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CLINICAL RESEARCH

Sex-related risks of recurrence of atrial fibrillation after ablation: Insights from the Guangzhou Atrial Fibrillation Ablation Registry

Risque de récurrence après ablation de fibrillation atriale liée au genre : données du registre Guangzhou Atrial Fibrillation ablation registry

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Abbreviations: AF:, atrial fibrillation; BNP:, B-type natriuretic peptide; CA:, catheter ablation; CI:, confidence interval; CRP:, C-reactive protein; eGFR:, estimated glomerular filtration rate; HR:, hazard ratio; LAD:, left atrial diameter.

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KEYWORDS
Atrial fibrillation
;Catheter ablation
;Female

Summary
Background. — Female sex has been linked with worse prognosis in patients with atrial fibrillation (AF). Clinical risk stratification of women with AF may help decision-making before catheter ablation (CA).
Aim. — To evaluate arrhythmia outcomes and the predictive value of clinical scores for arrhythmia recurrence in a large cohort of Chinese patients with AF undergoing CA.
Methods. — A total 1410 of patients (68.1% men) who underwent AF ablation with scheduled follow-up were analysed retrospectively. Baseline characteristics and ablation outcome were compared between men and women. The predictive values of risk scoring systems for AF recurrence were assessed in women.
Results. — Recurrence, early recurrence and complications after CA were similar in women and men over similar follow-up periods (20.7 ± 8.0 vs 20.7 ± 9.1 months; $P > 0.05$). Compared with men, women with AF recurrence were older and had a larger left atrial diameter (LAD), less paroxysmal AF, lower left ventricular ejection fraction, lower estimated glomerular filtration rate (eGFR) and higher serum concentrations of B-type natriuretic peptide (BNP) and C-reactive protein (CRP) (all $P < 0.01$). Multivariable analysis showed that age, non-paroxysmal AF, body mass index, coronary artery disease, LAD, early recurrence, eGFR, BNP and CRP were independent risk factors with sex differences (all $P < 0.05$) in the whole cohort. In women, only non-paroxysmal AF, early recurrence, BNP, CRP (all $P < 0.01$) and history of stroke/transient ischaemic attack ($P = 0.016$) were independent risk factors. Of the clinical scoring systems tested, MB-LATER, APPLE, CAAP-AF and BASE-AF_2 scores (C-indexes 0.73, 0.72, 0.68 and 0.72, respectively; all $P < 0.01$) had a modest predictive value for AF recurrence after CA in women.
Conclusions. — CA for AF has similar recurrence risks in women and men, but there are sex differences in the clinical characteristics and risk factors associated with AF recurrence.

MOTS CLÉS
Fibrillation atriale ;
Ablation par
cathéter ;
Genre féminin

Résumé
Justification. — Le genre féminin serait associé à un plus mauvais pronostic chez les patients en fibrillation atriale. La stratification clinique du risque chez la femme en fibrillation atriale pourrait contribuer à optimiser la décision thérapeutique avant indication d'une ablation par cathéter.
Objectifs. — Évaluer l'évolution au décours d'une ablation et la valeur prédictive des scores de risque clinique pour prédire la récurrence d'arythmie dans une cohorte de patients chinois en fibrillation atriale ayant bénéficié d'une ablation par cathéter.
Méthode. — Un total de 1410 patients, 68.1 % de genre masculin ayant bénéficié d'une ablation par cathéter de fibrillation atriale, ont été analysés rétrospectivement. Les caractéristiques de base et au décours de l'ablation pour fibrillation atriale ont été comparées en fonction du genre, masculin ou féminin. La valeur prédictive des scores de risque clinique pour la prédiction de la récurrence de fibrillation atriale a été évaluée en particulier chez les patientes.
Résultats. — La récurrence, la récurrence précoce et les complications après ablation de fibrillation atriale étaient similaires dans les deux genres, avec des périodes de suivi similaires, ($20,7 \pm 8$ versus $20,7 \pm 9,1$ mois, $p > 0,005$). Comparativement aux hommes, les femmes ayant une récurrence de fibrillation atriale sont plus âgées, et ont un diamètre de l'oreillette gauche plus important, moins de fibrillation atriale paroxystique, une FEVG moindre, un débit de filtration glomérulaire moindre et des concentrations sériques plus élevées de BNP et de CRP ($p < 0,001$ pour tous ces valeurs et paramètres). L'analyse multivariée montre que l'âge, le caractère non paroxystique de la FA, l'index de masse corporelle, la maladie coronaire, le diamètre de l'oreillette gauche, la récurrence précoce, le taux de filtration glomérulaire, le BNP et la CRP sont des facteurs de risque indépendants des différences observées ($p < 0,005$ pour tous les paramètres cités), au sein de la cohorte. Chez les femmes, seul le caractère non paroxystique de la FA, la récurrence précoce, les taux de BNP et de CRP ($p < 0,01$ pour tous ces paramètres) ainsi que l'antécédent d'accident vasculaire cérébral ou d'accident ischémique transitoire ($p = 0,016$), sont des facteurs de risque indépendants. Parmi les scores de risque clinique de récurrence de fibrillation atriale évalués, MB-later, APPLE, CAAP-AF et BASE-AF2,

