

Factors associated with early atrial fibrillation after ablation of common atrial flutter

A single centre prospective study

A. Da Costa, C. Romeyer, S. Mourrot, M. Messier, A. Cerisier, E. Faure and K. Isaz

Division of Cardiology, University Jean Monnet of Saint-Etienne, Saint-Etienne, France

Background The occurrence of early atrial fibrillation (≤ 6 months) after ablation of common atrial flutter is of clinical significance. Variables predicting this evolution in ablated patients without a previous atrial fibrillation history have not been fully investigated.

Objectives The aim of the present study was: (1) to identify predictive factors of early atrial fibrillation (≤ 6 months) in the overall population following atrial flutter catheter ablation; (2) to identify predictive variables of early atrial fibrillation following (≤ 6 months) atrial flutter catheter ablation within a subgroup of patients without documented prior atrial fibrillation.

Methods This study prospectively included 96 consecutive patients (age 65 ± 13 years; 18 women) over a 12-month period. Their counterclockwise flutter was ablated by radiofrequency, by the same operator, with an 8-mm-tip catheter. Clinical, electrophysiological and echocardiographic data were collected and 27 variables were retained for analysis: age; gender; type of atrial flutter (permanent vs paroxysmal); symptom duration (months \pm SD); pre-ablation history of atrial fibrillation; structural heart disease; left ventricular ejection fraction (%); left atrial size (mm); cava–tricuspid isthmus dimension; septal isthmus dimension; systolic pulmonary pressure $>$ or ≤ 30 mmHg; right atrial area; left atrial area; isthmus block; number of radiofrequency applications (\pm SD); antiarrhythmic drugs at discharge; left ventricular diastolic diameter; left ventricular systolic diameter; left ventricular telediastolic volume; left ventricular telesystolic volume; A-wave velocity ($\text{cm} \cdot \text{s}^{-1}$); E-wave velocity ($\text{cm} \cdot \text{s}^{-1}$); E/A; isovolumetric relaxation time; E-wave deceleration

time; significant mitral regurgitation and flutter cycle length (ms).

Results Of the 96 consecutive ablated patients, early atrial fibrillation was documented in 16 patients (17%). Atrial fibrillation occurred 30 ± 46 days (range 1 to 171 days) after ablation. Univariate analysis associated an early occurrence of atrial fibrillation with: atrial fibrillation history, left ventricular ejection fraction, left atrial size, left ventricular telesystolic volume, A-wave velocity, significant mitral regurgitation and flutter cycle length. Multivariate analysis using a Cox model found that the only independent predictors of early atrial fibrillation were left ventricular ejection fraction and pre-ablation history of atrial fibrillation. In the subgroup without prior atrial fibrillation history ($n=63$; 66%), the only independent predictor of early atrial fibrillation was the presence of a significant mitral regurgitation.

Conclusions In a subgroup of patients without atrial fibrillation history, 8% of patients revealed an early atrial fibrillation. Mitral regurgitation is a strong predictive factor of early atrial fibrillation occurrence with 80% sensitivity, 78% specificity and 98% negative predictive value. These data should be considered in post-ablation management. (Eur Heart J 2002; 23: 498–506, doi:10.1053/euhj.2001.2819) © 2001 The European Society of Cardiology

Key Words: Atrial flutter, atrial fibrillation, electrophysiology, catheter ablation.

See page 441, doi: 10.1053/euhj.2001.2912 for the Editorial comment on this article

Revision submitted 20 April 2001, accepted 13 June 2001, and published online 19 September 2001.

Correspondence: Dr Da Costa, Service de Cardiologie, Hôpital Nord, Centre Hospitalier Universitaire de Saint-Etienne, 42 055 Saint-Etienne Cedex 2, France.

Introduction

Debate continues regarding the optimal approach for atrial flutter treatment, and it is now accepted that common or typical atrial flutter is the consequence of a macro-reentrant circuit constrained in the right atrium between two natural endocardial barriers^[1,2]. Radiofrequency catheter ablation of the inferior vena cava–tricuspid isthmus is the treatment of choice when considering its high efficacy. One controlled study with medication addressing atrial flutter exists to date^[3]. With the high peri-ablation success rate, the early and long-term management of patients undergoing this procedure now needs to be determined^[4]. Recently, Gilligan and colleagues showed that all patients with a history of atrial fibrillation required antiarrhythmic drugs or anticoagulant therapy following a successful radiofrequency catheter ablation procedure^[4]. Other studies have investigated factors predictive of atrial fibrillation occurrence and a group at high risk of early atrial fibrillation have been identified^[5–9]. It seems that pre-existing left ventricular dysfunction and electrophysiological substrate determine atrial fibrillation occurrence, but these studies included all patients with and without a history of atrial fibrillation^[5–9]. Echocardiographic parameters such as right atrial anatomy were not fully investigated^[7]. The aim of the present study was: (1) to identify factors predictive of early atrial fibrillation (≤ 6 months) in the overall population following atrial flutter catheter ablation; (2) to identify variables predictive of early atrial fibrillation following (≤ 6 months) atrial flutter catheter ablation within a subgroup of patients without documented prior atrial fibrillation.

