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CLINICAL RESEARCH

Epicardial fat thickness predicts atrial fibrillation recurrence after a first pulmonary vein isolation procedure using a second-generation cryoballoon

La graisse épicardique prédit la récidive de fibrillation atriale dans les suites d'une première procédure d'isolation des veines pulmonaires par cryothérapie via le ballon de 2e génération

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KEYWORDS
Atrial fibrillation;
Epicardial adipose tissue

Summary
Background. — Atrial fibrillation is the most common arrhythmia in adults. A relationship between epicardial adipose tissue and atrial fibrillation has recently been reported.
Aim. — To evaluate the impact of epicardial fat thickness on the outcome of patients who underwent a first pulmonary vein isolation procedure using a second-generation cryoballoon.
Methods. — From February 2012 to February 2017, all patients who underwent a first pulmonary vein isolation procedure using a second-generation cryoballoon at Rouen University Hospital were included. Data were collected retrospectively. Epicardial fat thickness was assessed by cardiac magnetic resonance imaging. The primary endpoint was documented atrial fibrillation recurrence at 4 months.

Abbreviations: AF, atrial fibrillation; CI, confidence interval; cMRI, cardiac magnetic resonance imaging; EFT, epicardial fat thickness; ROC, receiver operating characteristic.

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Results. — A first pulmonary vein isolation procedure using a second-generation cryoballoon was performed in 288 patients; among them, 231 patients (80.2%) underwent cardiac magnetic resonance imaging. Epicardial fat thickness could be measured accurately in 206 patients (71.5%). Recurrence of atrial fibrillation at 4 months occurred in 32/206 patients (15.5%). In the multivariable analysis, factors predictive of atrial fibrillation recurrence at 4 months were: epicardial fat thickness (hazard ratio 1.96, 95% confidence interval 1.20—3.18; $P = 0.007$), the presence of high left atrium enlargement (hazard ratio 4.63, 95% confidence interval 1.17—18.38; $P = 0.03$) and atrial fibrillation recurrence before hospital discharge (hazard ratio 7.55, 95% confidence interval 2.50—22.81; $P < 0.001$).
Conclusion. — Epicardial fat thickness is a predictive factor for atrial fibrillation recurrence after a first pulmonary vein isolation procedure using a second-generation cryoballoon.

MOTS CLÉS
Fibrillation atriale ;
Graisse épicardique

Résumé
Introduction. — La fibrillation atriale est une arythmie cardiaque fréquente dans la population adulte. Un lien entre la graisse épicardique et la fibrillation atriale a récemment été mis en évidence.
Objectif. — L'objectif de cette étude était d'évaluer l'impact de l'épaisseur de la graisse épicardique sur le devenir des patients ayant eu une première procédure d'isolation des veines pulmonaires par cryothérapie via le ballon de 2e génération.
Méthodes. — De février 2012 à février 2017, tous les patients ayant eu une première procédure d'isolation des veines pulmonaires par cryothérapie via le ballon de 2e génération au centre hospitalier universitaire de Rouen ont été inclus. Les données ont été collectées rétrospectivement. L'épaisseur de graisse épicardique a été évalué par IRM cardiaque. Le critère de jugement principal était la survenue d'une récidive de fibrillation atriale à 4 mois.
Résultats. — Une première procédure d'isolation des veines pulmonaires par cyrothérapie via le ballon de 2e génération a été réalisée chez 288 patients. Parmi eux, 231 (80,2 %) ont eu une IRM cardiaque. L'épaisseur de graisse épicardique a pu être évaluée avec précision chez 206 patients (71,5 %). Des récurrences de fibrillation atriale ont été mise en évidence chez 32/206 patients (15,5 %). En analyse multivariée, les facteurs prédictifs identifiés de récurrence de fibrillation atriale à 4 mois étaient : l'épaisseur de graisse épicardique (HR 1,96, IC95 % 1,20—3,18 ; $p = 0,007$), la présence d'une dilatation importante de l'oreillette gauche (HR 4,63, IC95 % 1,17—18,38 ; $p = 0,03$) et la récidive de fibrillation atriale avant sortie d'hospitalisation (HR 7,55, IC95 % 2,50—22,81 ; $p < 0,001$).
Conclusion. — L'épaisseur de graisse épicardique est un facteur prédictif de récidive de fibrillation atriale en post-procédure d'isolation des veines pulmonaires par cryothérapie via le ballon de 2e génération.

Background

Atrial fibrillation (AF) is the most common arrhythmia, with a prevalence of 3% in adults and a predicted increase in incidence in the coming years [1]. Some factors are associated with the occurrence of AF, especially arterial hypertension, diabetes, obstructive sleep apnoea syndrome, obesity, age, sex and genetic disorders [2]. Recent studies have reported an association between epicardial adipose tissue and AF, with a higher thickness or volume in patients with AF, particularly in those with non-paroxysmal AF [3,4]. Furthermore, it seems that the greater the epicardial adipose tissue, the higher the risk of AF recurrence after a first pulmonary vein isolation using radiofrequency [5] or a first-generation cryoballoon [6]. No data are yet available regarding the evaluation of epicardial adipose tissue and the results of ablation using a second-generation cryoballoon.

The objective of this study was to evaluate the impact of epicardial fat thickness (EFT) on the outcome of patients who had a first pulmonary vein isolation procedure using a second-generation cryoballoon.

