

Angiographic Anatomy of the Inferior Right Atrial Isthmus in Patients With and Without History of Common Atrial Flutter

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Background—Although most ablative procedures undertaken for common atrial flutter target the inferior right atrial isthmus, comparative studies of the morphology of this area are lacking. Our study examines its angiographic anatomy, making correlations with postmortem specimens, to provide a better understanding of the anatomic substrate of this arrhythmia.

Methods and Results—The gross morphological features and dimensions of the area between the orifice of the inferior caval vein and the attachment of the septal leaflet of the tricuspid valve were determined from angiograms made in 23 patients with documented atrial flutter and 30 control subjects. For comparison, we studied 20 normal heart specimens. When viewed in right anterior oblique projection, 2 morphologically distinct areas were identified. In the specimens, the inferior isthmus measured a mean length of 30 ± 4 mm, not significantly different from the dimensions obtained from angiograms of control subjects. The mean length of the isthmus, however, was greater in patients with common atrial flutter than those without (37 ± 8 versus 28 ± 6 mm). Patients with atrial flutter and structural heart disease had an even longer isthmus than those with flutter alone (39.6 ± 8 versus 33 ± 7 mm). Compared with those without flutter, the atrial diameter was also larger in patients with flutter (57.6 ± 9 versus 48.5 ± 6 mm). Reevaluation carried out at follow-up 10 ± 2 months after ablation did not show any reduction in atrial size, although contractility improved.

Conclusions—The inferior isthmus and right atrium in patients with common atrial flutter were significantly larger than those in a control population. (*Circulation*. 1999;99:3017-3023.)

Key Words: atrial flutter ■ atrium ■ angiography ■ catheter ablation

Debate continues regarding the specific anatomic and functional substrates of atrial flutter (atrial fibrillation, AF). It is now accepted that so-called common or typical AF is the consequence of a macro-reentrant circuit constrained in the right atrium between 2 natural endocardial barriers. These are the AV junction on 1 side and the terminal crest, with its continuation into the eustachian ridge, on the other.¹⁻³ Maintenance of the reentrant circuit requires not only the presence of zones of slow conduction but also the functional block produced by natural obstacles or barriers.⁴⁻⁶ In patients with typical atrial flutter, previous electrophysiological studies^{7,8} suggested that the zone of slow conduction might be located in the inferior right atrial isthmus, the muscular atrial wall between the orifice of the inferior caval vein and the hinge of the tricuspid valve. Other recent studies^{6,9} have supported the concept that the eustachian ridge forms a further functional linear barrier to conduction, extending as it does from the

lateral margin of the inferior caval vein to the superior wall of the coronary sinus. Although the electrophysiological substrate has been widely studied in humans with AF, no close examination has been made of the anatomy of the isthmus area in patients with or without a history of AF. It is axiomatic that detailed knowledge of the anatomy of this area may help to clarify the mechanism and increase our understanding of the anatomic substrate for development of AF. In the present study, therefore, right atrial angiography was used to determine the gross morphology and dimensions of this area in patients with and without common AF. Results were compared with those obtained from normal heart specimens.

Methods

Heart Specimens

We examined 20 formalin-fixed hearts obtained from patients who died of noncardiac causes (14 men; mean age, 47 ± 13 years;

