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Sex-related differences in presentation, treatment, and outcome of patients with atrial fibrillation in Europe: a report from the Euro Observational Research Programme Pilot survey on Atrial Fibrillation

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Aims Sex differences in the epidemiology and clinical management of AF are evident. Of note, females are more symptomatic and if age >65, are at higher risk of thromboembolism if incident AF develops, compared with males.

Methods and results In an analysis from the dataset of the Euro Observational Research Programme on Atrial Fibrillation (EORP-AF) Pilot survey ($n = 3119$), we examined sex-related differences in presentation, treatment, and outcome of contemporary patients with AF in Europe.Female subjects were older ($P < 0.0001$), with a greater proportion aged ≥75 years, with more heart failure and hypertension. Heart failure with preserved ejection fraction was more common in females ($P < 0.0001$), as was valvular heart disease ($P = 0.0003$). Females were more symptomatic compared with males with a higher proportion being EHRA Class III and IV ($P = 0.0012$). The more common symptoms that were more prevalent in females were palpitations ($P < 0.0001$) and fear/anxiety ($P = 0.0007$). Other symptoms (e.g. dyspnoea, chest pain, fatigue, etc.) were not different between males and females. Health status scores were significantly lower for females overall, specifically for the psychological and physical domains (both $P < 0.0001$) but not for the sexual activity domain ($P = 0.9023$). Females were less likely to have electrical cardioversion (18.9 vs. 25.5%, $P < 0.0001$), and more likely to receive rate control ($P = 0.002$). Among patients recruited in hospital and discharged alive ($n = 2009$), documented contraindications to vitamin K antagonist (VKA) were evident in 23.8% of females. A CHA_2DS_2-VASc score ≥2 was found in 94.7% of females and 74.6% of males ($P < 0.0001$), with oral anticoagulants being used in 95.3 and 76.2%, respectively ($P < 0.0001$). A HAS-BLED score of ≥3 was found in 12.2% of females and 14.5% of males. Independent predictors of VKA use in females on multivariate analysis were CHA_2DS_2-VASc score ($P = 0.0007$), lower HAS-BLED score ($P = 0.0284$), and prosthetic mechanical valves ($P = 0.0276$).

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Conclusion The EORP-AF Pilot survey provides contemporary data on sex differences in clinical features and management of AF patients participating in the EORP-AF Pilot registry. Female subjects were older and more symptomatic, compared with males, and were more likely to receive rate control. Also, female patients were at higher stroke risk overall, but oral anticoagulation was used in a high proportion of patients.

Keywords Atrial fibrillation • Female • Anticoagulation • Survey

Introduction

Atrial fibrillation (AF) is the common sustained cardiac rhythm disorder, and is associated with a high risk of mortality and morbidity from stroke and thromboembolism, heart failure (HF), impaired cognitive function, and poor quality of life (QoL). Recent projections based on the Rotterdam study suggest that from 2010 to 2060, the number of adults 55 years and over with AF in the European Union will more than double, to 17.9 million (95% confidence interval: 13.6–23.7 million) assuming the age- and sex-specific prevalence remains stable.[1]

Sex differences in the epidemiology and clinical management of AF are evident. Of note, females are at particularly high risk if incident AF develops.[2,3] In the EuroHeart survey report from 2007, Dagres *et al.*[4] reported that compared with males, female subjects were older, had a lower QoL, had more comorbidities, more often had HF with preserved left ventricular systolic function, and less often had HF with systolic dysfunction. Among patients with typical AF symptoms, there was no gender-related difference in the choice of rate or rhythm control. Prescription of oral anticoagulants (OAC) was identical in both genders.

Since the EuroHeart survey was conducted a decade ago, the European Society of Cardiology (ESC) has produced new guidelines and additional studies have addressed the impact of rate vs. rhythm control, and the use of catheter ablation.[5] Also, the contemporary management of AF has shifted towards being more patient-centred and symptom-directed. In addition, the availability of non-vitamin K oral anticoagulants (NOACs) has also improved opportunities for stroke prevention, given their efficacy, safety, and relative convenience.[6,7]

In this analysis from the baseline dataset of the Euro Observational Research Programme on Atrial Fibrillation (EORP-AF) Pilot survey, we examined sex-related differences in presentation, treatment, and outcome of contemporary patients with AF in Europe.

