Catheter Ablation of Atrioatrial Conduction as a Cure for Atrial Arrhythmia After Orthotopic Heart Transplantation

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Objectives. We present three patients in whom atrial arrhythmia was treated by ablation of electrical conduction across a surgical suture line.

Background. Conduction across the suture line separating the donor and native right atria has recently been described after orthotopic heart transplantation.

Methods. Mapping and pacing of both grafted and recipient right atrium was performed to assess the relation between both atria and its relevance to clinical arrhythmia, prior to successful radiofrequency at the site of electrical communication.

Results. In cases 1 and 3, atrioatrial conduction was bidirectional. In both, two types of P waves were observed during sinus rhythm. In case 2, conduction from the recipient to the grafted atrium yielded a very particular surface ECG pattern of atrial extrasystole. The block being unidirectional, the recipient atrial sinus rhythm was not perturbed and behaved like an atrial parasystole. Ablation was performed during sinus rhythm in case 1, recipient right atrial pacing in case 2 and grafted right atrial pacing in case 3 at the site with the shortest conduction time to the other tissue. At the successful ablation site multiple component potentials were recorded. Respectively, 1, 4 and 2 radiofrequency pulses were followed by total atrioatrial conduction interruption. No tachycardia could be induced at the end of the procedure and late follow-up was event free.

Conclusions. The existence of arrhythmogenic atrioatrial conduction should be taken into account when evaluating atrial arrhythmias in the transplanted heart because it is potentially curable by radiofrequency catheter ablation.

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Patients

In this study the term atrioatrial conduction refers to electrical coupling of both the native and grafted atria. Of 4 patients in whom atrioatrial conduction was documented after an electrophysiological study performed for evaluation of palpitations, 3 patients presented with arrhythmia for which the presence of this abnormality was felt to be responsible for the clinically occurring arrhythmia.

Patient 1. Patient 1 was transplanted in April 1989 at the age of 42 for end-stage dilated cardiomyopathy. While this patient never had an arrhythmia in the pre- and perioperative period, frequent extrasystoles were noted during subsequent routine follow-up examination. A 24-h Holter recording was done 5 months after surgery and frequent premature atrial contractions, including salvos and runs of nonsustained atrial tachycardia (up to 20 s), were recorded. In the following 2 years, two episodes of atrial flutter subsequently led to external DC cardioversion after pacing and chemical cardioversion had failed.

Patient 2. Patient 2 was successfully treated for promyelocytic leukemia. He then developed daunorubicin-related cardiomyopathy for which he was transplanted in April 1989 at the age of 18. Although no arrhythmia had been observed preoperatively, frequent premature atrial contractions (PACs) were noted after the tenth postoperative week. They were always present in each of the 7 24-h Holter recordings (up to 17,000/24 h) with a nocturnal preponderance and were often accompanied by right bundle branch block aberrancy. Serial endocardial biopsies showed only mild rejection that did not require specific therapy. In February 1992, an electrophysiological study was performed after three episodes of palpitations accompanied by dizziness and dyspnea reoccurred within...
a 9-month period despite empirical treatment with flecaïnide. During this study atrioatrial conduction was observed. Although no arrhythmia was induced by programmed atrial stimulation of both right atria, digoxin was added. Symptoms were not controlled by antiarrhythmic drugs and in September 1993 salvos of atrial tachycardia were seen on a Holter recording. A second electrophysiological study done the same month did not show evidence of atrioatrial conduction nor inducible arrhythmia. Because of a recurrence of another episode of palpitation with dizziness and evidence of donor right atrial capture on Holter monitoring, a third electrophysiological study was performed in May 1994. Part of the data pertaining to this patient have been published (Patient 1, reference 1).

Patient 3. Patient 3 underwent orthotopic heart transplantation in November 1989 at the age of 51 for end-stage heart failure due to dilated cardiomyopathy. Other than an episode of atrial flutter at week 6 for which he received a short course of oral amiodarone, the postoperative period was event free. Myocardial biopsies and control coronary angiography were within normal limits for 5 years. In December 1994, he had an episode of poorly tolerated atrial tachycardia at a rate of 200 beats/min.

