Efficacy of Radiofrequency Ablation for Control of Intraatrial Reentrant Tachycardia in Patients With Congenital Heart Disease

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Background. Intraatrial reentrant tachycardia (IART) is a common problem in patients with congenital heart disease (CHD). The progression of clinical symptoms of IART and their response to radiofrequency (RF) ablation are not yet well described.

Objectives. The objective of the study was to determine the early and midterm success rates of RF ablation in effecting a reduction of clinical arrhythmic events in patients with IART and CHD.

Methods. Clinical records of patients undergoing early, successful RF ablation were analyzed retrospectively to document the occurrence and frequency of documented IART, cardioversion and arrhythmia-related hospital visits before and after ablation.

Results. Fifty-five catheterizations for intended RF ablation of IART were performed in 45 patients (mean [±SD] age 24.5 ± 10.5 years, 40 after surgical palliation of CHD). Early success was achieved for one or more IART circuits in 33 patients (73%). Mean clinical follow-up of those patients with successful ablation is 17.4 ± 11.3 months (total 574 patient-months). Documented IART recurrence was noted after 21 (53%) of 40 early, successful catheterizations in 17 (52%) of 33 patients, with a mean time to

recurrence of 4.1 months, often with electrocardiographically novel configurations. A more prolonged and frequent history of IART was a univariate risk factor for recurrence. Seven patients underwent repeat RF ablations, and eight patients were restarted on antiarrhythmic medications after ablation. Two patients who had severe ventricular dysfunction before RF ablation died 1.5 and 11 months after RF ablation without known arrhythmia recurrence. Clinical events related to IART increased steadily in frequency for 24 months before RF ablation. Radiofrequency ablation resulted in a reduction of event frequency to levels significantly lower than those in the 12-month period before RF ablation and not significantly different from those levels observed at baseline 3 to 4 years before RF ablation.

Conclusions. In patients with successful RF ablation, the frequency of subsequent events was reduced compared with the 2 preceding years. However, recurrence of IART in patients who showed clinical improvement was frequent, and often revealed the presence of new IART configurations.

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Intraatrial reentrant tachycardia (IART) is common after repair or palliation of many types of congenital heart disease (CHD), and its prevalence increases over time (1–7). Although some patients with IART are minimally symptomatic, associated morbid events may include hemodynamic deterioration, thromboembolism and death (8–10). Experience with the use of antiarrhythmic agents and atrial pacing techniques to suppress IART or its symptoms has been unsatisfactory (8,11–13). Early reports of the early efficacy of radiofrequency (RF) ablation to modify the complex IART substrate in these patients suggest that this approach, although technically challenging, may provide a useful alternative therapy (14–16).

The primary purpose of this study was to analyze the intermediate-term follow-up of IART after RF therapy. Because the assessment of clinical response to therapeutic intervention in this arrhythmia is complicated by a lack of knowledge of the natural history of recurrent IART, we have also outlined the time course of well documented clinical events related to IART experienced by our study patients before RF ablation, and we have quantified the frequencies of such events before and after RF ablation.

Methods

Patient selection. The study group was composed of patients undergoing catheterization for intended RF ablation of IART at Children's Hospital of Boston between April 1993 and May 1996. This group included 10 patients in whom the early efficacy of RF ablation for IART has been previously reported (14). Additional preprocedural and follow-up data from this subgroup are included in the current study. Informed consent for ablation was obtained under a protocol approved by the Clinical Investigations Committee of Children's Hospital.

Abbreviations and Acronyms

CHD = congestive heart disease
ECG = electrocardiographic
IART = intraatrial reentrant tachycardia
RF = radiofrequency

Definition of IART. Intraatrial reentrant tachycardia was defined as a rapid atrial rhythm that was independent of atrioventricular conduction, with sudden onset and termination and a constant cycle length (17). Other electrophysiologic criteria determined by esophageal or intracardiac study, or both, confirming the diagnosis included the ability to initiate, terminate and entrain the tachyarrhythmia using atrial stimulation and the demonstration of a nonsinus mechanism by an atrial activation sequence. Because multiple configurations of IART were inducible in some patients, circuits were initially selected for mapping and ablation if they were similar in electrocardiographic (ECG) configuration and cycle length to previously documented tachycardias.

