In-hospital and 12-month follow-up outcome from the ESC-EORP EHRA Atrial Fibrillation Ablation Long-Term registry: sex differences

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Aim

The purpose of this study was to compare sex differences of atrial fibrillation (AF) catheter ablation (CA) and to analyse the opportunities for improved outcomes.

Methods and results

All data were collected from the Atrial Fibrillation Ablation Long-Term registry, a prospective, multinational study conducted by the ESC-EORP European Heart Rhythm Association (EHRA) under the EURObservational Research Programme (ESC-EORP). A total of 104 centres in 27 European countries participated. Of 3593 included patients, 1146 (31.9%) were female. Female patients were older (61.0 vs. 56.4 years; \( P < 0.001 \)), had more comorbidities (hypertension, diabetes, and obesity), more episodes of arrhythmias per month (6.9 vs. 6.2; \( P < 0.001 \)), and a higher average EHRA score (2.6 vs. 2.4; \( P < 0.001 \)). The duration of the procedure was shorter in females (160.1 min vs. 167.9 min; \( P < 0.001 \)), irrespective of additional ablation lesions added to pulmonary vein isolation. Overall cardiovascular complications were more frequent in women than in men (5.7% vs. 3.4%; \( P < 0.001 \)). Furthermore, cardiac perforations (3.8% vs. 1.3%; \( P = 0.011 \)) and neurological complications (2.2% vs. 0.3%; \( P = 0.004 \)) were found in females in less experienced centres than in experienced ones. On a final note, at 12 months, AF recurrence rate was similar in females and males (34.4% vs. 34.2%; \( P = 0.897 \)), but more females were still on antiarrhythmic drugs (50.6% vs. 44.1%; \( P < 0.001 \)) when compared with men.

Conclusion

Females underwent CA procedures for AF less frequently than males throughout Europe, despite more recurrent symptoms. With the same success rate, severe acute complications remained considerable in females, especially in less experienced centres.

Keywords

Atrial fibrillation • Catheter ablation • Sex differences • Gender differences • Registry
Introduction
Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, with a continuously increasing incidence. Several studies have investigated sex-related differences in AF. New data on clinical presentation and interventional treatment outcomes have become available. Epidemiological studies have revealed that the risk of incident AF in men is approximately twice that of women. Atrial fibrillation is also more frequent at a given age in men than in women. Variability increases markedly one decade later in women than in men. Women with AF are more symptomatic than men and display different comorbidities.

The investigation of sex differences in the management of AF has led to conflicting results. Recent data suggest that a gender-related risk of thromboembolic events may not be increased in women, as is currently set forth. Regarding interventional treatment, women tend to be referred for AF catheter ablation (CA) less frequently, and at an older age, than men. Some other studies have suggested higher procedural risk of complications in women. Although several analyses have reported comparable CA outcomes between both sexes, there is still a need to gather more evidence in this respect. For further studies, the usage of a more homogeneous data set from the following viewpoints would be advisable: gender, age, comorbidities, and experience level of centres in scope.

Methods
Sex differences were analysed in the clinical profile of patients submitted to CA, in-hospital and 12-month follow-up of the AF Ablation Long-Term registry, a prospective, multinational, observational study conducted by the European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC) under the EURObservational Research Programme (EORP).

Study design and setting
Twenty-seven individual National Societies of Cardiology in Europe were invited to participate in the registry. National Coordinators were responsible for obtaining approval of their national and/or local Institutional Review Board. A total of 104 centres were asked to voluntarily enroll 20–50 consecutive patients scheduled for the first and/or repeat AF ablation, between April 2012 and April 2015, and to perform a follow-up after 12 months. All patients signed an informed consent before collection of any data. Symptoms of AF in women persistent or persistent AF who previously failed antiarrhythmic drugs (AADs) were considered as having Class IIa indication for CA. On the other hand, AF refractory to AADs, as well as AF patients with refractory heart failure, who did not undergo ablation procedure were excluded from the analysis.