Methods

In all three patients the electrophysiological study was performed according to a protocol which is routinely used for atrial tachycardia ablation (2). Briefly, in addition to a regular quadripolar catheter positioned in the His bundle area, two multipolar catheters (at least one of which had a 4-mm tip) were inserted. These were moved into both right atria in order to recognize and evaluate the presence of conduction across the suture line and to precisely localize the zone where this conduction occurred using pace mapping techniques and recording of local fractionated electrograms.

Incremental atrial pacing and programmed atrial stimulation were performed in both right atria. Mapping was done after positioning one catheter at a fixed donor or recipient right atrial site and pacing at a fixed rate. The other catheter was sequentially moved in a careful search of the area where the shortest conduction time between the atrial electrogram of the pacing and the mapping catheters was observed. This was considered to be the (or the closest possible) atrioatrial conduction site. Special attention was paid to the recording of double potentials bridging the gap between both atrial electrical activities in a similar fashion to that which is observed in accessory pathway ablation. Electrogram gains were manipulated from 5 to 0.2 mV/cm in order to obtain electrograms of similar sizes.

Radiofrequency pulses were delivered at the atrioatrial conduction site using radiofrequency pulses of 20–30 W for 60–90 s using an Osypka HAT 200 S generator until evidence of total interruption of atrioatrial conduction occurred. This was further checked during spontaneous sinus rhythm by pacing at various atrial sites.

Results

Electrophysiological findings. Patient 1. In this case atrioatrial conduction was bidirectional and permanent. This did not allow any atrial dissociation to be visible on surface ECG. Most of the time the dominant rhythm showed flat P waves in the inferior leads followed by a slightly negative component. P waves were all positive in the precordial leads. Intracardiac recordings showed alternans of recipient and grafted sinus rhythm as the dominant rhythm. In the upper panel of Figure 1, the most frequent surface electrocardiogram (ECG) is shown. This results from the dominance of the grafted (donor) atrial sinus rhythm. The prolonged conduction time to the recipient is responsible for the P wave prolongation. The slight increase in the initial negative deflection that is superimposed on the QRS in lead II corresponds to the beginning of the recipient electrical activity. On the other hand, when the dominant sinus rhythm was of the recipient right atrium (Fig. 1, lower panel), P wave duration and PR interval are dramatically increased and there is a frank distortion of P wave morphology. The initial portion of the P wave is biphasic yet mostly positive, and is followed after an isoelectric component by a frankly negative component, and eventually by the resulting QRS. Similarly to the P wave resulting from area in the vicinity of the coronary sinus ostium, the inverted (ascending) nature of the second atrial component suggests electrical connection at a relatively low grafted atrial site. The same observations were made during pacing both native and grafted right atria.

Incremental grafted right atrial pacing showed evidence of 1:1 conduction to the recipient right atrium up to a cycle length
of 250 ms with a 15 ms delay. The time elapsed between the pacing spike in the grafted right atrium and the beginning of the recipient right atrial electrogram reached 240 ms. Programmed recipient atrial stimulation with a basic drive train of 600 ms showed an atrioatrial conduction effective refractory period of 210 ms. Incremental recipient right atrial pacing allowed conduction to occur up to a cycle length of 280 ms. No sustained atrial tachycardia could be induced despite delivery of up to two extrasystoles and burst pacing in both right atrial chambers.