Methods

The full baseline features and results from the EORP-AF Pilot survey have been previously published.[8] In this ancillary analysis, we focused on sex differences in clinical features and management. In brief, the EORP-AF registry population comprised consecutive in- and outpatients with AF presenting to cardiologists in participating ESC countries. Consecutive patients were screened for eligibility at the time of their presentation to a cardiologist (hospital or medical centre). All patients provided written informed consent. Patients with the primary or secondary recorded diagnosis of AF were included.

Patients were officially enroled in the EORP-AF only if an electrocardiogram (ECG) diagnosis (12-lead ECG, 24 h Holter, or other electrocardiographic documentation) confirming AF was made.[8] The qualifying episode of AF should have occurred within the last year, and patients did not need to be in AF at the time of enrolment. For the pilot phase, nine countries formally participated. A minimum of 20 consecutive patients per centre were to be enroled, with a target of 3000 patients. Enrolment into the registry started in February 2012, and the end of enrolment was March 2013.

Statistical analyses

Univariate analysis was applied to both continuous and categorical variables. Continuous variables were reported as mean ± SD or as median and interquartile range (IQR). Among-group comparisons were made using a non-parametric test (Kruskal–Wallis test). Categorical variables were reported as percentages. Among-group comparisons were made using a χ^2 test or a Fisher's exact test if any expected cell count was less than five.

A multiple logistic regression was used to determine the predictors of antithrombotic therapy use including into the model all the candidate variables. Following that, the search of the best predictive model was performed by using the programme R and the package 'glmulti' which automatically generated all possible models (i.e. combinations of predictors) with the specified response and explanatory variables, and found the best models in terms of the Akaike Information Criterion. The search option was set to genetic algorithm and all the two-way interactions were neglected. The search of the best predictive model was performed on the following candidate variables: prosthetic mechanical valve, hyperthyroidism, hypothyroidism, peripheral vascular disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease, malignancy, liver disease, sleep apnoea, haemorrhagic events, ischaemic thrombo-embolic complications, age, body mass index, heart rate, systolic blood pressure, diastolic blood pressure, CHA_2DS_2-VASc score, and HAS-BLED score. *P* values <0.05 were considered significant.

Results

In the dataset of the Euro Observational Research Programme on Atrial Fibrillation (EORP-AF) Pilot survey ($n = 3119$), female subjects were older ($P < 0.0001$), with a greater proportion aged ≥75 years. There was no difference in proportion of AF subtype (paroxysmal, persistent, permanent, etc.) between males and females (*Table 1*). First detected (or new-onset) AF was evident in 27.9% of females, compared with 31.9% of males.

Of the various comorbidities, the commonest were HF and hypertension (*Table 1*). Non-ischaemic HF being more common in females ($P = 0.0001$) and lower prevalence of moderate–severe systolic dysfunction and coronary artery disease (both $P < 0.0001$). Heart failure with preserved ejection fraction was more common in females ($P < 0.0001$), as was valvular heart disease ($P = 0.0003$) although the high-reported figure includes mild valvular abnormalities even