les index-C sont respectivement de 0,73, 0,72, 0,68 et 0,72, toutes valeurs avec $p < 0,01$ et ont une valeur prédictive de la récurrence de FA modeste au décours d'une ablation, chez la femme.
Conclusion. — L'ablation par cathéter de fibrillation atriale a un risque de récurrence similaire dans les deux genres mais des différences sont observées pour ce qui concerne les caractéristiques cliniques et les facteurs de risque associés aux récurrences de FA.

Background

Some sex-related differences are evident in the AF population, with women being older and more symptomatic, and having more cardiac co-morbidities, heart failure with preserved systolic function and a lower quality of life compared with men [1]. Sex differences are also found in the AF substrate, including fibrosis of the left superior pulmonary vein or inflammation [2,3].

Management differences are also evident, with women being referred less frequently to special arrhythmia clinics than men [4]. Women are also less likely to receive invasive rhythm control, including electrical cardioversion, catheter ablation (CA) and maze surgery [5—7], but are more likely to accept antiarrhythmic drugs [8]. Being less anticoagulated, women experience more stroke [9] or a worse prognosis accompanied with a higher risk than men [10].

Sex differences in outcomes of CA are also evident between women and men. Women undergoing CA are often reported to have less successful outcomes and more complications [11], but similar outcomes [12] and safety results have also been reported. Sex-related outcomes have not been reported in surgical ablation [13].

Although reported sex differences in outcomes after CA for AF have been contradictory, clinical risk stratification of women with AF may help decision-making before they undergo CA. We evaluated arrhythmia outcomes and the predictive value of clinical scores for arrhythmia recurrence in a large cohort of Chinese patients with AF undergoing CA.

Methods

A total of 1423 consecutive symptomatic and drug-refractory patients with non-valvular AF who underwent single ablation between June 2011 and August 2015 in the Guangdong General Hospital were enrolled retrospectively into this study. Baseline characteristics, ablation variables, complications and arrhythmia outcome were collected until 31 December 2016. The study protocol was approved by the Clinical Research Ethics Committee of Guangdong General Hospital. Thirteen patients were withdrawn during the follow-up period, and data from 1410 patients were included in the final analysis.

Paroxysmal AF was defined as AF that terminated spontaneously or with intervention within 7 days; persistent AF was defined as AF that lasted ≥ 7 days; and long-standing persistent AF was defined as AF that lasted > 1 year [14]. The term ''non-paroxysmal'' AF included persistent AF and long-standing persistent AF.

Any recorded atrial tachycardia that lasted ≥ 30 seconds was defined as recurrence. Recurrences that occurred within the first 3 months (blanking period), 3—11 months and ≥ 12 months after the procedure were defined as early recurrences, late recurrences and very late recurrences, respectively. All late and very late recurrences in this study were classed as recurrences. The HATCH, $CHADS_2$, CHA_2DS_2-VASc, MB-LATER, APPLE, BASE-AF_2 and CAAP-AF scores were tested in this study (for score definitions, see Table S1), as reported previously [15].

Ablation procedure

All patients accepted anticoagulation administration and transoesophageal echocardiography or left atrial computed tomography detection to prevent and exclude thrombosis of the left atrium before the procedure. Management of anticoagulants, antiarrhythmic drugs and the invasive ablation protocol followed current guideline recommendations [16].