**Patient 2.** At the beginning of the procedure, atrial tachycardia with 3:1 atrioventricular transmission was recorded but ended during positioning of the catheters. Immediately thereafter conduction from the recipient to the grafted atrium yielded a very particular surface ECG pattern of atrial extrasystole with rate dependent right bundle branch block (Fig. 2). Fig. 3A depicts the interaction of the two right atrial sinus rhythms. When the recipient atrial discharge fell late in the diastole of the grafted atrium, the latter was invariably excited, giving rise to a surface ECG characteristic of atrial extrasystole. Because block was unidirectional, the recipient atrial sinus rhythm was not perturbed and behaved like an atrial parasystole. Finally, due to the regular resetting of the grafted sinus rhythm, the resulting surface ECG pattern was that of atrial trigeminy. Incremental and programmed recipient and grafted atrial pacing confirmed unidirectional conduction towards the grafted right atrium at various rates (Fig. 3B and C). Neither incremental nor programmed grafted right atrial stimulation induced tachycardia in this chamber were able to perturbate the recipient right atrial sinus rhythm (Fig. 3C).

**Patient 3.** Evidence of grafted to native right atrial conduction was visible on the surface ECG because two types of P waves were observed during sinus rhythm (Fig. 4). The most frequent morphology is shown in the right part of the tracing. There was a low voltage slightly positive P wave in the inferior leads invariably followed by a hardly distinguishable PR interval during which the ascending baseline mimicked the WPW pattern. This pattern was found to be stable and repetitive, and always resulted in recipient right atrial capture thereby excluding randomly occurring fusion. The other type of P wave was taller with a flat PR interval. When the impulse arose in the grafted right atrium, subsequent propagation to the recipient right atrium gave rise to the second component of the P wave mimicking ventricular preexcitation over an accessory pathway. On the other hand, a tall P wave and flat PR interval were seen when the native sinus discharge was conducted to the grafted atrium.

Incremental recipient atrial pacing was followed by 1:1 atrioatrial conduction to the grafted right atrium down to a cycle length of 280 ms. Faster pacing cycles were accompanied by 2:1 atrioatrial conduction. Incremental grafted atrial pacing yielded 1:1 atrioatrial conduction down to a cycle length of 240 ms and induction of an atrial tachycardia in the native atrium with a cycle length of 280–300 ms with 1:1 or 2:1 conduction to the grafted atrium (Fig. 5). Note that in this particular case, since the pattern of atrioventricular conduction was stable, the real (recipient right atrium) origin of the tachycardia could not be detected on the surface electrogram. Spontaneous termination of this tachycardia occurred after...
this recording. Programmed grafted right atrial stimulation resulted in induction of a native atrial tachycardia with a cycle length of 340 ms. Extrasystoles delivered in both chambers were not able to reset the tachycardia. The first attempt at transient tachycardia entrainment-mapping with recipient atrial pacing was followed by tachycardia termination.

**Ablation.** In the three cases ablation was performed only in the right atrium. Left atrial mapping as well as extensive mapping of the suture lines was not performed. Because of the distortion of atrial anatomy after surgery, precise location of the ablation site in reference to the normal anatomical structures was difficult. Additionally in our experience, the presence of multiple components or fractionated potentials is frequent after cardiac surgery. This rendered interpretation of local electrogram timing difficult, but suggested the presence of local block (i.e., the suture line). Therefore we elected to guide the ablation by the presence of such abnormal potentials with concomitant recording of a locally short conduction time.

In Patient 1, during grafted sinus rhythm, careful mapping of both right atria revealed a zone in the low anterolateral right atrium where a multiple component potential was recorded including an intermediate high voltage spike immediately preceding an “early” recipient atrial electrogram (Fig. 6). Because this was the site where the shortest grafted to recipient atrial conduction time was recorded we interpreted this recording to be arising at the probable location of electrical communication across the suture line (although the latter was not visible on fluoroscopy). In other locations, the conduction time was found to be longer and the electrograms more widely separated. This could be interpreted as the catheter straddling both sides of the suture line with electrotonic activation of the second component. A single radiofrequency pulse delivered at that site was followed by complete and permanent interruption of atrioatrial conduction after 12 s. On subsequent surface electrocardiograms, the dissociation of both atrial activities was obvious (Fig. 7).