Methods

Study population

From June 1999 to June 2000, 96 consecutive symptomatic patients with common counterclockwise atrial flutter were referred for catheter ablation and prospectively included in this study. Typical atrial flutter was diagnosed when the surface ECG showed flutter waves that were predominantly negative in leads II, III, aVF and positive in lead V₁, with a regular atrial rate between 240 and 340 beats \cdot min⁻¹. The intracardiac electrogram illustrated the following activation sequence: high right atrium then low right atrium, a counterclockwise inferior vena cava–tricuspid isthmus activation sequence followed by left atrial activation. The overall population included 78 men (81%) and 18 women (19%) (mean age of 65.5–13 years, range 21 to 90 years). Sixty-seven patients had chronic flutter (69.8%) and 29 patients had paroxysmal flutter (30.2%).

Electrophysiological testing and inferior vena cava–tricuspid isthmus mapping

Patients signed an informed consent, then stopped all antiarrhythmic drugs for at least five half-lives (with the

exception of amiodarone), and fasted to undergo an electrophysiological study. Two catheters were introduced through the right femoral vein into the right atrium. A 6-F quadripolar catheter with an inter-electrode distance of 5 mm (Bard Electrophysiology, Tewksbury, MA, U.S.A.) was advanced to the His-bundle position then a dodecapolar catheter with a 5-mm bipolar separation (Bard Electrophysiology, Tewksbury, MA, U.S.A.) was positioned in the coronary sinus. The distal tip was placed in the coronary sinus ostium for electrodes 1,2 (H1). Electrodes 3,4 (H2), 5,6 (H3), 7,8 (H4) were located close to the inferior vena cava–tricuspid isthmus, while electrodes 9,10 (H5), 11–12 (H6) recorded the low and high right atrial activations, respectively. An 8-F quadripolar deflectable catheter with an 8-mm tip electrode (Boston EP technologies, San Jose, U.S.A.) was used for the cava–tricuspid isthmus ablation. Surface ECGs (leads I, II, III and V₁) were filtered through a 1 to 500 Hz bandpass filter, while bipolar intracardiac electrograms were filtered at 30 to 500 Hz and amplified at high gain (0.1 mV \cdot cm⁻²). These were simultaneously recorded with the 12-lead surface ECG at paper speeds of 200 mm \cdot s⁻¹ and stored digitally with a polygraph (Cardiolab system, Prucka Engineering). All measurements were performed with the Cardiolab system. A programmable stimulator (Cardiostimulateur Medtronic, France) with a 2-ms output pulse width set at four times the threshold amplitude was used. Descending lateral, ascending septal right atrial activation, and lateral to medial isthmus activation during counterclockwise atrial flutter were confirmed by sequential mapping. A radiofrequency current (unmodulated, sine wave) was delivered in the unipolar mode between the distal ablation catheter tip and a cutaneous patch electrode, placed over the left scapula with a maximal target temperature of 60° for 60 s. Radiofrequency delivery by the same operator (A.D.C.) was applied point by point until a block could be obtained. For all measurements, the filter was set from 30 to 500 Hz. The end-point of the procedure was the achievement of a complete bi-directional isthmus block according to the method reported in detail in the landmark study by Poty *et al.*^[10] using activation mapping. A complete cava–tricuspid isthmus map with a 12-pole mapping catheter, according to Chen *et al.*, was used^[11]. Atrial flutter induction was attempted with proximal coronary burst pacing at cycle lengths as short as 180 ms at the end of the procedure. Thirty minutes after the bi-directional block was obtained, all patients underwent a post-ablation control.

Echocardiographic measurements

Transthoracic Doppler Echocardiography was performed within 24 h of the radiofrequency ablation procedure by one observer (S.M.) blinded to the patient's electrophysiological status. Ultrasound studies were performed with a Hewlett-Packard Sonos 1000 imaging system using a 2.5-MHz transducer. M-mode

measurements were made according to the recommendations of the American Society of Echocardiography^[12]. Left ventricular systolic function was evaluated on two-dimensional echocardiographic imaging of the left ventricle. Left ventricular volumes and ejection fraction were calculated by planimetry in the apical two- and four-chamber views with the modified Simpson rule^[13]. Left atrial long axis, short axis and area were obtained by planimetry of the atrial inner borders with maximized atrial chamber size at end-systole in the four- and two-chamber views^[14]. The pressure gradient between the right ventricle and right atrium during systole was measured using the simplified Bernoulli equation^[14]. Peak systolic pulmonary pressure was calculated from the sum of the gradient with the right atrial systolic pressure, estimated from inferior vena caval diameter and dynamics during respiration^[15]. All two-dimensional echocardiographic and Doppler-derived pulmonary pressure measurements were averaged over five cardiac cycles. Mitral regurgitation was assessed by traditional echocardiographic markers^[16–18]. Mitral regurgitation was considered significant when the graduation was \geq II+.

Right atrium anatomical two-dimensional echocardiographic measurements

Two-dimensional echocardiographic measurements of right atrium were obtained in the four-chamber apical view with the largest right atrial size visualized at the end of ventricular systole^[19]. The right atrial long axis was measured from the junction of the tricuspid valve and the interventricular septum to the roof of the right atrium. The right atrial short axis was measured as the maximum distance between the inner borders of the inter-atrial septum and the free wall of the right atrium. Right atrial surface area was estimated by planimetry. The septal isthmus length was measured as the distance between the junction of the tricuspid septal leaflet with the interventricular septum and the coronary sinus ostium, in a slightly modified four chamber projection. From the classic four-chamber view, slight posterior adjustments in the transducer orientation visualized the origin of the coronary ostium. The inferior vena cava–tricuspid isthmus length was measured as the distance from the lateral border of the tricuspid annulus to the inferior vena cava origin, in the subxiphoid view.