Mapping and ablation technique. The techniques used for RF ablation of IART were based on those previously reported (14). Mapping of areas demonstrating abnormal right atrial conduction were performed both in sinus rhythm and during IART. Areas of anatomic or functional conduction block, or both, were identified by observation of split electrograms or large shifts in electrographic timing associated with small movements of the mapping catheter, or both. Candidate zones of slow and/or protected conduction possibly critical to the IART circuit were identified by the presence of low amplitude, fractionated electrograms of long duration occurring in atrial electrical diastole, defined as the period occurring between surface P waves. These sites were tested using tachycardia entrainment at rates marginally faster than those of IART. Postpacing interval and comparison of entrained and spontaneous endocardial activation were used to ascertain whether paced sites lay within the tachycardia circuit and its protected zone (18). Attempts were made to demonstrate an entrainment response at a variety of anatomic sites, but if the IART was terminated by entrainment pacing or if sustained IART had been difficult to induce by programmed stimulation, or both, entrainment studies were limited to the areas of interest. Radiofrequency applications were targeted using the demonstration of concealed entrainment from a protected zone as a primary criterion, with secondary criteria including local atrial mid-diastolic/presystolic activation, fractionated diastolic atrial electrographic configuration and location in an isthmus between known anatomic or electrophysiologically identified areas of conduction block, or both.

Radiofrequency energy was generated using either a voltage-controlled (Radionics RFG-3C, Radionics, Inc.) or a temperature-controlled (Medtronic Cardiorhythm Atakr) RF generator. When RF applications were planned along the lateral atrial wall, the ability to stimulate the phrenic nerve at

the intended ablation site was assessed by pacing the site at high output (e.g., 10 mA $\times$ 2 ms) and assessing for the presence of diaphragmatic twitch. If the phrenic nerve was easily stimulated, alternate sites were sought. Applications were made during IART, and if the tachycardia terminated or became irregular or changed in rate within 15 to 20 s, the application was continued for 40 to 60 s. Additional lesion(s) were placed around the anatomic site of a successful ablation in an effort to increase the lesion size. If the site was thought to represent an anatomic isthmus, attempts were made to create a linear lesion between the nonconductive borders.

Attempts were then made to reinduce the ablated IART using programmed atrial stimulation. Isoproterenol was only used to increase the sensitivity of postablation testing when a high likelihood was considered to exist of either incomplete RF ablation of the targeted circuit or additional clinically relevant configurations of IART. When additional IART circuits of different cycle lengths, P wave configuration or activation sequence, or a combination of these, were identified and thought to represent clinically relevant tachycardias on the basis of previous ECG records, endocardial mapping and ablation procedures were repeated. For the purposes of follow-up, a successful ablation was defined as termination of one or more IARTs, including the primary targeted circuit, during RF application, without the subsequent ability to reinduce those targeted arrhythmias using programmed stimulation.

Assessment of clinical activity. Because increased frequency of arrhythmia symptoms or the need for early arrhythmia intervention may affect both the quality of the patient's life and the perceived need for additional intervention, attempts were made to quantify the frequency of clinical events per patient-month before and after early, successful RF ablation. Review of medical records and procedure notes were used to ascertain the dates of occurrence of the following types of events: 1) electrocardiographically documented occurrence of IART; 2) cardioversion by countershock, pacing or intravenous drug therapy; and 3) emergency room visit or hospital admission for management of arrhythmia or diagnostic evaluation of symptoms of arrhythmia. Patients and/or their guardians and physicians were interviewed by telephone to ensure continuous clinical follow-up for all patients to within 3 months of closure of the study period in November 1996.

Statistical analysis. Statistical analysis was performed using STATA version 4.0 (Stata Corp.). Dates of clinical events were converted to time interval (months) before and after RF ablation of IART; if a second successful RF procedure was performed, follow-up was referenced to the more recent procedure. Time intervals were grouped in 12-month periods ranging from 48 months before the initial RF procedure until the most recent follow-up visit. Event frequency (events per patient-month) was determined to be the number of events occurring in a given period divided by the number of patient-months of exposure for the entire group in that period. Event frequency was compared between periods using Poisson regression for comparison of rates. Continuous data are presented as either mean $\pm$ SD or median (range), as appropriate.