Methods

Study population

From February 2012 to February 2017, all patients who had a first pulmonary vein isolation procedure using a second-generation cryoballoon at Rouen University Hospital were included. Exclusion criteria were: age < 18 years, no pre-procedural cardiac magnetic resonance imaging (cMRI) or insufficient image quality on cMRI to measure EFT accurately. Data were collected retrospectively.

Measurement of EFT (Fig. 1)

EFT was measured on cMRI (1.5 T), initially performed to evaluate the anatomy of the left atrium and pulmonary veins before the ablation procedure. cMRI was preferred to other imaging techniques, such as cardiac tomodensitometry, because it is the technique used most frequently in the study population. Measures were performed in end-diastolic time, on the right ventricular free wall axial view. For each patient, a mean value for EFT was calculated after repeated measurements (at least four). Epicardial fat was identified as the white area between the myocardium and the visceral pericardium on T2 sequences. Intraobservation variability was evaluated on 100 patients selected at random; interobservation variability was evaluated on 20 patients selected at random. All measurements were performed by physicians who were blinded to the primary endpoint.

Pulmonary vein isolation procedure

The pulmonary vein isolation procedure was performed with a 28 mm second-generation cryoballoon (Medtronic, Minneapolis, MN, USA). The transspetal puncture was realised under transoesophageal echocardiography and fluoroscopic guidance. Phrenic nerve stimulation was applied during ablation of the right pulmonary veins. Successful isolation of the pulmonary veins was confirmed at the end of the procedure, and was defined as complete and persistent disappearance of the pulmonary vein potential. A single cryoballoon application was delivered for 240 seconds at each pulmonary vein antrum, without bonus application if the pulmonary vein potential disappeared during energy delivery. Anticoagulation therapy was not discontinued for the ablation procedure.

Postprocedural follow-up

A daily electrocardiogram was performed during the hospital stay. The day after the procedure, transthoracic echocardiography was performed to check pericardium and cardiac function. Patients were discharged at 48 hours in absence of adverse events. Two months after the procedure, 24-hour Holter monitoring was performed to search for recurrence of AF. Four months after the procedure, all patients had a clinical evaluation and an electrocardiogram. Additional electrocardiogram recordings were obtained in case of symptoms suggesting AF recurrence.

Endpoints

The primary endpoint was documented AF recurrence occurring during the first 4 months, after a blanking period of 2 months. However, recurrences within the first 2 months after ablation were considered to be significant if they led to hospitalization or a redo procedure. The timing of the primary endpoint was set at 4 months when an outpatient consultation was systematically scheduled for all patients, avoiding any loss to follow-up.

Secondary endpoints were: postprocedural AF recurrence before hospital discharge; EFT measurements; features of the ablation procedure (duration of the procedure, left atrial time and the number of pulmonary veins successfully isolated); adverse events; antiarrhythmic treatments during the follow-up period; and occurrence of redo procedures during follow-up.

Statistical analysis

Continuous variables are expressed as means ± standard deviations. Normal distribution was assessed by the Shapiro-Wilk test. Student's *t* test or the Mann-Whitney U test was used when appropriate. Categorical variables are expressed as percentages. The χ^2 test or Fisher's exact test was used when appropriate. Multivariable logistic regression was performed to identify factors predictive of AF recurrence at 4 months. A Cox proportional regression analysis was performed to identify factors predictive of a second pulmonary vein isolation procedure. Variables included in the regression analysis were those with a *P* value < 0.10 in the univariate analysis and those known to represent a risk of AF occurrence (type of AF, arterial hypertension, sex, diabetes, sleep apnoea syndrome, age and body mass index). The best cut-off values for EFT to predict AF recurrence and occurrence of a redo procedure were identified with a receiver operating characteristic (ROC) curve. The Youden index (sensitivity + specificity − 1) was calculated to define the best cut-off value. The Herrell C-index was calculated to confirm the area under the curve assessing the predictive value of EFT for occurrence of redo procedure. A redo procedure survival curve was plotted using a Kaplan-Meier model with a log-rank test. Spearman's rank test was used to assess correlations. Statistical significance was defined as a *P* value < 0.05. All tests were two-sided. The software used was SPSS Statistics V23 (SPSS Inc., Chicago, IL, USA).

Results

Study population

From February 2012 to February 2017, 670 patients had a pulmonary vein isolation procedure, 288 with a second-generation cryoballoon. Among them, 231 patients (80.2%) had cMRI, 35 patients (12.1%) had cardiac tomodensitometry and 22 patients (7.6%) did not have cardiac imaging before the procedure. Among the 231 patients who had cMRI, accurate measurement of EFT was obtained in 206 patients (Fig. 2). The baseline characteristics of the study population are shown in Table 1.