Reproducibility of two-dimensional measurements

The statistical validity of echocardiographic measurements was established for intra-observer and inter-observer data on: right atrium dimensions, inferior vena cava–tricuspid isthmus and septal isthmus lengths. These are analysed in 22 and 20 randomly selected patients, respectively, using the Bland-Altman agreement test^[20].

Follow-up

After catheter ablation, all patients underwent continuous ECG monitoring for at least 24 h before hospital discharge. Outpatient follow-up and electrocardiograms were programmed at 6 months and on recurring symptoms or palpitations.

Statistical analysis

Data are expressed as mean \pm SD. The differences among groups were analysed by ANOVA. A probability value of $P < 0.05$ was accepted as statistically significant. Univariate analysis assessed whether clinical, ECG variables or left ventricular ejection fraction predicted early atrial fibrillation. Univariate analysis was considered significant with a P -value below 0.05. Log rank survival tests determined statistically significant ($P < 0.05$) differences of categorical variables. Twenty seven variables, including anatomical right atrial data, were tested in the initial model: age; gender; the type of atrial flutter (incessant vs paroxysmal); symptom duration (months \pm SD); history of atrial fibrillation; structural heart disease (+ or –); left ventricular ejection fraction (%); left atrial size (mm); cava–tricuspid isthmus dimension (mm); septal isthmus dimension (mm); systolic pulmonary pressure $>$ or \leq 30 mmHg; right atrial area (cm²); left atrial surface area (cm²); isthmus block; number of radiofrequency applications (\pm SD); left ventricular diastolic diameter (mm); left ventricular systolic diameter (mm); left ventricular telediastolic volume; left ventricular telesystolic volume; A-wave velocity (cm \cdot s⁻¹); E-wave velocity (cm \cdot s⁻¹); E/A; E-wave deceleration time (ms); isovolumetric relaxation time (ms); mitral regurgitation (II+, III or IV grade), flutter cycle length (ms), and discharge with antiarrhythmic agents. Multivariate analysis was performed using a Cox model and incorporated all variables found statistically significant by univariate analysis (P value < 0.05). Sensitivity, specificity, predictive positive and negative predictive values of identified variable were established using standard formula: sensitivity (%) = true positives / (true positives + false negatives) \times 100, specificity (%) = true negatives / (true negatives + false positives) \times 100, predictive positive value (%) = true-positives / (true-positives + false positives) \times 100 and negative predictive value (%) = true-negatives / (true negatives + false-negatives) \times 100.

Results

Intra-observer and inter-observer variability for right atrial and isthmus two-dimensional measurements

Figures 1 and 2 show the results of intra-observer and inter-observer variability for the right atrial area,

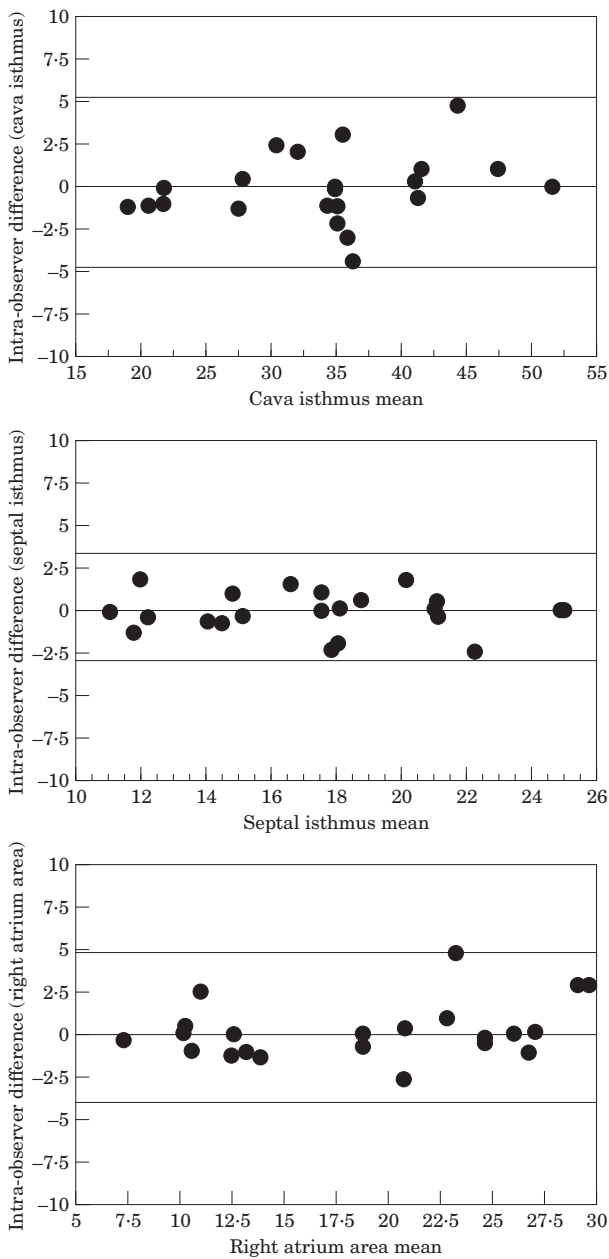


Figure 1 Intra-observer variability for right atrial area, inferior vena cava–tricuspid isthmus and septal isthmus two-dimensional measurements.