Table 1. Anatomic Diagnoses and Surgical Procedures

Anatomic Diagnosis	Surgical Procedure	No. (%) of Patients
Single ventricle	Fontan	22 (49%)
TGA	Mustard/Senning	8 (18%)
TOF/VSD	VSD repair	8 (18%)
ASD	ASD repair	2 (4%)
Cardiomyopathy	None	2 (4%)
Unrepaired CHD	None	2 (4%)
Normal	None	1 (2%)

ASD = atrial septal defect; CHD = congenital heart disease; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; VSD = ventricular septal defect.

Comparison between data sets was performed using the Student t test for unpaired data for continuous variables and the Fisher exact test for categoric variables. Statistical significance was determined as $p < 0.05$. Intervals for rates were calculated for 95% confidence by the binomial exact technique.

Results

Patient characteristics. Forty-five patients (24.5 ± 10.5 years [range 7.9 to 44.8]) were catheterized 55 times between April 1993 and May 1996. Seven patients underwent one or two repeat ablations for IART at intervals ranging from 9 days to 34 months. The underlying congenital lesions and surgical palliations of these patients are presented in Table 1. The mean age at which definitive cardiac surgical palliation was performed was 10.4 ± 8.1 years (range 0.2 to 26.6), and the mean age at onset of tachycardia was 16.4 ± 9.3 years (range 1.6 to 42.6). Patients had had a median of five documented episodes of IART before the first attempt at RF ablation (range 1 to 40). Before a successful ablation, 22 of 33 patients had undergone a total of 45 trials of antiarrhythmic medication (mean number of trials 2.0 [range 1 to 7 medications per patient). Thirteen patients had had implantation of a pacing system with an atrial pacing lead, and five patients were programmed in AAIT mode.

Early results of RF ablation. Spontaneous or inducible IART was present in 43 of 45 patients, with a median of 2 (range 1 to 5) IART circuits identified in each patient. In 41 of these patients, attempts were made to ablate the IART, resulting in early termination of 58 IART circuits in 40 catheterizations of 33 patients. Summary data are presented in Table 2.

Early procedural complications. One patient in whom an IART circuit was successfully ablated on the lateral wall of the right atrium suffered prolonged paresis of the right hemidiaphragm, which was clinically silent and resolved after 3 months. A second patient had a renal infarction discovered 3 days after an ablation attempt that did not include catheterization of the left heart. This resolved without sequela and was presumed to be secondary to a thromboembolic event associated with cardioversion from atrial flutter to sinus rhythm at the end of

Table 2. Early Success of Radiofrequency Ablation for Intraatrial Reentrant Tachycardia in Study Group

|	Patients* (n = 45)	Catheterizations* (n = 55)	Circuits IART† (n = 111)
Spontaneous or induced IART	43 (96%)	53 (96%)	—
Attempted RF ablation of IART	41 (91%)	50 (91%)	79 (71%)
Successful RF termination of IART	33 (73%)	40 (73%)	58 (52%)

*Number (%) of patients. †Number (%) of circuits. RF = radiofrequency; IART = intraatrial reentrant tachycardia.

the ablation attempt. A third patient had femoral venous cannulation site hemorrhage 6 h after the procedure that required a 1-U blood transfusion.

Recurrence of IART after RF ablation. IART was documented electrocardiographically after 21 (53%) of 40 early, successful RF ablation procedures (confidence interval 36% to 69%) in 17 (52%) of 33 patients (confidence intervals 34% to 69%). Among patients with recurrence, the median time until first recurrence was 2.1 months (range 1 day to 18.1 months). Figure 1 presents a Kaplan-Meier analysis for survival free of documented IART after early, successful RF ablation in this patient group, and suggests that recurrence is most likely to occur in the first 6 months after the procedure, with an actuarial likelihood of freedom from documented arrhythmia at 3 years of ~40%.