Table 1 Baseline

	Whole cohort	Female	Male	*P*-value
N	3119	1260	1859	
Demographics				
Age (years) (mean ± SD)	68.8 ± 11.5	71.7 ± 10.6	66.9 ± 11.7	<0.0001
Age (years) (median, IQR)	69 (62–77)	73 (65–79)	68 (60–76)	
Age ≥75 years (%)	33.7	42.2	27.9	<0.0001
Type of AF				
First detected (%)	30.3	27.9	31.9	0.1189
Paroxysmal (%)	26.5	28.5	25.1	
Persistent (%)	21.2	21.2	21.2	
Long-standing persistent (%)	4.8	5.0	4.6	
Permanent (%)	17.3	17.5	17.1	
Concomitant medical history				
Chronic HF (%)	47.5	47.5	47.5	0.9844
Chronic HF type—ischaemic (%)	47.3	40.4	51.9	0.0001
Chronic HF type—non-ischaemic (%)	52.7	59.6	48.1	
Systolic dysfunction: moderate–severe, EF < 35% (%)	12.0	6.4	15.6	<0.0001
Systolic dysfunction: mild, EF 35–45% (%)	15.9	11.7	18.6	
Systolic dysfunction: normal, EF > 45%	72.1	81.9	65.8	
HF with preserved systolic function, EF > 45% (%)	48.1	65.2	37.4	<0.0001
HF with systolic dysfunction, EF ≤ 45% (%)	51.9	34.8	62.6	
Hypertension (%)	70.7	74.7	68.0	<0.0001
Coronary artery disease (%)	36.4	31.3	39.8	<0.0001
Valvular heart disease (%)	63.4	67.3	60.7	0.0003
Hyperthyroidism (%)	3.0	3.7	2.5	0.0666
COPD (%)	11.0	9.6	11.9	0.0463
Diabetes mellitus (%)	20.6	20.9	20.3	0.6757
Previous stroke (%)	6.3	5.3	7.0	0.0551
Previous TIA (%)	4.1	4.3	3.9	0.5530
Chronic kidney disease (%)	13.1	11.8	14.0	0.0711
Haemorrhagic event (%)	5.9	6.0	5.8	0.7740
$CHADS_2$ scores				
0	12.6	10.0	14.3	<0.0001
1	27.1	24.3	29.1	
≥2	60.3	65.7	56.6	
CHA_2DS_2-VASc score				
0	5.7	0.0	9.6	<0.0001
1	12.6	5.7	17.2	
≥2	81.7	94.3	73.2	
HAS-BLED score				
0	21.7	16.7	25.1	<0.0001
1	37.7	40.2	35.9	
2	26.6	29.6	24.6	
≥3	14.0	13.5	14.4	
EHRA score				
Class I (%)	39.7	43.3	34.4	<0.0001
Class II (%)	30.9	31.2	30.5	
Class III (%)	23.9	20.7	28.7	
Class IV (%)	5.6	5.0	6.4	
Symptoms				
Currently symptomatic (%)	60.3	65.6	56.8	<0.0001
AF symptoms in the past (%)	58.0	64.2	54.6	0.0011

Continued

Table 1 *Continued*

	Whole cohort	Female	Male	*P*-value
Palpitations (%)	73.7	80.2	68.5	<0.0001
Fear/anxiety (%)	12.2	14.6	10.5	0.0007
Dyspnoea/shortness of breath (%)	53.7	55.7	52.1	0.1189
Chest pain (%)	23.5	23.1	23.8	0.7237
General non-wellbeing (%)	34.9	36.6	33.6	0.1636
Dizziness (%)	24.0	25.4	22.9	0.2160
Fatigue (%)	46.7	45.1	47.9	0.2328
Health status				
Score of psychological domain mean ± SD)	19.9 ± 8.04	18.5 ± 8.02	20.8 ± 7.92	<0.0001
Score of psychological domain (median, IQR)	20 (14–26)	18 (13–24)	21 (15–27)	
Score of physical domain (mean ± SD)	20.6 ± 9.51	18.8 ± 9.24	21.8 ± 9.5	<0.0001
Score of physical domain (median, IQR)	20 (13–28)	18 (12–25)	22 (14–29)	
Score of sexual activity domain (mean ± SD)	9.7 ± 4.22	9.6 ± 4.57	9.8 ± 3.98	0.9023
Score of sexual activity domain (median, IQR)	10 (7–14)	10 (6–15)	10 (7–13)	
Total score (mean ± SD)	48.3 ± 19.95	45.1 ± 19.38	50.6 ± 20.04	<0.0001
Total score (median, IQR)	49 (36–62)	46 (33–58)	51 (38–65)	

those detected with echocardiography. Hyperthyroidism, diabetes, prior stroke, chronic kidney disease, and prior bleeding event were not significantly different between males and females (all P = NS).

A $CHADS_2$ or CHA_2DS_2-VASc score ≥2 was more prevalent in females ($P < 0.0001$). A HAS-BLED score of ≥3 was found in 13.5% of females and 14.4% of males (*Table 1*).