Data collection
Data were collected using a web-based system. An electronic case report form was developed to capture the following information for each enrolled patient: enrolment, procedural, post-procedural, and 12-month follow-up data. Symptoms at baseline and 12-month follow-up were estimated through individual questionnaires. Centres planned their follow-up according to their usual clinical practice. There were no standardized recommendations across different centres for AAD administration. No specific QoL questionnaire was applied in this survey. The database was set up at the European Heart House of the ESC. The EORP Department of the ESC was responsible for close central data monitoring and auditing, detecting inaccuracies and inconsistencies.

Statistical analysis
Continuous variables were reported as median and interquartile range (IQR). Categorical variables were reported as percentages. Group comparisons were made using a χ2 test or Fisher’s exact test (if any expected cell count was <5). For quantitative variables with more than two possibilities, the Monte Carlo estimates of the exact P-values were used. Plots of the Kaplan–Meier curves for arrhythmia-free survival according to gender categories were performed. The survival distributions were compared using the log-rank test. A two-sided P-value <0.05 was considered statistically significant. To determine the hazard ratio of periprocedural complications, a Cox regression analysis was used. The covariates included in

What’s new?
- This study was a sub-analysis of the European Society of Cardiology (ESC)–EORP European Heart Rhythm Association (EHRA) Atrial Fibrillation (AF) Ablation Long-Term registry regarding sex differences in clinical profile of patients submitted to catheter ablation (CA), in-hospital complications and 12-month follow-up.
- Females underwent less frequently to CA being predominantly overweight, in their 60s, with multiple comorbidities and having a higher average EHRA score.
- Maintenance of sinus rhythm at 12-month follow-up after CA was similar in women and men, regardless of AF type prior to ablation; however, cardiac perforation and vascular complications occurred predominantly in female patients.
- Female sex was found to be a predictor of acute cardiovascular complications after CA of AF, especially in less experienced centres.
- For further studies, the usage of a more homogeneous data set from the following viewpoints would be advisable: gender, age, comorbidities, and experience level of centres in scope.
the multivariable regression model were chosen based on their clinical relevance and the significance in univariable analyses with a P-value of <0.10 and with at least 80% of data available, entered into the model with an automatic stepwise selection.

All analyses were performed using SAS statistical software version 9.4 (SAS Institute, Inc., Cary, NC, USA).

**Results**

**Patient population**

Overall, 3593 of 3630 included patients (99.0%) underwent AF ablation, of which one-third were women (31.9%). The geographical distribution of gender among those undergoing CA was as follows: the female patients were 27.9% in Northern, 29.3% in Western, 29.6% in Southern, and 37.6% in Eastern countries (Figure 1). The proportion of treated females was 31.66% in experienced centres and 31.23% in less experienced ones (P = 0.805).

**Clinical characteristics**

Clinical characteristics of patients included in the study are presented in Table 1. Median age was significantly higher in female patients (61.0 vs. 56.4 years; P < 0.001), and the proportion of older patients (≥65 years) was 34.2% vs. 18.3%; P < 0.001. The females more often had paroxysmal AF (73.8% vs. 64.7%, P < 0.001), compared with male patients, whereas the males more often had persistent AF (29.8% vs. 22.4%, P < 0.001) and long-standing persistent AF (5.6% vs. 3.8%, P < 0.001), compared to females. The time length of AF history was

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**Table 1** Gender differences regarding clinical characteristics of patients

