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Atrioatrial Conduction After Orthotopic Heart Transplantation

FREDERIC ANSELME, MD, NADIR SAOUDI, MD, MICHEL REDONNET, MD, BRICE LETAC, MD, FACC

Rouen, France

Objectives. **In two patients with orthotopic heart transplantation, the surface electrocardiogram suggested interaction between the donor right atrium and the recipient right atrium. An electrophysiologic investigation was performed to assess possible atrioatrial conduction.**

Background. **After orthotopic heart transplantation, both recipient and donor atrial activities are usually independent, but in humans they may synchronize for short periods during exercise.**

Methods. **Electrophysiologic recordings were made using standard techniques. The atrial electrode locations (anterior for the donor and posterior for the recipient right atria) were confirmed by fluoroscopy. Incremental and programmed donor and recipient right atrial pacing protocols were performed.**

Results. **Unidirectional conduction between native and graft atria occurred in both patients. This phenomenon was evident at rest, during normal sinus rhythm and at various pacing rates, resulting in frequent atrial bigeminy and trigeminy.**

Conclusions. **Possible atrioatrial conduction after orthotopic heart transplantation may potentially be arrhythmogenic for the chamber where extrasystoles occur. This should be taken into account in attempting to devise new pacing modes if both atria are rendered electrically common.**

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In human orthotopic heart transplantation, the posterior portion of the recipient right and left atria are left in situ, leaving the native sinus node and its neural connections undisturbed (1). The donor right atrium contains its own sinus node, which eventually becomes the pacemaker of the transplanted heart. Usually electrical impulses do not cross the atrial suture line, and the two sinus nodes beat independently (2). Commonly, their activities are recognized on standard surface electrocardiograms (ECGs) by the presence of two sets of P waves of different morphologies (recipient and donor), which are totally independent of each other.

We report here on the electrophysiologic evaluation of two patients in whom an interaction between the recipient and the donor right atrial depolarization was demonstrated after heart transplantation.

Methods

Patients. Patient 1, a 26-year old man, had promyelocytic leukemia that had been treated with daunorubicin (rubidomicin) (1,200 mg/m^2) at the age of 3 years. The disease progressed favorably, with the exception of signs of cardiac failure as a result of an anthracycline-related cardiomyopathy, which appeared in December 1986. Three years later, the patient underwent orthotopic heart transplantation. He recovered well, leaving the hospital after a 33-day stay. Regular endocardial biopsies showed only mild rejection episodes, which did not require any specific treatment. On successive ECGs, sporadic asymptomatic atrial extrasystoles were noted. A short episode of regular and fast palpitations led to hospital admission in February 1992. An endocardial biopsy was performed and failed to show any signs of rejection. An electrophysiologic diagnostic study was performed without antiarrhythmic treatment.

Patient 2, a 43-year old man with idiopathic congestive cardiomyopathy, underwent orthotopic heart transplantation in October 1989. During the early follow-up period, atrial flutter accompanied an acute rejection episode for which he was successfully treated. He was finally discharged on the 45th postoperative day. Routine endocardial biopsies revealed several episodes of mild rejection that were successfully treated with azathioprine. In April 1991, a subsequent episode of atrial flutter occurred, and flecainide, 200 mg daily, was begun. This dosage was increased to 300 mg daily after an episode of atrial tachycardia. The patient was readmitted 1 month later because of wide QRS tachycardia, for which an electrophysiologic diagnostic investigation was performed.

Electrophysiologic study. Under fluoroscopic guidance, four pacing electrodes were inserted via the femoral veins and were positioned in the recipient right atrium, donor right atrium, in the hisian area and at the apex of the right ventricle. The right atrial electrode locations (anterior for the donor and posterior for the recipient atrium) were confirmed by 30° right anterior oblique angle fluoroscopy. Sinus rhythm

From The Centre Hospitalier et Universitaire de Rouen, Hôpital Charles Nicolle, Groupe de Recherche VACOMED, Rouen, France.

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Address for correspondence: Dr. Nadir Saoudi, Centre Hospitalier et Universitaire de Rouen, Hôpital Charles Nicolle, Groupe de Recherche VACOMED, 1 rue de Germont, 76000 Rouen, France.