Symptoms and health status

Females were more symptomatic compared with males with a higher proportion being EHRA Class III and IV ($P = 0.0012$). Most patients were symptomatic, with more females (65.6%) currently symptomatic ($P < 0.0001$), or having past symptoms (64.2%, $P = 0.0011$). The more common symptoms that were more prevalent in females were palpitations ($P < 0.0001$) and fear/anxiety ($P = 0.0007$). Other symptoms (e.g. dyspnoea, chest pain, fatigue, etc.) were not different between males and females.

Health status scores were significantly lower for females overall, specifically for the psychological and physical domains (both $P < 0.0001$) but not for the sexual activity domain ($P = 0.9023$).

Diagnostic procedures

There were no sex differences in transthoracic echocardiography use ($P = 0.2319$) but transoesophageal echocardiography was less common in females. Thyroid function testing was not different between males and females. Coronary angiography and exercise testing were less common in females (*Table 2*).

Interventions performed/planned at enrolment

Females were less likely to have electrical cardioversion (18.9 vs. 25.5%, $P < 0.0001$), and more likely to have pharmacological cardioversion (28.2 vs. 22.4%, $P = 0.0002$). No differences were evident for ablation or devices (*Table 3*).

Treatment in relation to symptoms

In the presence of typical AF symptoms, females were less likely to receive rhythm control, and more likely to receive rate control ($P = 0.002$) (*Table 4*). In the absence of symptoms, rate control was offered to >50% in both males and females, but rhythm control was still used in a significant proportion.

Drug therapy at discharge in patients discharged alive

Antiarrhythmic drugs were used in 39.7 and 36.6% of males and females, respectively. The most common classes were Class Ic and III agents, with no sex differences (*Table 5*).

Angiotensin-converting enzyme inhibitors (ACEI) or angiotension receptor blockers (ARBs) were commonly used, with ACEI being more common in males. Digoxin ($P = 0.0056$) and diuretics ($P = 0.0259$) were more commonly used in females. There were no differences in use of beta-blockers or calcium-channel blockers.

Antithrombotic therapy, stroke, and bleeding risk

Among patients recruited in hospital and discharged alive ($n = 2009$), documented contraindications to vitamin K antagonist (VKA) were evident in 23.8 and 23.4% of females and males, respectively. None were discharged on no antithrombotic therapy. Oral anticoagulants were prescribed in 79.8 and 81.5% of females and males, respectively ($P = 0.3646$), the majority being VKAs (72.7% overall). A CHA_2DS_2-VASc score ≥2 was found in 94.7% of females and 74.6% of males ($P < 0.0001$), with OAC being used in 95.3 and 76.2%, respectively ($P < 0.0001$). A HAS-BLED score of ≥3 was found in 12.2% of females and 14.5% of males.

Antiplatelet drugs were more commonly prescribed in males (40.8 vs. 36.5%, $P = 0.049$), usually aspirin. Indobufen use was minimal

Table 2 Diagnostic procedures

	Whole cohort	Females	Males	*P*-value
N	3119	1260	1859	
Diagnostic procedures				
Transthoracic (%)	91.8	92.5	91.3	0.2319
Transoesophageal (%)	11.3	9.7	12.4	0.0202
Electrophysiological study (%)	4.2	3.3	4.8	0.0425
Thyroid hormone level measurement—*before* (%)[a]	53.6	53.5	53.9	0.9604
Thyroid hormone level measurement—*now* (%)[a]	40.6	37.7	46.4	0.1556
Thyroid hormone level measurement—*planned* (%)[a]	23.7	24.5	21.9	0.6814
Coronary angiography (%)	14.4	11.8	16.2	0.0007
Exercise test (%)	7.8	6.5	8.7	0.0251
Holter monitoring (%)	17.0	17.0	16.9	0.9649
CT scan (%)	5.6	5.7	5.6	0.8489
MRI scan (%)	1.2	1.0	1.3	0.3820
Other procedures (%)	6.5	5.8	7.0	0.1882

[a]For population who have hyperthyroidism or hypothyroidism.