Circumferential pulmonary vein isolation was performed in most patients, except those with confirmed foci. The freezing procedure was performed consecutively, as described previously [17]. Bidirectional conduction block was confirmed by pacing or administration of adenosine, and was documented as the endpoint of circumferential pulmonary vein isolation and cryoballoon catheter ablation. A cavotricuspid isthmus bidirectional block was done in patients with typical atrial flutter. Linear ablation of the left atrial roof or mitral isthmus and complex fractionated atrial electrograms were performed when necessary. Pharmaceutical (ibutilide or aminodarone) or electrical cardioversion was performed to restore the sinus rhythm when AF continued after the necessary ablation. Procedures were performed under monitoring of activated clotting time within 250—300 seconds once the trans-septal puncture succeeded.

Follow-up

Management of oral anticoagulants and antiarrhythmic drugs after ablation followed current practice guidelines [16]. A physical examination, 12-lead electrocardiogram and 24-hour Holter electrocardiogram were performed at discharge, at 1, 3 and 6 months, and every 6 months thereafter, during follow-up visits. Additional electrocardiograms or 24-hour Holter electrocardiograms were performed when there was any suspicion of recurrence. Arrhythmia recurrence was defined as the study endpoint. Patients without evidence of recurrence were followed up until 31 December 2016 or for a minimum of 12 months.

Statistical analysis

Categorical data are presented as frequencies and percentages, and continuous variables are described as means ± standard deviations. The χ^2 test or independent t test was used to compare differences between men and women, or women with and without recurrence. Differences in the predictive ability of characteristics between men and women were assessed by fitting a sex term in the Cox multivariable regression analysis. Cox multivariable regression analysis was used to determine the predictive ability of clinical characteristics for AF recurrence in women and men. A Kaplan-Meier curve was used to showed effect of a risk factor or clinical characteristic on the time survived without AF/atrial flutter events. Harrell's C-index was used to test the predictive probability of clinical risk scores. The predictive values of clinical scores were compared by the C-index change. A two-sided P value < 0.05 was considered statistically significant. Analyses were done using SPSS software, version 20.0 (IBM Corporation, Armonk, NY, USA) and R software, version 3.5.1 for Windows (RStudio, Inc., Boston, MA, USA).

Results

There were 450 (31.9%) women and 960 (68.1%) men included the final analysis. Female patients were older, with a higher serum concentration of B-type natriuretic peptide (BNP) and greater prevalence of paroxysmal AF, hypertension and diabetes mellitus (all $P < 0.01$). Male patients had a larger left atrial size and worse left ventricular contractive function (all $P < 0.01$). Compared with men, women had higher $CHADS_2$ and CHA_2DS_2-VASc scores (all $P < 0.01$). Women accepted more cryoballoon ablation, whereas men received more additional ablation (cavotricuspid isthmus or complex fractionated atrial electrogram) and electrical cardioversion (all $P < 0.05$). In-hospital complications, early recurrences and overall recurrences had no significant sex differences (Table 1).

Differences between female patients with and without recurrence

Female patients with AF recurrence were older, with a larger left atrial size, worse left ventricular contractive function, more non-paroxysmal AF and previous heart failure, higher serum concentrations of BNP and C-reactive protein (CRP) and a lower estimated glomerular filtration rate (eGFR) compared with female patients without recurrence (all $P < 0.05$). Women with AF recurrence underwent more electrical or pharmaceutical cardioversion and linear ablation during the procedure (all $P < 0.05$) (Table 2).

Sex-related risk factors associated with AF recurrences

Fitting an interaction term as sex, the multivariable analysis showed that age ($P < 0.01$), AF type ($P < 0.01$), body mass index ($P < 0.01$), coronary artery disease ($P = 0.037$), left atrial diameter (LAD) ($P < 0.01$), eGFR ($P < 0.01$), BNP ($P < 0.01$), CRP ($P < 0.01$) and early recurrence ($P < 0.01$) were the independent risk factors for AF recurrence with sex differences (Table 3).