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Table 1. Conduction Intervals and Refractory Periods

	Patient 1	Patient 2
DRA SCL	655	800
RRA SCL	840	880
AH	70	80
HV	55	60
AV FRP	300	360
DRA ERP	220	260
RRA ERP	240	260
DRA-RRA ERP	—	—
RRA-DRA ERP	330	—

Data are all expressed in milliseconds. AH = AV node conduction time; AV FRP = functional refractory period of AV node; DRA ERP = effective refractory period of donor right atrium; DRA-RRA ERP = effective refractory period of donor to recipient right atrial conduction; DRA SCL = sinus cycle length of donor right atrium; HV = His-Purkinje conduction time; RRA ERP = effective refractory period of recipient right atrium; RRA SCL = sinus cycle length of recipient right atrium.

conduction intervals, as well as refractory periods, were determined using standard techniques (3,4).

Results

Patient 1. Surface ECGs showed a normal sinus rhythm with a PR interval of 0.12 s and no visible recipient P waves. There was an incomplete right bundle branch block, which was accentuated during intermittent episodes of atrial trigeminy. Sinus rhythm conduction intervals and refractory periods were found to be normal (Table 1). During ventricular pacing there was retrograde ventriculoatrial (VA) conduction in the donor heart down to a pacing cycle length of 450 ms.

Surprisingly, we observed that when recipient atrial sinus discharges occurred between 270 and 500 ms after the donor atrial electrograms, they were consistently followed by a premature donor atrial beat at a constant coupling interval of 65 ms. The latter was conducted over the donor's normal pathway with a varying degree of right bundle branch block. Figure 1 shows that the result of increasing the prematurity of His bundle depolarization is a gradual parallel increase in the degree of right bundle branch block aberration.

The conjunction of atrioatrial conduction and intermittent donor right atrium resetting as a function of the respective sinus cycle lengths allowed emergence of regular donor right atrial periods (i.e., atrial trigeminy). Figure 2 shows a representative example. The first donor right atrial cycle is undisturbed because rA1 occurs 60 ms after dA1, far before the critical 270 ms necessary to permit transmission from recipient right atrial to donor right atrial. The recipient atrial sinus node regularly discharges at a cycle length of 840 ms (longer than that of the donor right atrial 655 ms). As a consequence, rA2 decreases 300 ms after dA2 and can be conducted to the donor right atrium, resulting in a premature donor atrial depolarization (dA3). The latter resets the DRA sinus node and causes this sequence to repeat itself for a prolonged period.

During incremental recipient atrial pacing, there was found to be 1:1 atrioatrial conduction down to a 400-ms cycle length (Fig. 3A). At shorter pacing cycle lengths, conduction time between recipient right atrium and donor right atrium progressively increased until the appearance of an intermittent second-degree type II local block. Further pacing cycle length shortening yielded alternation of 3:2 and 2:1 conduction for the same cycle. Finally, at even shorter pacing cycle lengths, stable 2:1 transmission was recorded (Fig. 3B). When programmed recipient right atrial stimulation was performed at a 600-ms pacing cycle length, the atrioatrial effective refractory period was 330 ms.

In contrast to what we observed during recipient right atrial pacing, the incremental donor right atrial pacing did not affect the recipient right atrial cycle because of a unidirectional donor-recipient right atrial conduction block. Likewise, despite the presence of retrograde VA conduction, the recipient right atrial cycle did not change during ventricular pacing.