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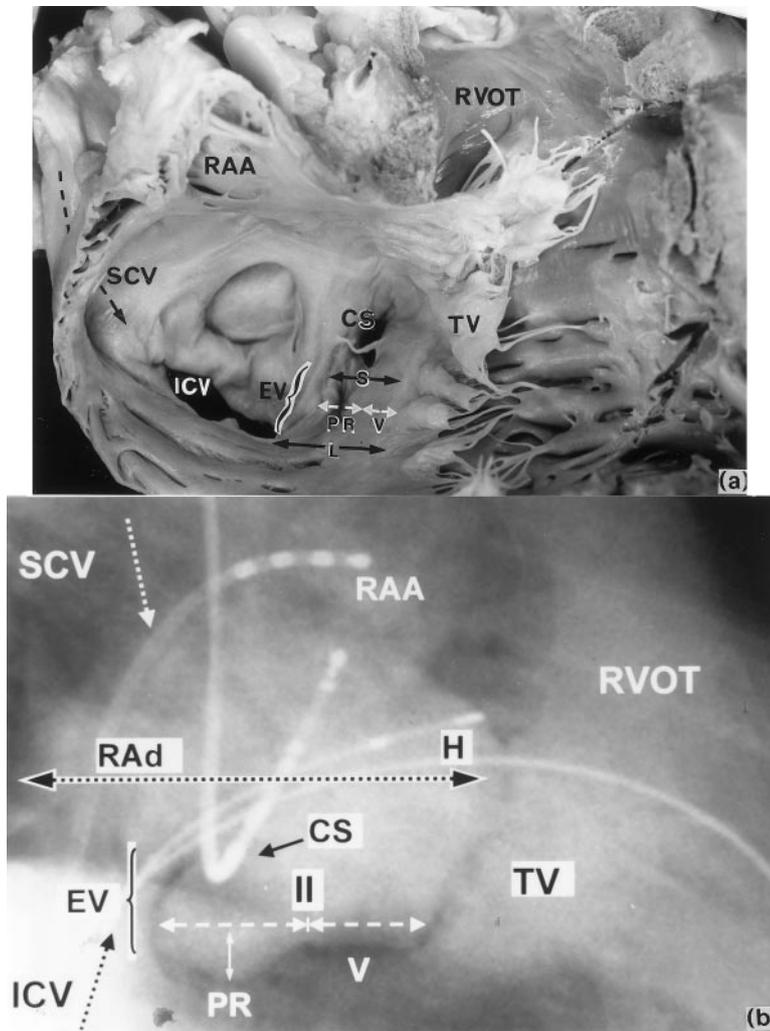


Figure 1. a, Heart specimen displayed in simulated RAO projection to show inferior isthmus, which comprises pouchlike recess (PR) and tricuspid vestibule (V). Black double arrows indicate shortest (S) and longest (L) distances between orifice of inferior caval vein (ICV) and hinge of tricuspid valve. Measurement for isthmus was taken along line of white arrows. b, Comparative right atrial angiogram in 45° RAO view of control subject. Inferior isthmus (II), eustachian valve (EV), and hinge of septal leaflet of tricuspid valve (TV) are visualized in 1 plane. Pouchlike area corresponds to inferior pouchlike recess; smooth area corresponds to vestibule of tricuspid valve (V) as observed in heart specimen. Dashed lines mark lengths of 2 components of inferior isthmus. CS indicates coronary sinus; H, His bundle catheter; RAA, right atrial appendage; RAd, right atrial diameter; RVOT, right ventricular outflow tract; and SCV, superior caval vein.

range, 40 to 53 years). The mean weight was 354 ± 67 g. The right atrium was dissected to display the area between the inferior caval vein and tricuspid valve in a simulated right anterior oblique (RAO) view. This area forms the inferior part of the right atrium and is inferior to the triangle of Koch. It is bounded anteriorly by the hinge of the septal leaflet of the tricuspid valve and posteriorly by the trabecular ramifications of the terminal crest. In an attempt to replicate the angiographic RAO view, the inferior isthmus was taken as a straight line between the hinge of the septal leaflet and a point at the insertion of the eustachian valve where the orifice of the inferior caval vein was largest as seen in profile. In this way, we avoided the shortest distance, nearest the septum, and the longest distance, which was more parietal (Figure 1). The length of the inferior isthmus was measured by placing a straight rule close to the endocardial surface, with care taken not to stretch the right atrium (Table 1). By cutting the heart along the line of the inferior isthmus, we could measure the width of the

smooth muscular vestibule extending between the trabeculated area and the hinge of the tricuspid valve (Figure 1). Each distance was measured 4 times in each heart, and the values were averaged. We also noted the maximal and minimal thicknesses of the atrial wall as profiled by the cut along the inferior isthmus.

Angiographic Studies

We enrolled 53 patients prospectively in the angiographic study. There were 23 patients (21 men; mean age, 59 ± 15 years; range, 26 to 75 years) seen consecutively with clinically documented typical AF who subsequently underwent successful radiofrequency ablation and 30 control subjects (16 men; mean age, 50 ± 14 years; range, 22 to 70 years). Requirements for inclusion as a control were absence of any history of AF, inability to induce this arrhythmia at electrophysiological study, and absence of structural heart disease.

In those with flutter, it had been recurrent for a mean of 8 years (range, 2 to 18 years) despite treatment with several antiarrhythmic agents (mean, 3 ± 1). Structural heart disease was present in 12 patients (coronary arterial disease in 7, dilated cardiomyopathy in 4, and surgically repaired atrial septal defect in 1). Atrial flutter was permanent in 16 patients and paroxysmal in 7 patients.