When testing men and women separately, the multivariable analysis showed that AF type ($P < 0.01$), early recurrence ($P < 0.01$), history of stroke/transient ischaemic attack ($P = 0.016$), BNP ($P < 0.01$) and CRP ($P < 0.05$) were risk factors for AF recurrence in women, whereas predictors of AF recurrence in men were age ($P < 0.01$), AF type ($P = 0.047$), coronary artery disease ($P < 0.01$), LAD ($P < 0.01$), eGFR ($P < 0.01$), BNP ($P < 0.01$), CRP ($P < 0.01$) and early recurrence ($P < 0.01$) (Table 3).

Clinical scores and AF recurrence

Harrell's C-indexes showed that the HATCH, $CHADS_2$ and CHA_2DS_2-VASc scores (C-indexes 0.56, 0.55 and 0.57, respectively ; all $P < 0.01$ and the MB-LATER, APPLE, CAAP-AF and BASE-AF_2 scores (C-indexes 0.73, 0.72, 0.68 and 0.72, respectively; all $P < 0.01$) had a modest predictive value for AF recurrence after CA in women (Table 4). Comparing differences in C-index, the MB-LATER score had a similar predictive value to the APPLE and BASE-AF_2 scores, but was significantly better than the other four scores (Table 5). The MB-LATER score showed a significantly different predictive ability in women with different scores (0—4) using Kaplan-Meier analysis ($P < 0.01$) (Fig. 1).

Discussion

In this large ''real-world'' Chinese dataset of AF ablation our main findings were as follows:

- sex-related differences were found in baseline characteristics and ablation variables, but not in ablation outcome;
- sex-related differences were found in the risk factors for AF recurrence;
- seven clinical scores (MB-LATER, APPLE, CAAP-AF, BASE-AF_2, HATCH, $CHADS_2$ and CHA_2DS_2-VASc) had modest or mild predictive ability for AF recurrence after CA in women. To our knowledge, this is the first report on sex-related risk factors for AF recurrence. Sex-related differences in clinical characteristics and ablation variables, but similar outcomes, were shown in our overall results.

Sex-related prognosis of AF and ablation outcome

Sex-related differences in clinical characteristics in the non-valvular AF population have been reported in many studies [5,6,8]. Women with AF are older, with a higher heart rate, more symptoms, a poorer quality of life and a worse prognosis, with increasing prevalence of persistent AF, stroke and death. Female sex has also been related to new-onset AF in patients with atrial flutter [18]. Compared with men, the prevalence of diabetes mellitus is higher in women, who also have a higher $CHADS_2$ score, leading to increased stroke risk [10]. Treatment of women with AF tends to be more conservative, with lower rates of oral anticoagulation, less selection of invasive rhythm control therapy and more antiarrhythmic drug side effects [7,8].

Table 1 Differences in characteristics between men and women.