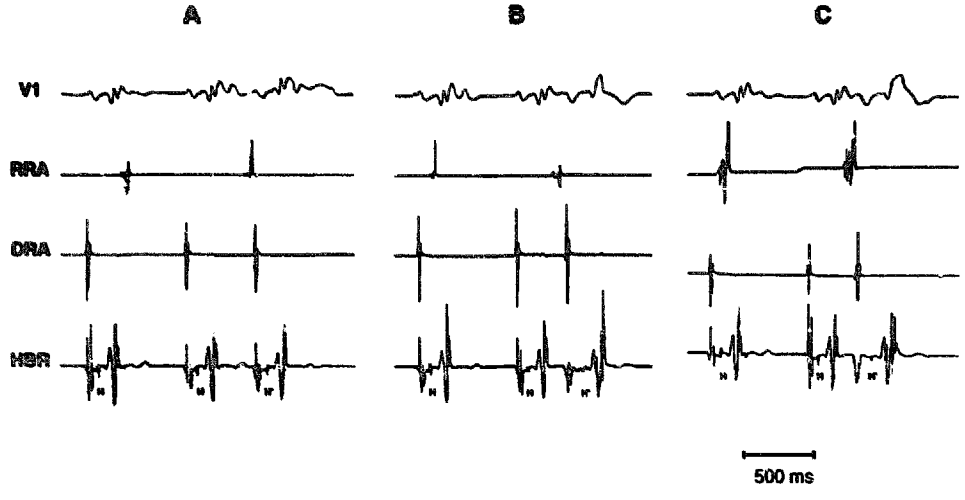


Figure 1. Patient 1. Recording during normal sinus rhythm. Varying degrees of block occurred in the right bundle branch after the premature beat. The recipient right atrium electrogram always preceded the donor right atrium electrogram. During stable donor atrial and HH cycle length (680 ms), the degree of ventricular aberration parallels that of the coupling interval of H′. A, H-H′ 480 ms; B, H-H′ 380 ms; C, H-H′ 370 ms. DRA = donor right atrium; HBR = His bundle recording; RRA = recipient right atrium; V1 = lead V_1 on surface electrocardiogram.

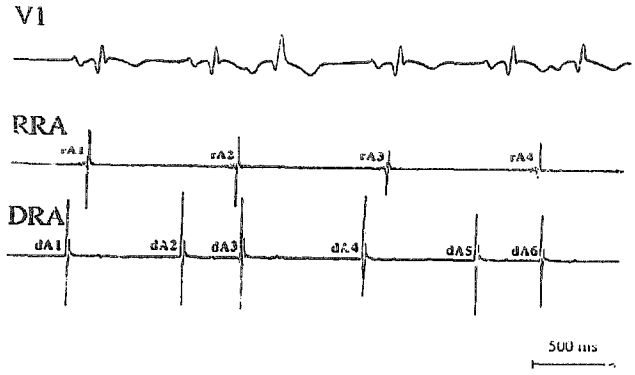


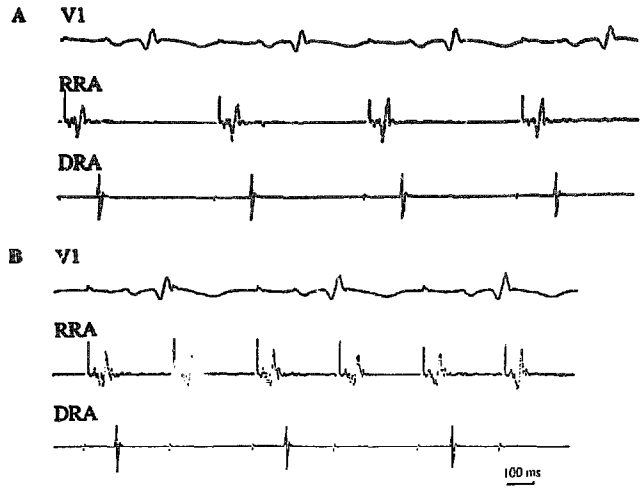
Figure 2. Patient 1. Recording during normal sinus rhythm. Although the recipient atrial cycle length was unchanged, there was trigeminy in the donor right atrium. The donor atrial premature beat was always preceded by that of the recipient, with a constant coupling interval of 65 ms. The first and third recipient sinus beats occurred earlier in the cycle of the donor atrium to produce a premature depolarization. Abbreviations as in Figure 1.

Patient 2. On the surface ECG there was a normal sinus rhythm with a PR interval of 0.18 s and an incomplete right bundle branch block. As in patient 1, the conduction intervals and the refractory periods of the transplanted heart were subnormal (Table 1).

During sinus rhythm there was a temporal window in the middle of the recipient right atrial cycle (between 440 and 700 ms after the recipient atrial electrogram) during which donor to recipient atrial conduction could occur with a constant coupling interval of 10 ms.

Figure 4 shows an example in which transmission from donor right atrium to recipient right atrium yielded recipient atrial bigeminy. The dA2 decreases 800 ms after rA1 and does not produce a premature recipient depolarization.

Figure 3. Patient 1. Recording during incremental recipient atrial pacing. A, The recipient atrium was driven at a cycle length of 640 ms, and a 1:1 conduction of donor atrium was established. B, The recipient atrial cycle length was set at 350 ms, yielding 2:1 conduction. Abbreviations as in Figure 1.