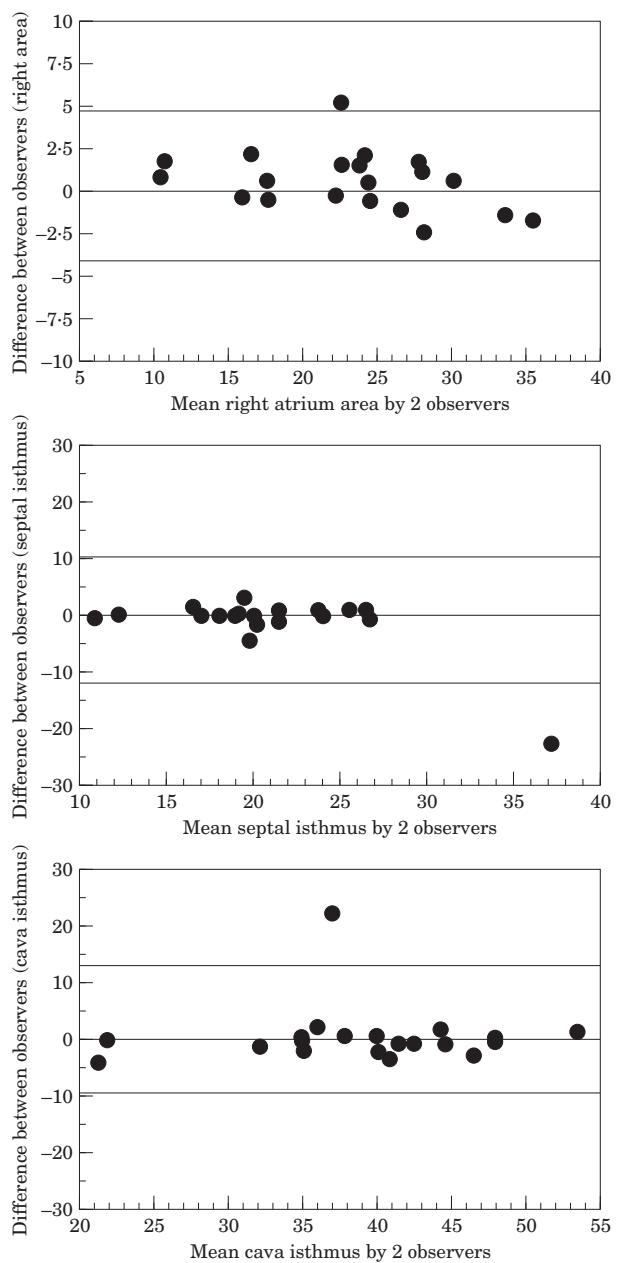


Figure 2 Inter-observer variability for right atrial area, inferior vena cava–tricuspid isthmus and septal isthmus two-dimensional measurements.

inferior vena cava–tricuspid isthmus and septal isthmus two-dimensional measurements.

Study population

Patient characteristics are summarized in [Table 1](#). Forty-seven patients (49%) had structural heart disease with 40 patients in the chronic flutter group (60%) and seven in the paroxysmal flutter group (24%). Structural heart disease included 23 coronary artery diseases, 14 dilated cardiomyopathies and 11 valvular heart diseases:

mitral regurgitation in four, mild mitral stenosis with regurgitation in four and aortic prosthesis in two cases. Twenty-six patients were discharged with antiarrhythmic drugs; 24 received drugs due to a history of pre-ablation atrial fibrillation (amiodarone in 14, Vaughan-Williams class Ic class in seven, sotalol in two and Vaughan-Williams class Ia in one): one due to previous symptomatic ventricular ectopic beats was placed on amiodarone and one was prescribed Vaughan-Williams class Ic for symptomatic repetitive atrial ectopic beats occurring early after ablation.

Table 1 Clinical, electrocardiographic and echocardiographic characteristics

| | Study population |
|--|------------------|
| Age (years) | 65.5 ± 13 |
| Gender (% female) | 18/96 (18.75%) |
| Structural heart disease | 47/96 (49%) |
| Flutter cycle length (ms) | 244 ± 34 |
| Plateau duration (ms) | 125 ± 32 |
| LA systolic diameter (mm) | 42.3 ± 8 |
| LV end-diastolic diameter (mm) | 52 ± 8 |
| LV end-systolic diameter (mm) | 36 ± 9 |
| LV ejection fraction (%) | 58.5 ± 13 |
| Systolic pulmonary pressure (mmHg) | 35.5 ± 12 |
| Septal isthmus length (mm) | 18 ± 5 |
| Inferior vena cava isthmus length (mm) | 38 ± 10 |
| LV end-diastolic volume (cm ³) | 110 ± 48 |
| LV end-systolic volume (cm ³) | 48 ± 35 |
| LA end-systolic area (cm ²) | 22 ± 6 |
| RA end-systolic area (cm ²) | 21 ± 7 |

LA=left atrium; LV=left ventricle; RA=right atrium.

Atrial flutter ablation

Patients underwent catheter ablation with the same operator (A.D.C.) and the end-point, bi-directional isthmus conduction block, was obtained in 91 patients (94.8%). The mean number of radiofrequency applica-

tions was 14 ± 12 (range from 1.5 to 67). No major complications were observed during follow-up. Five patients (5.2%) had an incomplete block (clockwise unidirectional block in four patients and counterclockwise unidirectional block for the last patient). In these five patients, atrial flutter was interrupted during radiofrequency catheter ablation and could not be induced. Early atrial flutter recurred in three of these patients (3.1%), and a second successful ablation achieved a bi-directional isthmus conduction block.