Of the 17 patients with documented recurrence of IART, seven have undergone 10 additional attempts at RF ablation. All seven second attempts and none of the three third ablation attempts had early success. The configurations of the ablated IARTs in some cases indicated tachycardia mechanisms different from those previously ablated (Fig. 2). Ten patients have required reinstitution or an increase of antiarrhythmic agents, or both. Of the 16 patients without documented recurrence of IART, 14 are free of arrhythmia and 2 have had nonsustained palpitations suggesting undocumented transient recurrence.

Figure 1. Recurrence of documented IART. Kaplan-Meier survival curve presenting time to first documented IART recurrence in patients who underwent an early, successful RF ablation for IART. **Triangles** represent follow-up in patients free from documented recurrence at time of study closure.
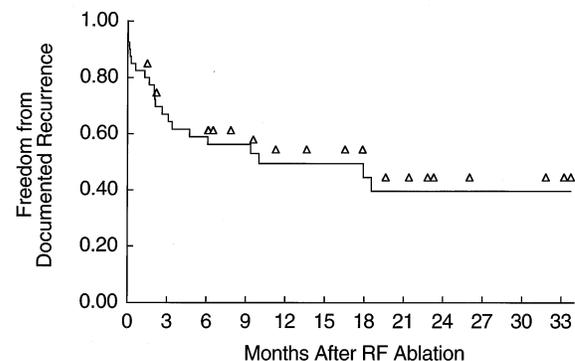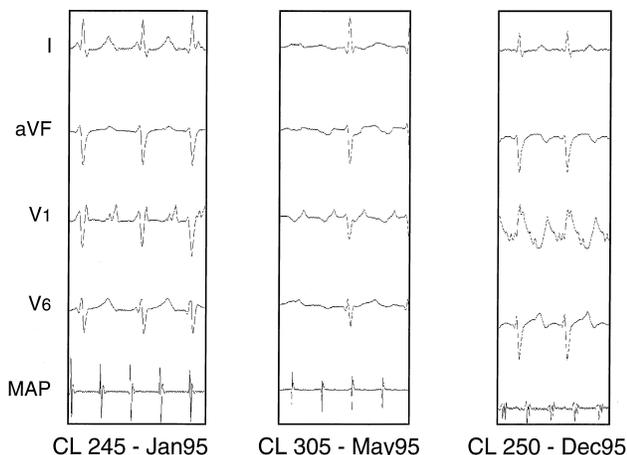
Figure 2. Multiple configurations of IART targeted in serial ablation attempts in one patient. CL = cycle length (ms); MAP = monophasic action potential.

Twelve receive no specific antiarrhythmic therapy and four are asymptomatic or have minimal symptoms on continued anti-arrhythmic therapy. On univariate analysis, frequency of prea-blation IART events was significantly increased in patients who had IART recurrence. Overall, the frequency of preablation cardioversions in patients who did not have a subsequent recurrence was 52% of that seen in patients who subsequently had a recurrence of IART (0.061 vs. 0.117 cardioversions per patient-month, p = 0.0005). Recurrence of IART was not predicted by type of operation, age at operation, age at RF ablation, total number of episodes of IART before ablation or number of IART circuits identified at the time of ablation.

Postprocedure deaths. Two patients, both with severe left ventricular dysfunction, died suddenly 11 and 1.5 months after RF ablation without documented recurrence of IART. The first of these patients had had multiple surgical procedures for palliation of severe aortic hypoplasia and subaortic stenosis, and continued to receive multiple antiarrhythmic medications after RF ablation for IART because of complex ventricular

ectopy and inducible sustained ventricular tachycardia. The second patient had severe dilated cardiomyopathy associated with iron overload and hemochromatosis.

Frequency of clinical arrhythmia events before and after RF ablation. Among patients who had an early, successful RF ablation, 26 of 33 had clinical records available for a period ≥48 months before RF ablation (mean duration of preablation clinical history 43.0 months). All patients had postablation follow-up of 17.4 ± 11.3 months from the most recent early, successful RF ablation (range 0.3 to 40.9 months, total posta-blation exposure 574 patient-months).