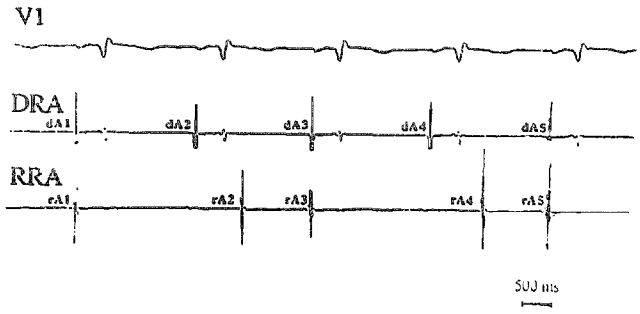
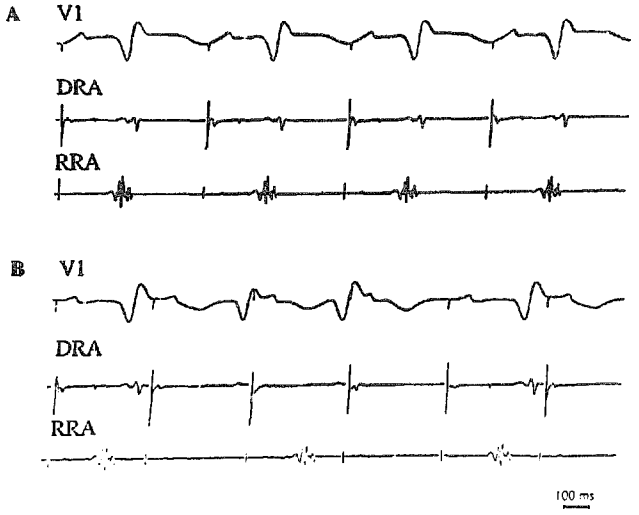


Figure 4. Patient 2. Recording during normal sinus rhythm. The donor sinus cycle length was constant, and the recipient atrial activity showed bigeminy. The premature recipient beat was preceded by the donor right atrial electrogram, with a constant coupling interval of 10 ms. The first and third donor atrial beats occurred later, after the recipient electrogram to be transmitted, possibly because of phase 4 block. Abbreviations as in Figure 1.

Because the donor right atrial cycle is shorter than the recipient cycle, dA3 decreases relatively earlier after rA2 than the previous beat (500 ms) and, as a result, can be followed by rA3 with a short coupling interval. The latter resets the recipient right atrial sinus node. Because of this, dA4 occurs late in the recipient atrial cycle and cannot be conducted to recipient right atrium. This stable sequence was repeated for a long period of time.

During incremental donor atrial pacing, 1:1 transmission to recipient right atrium appeared down to a pacing cycle length of 400 ms with a conduction time of 190 ms (Fig. 5A). For faster donor right atrial pacing, stable 2:1 conduction became established (Fig. 5B). During ventricular pacing, retrograde VA conduction allowed 1:1 synchronization be-

Figure 5. Patient 2. Recording during incremental donor atrial pacing. A, The donor right atrial pacing cycle length was 550 ms, with 1:1 propagation to recipient atrium. B, The donor right atrial pacing cycle length was decreased to 370 ms, and then the recipient atrium was excited with a ratio of 2:1. Abbreviations as in Figure 1.



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tween the donor right atrium and the recipient right atrium down to a pacing cycle length of 550 ms. Below this value, retrograde Wenckebach periods occurred.

Discussion

We report unidirectional atrioatrial conduction during atrial pacing in two patients who had undergone orthotopic heart transplantation. To our knowledge this phenomenon, which also could occur during sinus rhythm at rest, has never been reported before, either in experimental laboratory procedures in animals (5) or in previous studies dealing with sinoatrial function after cardiac transplantation (6–8).

Recording both donor and recipient atrial activity is relatively easy on surface ECG or by using either esophageal or endocardial electrodes (6,9). Usually the atrial suture line isolates the native atrium's own sinus node from the transplanted atrium. The electrical activities of both atria remain independent of each other, resulting in surface ECG dissociation between the recipient and the donor P waves (2,5).

A temporary synchronization between donor and recipient rates has been found during exercise (10). This was observed when the respective sinus rates approached a similar frequency, but it was never sustained (~3.5 min). However, this phenomenon was not noted in patients at rest, when recipient and donor rates were frankly different.