Early atrial fibrillation

Of the 96 consecutive patients undergoing ablation of common counterclockwise atrial flutter, early atrial fibrillation was documented in 16 patients (16.6%). Atrial fibrillation occurred at 29.7 ± 46 days (range from 1 to 171 days). Univariate analysis revealed that a history of atrial fibrillation, left ventricular ejection fraction, left atrial size, left ventricular telesystolic volume, A-wave velocity, significant mitral regurgitation (II+, III or IV grade) and flutter cycle length were associated with early atrial fibrillation (Table 2). Multivariate analysis using the Cox model found that the only independent predictors of early atrial fibrillation were left ventricular ejection fraction and pre-ablation history of atrial fibrillation (Table 3). Subgroup analysis of patients without

Table 2 Univariate predictors of early post-ablation atrial fibrillation in the overall population

| | Atrial fibrillation (n=16) | No atrial fibrillation (n=80) | P value |
|--|----------------------------|-------------------------------|---------|
| Age y ± SD | 60 ± 14 | 66 ± 13 | 0.07 |
| Gender (% female) | 18.8 | 18.75 | 0.99 |
| Type of atrial flutter (incessant vs paroxysmal) | 18.8% | 32.5% | 0.27 |
| Left ventricular ejection fraction | 49.3 ± 13 | 61 ± 12 | 0.0007 |
| Symptom duration (months ± SD) | 7 ± 13 | 13 ± 23 | 0.38 |
| Pre-ablation history of atrial fibrillation | 68.8 | 27.5 | 0.0024 |
| Structural heart disease (+ or -) | 66.7 | 52.5 | 0.20 |
| Left atrial size (mm) | 47 ± 8 | 41 ± 8 | 0.0054 |
| Cava tricuspid isthmus (mm) | 37 ± 9 | 38 ± 10 | 0.83 |
| Septal isthmus (mm) | 19 ± 4 | 18 ± 5 | 0.69 |
| Systolic pulmonary pressure (mmHg) | 37 ± 13 | 35 ± 13 | 0.47 |
| Right atrial area (cm ²) | 22 ± 8 | 21 ± 7 | 0.35 |
| Left atrial area (cm ²) | 23 ± 7 | 21 ± 6 | 0.3 |
| Radiofrequency applications (± SD) | 18 ± 9 | 14 ± 12 | 0.19 |
| Left ventricular diastolic diameter | 54 ± 10 | 51 ± 7 | 0.14 |
| Left ventricular systolic diameter | 39 ± 11 | 35 ± 8 | 0.11 |
| Left ventricular telediastolic volume (ml) | 125 ± 58 | 107 ± 45 | 0.12 |
| Left ventricular telesystolic volume (ml) | 67 ± 50 | 44 ± 31 | 0.007 |
| A-wave velocity (cm . s ⁻¹) | 0.53 ± 0.16 | 0.68 ± 0.3 | 0.027 |
| E-wave velocity (cm . s ⁻¹) | 0.9 ± 3 | 0.97 ± 0.4 | 0.62 |
| E/A | 1.9 ± 0.8 | 1.6 ± 0.9 | 0.31 |
| E-wave deceleration time (ms) | 172 ± 6 | 204 ± 68 | 0.07 |
| Isovolumetric relaxation time | 76 ± 18 | 72 ± 17 | 0.29 |
| Mitral regurgitation (%) | 53 | 23.5 | 0.029 |
| Atrial flutter cycle length (ms) | 260 ± 50 | 241 ± 30 | 0.043 |
| Antiarrhythmic drugs discharge | 31 | 27 | 0.8 |

Table 3 Univariate and multivariate predictors analysis of early post-ablation atrial fibrillation in the overall population using a Cox model

| | Univariate analysis | Multivariate analysis |
|---|---------------------|-----------------------|
| (1) Pre-ablation history of atrial fibrillation | 0.0024 | 0.0005 |
| (2) Left ventricular ejection fraction | 0.0007 | 0.022 |
| (3) Left atrial size (mm) | 0.0054 | 0.21 |
| (4) Left ventricular telesystolic volume (ml) | 0.007 | 0.37 |
| (5) A-wave velocity (cm . s ⁻¹) | 0.027 | 0.12 |
| (6) Significant mitral regurgitation | 0.029 | 0.8 |
| (7) Atrial flutter cycle length (ms) | 0.043 | 0.79 |

Table 4 Clinical and echocardiographic characteristics of the population without history of atrial fibrillation

Characteristics of the population without pre-ablation atrial fibrillation (n=63)

| | |
|--|----------|
| Age ± SD | 65 ± 14 |
| Gender (% female) | 19 |
| Flutter type (% paroxysmal) | 22.2 |
| Structural heart disease (%) | 44.4 |
| Left ventricular ejection fraction | 59 ± 13 |
| Symptoms duration (mo ± SD) | 13 ± 25 |
| Left atrial size (mm) | 42 ± 9 |
| Cava tricuspid isthmus (mm) | 39 ± 10 |
| Septal isthmus (mm) | 19 ± 5 |
| Systolic pulmonary pressure (mmHg) | 35 ± 13 |
| Right atrial area (cm ²) | 22 ± 7 |
| Left atrial area (cm ²) | 22 ± 7 |
| Radiofrequency applications (± SD) | 14 ± 12 |
| Left atrial size (mm) | 42 ± 9 |
| Left ventricular telediastolic volume (ml) | 99 ± 22 |
| Left ventricular telesystolic volume (ml) | 114 ± 48 |
| Mitral regurgitation (%) | 27% |
| Atrial flutter cycle length (ms) | 245 ± 28 |