The effect of early, successful RF ablation on the frequency of cardioversions for IART per patient-month of observation is presented in Figure 3. The study group was divided into patients in whom a recurrence of documented IART is known to have occurred and those patients who had not had a recurrence. Compared with a baseline period 24 to 48 months before ablation, the frequency of cardioversion increased steadily during the 24 months before ablation in both groups, with a marked increase noted in the 12-month period before ablation. After ablation, the frequency of cardioversion in those patients with recurrence reverted to a level that was lower than that experience during the 24 months before ablation (0.072 vs. 0.181 cardioversions per patient-month, p = 0.0004) and slightly higher but not significantly different from that observed during the baseline period (0.072 vs. 0.050 cardioversions per patient-month, p = 0.347). Similarly, the frequencies of documented episodes of IART and of hospital visits also showed a pattern of significant increase during the 24 months before RF ablation. After RF ablation, the frequencies of both reverted to levels lower than those observed during the 24-month preablation period (0.124 vs. 0.224 episodes of documented IART per patient-month, p = 0.005; 0.113 vs. 0.216 hospital visits per patient-month, p = 0.003), but higher than those observed during the baseline period 24 to 48 months before ablation (0.124 vs. 0.053 episodes of docu-mented IART per patient-month, p = 0.004; 0.113 vs. 0.050 hospital visits per patient-month, p = 0.008).

Figure 3. Frequency of cardioversion of IART per patient-month of observation, before and after RF cath-eter ablation. Cardioversion was defined as direct cur-rent countershock, overdrive atrial pacing or parenteral drug therapy, or a combination of these. Data are separated into two columns for each period, separating patients who had a documented recurrence of IART after early, successful RF ablation (**dotted bars**) from those who did not (**open bars**). Before ablation, both groups experienced a steady increase in the frequency of cardioversion during the 2 years before RF ablation attempt(s). Overall preablation event frequency was higher in patients who subsequently experienced a re-currence. Among patients who had a recurrence, posta-blation event frequency was decreased in comparison to the 2-year period immediately before RF ablation (p = 0.0004). Postablation event frequency was slightly but not significantly higher than the frequency computed 3 to 4 years before ablation (p = 0.347).
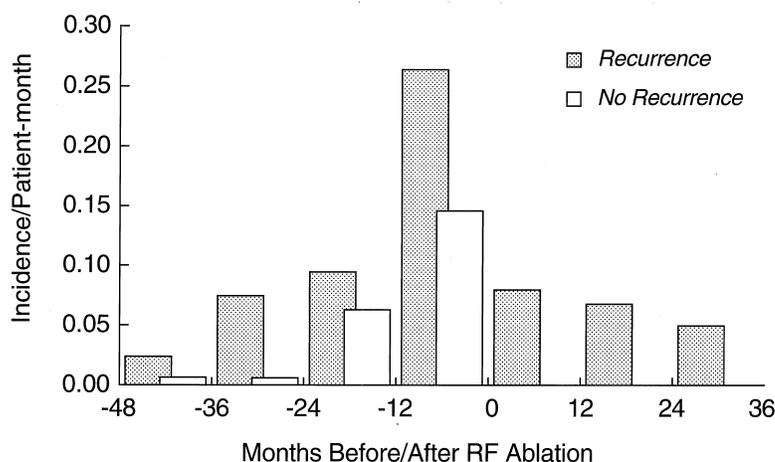
Discussion

The present study documents the intermediate-term results of RF ablation of IART in a group of patients with CHD. These results are set in the context of a retrospective review of clinical arrhythmia activity occurring in this patient group for the 48 month period preceding an RF ablation attempt, which revealed a steadily increasing frequency of clinical events associated with arrhythmia activity (i.e., cardioversion and arrhythmia-related hospital visits). Radiofrequency ablation was successfully used to terminate one or more IART circuits in 73% of patients brought to the catheterization laboratory with the intention to treat and in 81% of patients in whom an RF application was actually made. Over a mean follow-up period of nearly 18 months, IART recurred in 17 (53%) of the 33 patients who had an early, successful RF ablation. Recurrence was associated with a higher preablation frequency of clinical events and usually occurred within 6 months of early, successful RF ablation. The other 16 patients who had an early, successful RF ablation have been free of documented recurrence of their arrhythmia; this group constitutes 36% of the original study group of 45 patients. In addition, those patients who did have arrhythmia recurrence had improvement in their overall status in comparison to the 2-year period preceding ablation, as measured by clinical criteria of arrhythmia activity.