	Total	Men	Women	P[a]
	(n = 1410; 100%)	(n = 960; 68.1%)	(n = 450; 31.9%)	
Age (years)	57.8 ± 11.7	55.9 ± 11.8	59.9 ± 10.9	< 0.01
LAD (mm)	36.9 ± 5.2	37.3 ± 5.3	35.9 ± 5.3	< 0.01
BNP (pg/mL)	320 ± 456	229 ± 415	363 ± 555	0.014
CRP (mg/dL)	2.3 ± 3.7	2.2 ± 3.7	2.5 ± 3.9	0.21
eGFR (mL/min/1.73m^2)	87.2 ± 22.8	87.4 ± 20	87 ± 26.8	1.0
Body mass index (kg/m^2)	24.5 ± 3.3	24.7 ± 3.2	24 ± 3.4	< 0.01
LVEF (%)	64.7 ± 6.1	63.4 ± 6.3	65.4 ± 5.6	< 0.01
Follow-up (months)	20.7 ± 8.8	20.7 ± 9.1	20.7 ± 8.0	1.0
Non-paroxysmal AF	321 (22.8)	248 (25.8)[b]	73 (16.2)	< 0.01
Paroxysmal AF	1089 (77.2)	712 (74.2)	377 (83.8)	< 0.01
Bundle branch block	94 (6.7)	72 (7.5)	22 (4.9)	0.07
COPD	9 (0.6)	7 (0.7)	2 (0.4)	0.73
Alcohol	75 (5.3)	70 (7.3)	5 (1.1)	< 0.01
Smoking	244 (17.3)	219 (22.8)	25 (5.6)	< 0.01
History of CHF	72 (5.1)	48 (5)	24 (5.3)	0.75
Hypertension	508 (36.1)	310 (32.3)	198 (44)	< 0.01
Diabetes mellitus	143 (10.1)	82 (8.6)	61 (13.6)	< 0.01
History of stroke/TIA	84 (6)	52 (5.4)	32 (6)	0.23
CAD	105 (7.5)	72 (7.5)	33 (7.3)	1.0
Cryoballoon ablation	74 (5.3)	41 (4.3)	33 (7.3)	0.02
SMARTTOUCH® ablation catheter[b]	247 (17.5)	168 (17.5)	79 (17.6)	1.0
Electrical cardioversion	157 (11.2)	131 (13.7)	26 (5.8)	< 0.01
Drug cardioversion	221 (15.7)	157 (16.7)	64 (14.2)	0.35
CFAE ablation	35 (2.5)	20 (2.1)	15 (3.3)	0.20
CTI ablation	251 (26.2)	28 (24.6)	86 (19.1)	< 0.01
Linear ablation	266 (18.9)	195 (20.3)	71 (15.8)	0.049
Complications	12 (0.9)	9 (0.9)	3 (0.7)	0.38
Early recurrence	317 (22.5)	251 (26.1)	98 (21.8)	0.73
Recurrence	365 (25.9)	251 (26.1)	114 (25.3)	0.79
HATCH score	0.6 ± 0.9	0.6 ± 0.9	0.8 ± 0.9	< 0.01
$CHADS_2$ score	0.7 ± 0.9	0.6 ± 0.9	0.8 ± 1.0	< 0.01
CHA_2DS_2-VASc score	1.4 ± 1.4	1.0 ± 1.2	2.3 ± 1.3	< 0.01
APPLE score	0.8 ± 1.0	0.8 ± 1.0	0.9 ± 0.9	0.22
CAAP-AF score	3.5 ± 1.7	3.2 ± 1.7	4.2 ± 1.5	< 0.05

Data are expressed as number (%) or mean ± standard deviation. AF: atrial fibrillation; BNP: B-type natriuretic peptide; CAD: coronary artery disease; CHF: congestive heart failure; CRP: C reactive protein; CTI: cavotricuspid isthmus; CFAE: complex fractionated atrial electrogram; COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; TIA: transient ischaemic attack.

[a] χ^2 test or independent t test; statistically significant if $P < 0.05$.

[b] Biosense Webster Inc., Irvine, CA, USA

Reports on sex-related AF ablation outcomes have been inconsistent. In a German ablation registry (n = 3652), women who received ablation procedures were older, their procedures were less successful and they had more in-hospital complications compared with men [11]. In a smaller study (n = 221), sex-related differences were not found for the effectiveness and safety of AF ablation [12].

As in previous studies, women in our AF ablation cohort were older, with a greater prevalence of paroxysmal AF, hypertension and diabetes mellitus, as well as higher $CHADS_2$ and CHA_2DS_2-VASc scores compared with men. The proportion of women (31.9%) was similar to that in the German ablation registry (33%), but sex-related differences in success and safety were not found in our study. Procedure-related adverse events were small (0.9%) in our study; all complications were non-fatal, and only one intracranial haemorrhage occurred in a woman. Female sex and old age have been related to a higher prevalence of complications during the ablation procedure [19]. Although the women in our cohort were older than the men, they were slightly younger than in the German ablation registry cohort. Women seem to respond less favourably to AF ablation, and to have

Table 2 Differences in characteristics between women with or without recurrence of atrial fibrillation .