Table 5 Mitral regurgitation distribution in the subgroup without atrial fibrillation history

| | Mitral regurgitation (+) | Mitral regurgitation (-) | n=63 |
|-------------------------|--------------------------|--------------------------|------|
| Atrial fibrillation (-) | n=13 | n=45 | n=58 |
| Atrial fibrillation (+) | n=4 | n=1 | n=5 |

prior atrial fibrillation history (n=63/96; 66%), revealed atrial fibrillation in five patients (8%) (Table 4) and the only predictive factor was a significant mitral regurgitation in four of these (80% sensitivity). Mitral regurgitation was present after catheter ablation in 17/63 patients (grade II+ in 13, grade III in three and grade IV in one) without atrial fibrillation history. The distribution of this variable is shown in Table 5. Mitral regurgitation predicted the risk of atrial fibrillation with a specificity of 78%, a positive predictive value of 24% and shows a negative predictive value of 98%.

Discussion

Major findings

Despite technical refinements and low recurrence of atrial flutter in patients with bi-directional block, post-ablation fibrillation is frequently reported (18% to 30%) within the first months. Improved identification of patients at high risk for subsequent atrial fibrillation may facilitate their optimal management. This prospective study confirms that a higher risk of early atrial fibrillation exists for patients with a pre-existing left ventricular dysfunction and/or history of atrial fibrillation^[5-8]. Those without prior atrial fibrillation and with normal ventricular function were at lower risk for subsequent atrial fibrillation and the only predictive variable of early atrial fibrillation in the absence of prior atrial fibrillation is represented by a significant mitral regurgitation. One may wonder if these data highlight the haemodynamic role of mitral regurgitation in the occurrence of atrial fibrillation. This should be considered in planning post-ablation management in this selected group.

Univariate and multivariate factors predictive of early atrial fibrillation after atrial flutter ablation in the overall population

Factors predictive of early atrial fibrillation have been identified in epidemiological studies^[21-23], and more recently in atrial flutter post-ablation management reports^[5-8]. Thus, Philippon *et al.* found four factors predicting an increased risk of atrial fibrillation occurrence by univariate analysis of 11 clinical variables: (1) the presence of structural heart disease; (2) a prior clinical history of atrial fibrillation before atrial flutter ablation; (3) an inducible sustained atrial fibrillation after atrial flutter ablation and (4) a greater number of failed antiarrhythmic drugs before ablation^[7]. In their study, the inducibility of atrial fibrillation after ablation of atrial flutter was independently associated with late atrial fibrillation. No data were available concerning

more precise measures of left and right anatomical atrial parameters. Tai *et al.* analysed six clinical and six echocardiographic variables: three were univariate predictors of atrial fibrillation; the presence of structural heart disease, a history of atrial fibrillation before ablation and inducible atrial fibrillation after ablation. Multivariate analysis revealed only atrial fibrillation history and inducibility as predictive markers^[6]. Paydak *et al.* identified a high-risk subgroup with a 74% occurrence of atrial fibrillation when a history of atrial fibrillation and left ventricular dysfunction could be documented. Those patients with neither characteristics were at a lower 10% occurrence^[5]. The predictors were identical in patients with early or late atrial fibrillation manifestations. Seventeen variables were included and the univariate predictors of post-ablation atrial fibrillation were: age, atrial fibrillation history, left ventricular ejection fraction, left ventricular ejection fraction <50%, atrial enlargement and atrial fibrillation inducibility. The only independent variables by multivariate Cox regression were: history of spontaneous atrial fibrillation (relative risk 3.9) and left ventricular ejection fraction below 50% (3.8 rel. risk). Another study by Espaliat *et al.* evaluated 91 consecutive patients after atrial flutter catheter ablation, revealing an atrial fibrillation occurrence of 5.5% after an average of 11 ± 2 months^[24]. Recently, Anselme *et al.* published the long-term follow-up of 83 patients with a complete bi-directional isthmus block after atrial flutter ablation^[25]. Quality-of-life evaluation was performed in 63 patients at long-term follow-up (27.1 ± 8.5 months). Paroxysmal atrial fibrillation occurred in 36.4% after a mean of 14.7 months. Though a significant number of patients still complained of palpitations, the study demonstrated an improved quality of life^[25]. Our study, using univariate analysis and spanning 27 variables, revealed that atrial fibrillation history, left ventricular ejection fraction, left atrial size, left ventricular telesystolic volume, A-wave velocity, mitral regurgitation and flutter cycle length were associated with early atrial fibrillation. By multivariate analysis using the Cox model, we demonstrated two predictive factors of early atrial fibrillation, left ventricular ejection fraction and a history of clinical atrial fibrillation prior to the atrial flutter catheter ablation. Patients with prior history of atrial fibrillation are at higher risk of early recurrence than those without a clinical history of atrial fibrillation, 12/28 (48%) vs 5/63 (8%) ($P=0.0002$).