Table 3 Interventions performed/planned at enrolment

	Whole cohort	Females	Males	*P*-value
N	3119	1260	1859	
Interventions performed/planned at enrolment				
Electrical cardioversion (%)	22.8	18.9	25.5	<0.0001
Pharmacological conversion (%)	24.7	28.2	22.4	0.0002
Catheter ablation for AF[a] (%)	7.4	6.7	7.9	0.1905
Pacemaker implantation (%)	4.7	5.4	4.2	0.1017
ICD implantation (%)	1.1	0.6	1.4	0.0569
AF surgery (%)	0.4	0.3	0.4	>0.9999

AF, atrial fibrillation.
[a]Catheter ablation for AF includes any ablation for AF treatment.

Table 4 Treatment in relation to symptoms

	Whole cohort	Females	Males	*P*-value
N	3119	1260	1859	
Typical atrial fibrillation symptoms				
Rhythm control (%)	13.3	11.0	15.1	0.0020
Rate control (%)	29.1	33.1	26.0	
Rhythm control and rate control (%)	54.9	53.3	56.1	
Observation (%)	2.7	2.5	2.8	
No symptoms				
Rhythm control (%)	12.7	12.2	12.9	0.2191
Rate control (%)	53.9	51.5	55.2	
Rhythm control and rate control (%)	27.2	30.7	25.3	
Observation (%)	6.2	5.5	6.6	

(0.4%), while acetylsalicylic acid (ASA)/clopidogrel combination therapy was used in 7.8% of females and 10.5% of males ($P = 0.0426$). OAC and antiplatelet therapy were used in 4.0% of females and 6.1% of males ($P = 0.0412$).

Predictors of antithrombotic therapy use

According to the full model, the significant predictors of VKA use in females on multivariate analysis were CHA_2DS_2-VASc score ($P = 0.0007$), lower HAS-BLED score ($P = 0.0284$), and prosthetic mechanical valve ($P = 0.0284$) (see Supplementary material online, *Table S1*). Independent predictor of VKA use in males were lower HAS-BLED score ($P = 0.0337$) and prosthetic mechanical valve ($P = 0.0298$).

Significant predictors of antiplatelet drug use in females on multivariate analysis were younger age ($P = 0.0145$), CHA_2DS_2-VASc score ($P = 0.0249$), and higher HAS-BLED score ($P < 0.0001$), as well as the absence of chronic kidney disease ($P = 0.0001$), liver disease ($P = 0.0265$), haemorrhagic event ($P = 0.0003$), ischaemic thrombo-embolic events ($P = 0.012$), and prosthetic mechanical valves ($P = 0.0386$).

Multivariate predictors of antiplatelet drug use in males were younger age, lower blood pressure, and higher HAS-BLED score, as well as the absence of hyperthyroidism, chronic kidney disease, liver disease, haemorrhagic events, and ischaemic thrombo-embolic complications (see Supplementary material online, *Table S1*).