In Patient 2, because conduction was unidirectional, constant pacing was performed at various recipient right atrial sites in a search for the shortest time between the pacing artifact and the resulting onset of the grafted P wave. Figure 8 shows two representative examples of conduction times as a function of the pacing site. The site of shortest atrioatrial conduction was localized in the high right atrium in the vicinity of the grafted atrial sinus node. At this site multiple component electrical activity with a spiky electrogram in the middle was found. Four radiofrequency pulses were delivered and atrioatrial conduction was definitively interrupted.

In Patient 3 the lack of resetting effect of extrasystoles was interpreted as resulting from pacing relatively far from a small reentrant circuit, at a site that was probably located in the native right atrium but in close vicinity to the suture line. Because grafted to recipient atrial transmission was “better” than the reverse, ablation was performed during constant grafted right atrial pacing. Three radiofrequency pulses (20 W, 90 s) were delivered at a site where a double potential, with the second component immediately preceding the beginning of the native P wave, was recorded. Atrioatrial conduction disappeared within 2 s of the third pulse and complete atrioatrial dissociation ensued (Fig. 9). At the end of the procedure no tachycardia could be induced with pacing techniques initiated in either of the right atria.

**Figure 5.** Patient 3: induced atrial tachycardia with 2:1 and 1:1 atrioatrial conduction from the recipient to the grafted right atrium.

**Figure 6.** Patient 1: local electrogram at the successful ablation site during spontaneous grafted to recipient atrioatrial conduction. Proximal and distal recording bipole of the ablation catheter are straddling the suture line based on electrogram amplitude (see text for discussion). Abl = ablation catheter recording bipolar; d = distal, p = proximal.
to electrical propagation of the cardiac impulse across theoretically inexorable surgical suture lines. In a recent report from our laboratory, Anselme et al. described atrioatrial conduction after a heart transplant in a patient of this current series, as well as in another patient who did not undergo the ablation procedure (1). This phenomenon is exceptional, or is thought to be so, because complete electrical insulation usually occurs after surgery. Isolation by surgical incision of adjacent portions of atrial myocardium has been proposed as a long-term treatment of atrial arrhythmias (3). This is in fact the rationale of modern arrhythmia surgery (4–6).

Prevalence of atrioatrial conduction. In our series of 143 patients after orthotopic transplantation this phenomenon has in fact been documented four times. In all cases propagation was found to occur across the suture line late after scarring. It was found to be uni- or bidirectional in the cases reported here. Conduction from the native to the grafted right atrium was accompanied by symptoms associated with arrhythmias and ECG abnormalities that eventually led to the diagnosis. Pure grafted to native atrioatrial conduction resulting in native atrial arrhythmias are also at least theoretically possible. However, if conduction is unidirectional with no resulting perturbation of the grafted right atrium, it may be clinically undetectable and difficult to see on a surface ECG. In fact, because the patients are not systematically studied in our laboratory after heart transplantation, the overall prevalence of atrioatrial conduction is unknown. These observations are nevertheless of clinical relevance because, in addition to the surface ECG normalization, none of the patients experienced recurrences of a sustained arrhythmia during follow-up despite systematic withdrawal of antiarrhythmic drugs. The actual mechanism of atrial arrhythmogenesis should be a matter of continuing interest given the high prevalence of atrial arrhythmia in transplant patients in the absence of obvious rejection episodes. Additionally, up to 76% of the patients dying suddenly after heart transplantation are known to suffer from atrial arrhythmia independent of their ejection fraction (7,8).