Pathogenesis of IART. Intraatrial reentrant tachycardia complicates the management of many patients with CHD during the late postoperative period, affecting a large and increasing percentage of survivors who have undergone a variety of commonly performed palliative surgical procedures (1,3,6,7). The frequency with which IART occurs in these patients, combined with the results of studies that have defined the experimental substrate needed to initiate and sustain atrial macroreentrant tachycardias in animals (19–21), suggest that surgical scarring, fibrosis and hypertrophy of the atrial myocardium are likely to be implicated in its pathogenesis. Studies of patients who have had the Fontan procedure, who are particularly prone to IART, have demonstrated a high incidence of sinus node dysfunction and prolonged intraatrial conduction (22,23). Barriers to conduction that underlie these prolonged atrial activation times have been demonstrated in patients with CHD and recurrent IART using high density mapping techniques (24). The concomitant finding of severe sinus node dysfunction in many of these patients and the apparently salutary role of antibradycardia pacing in some patients (12) suggests that bradycardia may also play an important role, or at least be an additional marker for likely occurrence of this arrhythmia. Although IART is not uniformly associated with hemodynamic deterioration and may be clinically asymptomatic, it has also been associated with an increased risk of thrombosis, congestive heart failure and death (8–10,25). It was not possible to determine whether the two deaths in the current study were related to undiagnosed recurrence of IART. However, their occurrence emphasizes the severity of global cardiac disease in this patient group.
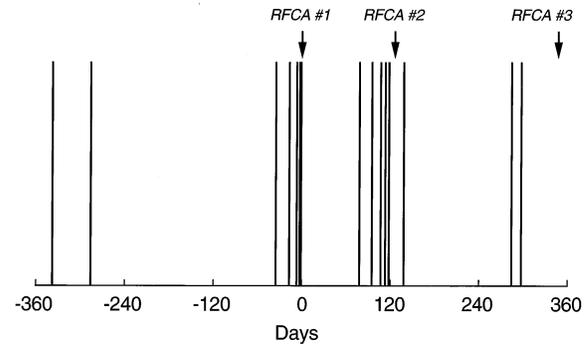

Figure 4. Documented IART episodes in one patient undergoing three serial RF ablations. In this patient, the first two RF ablations performed were successful early on at terminating the targeted IART circuits; the third attempt was unsuccessful. A steady increase in frequency of arrhythmia events is noted before each ablation attempt. **Arrows** indicate dates of ablation, and **vertical lines** the dates of documented IART. RFCA = radiofrequency catheter ablation.

Frequency and patterns of IART recurrence. Although the onset of IART has now been well documented (1–3,26), its natural history after the first occurrence has not been carefully studied. In the current study, the frequencies of clinical events attributable to IART increased significantly during the year before an attempt at RF ablation, with a smaller trend toward increased frequency noted in the 12 months before that. An example of this phenomenon is demonstrated in a single patient (Fig. 4). Although it stands to reason that the frequency of clinical arrhythmia events is likely to be greatest in any patient just before the time when a new therapeutic approach is proposed, the observation of a prolonged rise in such events extending back 12 to 24 months before the procedure strongly supports the anecdotal observation that clinical suppression of IART seems to become more difficult with time. The reason for this increase in frequency is not evident from these data, but may reflect continuing slow changes in those features of the atrial substrate thought to underlie this arrhythmia, such as fibrosis, hypertrophy and atrial enlargement, worsening severity of sinus node dysfunction or proarrhythmic effects of other attempted therapies.