	Total	With recurrence	Without recurrence	P^a
	(n = 450; 100%)	(n = 114; 25.3%)	(n = 336; 74.7%)	
Age (years)	59.9 ± 10.9	62.5 ± 9.6	59.2 ± 11.2	0.02
LAD (mm)	35.9 ± 5.3	37.8 ± 5.7	35.3 ± 5.1	< 0.01
BNP (pg/mL)	363 ± 555	885 ± 794	188 ± 281	< 0.01
CRP (mg/dL)	2.5 ± 3.9	4.5 ± 3.7	1.8 ± 3.7	< 0.01
eGFR (mL/min/1.73m^2)	87 ± 22.8	69.2 ± 28.8	93.1 ± 23.2	< 0.01
Body mass index (kg/m^2)	24 ± 3.4	24.4 ± 4.1	23.9 ± 3.5	0.14
LVEF (%)	65.4 ± 5.6	63.7 ± 6.9	66 ± 5.0	< 0.01
Follow-up (months)	20.7 ± 8.0	11.5 ± 7.8	23.9 ± 5.2	< 0.01
Non-paroxysmal AF	73 (16.2)	43 (37.7)*	30 (8.9)	< 0.01
COPD	2 (0.4)	1 (0.9)	1 (0.3)	0.44
Alcohol	5 (1.1)	1 (0.9)	4 (1.2)	1.00
Smoking	25 (5.6)	8 (7.0)	17 (5.1)	0.48
History of CHF	24 (5.5)	12 (10.1)	12 (3.6)	< 0.01
Hypertension	198 (44)	53 (46.5)	145 (43.5)	0.59
Diabetes mellitus	61 (13.6)	18 (15.8)	43 (12.8)	0.43
History of stroke/TIA	32 (6)	12 (10.5)	20 (6)	0.99
CAD	33 (7.3)	9 (7.9)	24 (7.1)	0.84
Cryoballoon ablation	33 (7.3)	8 (7)	25 (7.4)	1.0
SMARTTOUCH® ablation catheter[b]	79 (17.6)	19 (16.7)	60 (17.9)	0.89
Electrical cardioversion	26 (5.8)	19 (16.7)	7 (2.1)	< 0.01
Drug cardioversion	64 (14.2)	24 (21.1)	40 (11.9)	0.02
CFAE ablation	15 (3.3)	6 (5.3)	9 (2.7)	0.23
CTI ablation	8 6(19.1)	28 (24.6)	58 (17.3)	0.1
SVC ablation	32 (7.1)	6 (5.3)	26 (7.7)	0.53
Linear ablation	71 (15.8)	34 (29.8)	37 (11.0)	< 0.01
Early recurrence	98 (21.8)	59 (51.8)	39 (11.6)	< 0.01
HATCH score	0.8 ± 0.9	1.0 ± 1.1	0.7 ± 0.9	0.01
$CHADS_2$ score	0.8 ± 1.0	1.0 ± 1.1	0.8 ± 0.9	0.04
CHA_2DS_2-VASc score	2.3 ± 1.3	2.5 ± 1.5	2.2 ± 1.3	0.01
APPLE score	0.9 ± 0.9	1.5 ± 1.1	0.6 ± 0.8	< 0.01
CAAP-AF score	4.2 ± 1.5	5.1 ± 1.7	3.9 ± 1.4	0.07

Data are expressed as number (%) or mean ± standard deviation. AF: atrial fibrillation; BNP: B-type natriuretic peptide; CAD: coronary artery disease; CHF: congestive heart failure; CRP: C reactive protein; CTI: cavotricuspid isthmus; CFAE: complex fractionated atrial electrogram; COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; LAD: left atrial diameter; LVEF: left ventricular ejection fraction; SVC: superior vena cava; TIA: transient ischaemic attack.

[a] χ^2 test or independent t test; statistically significant if $P < 0.05$.

[b] Biosense Webster Inc., Irvine, CA, USA.

higher rates of procedural complications, but this may be improved with more acceptance of earlier ablation [20].

Our results showed that women had less prevalence of non-paroxysmal AF and a smaller left atrial size, whereas men accepted more linear ablation and electrical cardioversion during the procedure. These differences imply that women might have a less complicated left atrial substrate, contributing to similar AF ablation outcomes to men. Sex-related difference in maze surgery outcomes [13,21] have not been reported as yet.

Furthermore, the patients enrolled were all Chinese, and there should have been an ethnicity influence on the ablation result, as reported by GARFIELD-AF study [22].

Sex-related characteristics or risk factors for AF recurrence

Compared with those without recurrence, women with AF recurrence after CA in our cohort were older, with a larger left atrial size, higher serum CRP and BNP concentrations, higher prevalence of non-paroxysmal AF and history of heart failure, and a lower eGFR and left ventricular contractive function. This implies a highly complicated left atrial substrate, needing more linear ablation and electrical cardioversion during the procedure. Meanwhile, women with AF recurrence had higher $CHADS_2$ and CHA_2DS_2-VSCs scores, which corresponds with history of stroke/transient

ischaemic attack being one of the risk factors for AF recurrence in women.