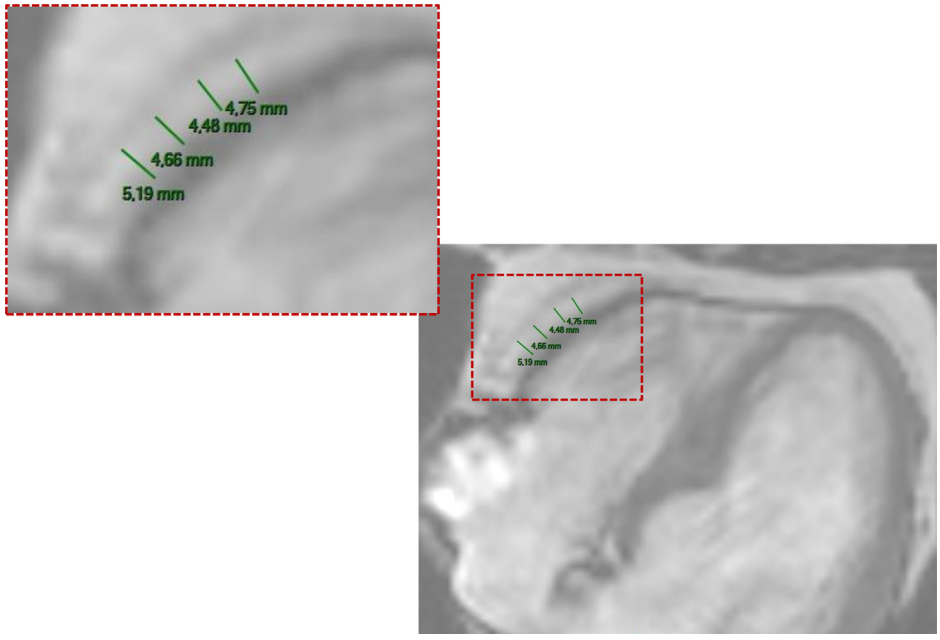

Figure 1. Measurement of epicardial fat thickness (EFT). EFT was measured on the axial view of the long side of the right ventricular free wall. For each patient, a mean value of EFT was calculated after repeated measurements (at least four). Measurements were performed in end-diastolic time.

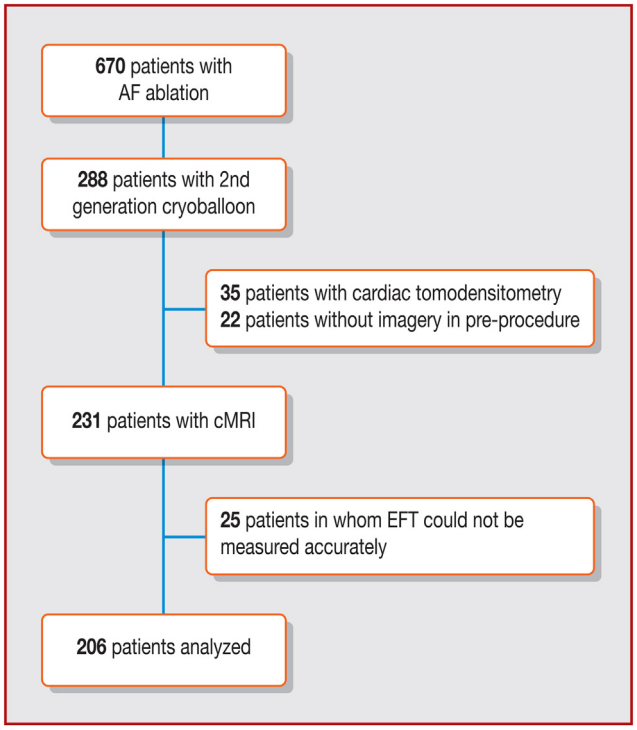

Figure 2. Flow-chart. AF: ablation fibrillation; cMRI: cardiac magnetic resonance imaging; EFT: epicardial fat thickness.

AF recurrence at 4 months

In the follow-up population, 15.5% ($n = 32$) of patients had documented AF recurrence at the 4-month clinical assessment; among them, 66.3% ($n = 18$) had a redo procedure. In patients with AF recurrence at 4 months, EFT was significantly higher than in the other patients: 4.9 ± 0.9 mm and 4.3 ± 0.9 mm, respectively ($P = 0.001$) (Table 2, Fig. 3). In the multivariable logistic regression analysis, the factors predictive of AF recurrence at 4 months were: EFT, the presence of high left atrium enlargement (left atrial volume ≥ 50 mL/m^2 or left atrial area ≥ 30 cm^2 or left atrial diameter > 50 mm) and AF recurrence before hospital discharge, independent of AF risk factors (Table 3).

Redo procedures

At a mean follow-up of 28.1 ± 16.6 months, the incidence of redo procedure was 11.2% ($n = 23$) in the study population. Redo procedures were performed a mean 13.2 ± 13.3 months after the first pulmonary vein isolation procedure. EFT was significantly higher in the redo procedure group than in the no redo group: 5.2 ± 0.9 mm and 4.3 ± 0.9 mm, respectively ($P < 0.001$) (Table 2, Fig. 3). In the multivariable Cox regression analysis, factors predictive of the redo procedure were EFT and documented AF recurrence at 4 months, independent of AF risk factors: hazard ratio 2.73, 95% confidence interval (CI) 1.43—5.22 ($P = 0.002$) and hazard ratio 106.3, 95% CI 20.51—551.12 ($P < 0.001$), respectively. Beyond AF risk factors, the other variables included in the multivariable Cox regression analysis were EFT, documented AF recurrence at 4 months, the duration of ablation procedure, an AF recurrence before hospital discharge and the presence of high left atrium enlargement.

In the redo procedure group, all patients had at least one pulmonary vein that was reconnected. A pulmonary vein-to-left atrium reconnection was observed at the right inferior pulmonary vein in 60.9% of patients, at the left superior pulmonary vein in 43.5% of patients, at the left inferior pulmonary vein in 43.5% of patients and at the right superior pulmonary vein in 26.1% of patients.