Predictive factors of early atrial fibrillation in post-atrial flutter ablation patients without atrial fibrillation history

It was determined that atrial flutter ablation is associated with a high procedural success rate^[5-7] and that patients with the association of atrial flutter and atrial fibrillation remain at high risk for atrial fibrillation^[26]. The risk of early atrial fibrillation in patients without

atrial fibrillation history is low, 8% in our study matching the approximately 10% reported^[5-7,27,28]. Predictors of atrial fibrillation occurrence are established by several studies and concern the overall atrial flutter population. Data analysing the lower risk subgroup, those patients without atrial fibrillation history, are sparse. The only marker of early atrial fibrillation identified in our study is the presence of a significant mitral regurgitation. This is not surprising as the most common organic heart disorder associated with atrial fibrillation is mitral valve dysfunction^[29]. In our study, mitral regurgitation is associated with the risk of early atrial fibrillation with a high sensitivity (80%), specificity (78%), high negative predictive value (88%) although a low positive predictive value (24%). In the general population, atrial fibrillation is more likely to occur in end-stage mitral regurgitation and when the left atria is enlarged^[30,31]. This overall population presenting with mitral regurgitation shows a decreased cardiac mortality with early surgery and a decreased cardiac morbidity (including less atrial fibrillation) when compared to more conservative management^[32].

Clinical implications

Patients with previous atrial fibrillation and/or with left ventricular dysfunction should be advised of the risk of recurrent symptoms due to atrial fibrillation. The embolic risk should be prevented with systematic anticoagulation. Data concerning the clinical determinants of subsequent atrial fibrillation and its medical management are sparse in patients without atrial fibrillation history. In this prospective study of 27 variables, we demonstrate the clinical significance of mitral regurgitation in the occurrence of early atrial fibrillation in this group. Although the atrial fibrillation high-risk group has been determined, early atrial fibrillation can exist in apparently lower risk groups such as those 10% without a history of atrial fibrillation. Thus, the presence of haemodynamically significant mitral regurgitation should lead to continued anticoagulation medication for at least 6 months, with regular follow-ups. The importance of this risk factor was not identified in the literature and has particular value in patient care after flutter ablation.

Study limitations

This study concerns a highly selected group of patients with medically refractory atrial flutter, which may reflect an increased risk of atrial fibrillation. The frequency of atrial fibrillation may be under-estimated because of asymptomatic and paroxysmal forms. Atrial fibrillation inducibility was not systematically investigated to avoid the potential consequences (prolonged hospitalization; anticoagulation; pharmacological or electrical cardioversion). One study's analysis^[5] found inducibility of

atrial fibrillation predictive of atrial fibrillation occurrence in the univariate mode only, multiple factors weakening its value in multivariate analysis. The improvement of left ventricular function as reported by Luchsinger *et al.*^[33] at a mean of 7 months following successful ablation could cast some doubt on the validity of some echocardiographic data acquired after ablation. Impractical to perform prior to the flutter ablation, our study design wished to avoid such doubt by uniformly analysing each patient immediately (24 h) after ablation, the data thus taken as representative of the patient's echocardiographic status almost at time=0, without the possibility of significant recovery. In addition, echocardiography was uniformly performed by one author, in a single laboratory with homogeneous methodology, in the expectation that these measurements and their evolution from the pre-ablation values would be similar in the two subgroups analysed.

Valvular diseases are known to be associated with atrial arrhythmia, and surgical treatment might be discussed before atrial flutter ablation. The management of patients with valvular heart disease^[33,34] depends on the clinical status, left ventricular function, mitral valve repair possibilities, age and other associated diseases^[35,36]. In our centre, according to these guidelines, surgical treatment for mitral regurgitation in paucisymptomatic patients often awaits potential improvement of functional or anatomical status expected after atrial flutter ablation, with mandatory evaluation at a long-term follow-up of 6 to 12 months^[34].

Conclusions

In the group of post-flutter ablation patients without a history of atrial fibrillation, the risk of early atrial fibrillation is 8% and the only predictive factor found is a significant mitral regurgitation. The negative predictive value of mitral regurgitation should be considered in planning post-ablation management.