Compared with men, the women had a higher serum BNP concentration—a known predictor of new onset non-valvular AF, and of prognostic value [23,24]. Indeed, BNP was an independent predictor of AF recurrence for both men and women in our study. CRP concentration [25,26] and chronic kidney disease [27,28] have been related to the onset, progression and recurrence of AF. Similar results were found in our cohort in both women and men, except for eGFR. BNP, CRP and eGFR were risk factors for AF recurrence with sex differences in our cohort. Reasons for these differences remain unknown.

Among the AF population, chronic obstructive pulmonary disease and coronary artery disease were related to AF recurrence, but occurred more frequently in men [29,30]. LAD is an accepted predictor of AF recurrence after CA [15], but only in men in our cohort. Sex-related LAD differences in our cohort might be one of the reasons for the similar arrhythmia outcome in men and women.

As reported by many studies [20], older age influences the progression and arrhythmia outcome of AF, and is included as one of the risk factors in many scoring systems. Age was a risk factor only in men in our cohort, but was related to a lower risk of AF recurrence. The mean age was < 60 years in both sexs, and should be related to this discriminating result.

Eight risk factors for AF recurrence were found using multivariable Cox regression analysis, by fitting an interaction term of sex. When testing women and men separately, we found that they had different risk factors for AF recurrence.

Predictive value of clinical scores in the female AF cohort

Apart from the biomarkers discussed above, eight clinical scores have been derived or tested in different AF ablation cohorts, but none has been specifically validated in a female cohort [15]. We tested seven of these scores, and found that the HATCH, $CHADS_2$, CHA_2DS_2-VASc, MB-LATER, BASE-AF_2, APPLE and CAAP-AF scores were significant predictors of AF recurrence in females. Although male sex was included as one of the risk factors in the MB-LATER score [31], the predictive value of this new score on AF recurrence was also validated in our female cohort. Furthermore, the score showed good predictive ability compared with the other scores, or when stratified into 0—4 points. This result was consistent with our previous study showing the predictive value of the MB-LATER score [32].

Study limitations

This was a single-centre retrospective observational study. Follow-up tools and methods were conservative, and some asymptomatic AF recurrence may have been missed. More intense monitoring, such as remote electrocardiogram monitoring and loop recorder implantation [33], could be considered.

Table 3 Multivariable analysis of risk factors for recurrence of atrial fibrillation after ablation.

Risk factors	HR (95% CI)	P[a]
With sex interaction[b]		
Age	0.96 (0.95 to 0.98)	< 0.01
AF type	1.56 (1.23 to 1.97)	< 0.01
Early recurrence	3.13 (2.49 to 3.95)	< 0.01
CAD	1.45 (1.02 to 2.07)	0.037
LAD	1.05 (1.02 to 1.07)	< 0.01
Body mass index (kg/m^2)	1.06 (1.02 to 1.10)	< 0.01
eGFR ($mL/min/1.73^2$)	0.97 (0.96 to 0.98)	< 0.01
BNP (pg/mL)	1.01 (1.00 to 1.001)	< 0.01
hsCRP (mg/dL)	1.06 (1.04 to 1.08)	< 0.01
Women		
AF type	2.32 (1.56 to 3.45)	< 0.01
Early recurrence	3.88 (2.59 to 5.82)	< 0.01
History of stroke/TIA	2.11 (1.15 to 3.89)	0.016
BNP (pg/mL)	1.00 (1.00 to 1.01)	< 0.01
hsCRP (mg/dL)	1.06 (1.02 to 1.09)	< 0.01
Men		
Age	0.97 (0.96 to 0.99)	< 0.01
AF type	1.34 (1.00 to 1.79)	0.047
CAD	1.75 (1.17 to 2.62)	< 0.01
LAD (mm)	1.05 (1.02 to 1.07)	< 0.01
Early recurrence	3.28 (2.47 to 4.35)	< 0.01
BNP (pg/mL)	1.00 (1.00 to 1.01)	< 0.01
hsCRP (mg/dL)	1.06 (1.04 to 1.08)	< 0.01
eGFR ($mL/min/1.73m^2$)	0.98 (0.97 to 0.99)	< 0.01