Table 1 Baseline characteristics of the study population.

	Total population ($n = 206$)	Documented AF recurrence at 4 months ($n = 32$)	No documented AF recurrence at 4 months ($n = 174$)	*P*
Age (years)	57.8 ± 10.7	59.1 ± 10.5	57.6 ± 10.8	0.53
Male sex	149 (72.3)	22 (68.8)	127 (73.0)	0.67
Body mass index (kg/m^2)	27.5 ± 4.4	28.2 ± 4.7	27.4 ± 4.3	0.33
Arterial hypertension	69 (33.5)	13 (40.6)	56 (32.2)	0.42
Diabetes	12 (5.8)	1 (3.1)	11 (6.3)	0.70
Dyslipidaemia	70 (34.0)	9 (28.1)	61 (35.1)	0.55
Smoking	88 (42.7)	13 (40.6)	75 (43.1)	0.85
Stroke	9 (4.4)	2 (6.3)	7 (4.0)	0.64
Obstructive sleep apnoea syndrome	19 (9.2)	3 (9.4)	16 (9.2)	1.0
Coronary artery disease	10 (4.9)	2 (6.3)	8 (4.6)	0.66
Alcohol consumption	3 (1.5)	1 (3.1)	2 (1.1)	0.40
Hyperthyroidism	7 (3.4)	0 (0)	7 (4.0)	0.60
CHA_2DS_2-VASc score	1.1 ± 1.1	1.4 ± 1.2	1.1 ± 1.1	0.11
Paroxysmal AF	193 (93.7)	29 (90.6)	164 (94.3)	0.44
Maximum duration of AF episode < 24 hours	174 (84.5)	28 (87.5)	146 (83.9)	0.80
Echocardiography variables				
LVEF	62.0 ± 9.2	61.0 ± 10.1	62.3 ± 9.0	0.78
High left atrium enlargement[a]	30 (14.6)	13 (40.6)	17 (9.8)	< 0.001
Treatment				
Beta-blocker	123 (59.7)	25 (78.1)	98 (56.3)	0.03
Cordarone	42 (20.4)	8 (25.0)	34 (19.5)	0.48
Flecainide	78 (37.9)	12 (37.5)	66 (37.9)	1.0
ACEI/ARB	53 (25.7)	9 (28.1)	44 (25.3)	0.83
Statin	50 (24.3)	7 (21.9)	43 (24.7)	0.83
Anticoagulation therapy				
Vitamin K antagonist	58 (28.2)	8 (25.0)	50 (28.7)	0.84
Rivaroxaban	87 (42.2)	15 (46.9)	72 (41.4)	0.57
Dabigatran	21 (10.2)	1 (3.1)	20 (11.5)	0.21
Apixaban	39 (18.9)	8 (25.0)	31 (17.8)	0.34
Serum creatinine concentration (μmol/L)	80.7 ± 18.1	79.3 ± 16.3	81.1 ± 18.6	0.70

Data are expressed as mean ± standard deviation or number (%). ACEI: angiotensin-converting enzyme inhibitor; AF: atrial fibrillation; ARB: angiotensin receptor blocker; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥ 75 years (doubled), diabetes, stroke/transient ischaemic attack/thromboembolism (doubled) — vascular disease, age 65—74 years and sex category (female); LVEF: left ventricular ejection fraction.

[a] High left atrium enlargement is defined as: left atrial volume ≥ 50 mL/m^2 or left atrial area ≥ 30 cm^2 or left atrial diameter > 50 mm.

EFT

EFT was independently associated with documented AF recurrence at 4 months and redo procedures. Intraobservation and interobservation variabilities in EFT measurement were 12.5 ± 9.9% and 14.3 ± 11.3%, respectively. The ROC curves showed an optimal cut-off value of 4.35 mm to identify patients at risk of AF recurrence at 4 months and patients at risk of redo procedures (area under the curve 0.683, 95% CI 0.582—0.783 [$P = 0.001$] and area under the curve 0.789, 95% CI 0.695—0.883 ($P < 0.001$, respectively) (Fig. 4). The Herrell C-index was 0.773 (95% CI 0.637—0.909; $P < 0.001$) and confirmed the predictive value of EFT for occurrence of redo procedure. The cut-off value of 4.35 mm was associated with a sensitivity of 0.75 and a specificity of 0.60 to predict AF recurrence, and a sensitivity of 0.91 and a specificity of 0.59 to predict redo procedures. Regarding redo procedures, a Kaplan-Meier curve was plotted for the comparison between patients with an EFT < 4.35 mm and those with an EFT ≥ 4.35 mm. Patients with an EFT > 4.35 mm had a higher rate of redo procedures compared with the other patients (21.9% vs 1.8%; $P < 0.001$, according to the log-rank test) (Fig. 5).

Table 2 Secondary endpoints in the study population.