Before every procedure, detailed information was given to all patients and control subjects, and written consent was obtained for the procedures. Angiographic and electrophysiological studies were performed at a single session.

Of the 23 patients with AF, 19 were reinvestigated with electrophysiological and angiographic studies, again at a single session, 6 to 12 months (mean, 10 ± 2 months) after their therapeutic ablation.

TABLE 1. Inferior Isthmus in the 3 Study Groups

	Postmortem Hearts (n=20)	Control Subjects (n=30)	Patients With Atrial Flutter (n=23)
Inferior isthmus	30 ± 4 (19–40)	28 ± 6 (17–38)	37 ± 8 (21–49)
Vestibule	12 ± 5 (8–15)	13 ± 4 (6–22)	17 ± 5 (9–30)
Inferior recess	17 ± 2 (9–23)	15 ± 4 (7–22)	20 ± 7 (12–31)

Values are length expressed as mean \pm SD (range) in millimeters.

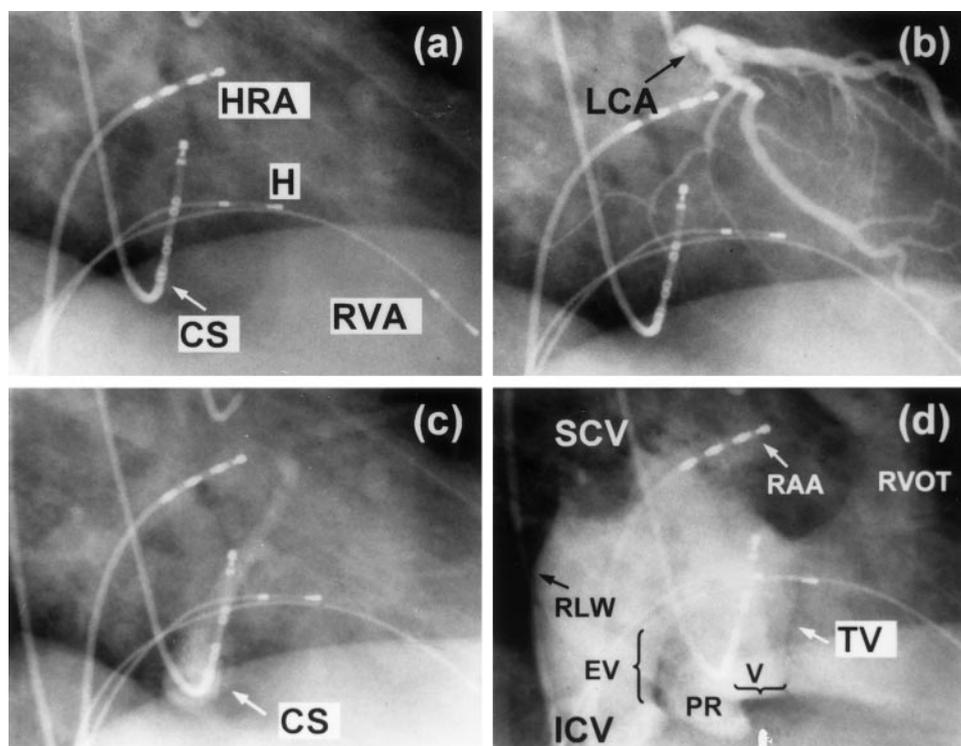


Figure 2. Four frames of fluoroangiographic images obtained from right atrial angiography and venous phase of left coronary arteriography performed in same study in control subject. Serial angiograms are in RAO projection. a, Fluoroscopic positions of catheters in high right atrium (HRA), coronary sinus (CS), His bundle recording site (H), and right ventricular apex (RVA). b, Angiographic display of left coronary artery (LCA). c, Coronary sinus venogram achieved during venous phase of arteriogram. d, Right atrial angiogram obtained by means of manual injections of contrast into inferior caval vein (ICV). Inferior isthmus profiled on angiograms at end-systolic phase is bordered by eustachian valve (EV) and septal leaflet of tricuspid valve (TV). Note pouchlike recess (PR) anterior to eustachian valve and inferior to orifice of coronary sinus and smooth vestibule (V) between pouch and tricuspid valvar annulus. RAA indicates right atrial appendage; RLW, right lateral wall; RVOT, right ventricular outflow tract; and SCV, superior caval vein.