Adjusted for age, AF type, AF duration, early recurrence, hypertension, stroke/TIA, CAD, LAD, LVEF, vascular disease, body mass index, eGFR, hsCRP and BNP. AF: atrial fibrillation; BNP: B-type natriuretic peptide; CAD: coronary artery disease; CI: confidence interval; HR: hazard ratio; LAD: left atrial diameter; eGFR: estimated glomerular filtration rate; hsCRP: high-sensitivity C-reactive protein; LVEF: left ventricular ejection fraction; TIA: transient ischaemic attack.

[a] Covariate categorical Cox regression analysis; statistically significant if $P < 0.05$.

[b] Fitting an interaction term of sex.

Table 4 Predictive value of clinical scores for recurrence of atrial fibrillation after catheter ablation in women.

	C index (95% CI)	P[a]
Score		
HATCH	0.56 (0.51 to 0.61)	< 0.01
$CHADS_2$	0.55 (0.50 to 0.61)	< 0.01
CHA_2DS_2-VASc	0.57 (0.52 to 0.62)	< 0.01
MB-LATER	0.73 (0.69 to 0.78)	< 0.01
APPLE	0.72 (0.69 to 0.77)	< 0.01
CAAP-AF	0.68 (0.63 to 0.73)	< 0.01
BASE-AF_2	0.72 (0.67 to 76)	< 0.01

CI: confidence interval.

[a] Statistically significant if $P < 0.05$.

Table 5 Predictive value of six scores compared with the MB-LATER score.

	C index change (95% CI)	P[a]
Score		
HATCH	0.17 (0.08 to 0.26)	< 0.01
$CHADS_2$	0.18 (0.11 to 0.24)	< 0.01
CHA_2DS_2-VASc	0.16 (0.08 to 0.24)	< 0.01
APPLE	0.01 (−0.05 to 0.06)	0.75
CAAP-AF	0.05 (0.00 to 0.10)	0.049
BASE-AF_2	0.02 (−0.03 to 0.06)	0.47

CI: confidence interval.
[a] Statistically significant if $P < 0.05$.

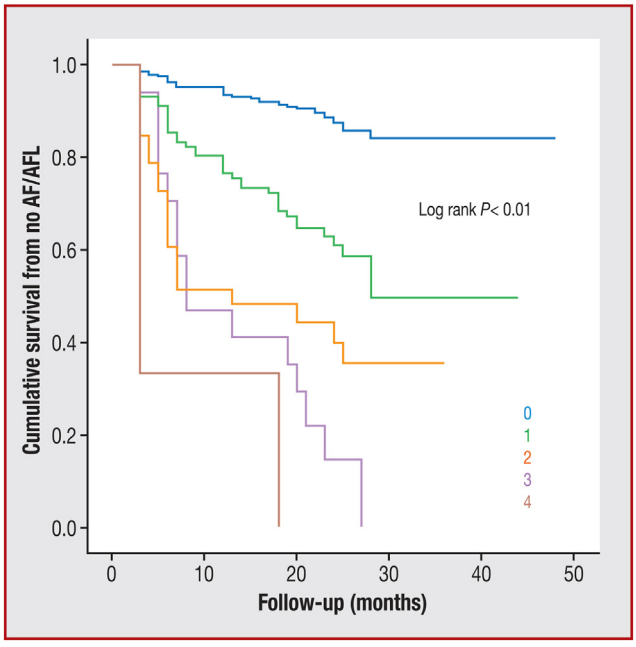

Figure 1. Kaplan-Meier curve of time to atrial fibrillation/atrial flutter (AF/AFL) events in women with different MB-LATER scores (0—4). Cum: cumulative.

Conclusions

CA for AF has similar recurrence risks in women and men, but there are sex differences in the clinical characteristics and risk factors associated with AF recurrence.

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Disclosure of interest

G. Y. H. L. Consultant for the companies Bayer/Janssen, BMS/Pfizer, Biotronik, Medtronic, Boehringer Ingelheim, Microlife and Daiichi-Sankyo. Speaker for the companies Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Microlife, Roche and Daiichi-Sankyo.

The other authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2018.10.006.

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