	Total population ($n = 206$)	Documented AF recurrence at 4 months ($n = 32$)	No documented AF recurrence at 4 months ($n = 174$)	*P*
Epicardial fat thickness (mm)	4.4 ± 0.9	4.9 ± 0.9	4.3 ± 0.9	0.001
AF recurrence before hospital discharge	14 (6.8)	6 (18.8)	8 (4.6)	0.02
Duration of ablation procedure (minutes)	79.1 ± 24.2	88.1 ± 26.4	77.5 ± 23.6	0.02
Left atrial time (minutes)	62.4 ± 20.8	67.8 ± 24.1	61.5 ± 20.2	0.39
Successful isolation of the four PVs	200 (97.1)	32 (100)	168 (96.6)	0.60
Adverse events				
Tamponade	2 (1.0)	1 (3.1)	1 (0.6)	0.29
Pericardial effusion	19 (9.2)	3 (9.4)	16 (9.2)	1.0
Femoral haematoma	1 (0.5)	0 (0)	1 (0.6)	1.0
Phrenic nerve paralysis	11 (5.3)	1 (3.1)	10 (5.7)	1.0
Postporcedural stroke	0 (0)			
Antiarrhythmic treatments during follow-up				
Beta-blocker	35 (17.0)	11 (34.4)	24 (13.8)	0.01
Cordarone	3 (1.5)	2 (6.3)	1 (0.6)	0.07
Flecainide	7 (3.5)	4 (12.9)	3 (1.8)	0.02

Data are expressed as mean ± standard deviation or number (%). AF: atrial fibrillation; PV: pulmonary vein.

Table 3 Predictors of atrial fibrillation recurrence, 4 months after a first pulmonary vein isolation procedure: Univariate and multivariable logistic regression analyses.

	Univariate analysis			Multivariable analysis		
	Hazard ratio	95% CI	*P*	Hazard ratio	95% CI	*P*
Epicardial fat thickness	1.91	1.27—2.88	0.002	1.96	1.20—3.18	0.007
AF recurrence before hospital discharge	4.79	1.54—14.92	0.007	4.63	1.17—18.38	0.03
Duration of ablation procedure	1.02	1.00—1.03	0.03	1.01	0.99—1.02	0.50
High left atrium enlargement[a]	6.31	2.66—15.0	< 0.001	7.55	2.50—22.81	< 0.001
Preprocedural beta-blocker	2.77	1.34—6.74	0.03	2.08	0.68—6.34	0.20
Beta-blocker in the follow-up period	3.27	1.40—7.64	0.006	2.01	0.66—6.11	0.22
Arterial hypertension	1.44	0.67—3.13	0.35	1.04	0.39—2.81	0.93
Diabetes	0.48	0.06—3.84	0.49	0.48	0.05—4.44	0.52
Sleep apnoea syndrome	1.02	0.28—3.73	0.98	0.72	0.16—3.31	0.68
Paroxysmal AF	0.59	0.15—2.27	0.45	1.89	0.29—12.29	0.51
Male sex	1.01	0.97—1.05	0.47	0.69	0.25—1.96	0.62
Body mass index	1.04	0.96—1.13	0.35	1.03	0.92—1.15	0.61
Age	0.97	0.94—1.01	0.11	1.01	0.97—1.06	0.62

AF: atrial fibrillation; CI: confidence interval.
[a] High left atrium enlargement is defined as: left atrial volume ≥ 50 mL/m^2 or left atrial area ≥ 30 cm^2 or left atrial diameter > 50 mm.

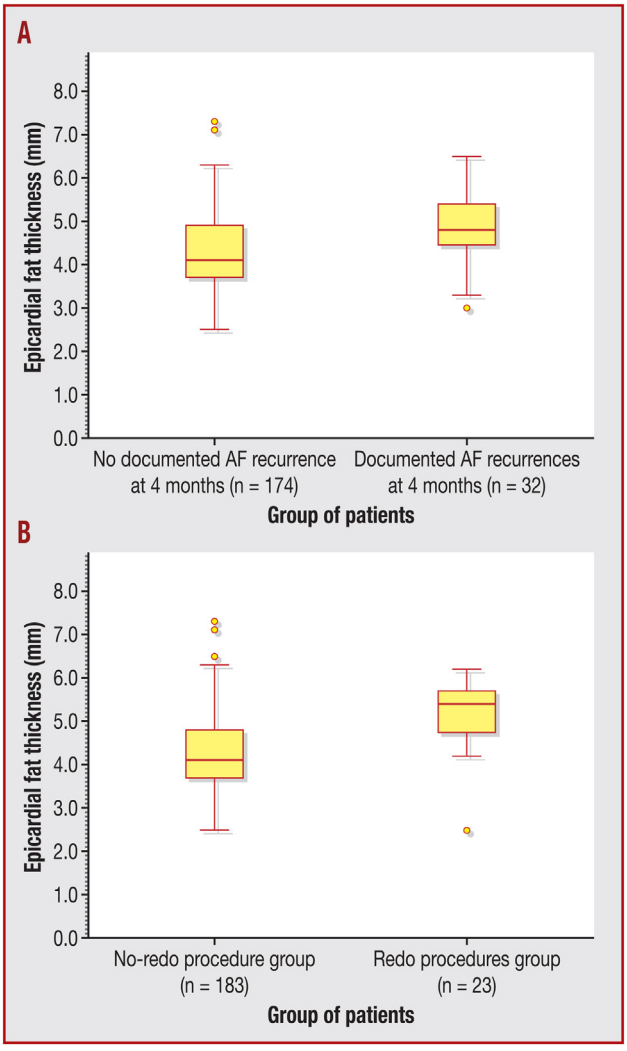

Figure 3. Box plots of epicardial fat thickness (EFT) according to patient group. A. Comparison of EFT between patients with and without documented AF recurrence at 4 months ($P = 0.001$). B. Comparison of EFT between patients who did and did not have a redo procedure ($P < 0.001$).