<table>
<thead>
<tr>
<th>Cardiovascular risk factors (%)</th>
<th>Total (N = 3593)</th>
<th>Male (N = 2447)</th>
<th>Female (N = 1146)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (kg/m²) &gt;30 kg/m² (%)</td>
<td>1047/3333 (31.4%)</td>
<td>620/2268 (27.3%)</td>
<td>427/1065 (40.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>347/3583 (9.7%)</td>
<td>215/2441 (8.8%)</td>
<td>132/1142 (11.6%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Active smokers</td>
<td>353/3432 (10.3%)</td>
<td>297/2331 (12.7%)</td>
<td>56/1101 (5.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>1159/3517 (33.0%)</td>
<td>755/2399 (31.5%)</td>
<td>404/1118 (36.1%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>146/3481 (4.2%)</td>
<td>118/2356 (5.0%)</td>
<td>28/1125 (2.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Underlying disorders (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1954/3579 (54.6%)</td>
<td>1245/2438 (51.1%)</td>
<td>709/1141 (62.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>449/2380 (18.9%)</td>
<td>335/1540 (21.8%)</td>
<td>114/840 (13.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic heart failure</td>
<td>537/2418 (22.2%)</td>
<td>339/1569 (21.6%)</td>
<td>198/849 (23.3%)</td>
<td>0.333</td>
</tr>
<tr>
<td>Co-morbidities (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>84/3519 (2.4%)</td>
<td>56/2390 (2.3%)</td>
<td>28/1129 (2.5%)</td>
<td>0.804</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>57/3556 (1.6%)</td>
<td>39/2418 (1.6%)</td>
<td>18/1138 (1.6%)</td>
<td>0.945</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>83/3516 (2.4%)</td>
<td>62/2389 (2.6%)</td>
<td>21/1127 (1.9%)</td>
<td>0.182</td>
</tr>
<tr>
<td>Sleep apnoea</td>
<td>122/3321 (3.7%)</td>
<td>104/2339 (4.6%)</td>
<td>18/1106 (1.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>70/3556 (2.0%)</td>
<td>38/2420 (1.6%)</td>
<td>32/1136 (2.8%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Stroke/transient ischaemic attack</td>
<td>239/3582 (6.7%)</td>
<td>146/2437 (6.0%)</td>
<td>93/1145 (8.1%)</td>
<td>0.017</td>
</tr>
</tbody>
</table>
similar in females (4.2 ± 4.6 years) when compared with males (4.5 ± 5.4 years, P = 0.846).

Regarding cardiovascular risk factors associated with AF, women more frequently presented with obesity (body mass index >30 kg/m²), hypercholesterolaemia, diabetes mellitus, hypertension, and a previous stroke/transient ischaemic attack. In addition, women had a higher mean CHADS2 score (1.1 vs. 0.9; P < 0.001), CHA2DS2-VASc score (2.5 vs. 1.2; P < 0.001) and HAS-BLED bleeding score (0.6 vs. 0.5; P < 0.001). On the contrary, men were more frequently smokers, alcohol users, more affected by sleep apnoea disorder, coronary and peripheral vascular disease, as presented in Table 1.

**Atrial fibrillation ablation indication**

Severity of symptoms (94.1% vs. 89.7%; P < 0.001) and poor QoL (71.3% vs. 63.8%; P < 0.001) were more frequently reported in females than males as the reason for AF ablation. The patient’s wish to maintain a normal sinus rhythm was more prevalent in men (27.8% vs. 23.8%; P = 0.004) and Class IIa in males (10.9% vs. 7.9%; P = 0.004).

**Echocardiography evaluation**

A pre-procedural transthoracic echocardiogram showed a left atrial median diameter of 41.0 mm (IQR 37.0–46.0) in women and 43.0 mm (IQR 39.0–47.0) in men (P < 0.0001). A normal left ventricular ejection fraction (%) was present in females as in males 61.0 (IQR 59.0–65.0) vs. 60.0 (IQR 55.0–65.0) (P < 0.001).

**Ablation technique and results**

More than two-thirds of participating centres in the study were experienced, as presented in Table 2. Ablation procedure parameters are described in Table 2. Regarding CA strategy, there were no particular sex-related discrepancies. Substrate ablation, including left atrial roof line, cavotricuspid isthmus (CTI), and complex fractionated left atrial electrograms (CFAE), was performed in paroxysmal AF (7.8%, 16.7%, and 5.7%, respectively) and in persistent AF (25.6%, 20.7%, and 14.9%, respectively), however, the CA technique used was not sex-dependent. Autonomic ganglionated plexi (GP) ablation was performed in addition to PVI more frequently in females (10.3% vs. 7.3%, P = 0.010) with paroxysmal AF. No sex-related differences regarding anaesthesia type, mapping system, or energy sources utilized were observed. The most commonly used energy source was radiofrequency with open irrigation, followed by cryoballoon ablation. The median procedure duration was slightly shorter in female than in male patients. Mean radiation exposure dose and mean exposure time were not gender dependent.