Ernst (11) has reported grafting a pedicle of the sinoatrial node (including its nutrient artery) into the right ventricular myocardium in dogs. Two to 4 months later, ordinary surgical procedures to produce complete AV block did not result in the appearance of complete heart block. The complete AV block was eventually obtained only after the atrial pedicle was removed. The author concluded that 1:1 transmission from atrium to ventricle occurred across the graft. Although the mechanism of this phenomenon was unclear, mechanical transmission from the contractile piece of the atrium to the right ventricle could not be excluded.

Bexton et al. (12) reported a case in which recipient and donor atria remained synchronized during a variety of physiologic and nonphysiologic situations. During sinus rhythm as well as during fast donor right atrial pacing, the recipient atrial electrograms followed the donor atrial electrograms with a coupling interval of 90 ms. Similarly, there was a constant relation of donor to recipient atria during incremental graft atrial pacing. Disopyramide infusion slowed the rate of the denervated donor sinus node and increased that of the innervated recipient sinus node. For a short time period the latter became the dominant pacemaker. The absence of VA conduction did not allow analysis of the retrograde interaction between the two atria.

Although disopyramide infusion was not performed in this study, we found only unidirectional atrioatrial conduction and block during the various pacing maneuvers and did not find bidirectional atrioatrial conduction. During sinus rhythm, propagation was possible during a relatively narrow conduction window determined by the other atrium's cycle length. Additionally, during incremental atrial pacing, the conduction obeyed the classically described 1:1, 3:2, 2:1 ratios, suggesting decremental conduction properties through the suture line. This might be expected because of the anatomic obstacle (with a resulting high likelihood of depressed conduction) that is represented by the surgical suture between the two atria.

Although the recipient atrium is under neural influences, the transplanted heart is denervated, and in the absence of sympathetic stimulus the donor right atrial frequency is often faster than that of recipient right atrium. These different rates are necessary to allow the emergence of orderly transmission from one atrium to the other, generating long periods of either atrial bigeminy or trigeminy.

In Patient 1, we think that the activity was not transmitted early in the cycle because it either fell within the atrial refractory period or was stopped within the interatrial suture by a phase 3 block. Similarly, in patient 2, the absence of transmission late in the atrial cycle could result from an atrial myocardial cell phase 4 block. According to studies by Jalife et al. (13), the rate-dependent block may be associated with time-dependent variations in depolarized fiber excitability as well as in the slow response amplitude generated by these fibers. Cell automaticity is therefore not necessary for the occurrence of a bradycardia-dependent block.

Several theories have been postulated to explain the existence of interaction between recipient right atrium and donor right atrium. Segers' original work (14) showed that when two fragments of frog heart were placed in mutual contact, they began to contract exactly in phase at the rate of the more rapidly beating fragment, provided that the difference between the two intrinsic rates was <25%. This synchronization could come either from electrical activity occurring after mechanical isolation or from a mutual mechanical influence occurring after electrical isolation.

However, the electrotonic transmission theory appears to be the most attractive one to explain these observations. This is propagation through an area of impaired conductivity, which does not need to produce an action potential but may provide ionic channels for transmission of electrotonic influences. In a biologic parasystole model, Jalife and Moe (15) demonstrated that an "ectopic" (parasystolic) pacemaker can be electrotonically entrained across an area of depressed excitability within a wide range of rates both above and below its intrinsic frequency. It is therefore conceivable that transmission of an impulse through the atrial suture line occurs even though the suture cells are fibrotic and therefore not excitable. Several clinical examples of so-called modulated parasystole have been reported from surface ECG analyses (16).

Clinical implications. These electrophysiologic explorations clearly show an interaction between donor and recipient atria. If conduction from recipient to donor atrium can generate atrial extrasystoles, it could at least theoretically be arrhythmogenic and produce sustained supraventricular tachyarrhythmias such as atrial fibrillation. Propagation

from donor to recipient atria does not seem to have deleterious consequences unless, as recently proposed, electrotonic connection by means of bipolar atrial triggered pacing is used to restore normal chronotropic responsiveness after cardiac transplantation. In the study by Kacet et al. (17) on patients with donor heart symptomatic sinus node dysfunction, a single unipolar active fixation lead was positioned in each atrium and was connected to a bipolar AAT pulse generator. With this configuration, the native sinus node drove the graft atrium. In this type of pacemaker, recipient-donor atrial interactions could also generate malfunctions. Even if these interactions are likely to be unusual, they should probably be searched for by electrophysiologic exploration before implantation.

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