During follow-up, all 19 patients were in sinus rhythm without any episodes of AF. Of the remaining 4 patients, 2 had atrial fibrillation, and the other 2 declined to be reevaluated.

Angiographic Techniques and Methodology

Thirty minutes after the electrophysiological procedure, we performed right atrial angiography and coronary arteriography in all patients in sinus rhythm. Contrast was injected into the right atrium at the moment when the venous phase of coronary arteriography was visualized (Figure 2). This allowed the isthmus and the orifice of the coronary sinus to be displayed simultaneously.

Right atrial angiography was performed through an 8F sheath, 40 cm long, inserted into the internal femoral vein. Right atrial angiograms were obtained by means of manual injection of 20 mL of nonionic contrast (Hexabrix) into the inferior caval vein.

Coronary arteriography was performed with conventional 5F catheters. Filming was prolonged to visualize the coronary venous phase. Angiographic studies were filmed in the 45° RAO view and recorded on 35-mm cine film. From film records, 2 observers later performed blind qualitative and quantitative analyses using static atrial end-systolic and end-diastolic frames of the right atrial angiograms and ventricular end-systolic frames of the coronary arteriography.

Reevaluation by use of right atrial angiography (as above) was carried out in 19 patients 6 to 12 months after therapeutic ablation for AF with the same 45° RAO views as before.

Angiographic Analysis and Measurement of the Right Atrial Isthmus

From the right atrial angiograms, it was possible to visualize the inferior and superior caval veins, right lateral wall, eustachian

valve, area inferior to the triangle of Koch, and vestibule of the tricuspid valve (Figure 1). The inferior isthmus was profiled as the area between the eustachian valve and the hinge of the septal leaflet of the tricuspid valve. We were able to distinguish 2 components: a pouchlike area inferior and posterior to the orifice of the coronary sinus and a smooth area between the pouch and the tricuspid annulus. Selecting the frames with the largest linear dimension of the inferior isthmus, we measured both components. Depth of the pouchlike area was measured as the distance from the inferior margin of the mouth of the coronary sinus to the lowest part of the pouch. We correlated these dimensions with the diameter of the right atrium, which was obtained in the RAO view by measurement of the distance between the lateral atrial wall and the tricuspid valvar annulus. All measurements were corrected for degrees of magnification of the angiographic image by relation of the diameter of the catheter in each projection to its true diameter.

We further compared the dimensions of the right atrium and the inferior isthmus in patients with AF as obtained in sinus rhythm 30 minutes after the ablation procedure with the dimensions at reevaluation (10 ± 2 months after ablation). We also evaluated changes in the contractility of the right atrium on both occasions by estimating the contraction fraction (CF) of the right atrium using the ratio $CF = (EDA - ESA) / EDA$, where EDA is atrial end diastole and ESA is atrial end systole. For each patient, frames in RAO projection were selected for measurement of end-diastolic and end-systolic areas of the right atrium by digital planimetry. These frames showed the largest and smallest areas at atrial end diastole and end systole, respectively. The same method was used to obtain right atrial areas in the control group.

Statistical Analysis

Measurements were expressed as mean \pm SD (range) (Tables 1 and 2). Data concerning postmortem specimens, control subjects, and

TABLE 2. Patients With Atrial Flutter and Without Structural Heart Disease Compared With Patients With Atrial Flutter and Structural Heart Disease

	AF, No SHD (n=11)	AF With SHD (n=12)
Right atrium	56±7 (40–63)	59±10 (43–77)
Inferior isthmus	33±7 (21–44)	39.6±10 (27–49)
Vestibule	14±3 (9–19)	19±6 (14–30)
Inferior recess	19±5 (14–28)	20±5 (14–31)

SHD indicates structural heart disease. Values are length expressed as mean±SD (range) in millimeters.

patients with AF were compared by use of unpaired and paired *t* tests. Correlations between quantitative variables were performed by standard linear regression studies. A value of $P<0.05$ was considered not due to chance.