Efficacy of therapies for IART. Studies have suggested that the efficacy of antiarrhythmic drug therapy (11,13) and atrial antibradycardia and antitachycardia pacing (12) are of value only in selected patients, and may be associated with the potential for lethal complications. Several recent reports have shown that RF ablation techniques can be used to terminate IART early on (14–16), but the patient groups have been small and follow-up duration relatively short. The current study suggests that, given the current techniques available for mapping IART circuits and applying radiofrequency lesions, the risk of recurrence is high, occurring after about half of early, successful ablations, with a mean time to recurrence of 4 to 5 months. Although there is no clear control group for patients in this study, Weindling et al. (11) identified an 80% arrhythmia recurrence rate after 2 years of medical therapy in a larger group of patients also managed at Children's Hospital. The

frequency of clinical events in the current study was significantly decreased when comparing immediate preablation and postablation periods. Although it is possible that this change reflects periodic spontaneous variations in IART frequency, it seems reasonable to interpret this as a real effect of the ablation procedure. Such a hypothesis is strongly supported by the patients in the study who have experienced complete or substantial regression of their IART symptoms after ablation.

Recurrence of IART with different configurations. It was often difficult to discern clear differences between IARTs encountered in serial catheterizations. In some cases, however, it was possible to document clearly the emergence of new IART configurations at recatheterization. The diversity of anatomic substrates that may support IART circuits has been demonstrated by ablation studies in which multiple IARTs are encountered and by the utilization of several distinct atrial sites as successful targets for ablation (14,15). More recently, this diversity has been visualized using high density endocardial mapping techniques (24). These data allow speculation that successful ablation of a dominant IART circuit in these arrhythmia-prone atria may allow the subsequent clinical emergence of new arrhythmia circuits that are critically dependent on other areas of the atrial myocardium. Possible proarrhythmic effects of the RF lesions themselves must also be considered. Thus, the techniques currently in use to target vulnerable sites for RF application in specific arrhythmia circuits may have to be modified to result in a more generalized modification of the atrial myocardial substrate, as has been proposed for the prophylaxis of atrial fibrillation (27,28).

Study limitations. Although the patients reported in this study have been prospectively followed since ablation, documentation of clinical events before ablation and the choice and timing of therapeutic interventions varied considerably between patients. For this reason, the clinical events for review were chosen to obtain the best available picture of the intensity of arrhythmia activity, as measured by events that were most likely to be well documented in the clinical record (cardioversions, hospital admissions). It is unlikely that clinical arrhythmia events, as defined for this study, have occurred without our knowledge during the follow-up period after ablation, but it is possible that the preablation history of clinical arrhythmia events was incomplete for some patients, which could have decreased our estimates of the frequency of preablation events. In some cases, multiple therapeutic failures or physician preference, or both, resulted in long periods of IART tolerated without a hospital visit or an attempt at cardioversion. Frequency of ECG documentation of IART was used as a proxy for arrhythmia intensity in these asymptomatic or minimally symptomatic patients; the results of that analysis were not different from the analyses of cardioversion or hospital visits.

An additional limitation of this study is the difficulty in ascertaining the identity of individual IART circuits electrocardiographically, because of slow cycle lengths favoring 1:1 conduction, low P wave amplitudes and unpredictable effects of previous ablation attempts and passive activation of atrial

tissue on P wave configuration. Although we were able to demonstrate that recurrent IART circuits clinically distinct from those ablated *could* occur (see Fig. 2), in the absence of careful intracardiac mapping, it was not possible to determine whether a given IART recurrence represented a new or previously targeted circuit. Thus, we cannot quantify the relative importance of inadequate ablation technique versus novel arrhythmogenesis in determining the frequency of recurrence.

Conclusions. Radiofrequency ablation is a useful adjunct for the treatment of IART in patients with CHD who are experiencing frequent arrhythmia recurrences. In this group, successful RF ablation resulted in good intermediate-term arrhythmia control in a subset of our study group and in an overall reduction in the frequency of clinical arrhythmia-related events observed and treated. However, early and late recurrence of IART occurred in more than half of the patients in whom the ablation procedure was deemed "successful" early on, and new IART circuits frequently presented themselves. Thus, this targeted RF ablation technique was more likely to be palliative than curative in this group. Although the electrophysiology of individual IART circuits indicates that they possess an excitable gap and are curable by targeted ablation of an anatomically relevant conductive isthmus, this pattern of recurrence suggests that a long-term cure or prophylaxis for this arrhythmia syndrome must address a more complex arrhythmia substrate that has the potential to support multiple such circuits.

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