Mechanism of atrioatrial conduction across inexcitable suture lines. The mechanism of electrical propagation of impulses across a suture line is not well understood. As early as in 1947, animal experiments suggested that mechanical excitation can lead to mutual synchronization of two closely spaced pacemakers firing at similar rates (9). More recently, in animal preparations, Jalife and Moe (10) described electrotonic transmission of impulses across a gap of totally inexcitable tissue and further analysis of this type of impulse propagation provided a scientific explanation for the so-called Wedensky facilitation (11). In a three-compartment preparation where the central segment was depolarized at a level at which the sodium channels are largely inactivated, Antzelevitch and Moe showed that, depending on the local conditions within the central segment, conduction across the gap could be prompt, abolished or delayed (12). Electrotonically mediated delayed transmission was at times even able to reexcite the proximal segment thus generating coupled reflections. Our observation may represent the clinical counterpart of their findings since in
Figure 7 the double spikes recorded by both bipoles of the ablation catheter may be interpreted as showing reflected reentry (as seen with filtered electrograms). The variation of amplitude of the two components of the electrograms as a function of the recording bipolar may represent preferential recording of the RRA side of the suture line for the proximal bipolar, and of the GRA side for the distal one, with far-field recording of the other side for both bipoles. An alternate explanation may be that electrotonic transmission across the suture line is shown by the larger deflection in the distal bipolar and the smaller deflection in the proximal (delayed electrotonic transmission) which in turn is followed by the larger deflection representing RRA activation. In this case the second (smaller) deflection in the distal bipolar of the ablation catheter may indeed represent local (nontransmitted) reflection back to the grafted right atrium. Transient enhanced excitability distal to a site of block has also been suggested by Prinzmetal and was recently demonstrated by Munsif in a model of preexcitation induced by subthreshold ventricular stimulation (13,14).

These observations led to the development of a series of modern concepts of cardiac physiology such as mutual entrainment of cells and the proposal of new mechanisms of arrhythmogenesis such as reflection or parasystolic modulation (15–19). Their clinical correlates have recently been observed in humans further supporting the high likelihood of the natural occurrence of these phenomena (20,21).

Radiofrequency ablation of atrioatrial conduction. Ablation was not targeted at the primary arrhythmia focus in patient 1 and 2 because no sustained arrhythmia could be induced in any chamber, thereby prohibiting activation mapping. Moreover in patient 2 two previous electrophysiological studies did not allow induction of any arrhythmia. In patient 3, two different types of atrial tachycardia were induced in the recipient right atrium that propagated to the grafted atrium. The presence of several types of atrial tachycardias is associated with a lower success of direct myocardial ablation. Additionally, although it could not be definitely proven that the mechanism of spontaneous tachycardia was due to the presence of abnormal bilateral atrioatrial conduction, recipient atrial tachycardia induction during grafted atrial pacing, led us to think that this could have been part of the natural pathogenic process in tachycardia initiation. A case report and an abstract dealing with the same topic have been reported (22,23). Finally, the frequent evolution of the recipient atrium towards atrial fibrillation with the ensuing possible conduction to the grafted atrium also provides support for the idea that atrio-atrial conduction ablation can be used for late prevention of grafted atrial fibrillation (analogous to His bundle ablation in cases of symptomatic recurrent atrial fibrillation). The radiofrequency technique used in this study is derived from standard techniques that are routinely used in ablation of other type of tachycardia. De Bakker et al. have shown in human hearts that fractionated potentials were either recorded at sites contiguous to a line of block or were shown to be related to the presence of fibrous tissue separating myocardial fibers giving rise to separate conducting paths within the same chamber (24). We interpreted the presence of such abnormal potentials as markers of the proximity of the suture line. A similar mapping approach has been used in the paper by Baker et al. for tachycardias for which the reentrant circuit turned around the scar. Recording of double potentials helped to localize the surgical scar and ablation pulses were then delivered between the surgical suture line and an anatomical obstacle that was the inferior (8 cases) or superior (2 cases) vena cava or the tricuspid annulus (7 cases). This is now routinely performed in the so-called “scar flutter” or “incisional tachycardia” after surgery of the atrium. In this paper we also looked for double potentials for localization of the suture line. Then we looked for the shortest local conduction time between these potentials, thus suggesting local evidence of conduction at this given site across the scar. This proved to be the optimal site because delivery of ablation pulses resulted in total interruption of conduction across the suture line. The ablation line was not extended to an anatomical barrier. Our technique intends to treat reentrant tachycardia utilizing conduction across the scar and/or to isolate both grafted and recipient atria. Ablation of a multiple component potential preceding an early atrial depolarization (as in patient 1 and 3) is similar to the approach used in ablation of overt accessory pathway (25). Similar to that which is observed in natural atrial disease, analysis of the spontaneous morphology of the composite P wave during atrioatrial conduction already suggests the site of electrical atrial propagation (26,27). Among the techniques that could have potentially been useful in evaluating potential target sites for ablation is the evaluation of the effects of local subthreshold stimulation (28–32). Although it has clearly been shown in animal models and during human electrophysiological studies that, using the latter technique local inhibition of conduction could reproducibly be obtained, we do not routinely apply it to optimize the location of the ablation site. However, this technique might be of help especially in cases where abnormal electrograms are widespread along the suture lines. Finally, the lack of late symptoms and of any arrhythmia during follow-up further validates the link between atrioatrial conduction and atrial arrhythmia, as well as the efficacy of radiofrequency ablation for this new indication.