**Peri-procedural anticoagulant management**

Ablation was performed on uninterrupted vitamin K antagonists with an INR target of 2.3 (IQR 2.0–2.5) or non-vitamin K antagonists in 36% of cases, without any difference between females and males. All patients continued to be treated with anticoagulant therapy from discharge onwards.

**Complications related to the ablation procedure**

In-hospital complications of CA procedures occurred in 7% of cases, 9.5% in females and 5.8% in males (P < 0.001), as presented in Table 3. Cardiac perforation, bradycardia requiring pacemaker implantation,
and vascular complications (e.g. femoral artery pseudo-aneurysm) occurred predominantly in female patients. Neurological events, pulmonary, or gastrointestinal side effects occurred in less than 1% of cases, irrespective of gender or type of procedure performed. A single death occurred in a female due to atrio-oesophageal fistula. Cardiac perforations (1.9% vs. 0.9%, \( P = 0.016 \)) and neurological complications (1.5% vs. 0.4%, \( P < 0.001 \)) were more frequent in less experienced centres when compared with more experienced ones. The rest of complications were comparable among centres. When analysing by gender, the incidence of cardiac perforation for female patients was higher in less experienced (3.8%) than in experienced centres (1.3%) (\( P = 0.011 \)). On the other hand, no significant differences were found for centre experience in males (1% vs. 0.7%, respectively; \( P = 0.425 \)). Neurological complications were also higher for females in less experienced centres (2.2% vs. 0.3% in experienced centres; \( P = 0.004 \)). Yet again, no significant differences were found in males (1.1% vs. 0.5%, respectively; \( P = 0.102 \)).

Female sex was found to be an independent factor for CA complications (HR 1.420, 95% CI 1.028–1.960; \( P = 0.011 \)) in multivariable analysis (Supplementary material online, Table S1). None of the other investigated parameters (age, diabetes, hypertension, chronic kidney disease, previous thromboembolism, CHADS\(_{2}\)-VASc score, CHA\(_{2}\)DS\(_{2}\)-VASc score, left atrial dimension, type of procedure, or energy source) was identified as a predictor of major complications. However, no general anaesthesia during CA procedure seems to be associated to less complications (HR 0.645, 95% CI 0.421–0.987; \( P = 0.043 \)) in univariable, as well as in multivariable analysis.

**12-month follow-up results**

At 12-months, the rate of AF recurrence was similar in females vs. males (34.4% vs. 34.2%; \( P = 0.897 \)). Freedom of arrhythmias was also similar in male and female patients (65.8 vs. 65.5%; \( P = 0.897 \)). More females received AADs after blanking period compared with males (50.8% vs. 43.1%, \( P < 0.001 \)), and they remained more on AADs after the 12-month follow-up (50.6% vs. 44.1%; \( P < 0.001 \)). Patients treated with AAD were more symptomatic (60% vs. 34%; \( P < 0.001 \)) and had presented with events more frequently than patients without AAD therapy (50.9% vs. 24.8%; \( P < 0.001 \)). When AF recurred, the longest episode had a similar duration in females (17.37 ± 56 days) vs. males (29.3 ± 76 days) (\( P = 0.062 \)). The same percentage of electrical cardioversions was performed in the case of recurrences in females (45.7%) vs. males (45.8%) (\( P = 0.973 \)), as well as repeat ablation (21.3% vs. 22.1%, \( P = 0.783 \)). The female group remained more symptomatic (50.4% vs. 40.3%, \( P < 0.001 \)), complaining of palpitations, fatigue, and dyspnoea, with a higher mean EHRA score (1.6 vs. 1.4; \( P < 0.001 \)). Females came to routine consultations more frequently (3.1 vs. 2.7 consultations/1 year; \( P < 0.001 \)). The EHRA score showed an equal improvement of symptoms after CA, from a mean EHRA score of 2.6 ± 0.6 at baseline to 1.6 ± 0.7 at 12 months in females (\( P < 0.001 \)), respectively from 2.4 ± 0.6 to 1.4 ± 0.7 in males (\( P < 0.001 \)) (Figure 2).