Results

Gross Morphological Features of the Inferior Isthmus

The inferior isthmus corresponded to an imaginary line (or band) that stretched from the attachment of the eustachian valve posteriorly to the hinge of the septal leaflet of the tricuspid valve anteriorly (Figure 1). This line, when traced on heart specimens, followed the contours of the endocardial surface, although the dimensions were measured linearly. From the eustachian valve, the line first passed anteriorly through an area that usually is membranous and lacking in atrial musculature. We have previously described this area as the posterior component of 3 morphological sectors within the isthmus.¹⁰ The second component was usually trabeculated. The third component, located anteriorly, was the smooth vestibule of the tricuspid valve. When heart specimens were cut along the line, producing a profile of the inferior wall of the right atrium, the contour of the endocardial surface was fairly constant. The posterior and middle sectors, when taken together, formed a pouchlike inferior recess. Irregular trabeculations of various thicknesses (0.2 to 6 mm from subepicardium to endocardium) separated by thinner areas of myocardium or membrane lined the anterior extent of the pouch. The smooth vestibule, in contrast, was made up of a thin layer of myocardium (0.5 to 5 mm from subepicardium to endocardium) that had a relatively homogenous gross appearance.

Dimensions of the Isthmus: Angiographic and Anatomic Comparisons

The overall angiographic features of the isthmus were similar, with a pouchlike area and a smooth area distinguishable in all patients. The pouchlike area corresponded to the posterior sector combined with the middle sector; the smooth area corresponded to the vestibule of the tricuspid valve as observed in the heart specimens (Figure 1). The mean angiographic lengths of the inferior isthmus and its 2 components in the control group and patients with AF compared with the corresponding measurements obtained from the heart specimens are listed in Table 1.

Compared with heart specimens, no significant differences were found in the overall lengths obtained from angiograms of patients without flutter. Furthermore, anatomic dimensions of the inferior recess and vestibule of the tricuspid valve were comparable (Table 1). In both groups, control and postmortem hearts, there were no significant differences between measurements obtained from women and men. The angiographic dimensions of the right atrium in the RAO view correlated with the dimensions of the inferior isthmus ($r=0.68$, $P<0.005$). Age and body surface area were unrelated to these measurements. In the specimens, a weak correlation existed between length of the inferior isthmus and heart weight ($r=0.56$, $P<0.05$).

Right atrial angiograms showed larger linear dimensions of the right atrium (57.6 ± 9 mm; range, 35 to 63 mm) in patients with AF than in control subjects (48.5 ± 6 mm; range, 40 to 77 mm; $P<0.001$). The mean CF of the right atrium in patients with AF during sinus rhythm when measured 30 minutes after ablation was 0.23 ± 0.06 compared with 0.51 ± 0.1 in control subjects. We also noted a slower “washout” of contrast in these patients at that time. This indicated decreased blood flow from the right atrium, presumably because of its larger dimensions and lesser compliance. This phenomenon of slower washout was not seen at follow-up.

The mean length of the isthmus and its 2 components was significantly larger in patients with than in those without common AF ($P<0.001$; Table 1). Representative angiograms demonstrating the differences between the 2 groups are shown in Figure 3. The mean depth of the pouchlike area showed a wide range in its measurements (0.5 to 8 mm), but no significant differences were found between groups. There was no correlation between measurements of the inferior isthmus and time of onset of symptoms. Nonetheless, the inferior isthmus was larger in the 16 patients with clinically incessant atrial flutter (38.7 ± 9 mm) than in those whose episodes of flutter were paroxysmal (32.5 ± 6 mm; $P<0.05$). Furthermore, although no significant differences were found in right atrial dimensions (56.7 ± 8 versus 58 ± 10 mm, respectively), the mean CF was smaller in patients with incessant compared with paroxysmal episodes of flutter (0.18 ± 0.04 versus 0.27 ± 0.06). In the 12 patients with structural heart disease, the dimensions of the inferior isthmus were greater compared with patients with flutter but no structural heart disease ($P<0.005$; Table 2). These differences in isthmus measurements were due to a wider vestibule of the tricuspid valve ($P<0.05$). When we compared the angiographic features and dimensions of the inferior isthmus in patients without structural heart disease with the control group, we found that the inferior recess was larger in patients with atrial flutter ($P<0.05$), resulting in a longer inferior isthmus ($P<0.05$).

There were no significant differences in overall dimensions of the right atrium and inferior isthmus in patients with atrial flutter measured in sinus rhythm after ablation and at reevaluation 10 ± 2 months later. We found that the mean right atrial function estimated by use of the CF of the right atrium, however, improved significantly ($P<0.001$).