Table 5 Drug therapy at discharge in patients discharged alive

	Whole cohort	Women	Men	*P*-value
N	2009	823	1186	
CHA_2DS_2-VASc ≥1 (%)	94.7	100.0	91.1	<0.0001
CHA_2DS_2-VASc ≥2 (%)	82.8	94.7	74.6	<0.0001
Documented contraindications to VKA (%)	23.6	23.8	23.4	0.8456
Antiarrhythmic drugs				
Antiarrhythmic drugs (%)	37.9	39.7	36.6	0.1538
Class Ia (quinidine) (%)	0.0	0.0	0.0	NA
Class Ic (flecainide/propafenone) (%)	9.3	9.6	9.0	0.6608
Propafenone (%)	5.8	7.6	4.6	0.0049
Flecainide (%)	3.5	2.1	4.5	0.0039
Class III (amiodarone/sotalol/ibutilide[a]) (%)	28.7	30.5	27.5	0.1424
Amiodarone (%)	25.9	27.2	25.0	0.2701
Dronedarone (%)	0.3	0.1	0.4	0.4106
Sotalol (%)	2.9	3.4	2.6	0.3020
Other antiarrhythmics (%)	0.1	0.0	0.2	0.5161
Antithrombotic drugs				
No antithrombotic medication (%)	3.4	3.0	3.7	0.4158
Antithrombotic treatment (%)	96.3	96.7	96.0	0.4247
Oral anticoagulants[b] (%)	80.8	79.8	81.5	0.3646
CHA_2DS_2-VASc = 0	4.7	0.0	7.9	<0.0001
1	11.4	4.7	15.9	
≥2	83.9	95.3	76.2	
HAS-BLED 0	23.3	18.4	26.6	0.0002
1	35.6	38.4	33.8	
2	27.5	31.1	25.2	
≥3	13.6	12.2	14.5	
VKA antagonists (%)	72.7	71.8	73.4	0.4456
Dabigatran	6.9	6.8	7.0	0.8657
Rivaroxaban	1.5	1.6	1.4	0.6727
Apixaban	0.0	0.0	0.0	NA
Antiplatelet drugs[c]	39.0	36.5	40.8	0.0490
ASA (%)	34.9	32.1	36.8	0.0324
Clopidogrel (%)	13.3	11.6	14.5	0.0599
Ticlopidine (%)	0.1	0.1	0.1	>0.9999
Clopidogrel/ASA (%)	9.4	7.8	10.5	0.0426
Prasugrel (%)	0.3	0.1	0.3	0.6543
Ticagrelor (%)	0.3	0.4	0.3	0.6941
Indobufen (%)	0.4	0.4	0.3	>0.9999
OAC and ASA and (clopidogrel or ticagrelor or prasugrel) (%)	5.2	4.0	6.1	0.0412
Other				
ACEIs (%)	46.5	42.3	49.4	0.0017
ARBs (%)	20.4	23.8	18.0	0.0017
DRI, aliskiren (%)	0.3	0.2	0.3	>0.9999
Beta-blockers (%)	71.5	70.0	72.5	0.2179
Digoxin (%)	21.9	25.0	19.8	0.0056
Diuretics (%)	57.3	60.2	55.2	0.0259
Aldosterone blockers (%)	29.9	29.3	30.4	0.5646
DHP calcium-channel blockers (%)	13.1	13.6	12.7	0.5250
Non-DHP calcium-channel blockers (%)	5.8	6.2	5.5	0.4959
Statins (%)	52.9	50.9	54.2	0.1360
Oral antidiabetics (%)	15.1	16.1	14.4	0.2897

Continued

Table 5 *Continued*

	Whole cohort	Women	Men	*P*-value
Insulin (%)	6.4	6.9	6.1	0.4395
Thyroid-suppressing drugs (%)	2.5	2.6	2.5	0.8782
Beta 2 agonists (%)	1.8	1.5	1.9	0.4188
Anticholinergic agents (%)	2.2	1.7	2.6	0.1747

[a]Ibutilide is absent in the CRF.
[b]Oral anticoagulants: Vitamin K antagonists, dabigatran, rivaroxaban, apixaban.
[c]Antiplatelets: ASA, indobufen, clopidogrel, prasugrel, ticagrelor, ticlopedin.

Discussion

In this analysis, we report sex differences in clinical features and management of AF patients managed by European cardiologists participating in the EORP-AF Pilot registry. We show that female subjects were older and more symptomatic (with lower health status scores for psychological and physical domains), compared with males. Secondly, females had more non-ischaemic HF and HF with preserved ejection fraction. Thirdly, despite more symptoms, females were offered less rhythm control and often managed by rate control. Fourthly, females were at higher stroke risk overall (although prior stroke history was more common in males), and oral anticoagulation was used in a high proportion (95.3% of females vs. 76.2% of males) with documented contraindications to VKA in ~23%.

Females were more symptomatic compared with males with a higher proportion being EHRA Class III and IV, especially from palpitations and fear/anxiety. Interestingly, other symptoms (e.g. dyspnoea, chest pain, fatigue, etc.) were not different between males and females. Indeed, AF confers a significant morbidity given that health status scores were significantly lower for females overall, specifically for the psychological and physical domains but not for sexual activity domain. It remains uncertain whether these QoL scores reflect the type of patient enroled, differences in the effect AF have on the patients, or instead may simply reflect other differences between men and women and would therefore also be present if men and women without AF were compared.