After 12-month follow-up, more females than males were treated with long-term antithrombotic therapy based on vitamin K (44.0% vs. 36.6%; \( P < 0.001 \)) or non-vitamin K antagonists (22.9% vs. 19.3%; \( P = 0.022 \)). Generally, almost a quarter of patients (21.4%) with long-term antithrombotic therapy applied through drugs such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (49.3% vs. 40.8%; \( P < 0.001 \)), aldosterone blockers (4.9% vs. 2.3%; \( P < 0.001 \)), or statins (31.8% vs. 25.7%; \( P < 0.001 \)).
Discussion

This study is a sub-analysis of the AF Ablation Long-Term registry results regarding sex differences in clinical profile, pre-/post-procedural parameters, and also 12-month follow-up of patients who underwent CA for AF. The main strength of this research is the registry size. The results showed that females had the same rate of sinus rhythm maintenance at 12 months after CA as males, but more post-procedural cardiovascular complications, especially in less experienced centres.

Gender differences in patient referral to catheter ablation procedure

Data analysis of this registry clearly showed that the proportion of females treated by CA was lower than in males. Several studies showed that women were referred less often for CA. The percentage of women referred for ablation in these studies ranged from 15.8% to 33.2%. The findings of this study were consistent with data of EORP-Atrial Fibrillation General Registry, where the proportion of females was also lower (39.4% female vs. 60.6% men). The fact that fewer women than men underwent ablation could raise the suspicion of bias against referring women. It could also be the result of personal choice of male patients who were more willing to accept interventional treatment before AAD, or simply having less symptoms, which was supported by the fact that their indication for CA was mainly IIb according to standard guidelines.

The above sex differences in the use of CA in AF management were relatively homogeneous throughout Europe; CA in females remained significantly lower (below 30%) irrespective of region or centre’s experience. This might primarily reflect the fact that AF prevalence per 100 000 inhabitants was higher in men when compared with women, according to a statistical analysis of the global burden of AF.

Our study also showed that women were treated by CA at an older age when compared with men. However, a similar length of history of AF before CA in both genders suggested that an advanced age of women at CA procedure was not related to late referral, but to higher prevalence of AF in women in older age groups. This was in line with recent epidemiological data documenting that females developed AF a decade later than males. For all these reasons, it was not surprising in this study that females who were in their 6th decade had more comorbidities than men, who were significantly younger.

Gender differences in symptoms

This study showed that women had more episodes of arrhythmia per month with a higher heart rate during AF when compared with men. Other studies confirmed that women were more symptomatic from AF and had a lower QoL, probably because of increased heart rates. It seemed that the mean heart rate at the onset of AF was higher in women than in men. In addition, women with AF were more likely to experience longer (>24 h) symptomatic episodes, more frequent recurrences of AF and a lower QoL due to depression caused by decreased physical and mental health status. Thus, we could deduce that AF events’ frequency and cardiac rate were more accurate parameters to indicate ablation, while EHRA score could also reflect age and associated comorbidities.

Predictors of success rate and recurrences after catheter ablation procedure in women

In this study, maintenance of sinus rhythm at 12-month follow-up was similar in women and men, regardless of AF type prior to ablation. Moreover, the results of this European registry were supported by other studies showing an efficacy of AF ablation in women in the range of 66–89% up to 12 months of follow-up.
Regarding the ablation technique, substrate ablation was added to PVI according to the type of AF (persistent vs. paroxysmal) and not based on gender. There was the same proportion of left atrial lines, right atrial lines, CTI, and CFAE in both genders. Ablation of autonomic GP seemed to be more frequently used in females with paroxysmal AF; this could be related not necessarily to gender, but more to technique preferences in Eastern Europe, where the percentage of comorbidities. Therefore, associated comorbidities were mostly involved in AF recurrences.2