Deleterious effects of the remnant atrium. Orthotopic heart transplantation using the classic Lower and Shumway technique allows a significant portion of the right atrium to remain in place (33–35). Although its original vascularization has disappeared, pericardial collaterals are usually sufficient to allow survival of a substantial amount of atrial tissue with its own intrinsic electrical activity. In case of preoperative chronic atrial fibrillation the atrial remnant is therefore expected to remain so or at times to return to an atrial rhythm because of the dramatic reduction of the atrial mass. Although the classic Lower and Shumway technique has been considered to be the gold standard for more than two decades, the loss of atrial anatomy with its ensuing loss of cardiac function, the electrical atrial asynchrony, the high prevalence of tricuspid and mitral valve regurgitation, and the higher potential for left atrial thrombosis have paved the way for the development of bicaval...
or total orthotopic transplantation (35–38). As shown in this study, the clear arrhythmogenic potential of atrioatrial conduction further demonstrates the advantages of total excision of the recipient atrium.

**Study limitations.** The clinical cure that was relatively easily obtained in this study was related to the easy access to a single limited pathway of communication between both right atria. Although clinical experience does not suggest such, it is unknown whether several or larger pathways may exist rendering radiofrequency less likely to be successful. Patient 3 suffered from only a single episode of atrial tachycardia, and it is uncertain whether the quiet postablation outcome is related to ablation of atrioatrial conduction. Although tachycardia was rendered noninducible after atrioatrial conduction interruption, this has recently been shown to be a relatively weak end point for prediction of late success after radiofrequency ablation (39,40). Identification of a block of conduction in a structure which is necessary for tachycardia initiation of perpetuation is a better marker but this does not apply to the induced tachycardia in patient 3 (41). However, because recipient right atrial tachycardia could be induced with grafted right atrial pacing, and because both sinus rhythms constantly interfered, we think that ablation has probably played a beneficial role in the late outcome of this patient.

**Conclusion.** Total orthotopic heart transplantation has recently been proposed as an alternative to the standard procedure. It is still controversial and preliminary studies have shown that it is feasible and have suggested that there are anatomic and physiologic benefits related to normalization of atrial size and function. The possibility of arrhythmogenic atrioatrial conduction with the classic Lower and Schumway technique is a new factor that should be taken into account when comparing the risk/benefit ratio of these procedures. In our institution these observations, as well as the higher risk of left atrial appendage thrombi, have dramatically changed our transplantation approach. At this time only total orthotopic heart transplantation is performed. Finally, because of the high incidence of atrial arrhythmia in heart transplant patients using the classic technique, prospective studies should be initiated to evaluate the prevalence of atrioatrial conduction, its clinical impact and its potential cure by radiofrequency ablation.

**References**


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