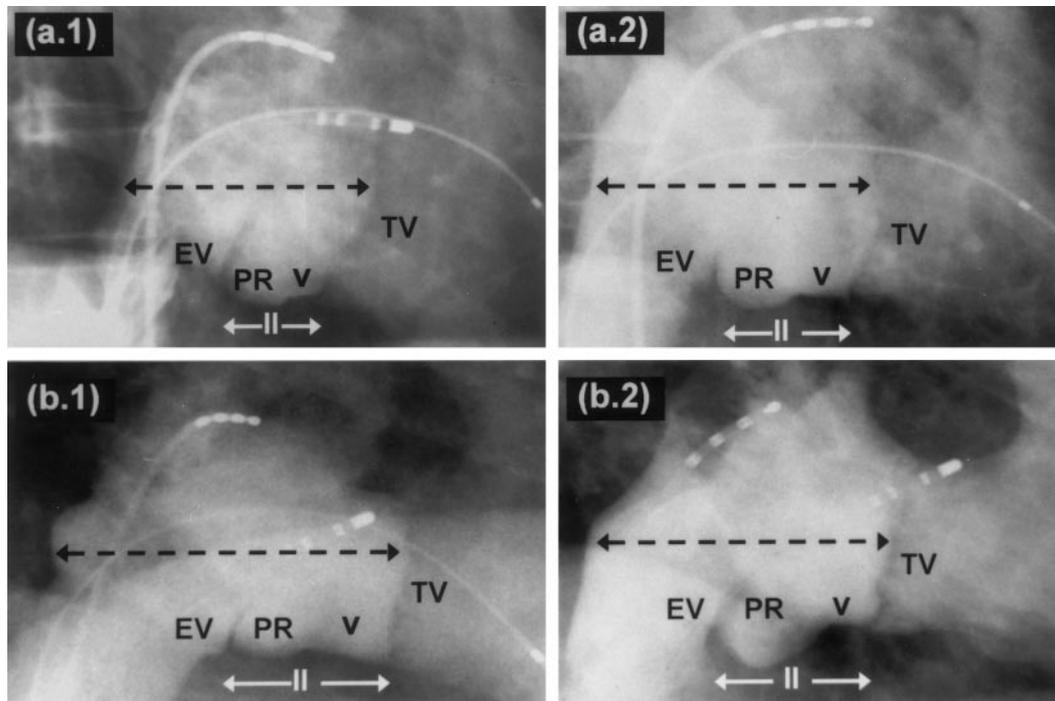


Figure 3. Comparative right atrial angiograms in RAO projection of (a) 2 control subjects and (b) 2 patients with common AF. Note inferior isthmus (II) and right atrium (dashed line) are larger in patients with common AF. a.1, Angiogram shows small inferior isthmus in patient without AF. Measurements of inferior isthmus and vestibule (V) of tricuspid valve (TV) are 19 and 6.5 mm, respectively. b.1, Note larger vestibule (19 mm) of tricuspid valve in patient with common AF and coronary arterial disease compared with another patient from control group (a.2) whose overall isthmus length is 26 mm with vestibule measuring 9.7 mm. b.2, Patient with AF not accompanied by structural heart disease. Pouchlike recess (PR) measures 22.5 mm, resulting in larger dimension of inferior isthmus (32 mm) vs normal. EV indicates eustachian valve.

at follow-up (0.23 ± 0.06 versus 0.53 ± 0.1). The mean CF at reevaluation of patients with previous AF was found to be similar to that previously obtained in the control subjects (0.51 ± 0.1), suggesting a recovery of atrial function.

Discussion

Although right atrial architecture is known to be crucial to the development and maintenance of the circuit for typical AF,⁴⁻⁹ the specific anatomic and functional substrates remain controversial. Slow conduction in the area bounded by the tricuspid valve and inferior caval vein seems to be mechanistically important,^{11,12} the more so since ablative lesions placed in this isthmic area by means of radiofrequency energy have proved to be effective in interrupting the circuit.^{13,14} Although global enlargement of the right atrium in the setting of AF is recognized, our study describes, for the first time as far as we are aware, the gross morphological features and dimensions of the isthmus as seen on angiography in patients with and without typical AF. This study also compares the size and mode of contraction of the right atrium in sinus rhythm immediately after successful ablation and at later follow-up, providing new information on atrial behavior during these periods.

