met een lang, slank uiterlijk en donker haar, één pot nat is. Echter, voor echte Brabanders zoals ik geldt, dat "Limlanders" nog erger zijn dan Hollanders. Maar alle gekheid op een stokje, ik zal onze ablatiesessies en zeker de DFT testen, onder het genot van stevige rockmuziek of heavy metal, nooit vergeten. Je geest gaat er lekker van open en inmiddels ben ik ook een liefhebber geworden.

Alle specialisten, verpleegkundigen, technici en secretaresses van de afdeling klinische electrofysiologie van het Erasmus MC. We hebben een gezellige tijd gehad samen en ik dank jullie met name voor de "ijzige" kalmte, die jullie hebben opgebracht tijdens de cryosessies. Het blijft lovenswaardig dat jullie aardig tegen me zijn gebleven, ook nadat ik het pandje had verlaten en op vrijdag voor een "totaal blok" van de wekelijkse beslommeringen zorgde.

De cardiologen uit het MCA, mijn "maten", zoals dat zo mooi heet. Ik zeg altijd maar: "vrienden heb ik niet, alleen maar vage kennissen". Dat neemt niet weg, dat jullie zorgen voor een goede, ambitieuze groep, alwaar ik nu al meer dan 3 jaar met veel plezier samenwerk. Ik denk dat wij het juiste "ritme" te pakken hebben.

De cardiologen/electrofysiologen, verpleegkundigen, technici en secretaresses van de afdeling klinische electrofysiologie van het AMC. In onzer beide beleving is een goede samenwerking tussen een academisch ziekenhuis en een perifere kliniek onontbeerlijk. Als het aan mij ligt houden we deze "parasystolie" nog lang gaande.

Mijn ouders, "ons" pa en ma. Wij zijn het nooit zo gewend geweest om onze diepere gevoelens bloot te leggen, maar bij deze wil ik toch een keer een uizondering maken. Ik ben jullie oprecht, vanuit het diepst van mijn hart, dankbaar voor het warme, liefdevolle nest waarin ik ben opgegroeid. Wat jullie met al de beperkte mogelijkheden en financiën niet alleen mij, maar ook mijn zus hebben gegeven, vind ik nog steeds onvoorstelbaar. Niets was teveel en jullie hebben letterlijk alles opzij gezet om te zorgen dat wij zo goed mogelijk terecht kwamen. Als jullie nu ook nog voor een goede erfenis zorgen… (geintje).

Mijn kinderen, Lars (de witte parel uit de Andes, voetbalnaam: Larsinho), Anne (Annie, hou jij mijn tassie effe vast, die kleine). Ik moet zeggen dat ik vreselijk heb moeten wennen aan jullie twee "hapsnurkers". Het verkrijgen van het vaderschap is geen sinicure en is iets wat je moet leren. Natuurlijk waren, en zijn jullie nog steeds de liefste kinderen ter wereld. Maar laten we eerlijk zijn, wie zit in het begin te wachten op een baby die niets anders kan dan huilen, piesen en poepen, en die er ook nog eens voor zorgt dat je vrijwel niets meer spontaan kunt ondernemen. Inmiddels zijn jullie echter een wezenlijk onderdeel van mijzelf geworden en kan ik me geen leven zonder voorstellen. Jullie zijn mooi "speelgoed" geworden waarvan ik elke dag kan genieten. Ik hoop dat ik jullie beide nog wat goeds voor de toekomst mee kan geven en anders "sla ik het er wel in".

Lest best, Foek, mijn dierbare echtgenote en toegewijde moeder. Wat een doorkijkjurk op de klasse-afdeling allemaal teweeg kan brengen! Jij bent de reden waarom ik van alles in de wereld nog steeds het liefste thuis ben. Laten we hopen dat dit altijd zo blijft.

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Curriculum vitae

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Tijdens opleiding Cardiologie 1 à 2 dagen per week werkzaam op de afdeling Klinische Electrofysiologie in het St. Antonius Ziekenhuis te Nieuwegein tot 1 oktober 1998

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