In the presence of typical AF symptoms, females were less likely to receive rhythm control, and more likely to receive rate control. This is interesting given that rhythm control is associated with an improvement in functional capacity.[9] In the absence of symptoms, rate control was offered to >50% in both males and females in the present analysis.

Among patients recruited in hospital and discharged alive, OAC were prescribed in a high proportion of females (79.8%), and 94.7% in those with CHA_2DS_2-VASc score ≥2. This is an improvement since the previous EuroHeart survey a decade ago[10] and reflects the increasing evidence that female gender is an independent predictor of stroke risk, in the presence of ≥1 stroke risk factors.[11] Of note, overall mean stroke risk in our cohort was higher in females, despite a history of prior stroke being higher in males in spite of their younger age. However, females with lone AF (and age <65) are at low risk,[12,13] and the ESC guidelines recommend no antithrombotic therapy use in such patients with a CHA_2DS_2-VASc score of 0 (males) or 1 (females).[5] Also, stroke rates in females while taking VKAs are higher than in males,[4] and may be a reflection of less optimal time in therapeutic range (TTR).[14] Also, impaired renal function may partly explain the higher stroke rate in females compared with males.[15] Follow-up data from the EORP-AF Pilot would provide outcome data, and the antecedents to such events.

Our data are broadly consistent with the EuroHeart survey data, where Dagres *et al.*[4] reported that females with AF had more comorbidities, more HF with preserved systolic function, and a lower QoL than men. In the subjects with atypical or no symptoms, females were treated more conservatively with less rhythm control than men. In this analysis, females had a higher chance for stroke than males, with an odds ratio 1.83 on multivariable regression analysis.

Among a group of healthy women in the Women's Health Study, Conen *et al.*[2] reported that new-onset AF was independently associated with all-cause, cardiovascular, and non-cardiovascular mortality, with some of the risk potentially explained by non-fatal cardiovascular events. Similarly, the Copenhagen City Heart Study found that AF is a much more pronounced risk factor for stroke and cardiovascular death in women than in men.[16] The potential mechanisms behind the increased risk of stroke in AF associated with female sex have been subject to much research interest.[17]

Limitations

As our female subjects were older and had higher risk, this may have affected some of the observed differences in our modest sized cohort. We did not have data on quality of anticoagulation control, with no data on TTR, which is highly relevant given that TTR is a major determinant of thromboembolism, bleeding, and death in patients being treated with VKA.[18,19] Also, we did not have detailed data on biochemical parameters, precise details on socioeconomic factors, nor outcomes which will be addressed by the ongoing follow-up phase of the EORP-AF Pilot, due to report in late 2014. Finally, one cannot determine how much differences in the treatment between men and women were influenced by patient preference as opposed to baseline differences and physician bias *per se*. Also, the possibility arises that inclusion of patients in the registry might have influenced their care. All our patients had AF, and we cannot determine if the observed sex differences would have been apparent even if we were studying non-AF patients.

Conclusion

In conclusion, the EORP-AF Pilot survey provides contemporary data on sex differences in clinical features and management of AF patients participating in the EORP-AF Pilot registry. Female subjects were older and more symptomatic, compared with males, and managed more commonly with rate control. Also, female patients were at higher stroke risk overall, but oral anticoagulation was used in a high proportion of patients.

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Investigators: The full list was provided in the primary paper describing the baseline data, by Lip *et al.*[8]

Conflicts of interest: G.Y.H.L. is a consultant for Bayer, Medtronic, Sanofi, BMS/Pfizer, Daiichi-Sankyo, and Boehringer Ingelheim, and has been a speaker for Bayer, BMS/Pfizer, Boehringer Ingelheim, Daiichi-Sankyo, and Medtronic. L.H.R.: is a speaker bureaus for Bayer, BMS/Pfizer, Janssen Pharmaceuticals, Takeda, Roche Diagnostics, and Boehringer Ingelheim. G.B. has received speaker fees from Medtronic Inc. and Boston Scientific. C.L., G.-A.D., M.S., Z.K., L.H.R., M.I.P., O.T., P.C., C.F.H., B.M., A.P.M., and L.T. have no conflicts to declare in relation to this manuscript.

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