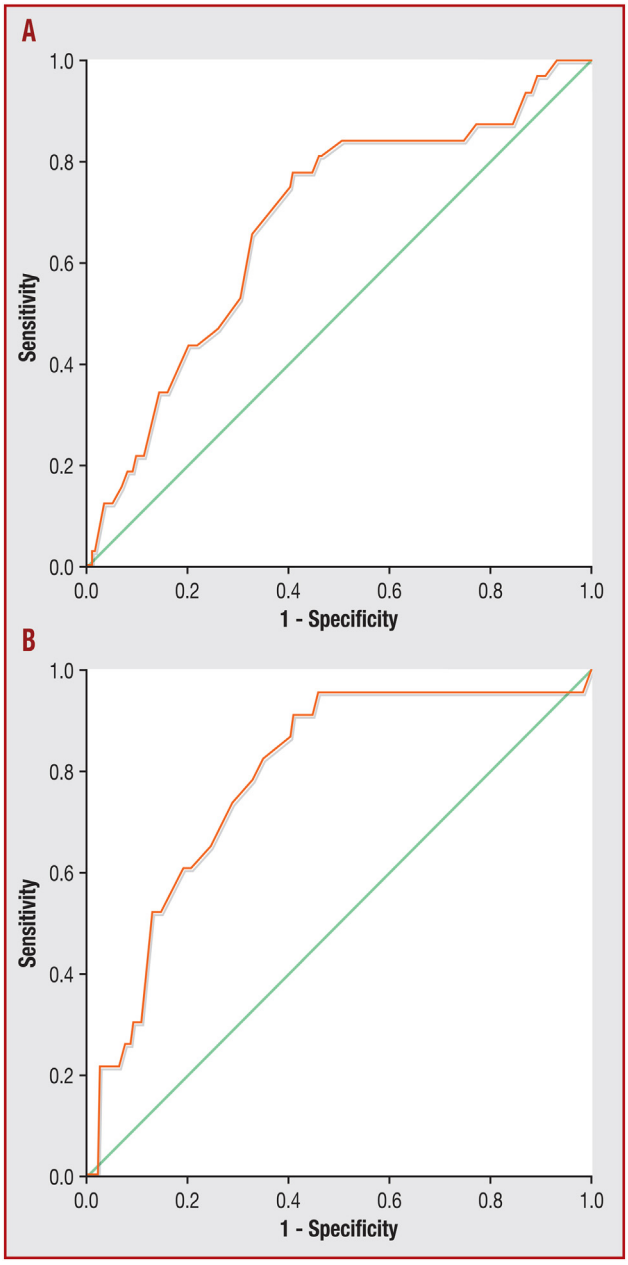

Figure 4. Receiver operating characteristic (ROC) curves. A. ROC curve of epicardial fat thickness (EFT) in the prediction of atrial fibrillation recurrence at 4 months (area under the curve = 0.68, 95% confidence interval 0.58–0.78; $P = 0.001$). B. ROC curve of EFT in the prediction of redo procedures (area under the curve = 0.789, 95% confidence interval 0.695–0.883; $P < 0.001$).

EFT and body mass index were not correlated ($r = 0.135$; $P = 0.06$) (Fig. 6). Left atrial diameter and EFT were not correlated ($r = 0.133$; $P = 0.12$).

Discussion

Our results show a clear relationship between EFT and patient outcome after a first pulmonary vein isolation procedure using a second-generation cryoballoon. A higher EFT value was predictive of AF recurrence at 4 months and redo procedures, independent of measured AF risk factors.

Epicardial adipose tissue is part of the heart's anatomy by its contiguity with the myocardium and coronary arteries. The association of epicardial adipose tissue with cardiovascular events, such as myocardial infarction [7] and atrial fibrillation [8,9], has already been reported; its paracrine and vasocrine functions seem to play a role in this phenomenon. Secretion of cytokines and proinflammatory mediators contribute to local homeostasis. However, a disruption in this balance may provide alterations in myocardial cell functioning, leading to a pathological state [10]. Some studies have reported a relationship between left atrium size and epicardial adipose tissue thickness or volume [11], which may contribute to electrophysiological disorders leading to AF. Correlation between diastolic dysfunction and EFT may play a role [12,13]. Moreover, even in the absence of left atrium enlargement, local secretion of tumour necrosis factor, interleukin-6 and free fatty acid by epicardial adipose tissue has been associated with AF [10,14,15]. Besides, the