Usefulness of Right Atrial Angiography in the Study of the Inferior Isthmus

Interpretation of cardiac anatomy derived from fluoroscopic examination during an electrophysiological proce-

dures has previously been abstract because the electrophysiologist had to imagine the anatomic landmarks from such weak references as the cardiac shadow and catheter position. Angiographic techniques, when used in the electrophysiological environment, have proved useful in identifying coronary venous anomalies during ablation of epicardial accessory pathways¹⁵ and in elucidating the anatomy of the triangle of Koch and right AV junction.¹⁶ In our study, we sought to overcome the limitations of previous investigations that studied the anatomy of the low right atrium area without the benefit of angiographic contrast. Simple fluoroscopy does not define the orifices of the inferior caval vein and tricuspid valve. Angiography, in contrast, has enabled us to visualize structures such as the eustachian valve, coronary sinus, caval veins, and tricuspid valve, as well as other cardiac structures not seen on conventional fluoroscopy as used in the electrophysiology laboratory. Our study also produced excellent correlation between isthmus measurements made during life and at postmortem examination, thus establishing the validity of the technique.

Interest is now increasingly focused on the anatomic substrates of the different arrhythmias. Several nonfluoroscopic and computer-based techniques have been introduced recently to visualize the cardiac anatomy.^{3,17,18} No systematic investigations, however, have been made of the dimensions of the inferior isthmus with these procedures. With widely used fluoroscopic projections, our results

will, we hope, improve understanding of this critical area of the so-called low right atrium during ablation procedures. They will provide a yardstick for future investigations that use electroanatomic mapping techniques, when it may prove possible to distinguish the different morphological components of the isthmus.

Anatomic Determinants for the Development of Atrial Flutter

Even though our anatomic findings in the normal heart may provide a clue to the potential substrate for areas of slow conduction essential for reentry, questions still remain as to the precise mechanism for the development of common AF and the reason why flutter does not develop in every human heart. It has been reported recently^{12,13} that conduction velocity in the isthmus during pacing in sinus rhythm was slower in patients with typical AF compared with those without any history of AF, further stressing the necessity to investigate the anatomy and dimensions of this crucial area. Our study shows that the overall dimensions of the right atrium and inferior isthmus are larger in patients with AF compared with the control population. The relationship between right atrial enlargement and atrial arrhythmias has been previously shown in animal models and experimental studies.^{19–21} Atrial enlargement, presumably caused by stretching, with resultant thinning of the musculature may provide the potential anatomical substrate for the recognized areas of slow conduction.⁵ The cause of the enlargement has not been investigated. In patients with structural heart disease, it is reasonable to suggest that the right atrium may be involved, resulting in atrial disease. We have shown that even in patients with AF but without structural heart disease, the inferior isthmus is longer compared with control subjects. Although the relationship between atrial enlargement and AF is evident, it is still unclear whether AF results in atrial tachycardiomyopathy, leading to larger right atrial dimensions or conversely whether previous atrial enlargement predisposes to the development of flutter. Restoration of normal sinus rhythm after ablation in patients with chronic AF and cardiomyopathy has been shown to result in substantially improved left ventricular function.²² But the effect of restoration of sinus rhythm on right atrial function has not been examined. We found that right atrial dimensions in patients with a history of AF were similar in sinus rhythm immediately after ablation and at reevaluation. It remains to be shown with longer follow-up whether the atrium will reduce in size or whether AF will recur in the setting of persistent atrial enlargement. Persistence of an enlarged right atrium but with normal contractility after ablation suggests that a previously dilated right atrium might contribute to AF. It may, of course, also simply be a residual feature. It is the enlargement of the isthmus, particularly its inferior recess, that we believe may set the scene for development of common AF.

A further finding in our study is that a recovery time is needed after ablation to achieve contractility that is comparable to the normal heart. A serial study is required to

determine the minimum time needed, because “recovery” was found in all our patients by the time of reevaluation.

Study Limitations

When correlating anatomic with angiographic measurements, we used 2 different populations because no data were available for patients undergoing both postmortem examination and previous angiographic study. In consideration of prolonged exposure to radiation, our analysis was limited to the dimensions of the inferior isthmus by use of a single, and standard, RAO projection. In estimating the contractility of the right atrium, we used area measurements to avoid assumptions on atrial geometry. The CF thus calculated is a useful, albeit crude, indicator of atrial function.

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