In literature, female gender was found to be a predictor of AF recurrence,18 but this was not confirmed by this study. Even though the CHA2DS2-VASC score, which included female gender, was found to be a predictor, it could be speculated that gender itself was insignificant since the CHADS2 score was also an independent predictor of recurrence in this study. Therefore, associated comorbidities or who underwent more complex CA procedures: PVI plus substrate ablation (lines lesions, CFAE). Also, the smaller size of the left atrium in women patients neither influences procedure duration, total fluoroscopy time of CA procedure, nor success rate. However, other studies have observed that anatomical differences in left atrial size could have a negative effect on the success rate of AF ablations.18

**Procedural complications**

Though rare, major cardiac complications and peripheral/vascular complications of CA procedure were more frequent in women. In fact, there was a single death reported in a female patient. In our study, female sex was identified to be a predictor of acute major cardiovascular complications after CA of AF. When diving deeper, the experience level of centres included in the study had a further influence on female patients. To be precise, major complications such as cardiac perforation and neurological complications occurred more frequently in less experienced centres, while this was not the case for male patients.

More serious complications did not occur in patients with comorbidities, or who underwent more complex CA procedures: PVI plus substrate ablation (lines lesions, CFAE). Also, the smaller size of the female heart was not an increasing factor of complications.

**Impact of catheter ablation on symptoms and EHRA score**

After 12 months, the female group remained more symptomatic, complaining of palpitations, fatigue, and dyspnoea. Even though the EHRA score showed a clear improvement of symptoms in both genders, females still remained more symptomatic overall, whilst having the same rate of stable sinus rhythm, the same duration of their longest episode of AF, the same number of cardioversions, and repeat AF ablations, as male patients. In this study, AAD therapy was used more in symptomatic patients and patients with AF recurrences. Females remained under AADs during the follow-up more frequently than males, mainly because of symptoms rather than documented recurrences. The latter were similar between sexes. The presence of AAD therapy in female group could be an explanation for the same rate of recurrences despite females being older and having more comorbidities.

**Study limitations**

This was a registry-based study with voluntary participation of the centres involved. The key points to consider when analysing the registry data included study design, data sources, patient selection, comparison groups, and sampling strategies. Nevertheless, it is worth mentioning sources of bias and ways to address them, as listed below.

First and foremost, the method of creating the registry permitted freedom of patient selection and ablation technique strategy, which could have been an incentive to enrol, for example, patients with low risk of complications. This, in turn, could have biased the registry results with statistically lower event rates. Furthermore, the registry did not collect additional data on the population from which the patients were referred for CA, such as: the given patients were not addressed or simply did not accept the procedure.

Secondly, although the protocol required ablated patients to be consecutively included in the registry, this condition was not systematically audited, thereby we cannot exclude a certain degree of underestimation of complication rates. Since each site was only asked to enroll 20–50 patients in a row, there was a risk that smaller centres could have been over-represented in the data set. Thus, the overall proportion of women and the outcomes might be skewed.

Finally, the ablation results could have been prone to error because of the evaluation method of AF recurrences during patient follow-up. The main inadequacy was the non-mandatory ECG monitoring of AF recurrences. Instead, most patients were evaluated through face-to-face or telephone questionnaires, during which they simply had to describe their symptoms and the ECG report if any. What’s more, there was no officially approved QoL to properly estimate the physical and mental status of patients throughout the study.

**Conclusions**

All in all, this study provides important insights of gender differences in the management of AF.

The study showed that across Europe, AF ablation procedures were less frequently performed in females’ clinical practice. Catheter ablation was performed predominantly in overweight women in their 60s, with multiple comorbidities, more frequently with highly symptomatic paroxysmal AF and a higher EHRA score. With the same AF procedural success rate, severe acute cardiovascular complications remained considerable in females, even more so in centres with less experience. This finding was valid regardless of procedure type.

For further studies, the usage of a more homogeneous data set from the following viewpoints would be advisable: gender, age, comorbidities, and experience level of centres in scope.

**Supplementary material**

Supplementary material is available at Europace online.

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