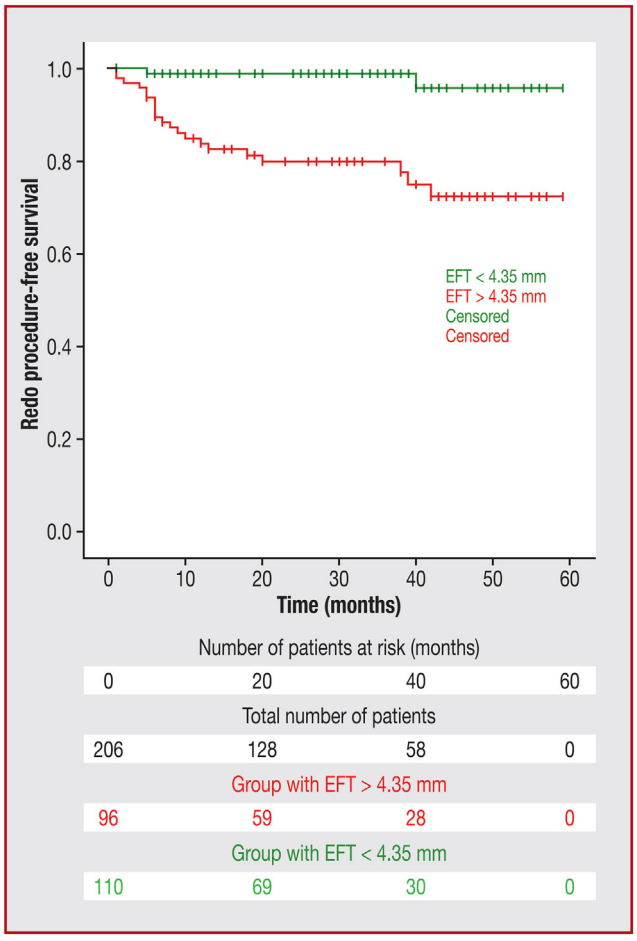

Figure 5. Kaplan-Meier survival curve of redo procedure after a first pulmonary vein isolation procedure according to epicardial fat thickness (EFT). The cut-off value was 4.35 mm. Patients with EFT > 4.35 mm had a higher rate of redo procedure (log-rank test, $P < 0.001$).

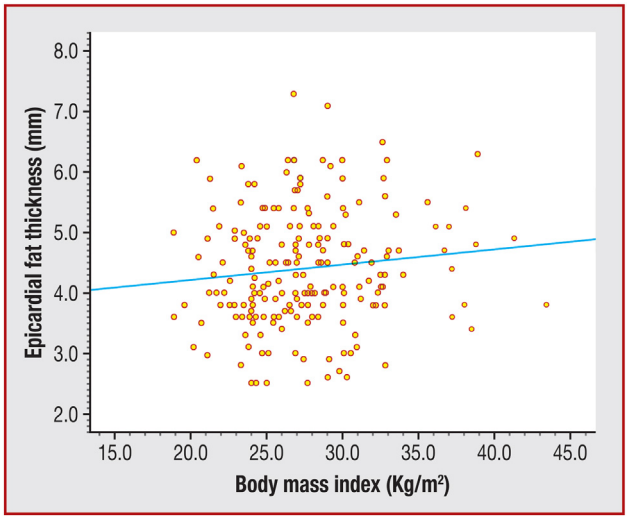

Figure 6. Epicardial fat thickness according to body mass index. Absence of correlation ($r = 0.135$; $P = 0.06$).

induction of atrial fibrosis by epicardial adipose tissue has already been reported [16].

In our study, EFT was predictive of AF recurrence after a first pulmonary vein isolation procedure using a second-generation cryoballoon. This observation is consistent with results from studies using other energy techniques. Chao et al. [5] found that EFT was associated with recurrence of AF after radiofrequency ablation in patients with paroxysmal or non-paroxysmal AF. Contrary to our results, they found other factors predictive of recurrence, such as the $CHADS_2$ (Congestive heart failure, Hypertension, Age $\geq$ 75 years, Diabetes, Stroke/transient ischaemic attack/thromboembolism [Doubled]) score and the type of AF (non-paroxysmal AF). In a more recent study [6], Canpolat et al. reported that EFT was predictive of AF recurrence after a first pulmonary vein isolation procedure using a first-generation cryoballoon; other predictive factors were left atrial diameter and early recurrence of AF. These authors found a correlation between C-reactive protein concentration and EFT, and a possible relationship between AF, inflammation and epicardial adipose tissue.

The relationship between EFT and redo procedures emphasizes the potential impact of epicardial adipose tissue on the outcome of AF ablation procedures. Nevertheless, during our redo procedures, we always found at least one pulmonary vein reconnected to the atria. The physiopathological mechanism explaining the link between epicardial adipose tissue and AF recurrence leading to redo procedure is therefore not so clear. It is unlikely that epicardial adipose tissue alone is responsible for pulmonary vein-to-left atrium reconnection. However, we know from electrophysiological studies systematically performed weeks or months after pulmonary vein isolation that pulmonary vein-to-left atrium reconnection is common, even in asymptomatic patients [17]. These observations suggest that epicardial fat, thanks to its secretions, rather promotes pulmonary vein activities (ectopies) responsible for AF recurrence.

Contrary to other studies [6,18], we did not observe a correlation between epicardial adipose tissue (evaluated by EFT) and either body mass index or left atrial diameter. As visceral adipose tissue in diabetes, epicardial adipose tissue should be considered as an autonomic entity with its own function.

In this study, we used cMRI to assess epicardial adipose tissue, measuring the thickness along the right ventricular free wall. A volumetric assessment or a measure at the left atrial posterior wall would have been more logical. However, it appeared to be the only site where EFT could be measured reliably. Despite this limitation, our results seem consistent with other data using echocardiography, cMRI or cardiac tomodensitometry [5,19,20]. Moreover, Kim et al. observed a correlation between EFT evaluated along the right ventricular free wall and epicardial fat volume [21]. In addition, EFT measured along the right ventricle appeared simple and reliable, as attested by the low interobservation and interobservation variabilities.