References

- [1] Disertori M, Inama G, Vergara G, Guarnerio M, Del Favero A, Furlanello F. Evidence of a reentry circuit in the common type of atrial flutter in man. *Circulation* 1983; 67: 434–40.
- [2] Shah DC, Jais P, Hiassaguere M *et al.* Three-dimensional mapping of the common atrial flutter circuit in the right atrium. *Circulation* 1997; 96: 3904–12.
- [3] Natale A, Newby KH, Pisano E *et al.* Prospective randomized comparison of antiarrhythmic therapy versus first line radiofrequency ablation in patients with atrial flutter. *J Am Coll Cardiol* 2000; 35: 1898–904.
- [4] Gilligan DM, Zakaib JS, Amir C *et al.* Radiofrequency ablation of atrial flutter: is it a definitive cure or simply one step in the management of chronic atrial disease. *PACE* 2000; 23: 553.
- [5] Paydak H, Kall JG, Burke MC *et al.* Atrial fibrillation after radiofrequency ablation of type I atrial flutter. Time to onset, determinants, and clinical course. *Circulation* 1998; 98: 315–22.
- [6] Tai CT, Chen SA, Chiang CE *et al.* Long term outcome of radiofrequency catheter ablation for typical atrial flutter: risk prediction of recurrent arrhythmias. *J Cardiovasc Electro-physiol* 1998; 9: 115–21.
- [7] Phillipon F, Plumb VJ, Epstein AE, Kay N. The risk of atrial fibrillation following catheter ablation of atrial flutter. *Circulation* 1995; 92: 430–5.
- [8] Della Bella P, Riva S, Galimberti P. Should ablation of atrial flutter be discouraged in patients documented atrial fibrillation. *Cardiologia* 1999; 44: 439–42.
- [9] Frey B, Kreiner G, Binder T, Heinz G, Baumgartner H, Gossinger. Relation between left atrial size and secondary atrial arrhythmias after successful catheter ablation of common atrial flutter. *PACE* 1997; 20: 2936–42.
- [10] Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter. Further insights into the various types of isthmus block: application to ablation during sinus rhythm. *Circulation* 1996; 94: 3204–13.
- [11] Chen J, De Chillou C, Basiouny T *et al.* Cavotricuspid isthmus mapping to assess bidirectional block during common atrial flutter radiofrequency ablation. *Circulation* 1999; 100: 2507–13.
- [12] Shan DJ, De Maria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978; 58: 1072–83.
- [13] Schiller NB, Shah PM, Crawford M, *et al.* Recommendations for quantification of the left ventricle by two-dimensional echocardiography: American Society of echocardiography Committee on Standards, subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989; 2: 358–67.
- [14] Gutman J, Wang YS, Wahr D, Schiller NB. Normal left atrial function determined by 2-dimensional echocardiography. *Am J Cardiol* 1983; 51: 336–40.
- [15] Yock PG, Popp RL. Non-invasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. *Circulation* 1984; 70: 657.
- [16] Helmeke F, Nanda F, Hsiung M *et al.* Colour Doppler assessment of mitral regurgitation with orthogonal planes. *Circulation* 1987; 75: 175–83.
- [17] Enriquez-Sarano M, Bailey K, Seward J, Tajik A, Krohn M, Mays J. Quantitative Doppler assessment of valvular regurgitation. *Circulation* 1993; 87: 841–8.
- [18] Enriquez-Sarano M, Seward J, Bailey K, Tajik A. Effective regurgitant orifice area: a non invasive Doppler development of an old hemodynamic concept. *J Am Coll Cardiol* 1994; 23: 443–51.
- [19] Bommer W, Weinert L, Neumann A, Neef J, Mason D, DeMaria A. Determination of right atrial and right ventricular size by two-dimensional echocardiography. *Circulation* 1979; 60: 91–100.
- [20] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurements. *Lancet* 1986; 1: 307–10.
- [21] Kannel WB, Abbott RD, Savage DDD, McNamara PM. Epidemiologic features of atrial fibrillation: the Framingham study. *N Engl J Med* 1982; 306: 1018–22.
- [22] Furberg CD, Psaty BM, Maniolo TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the cardiovascular health study). *Am J Cardiol* 1994; 74: 236–41.
- [23] Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of non rheumatic atrial fibrillation: the Frammingham Heart Study. *Circulation* 1994; 89: 724–30.
- [24] Espaliat E, Lagrange P, Boveda S *et al.* Radiofrequency ablation in auricular flutter. Predictive factors of primary success and medium term results. *Arch Mal Coeur Vaiss* 1999; 92: 29–34.
- [25] Anselme F, Saoudi N, Poty H, Douillet R, Cribier A. Radiofrequency catheter ablation of common atrial flutter. Significance of palpitations and quality-of-life evaluation in patients with proven isthmus block. *Circulation* 1999; 99: 534–40.

- [26] Saxon LA, Kalman JM, Olgin JE *et al.* Results of radiofrequency catheter ablation for atrial flutter. *Am J Cardiol* 1996; 77: 1014–16.
- [27] Chen SA, Chiang CE, Wu TJ *et al.* Radiofrequency catheter ablation of common atrial flutter: comparison of electrophysiologically guided focal ablation technique and linear ablation technique. *J Am Coll Cardiol* 1996; 27: 860–8.
- [28] Fisher B, Jais P, Sha D *et al.* Radiofrequency catheter ablation of common atrial flutter in 200 patients. *J Cardiovasc Electro-physiol* 1996; 7: 1225–33.
- [29] Chua YL, Schaff HV, Orszulak TA, Morris JJ. Outcome of mitral valve repair in patients with preoperative atrial fibrillation. Should the maze procedure be combined with mitral valvuloplasty? *J Thorac Cardiovasc Surg* 1994; 107: 408–15.
- [30] Levy S. Factors predisposing to the development of atrial fibrillation. *Pace* 1997; 20: 2670–74 (Part II).
- [31] Diker E, Aydogdu S, Ozdemir M *et al.* Prevalence and predictors of atrial fibrillation in rheumatic valvular heart disease. *Am J Cardiol* 1996; 77: 96–8.
- [32] Ling LH, Enriquez-Sarano M, Seward JB *et al.* Early surgery in patients with mitral regurgitation due to flail leaflets: a long-term outcome study. *Circulation* 1997; 96: 1819–25.
- [33] Luchsinger JA, Steinberg JS. Resolution of cardiomyopathy after catheter ablation of atrial flutter. *J Am Coll Cardiol* 1998; 32: 205–10.
- [34] Carabello BA, Crawford FA. Valvular heart disease. *N Engl J Med* 1997; 337: 32–41.
- [35] Carabello B, De Leon AC, Edmunds LH *et al.* ACC/AHA guidelines for management of patients with valvular heart disease. *J Am Coll Cardiol* 1998; 32: 1486–588.