Study limitations

Data were collected retrospectively with inherent limitations. EFT was measured using cMRI, which was initially performed to evaluate the anatomy of the left atrium and

pulmonary veins before the ablation procedure. cMRI was not synchronized on heart beats.

Although thickness of epicardial adipose tissue varies according to the myocardial region, measurements were performed in the same area along the right ventricle. Because of technical restrictions related to MRI, we measured the thickness of the epicardial fat, whereas a volumetric assessment would have been more accurate.

Evaluating the potential link between EFT and left atrial fibrosis on cMRI could have been interesting. However, as cMRI was initially performed to depict left atrial anatomy only, no late gadolinium enhancement sequences were realized.

Conclusion

In this study, EFT was found to be an independent predictive factor for AF recurrence and redo procedures after a first pulmonary vein isolation procedure using a second-generation cryoballoon. In accordance with other studies, epicardial adipose tissue seems to be intimately bound to AF physiopathology, even if the true mechanisms have yet to be elucidated. Nevertheless, other studies should be performed to confirm these results. Indeed, a better understanding of this relationship would be helpful to tailor the ablation strategy according to the amount of epicardial fat in a given patient.

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Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37:2893—962.
[2] Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Europace 2012;14:528—606.
[3] Al Chekakie MO, Welles CC, Metoyer R, et al. Pericardial fat is independently associated with human atrial fibrillation. J Am Coll Cardiol 2010;56:784—8.
[4] Batal O, Schoenhagen P, Shao M, et al. Left atrial epicardial adiposity and atrial fibrillation. Circ Arrhythm Electrophysiol 2010;3:230—6.
[5] Chao TF, Hung CL, Tsao HM, et al. Epicardial adipose tissue thickness and ablation outcome of atrial fibrillation. PLoS One 2013;8:e74926.
[6] Canpolat U, Aytemir K, Yorgun H, Asil S, Dural M, Ozer N. The impact of echocardiographic epicardial fat thickness on outcomes of cryoballoon-based atrial fibrillation ablation. Echocardiography 2016;33:821—9.
[7] Mahabadi AA, Berg MH, Lehmann N, et al. Association of epicardial fat with cardiovascular risk factors and incident myocardial infarction in the general population: the Heinz Nixdorf Recall Study. J Am Coll Cardiol 2013;61:1388—95.
[8] Thanassoulis G, Massaro JM, O'Donnell CJ, et al. Pericardial fat is associated with prevalent atrial fibrillation: the Framingham Heart Study. Circ Arrhythm Electrophysiol 2010;3:345—50.
[9] van Rosendael AR, Dimitriu-Leen AC, van Rosendael PJ, et al. Association between posterior left atrial adipose tissue mass and atrial fibrillation. Circ Arrhythm Electrophysiol 2017;10:e004614.
[10] Iacobellis G. Local and systemic effects of the multifaceted epicardial adipose tissue depot. Nat Rev Endocrinol 2015;11:363—71.
[11] Yorgun H, Canpolat U, Aytemir K, et al. Association of epicardial and peri-atrial adiposity with the presence and severity of non-valvular atrial fibrillation. Int J Cardiovasc Imaging 2015;31:649—57.
[12] Chu CY, Lee WH, Hsu PC, et al. Association of increased epicardial adipose tissue thickness with adverse cardiovascular outcomes in patients with atrial fibrillation. Medicine (Baltimore) 2016;95:e2874.
[13] Iacobellis G, Leonetti F, Singh N, Sharma M. Relationship of epicardial adipose tissue with atrial dimensions and diastolic function in morbidly obese subjects. Int J Cardiol 2007;115:272—3.
[14] Lin YK, Chen YC, Chang SL, et al. Heart failure epicardial fat increases atrial arrhythmogenesis. Int J Cardiol 2013;167:1979—83.
[15] Mazurek T, Kiliszek M, Kobylecka M, et al. Relation of proinflammatory activity of epicardial adipose tissue to the occurrence of atrial fibrillation. Am J Cardiol 2014;113:1505—8.
[16] Venteclef N, Guglielmi V, Balse E, et al. Human epicardial adipose tissue induces fibrosis of the atrial myocardium through the secretion of adipo-fibrokines. Eur Heart J 2015;36:795—805.
[17] Miyazaki S, Taniguchi H, Hachiya H, et al. Clinical recurrence and electrical pulmonary vein reconnections after second-generation cryoballoon ablation. Heart Rhythm 2016;13:1852—7.
[18] Nagashima K, Okumura Y, Watanabe I, et al. Association between epicardial adipose tissue volumes on 3-dimensional reconstructed CT images and recurrence of atrial fibrillation after catheter ablation. Circ J 2011;75:2559—65.
[19] Stojanovska J, Kazerooni EA, Sinno M, et al. Increased epicardial fat is independently associated with the presence and chronicity of atrial fibrillation and radiofrequency ablation outcome. Eur Radiol 2015;25:2298—309.
[20] Wong CX, Abed HS, Molaee P, et al. Pericardial fat is associated with atrial fibrillation severity and ablation outcome. J Am Coll Cardiol 2011;57:1745—51.
[21] Kim BJ, Kang JG, Lee SH, et al. Relationship of echocardiographic epicardial fat thickness and epicardial fat volume by computed tomography with coronary artery calcification: data from the CAESAR Study. Arch Med Res 2017;48:352—9.