Gender Differences in Clinical Presentation and One-Year Outcomes in Atrial Fibrillation

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Supplementary Tables 1-9

Supplementary Tables 1: Baseline characteristics of PREFER in AF study participants without follow-up by gender.

Variables	Women without Follow up N=340	Men without Follow up N=474
Risk factors		
Age, years (SD)	72.5 (10.9)	67.4 (12.7)
Body mass index, kg/m² (SD)	27.9 (5.3)	27.9 (4.5)
Systolic blood pressure, mm Hg (SD)	134.6 (16.5)	131.5 (16.6)
Ever smoking, N (%)	68 (20.4)	238 (50.9)
Alcohol excess (≥8 units/week), N (%)	3 (0.9)	15 (3.3)
Lack of guideline compliance in anticoagulant therapy, N (%)	10 (3.0)	12 (2.6)
EHRA score >2, N (%)	218 (65.1)	253 (54.2)
CHA_2DS_2-VASc ≥2†, N (%)	258 (94.5)	283 (74.1)
HASBLED ≥2, N (%)	176 (73.6)	193 (57.6)
Disease history		
Diabetes mellitus, N (%)	85 (25.3)	110 (23.5)
Dyslipidaemia, N (%)	155 (46.6)	198 (42.4)
Chronic renal insufficiency, N (%)	33 (10.1)	52 (11.2)
Chronic hepatic disease, N (%)	11 (3.3)	12 (2.6)
Hyperthyroidism, N (%)	18 (5.4)	12 (2.6)
Chronic obstructive pulmonary disease, N (%)	29 (8.7)	58 (12.4)

Variables	Women without Follow up N=340	Men without Follow up N=474
Major gastrointestinal/ cerebrovascular/other bleeding events, N (%)	13 (3.8)	13 (2.7)
Prevalent cardiovascular disease (CHD, peripheral arterial disease, MI infarction), N (%)	53 (16.1)	116 (25.3)
Stent insertion, N (%)	22 (6.7)	48 (10.4)
Heart valve dysfunction, N (%)	136 (40.5)	138 (29.7)
Heart valve replacement, N (%)	19 (5.7)	18 (3.9)
Heart failure, N (%)	70 (20.8)	112 (24.1)
Previous ischemic stroke/ TIA/other ischemic-thromboembolic event, N (%)	142 (50.0)	184 (50.3)
Sinus rhythm at baseline, N (%)	133 (39.6)	166 (35.9)
Adequate heart rate control (60-100 bpm) at baseline, N (%)	142 (50.0)	184 (50.3)
Medication		
Antiplatelet agents, non-steroidal antinflammatory drugs, N (%)	79 (23.4)	103 (22.0)
Antiarrhythmic drugs,N(%)	216 (63.5)	271 (57.2)

Mean and standard deviation (SD) and number and percentages are presented.
N=17 individuals without follow-up information had missing data on gender and are therefore not shown in the table.
*Univariate odds ratios for gender were obtained by logistic regression adjusted for age and country.
†CHA_2DS_2-VASc score included the extra point for female gender. CHD, coronary heart disease; TIA, transient ischemic attack. **Medication as used in the HAS-BLED score.
Lack of guideline compliance indicates lack of treatment with oral anticoagulant in the previous 12 months despite guideline indication without contraindication.

Supplementary Table 2 Baseline variables entered into the stepwise regression analysis.

Variables
Age
Gender
Country (Austria, Switzerland, Germany pooled together)
Systolic blood pressure
Body mass index
Ever smoking
Lack of compliance
European Heart Rhythm Association (EHRA) score
Dyslipidaemia
Hyperthyroidism
Chronic renal insufficiency
Chronic hepatic disease
Diabetes mellitus
Chronic obstructive pulmonary disease
Prevalent cardiovascular disease (coronary heart disease, peripheral arterial disease, myocardial infarction)
Previous ischemic stroke/transient ischemic attack/ischemic-thromboembolic event (e.g. arterial embolism)
Major gastrointestinal/cerebrovascular/other bleeding
Chronic heart insufficiency/reduced left ventricular ejection fraction
Heart valve dysfunction (e.g. stenosis, insufficiency)
Heart valve replaced
Stent insertion
Electrical cardioversion
Ablation (pulmonary vein isolation)
Pharmacological cardioversion
Antiplatelet agents, non-steroidal anti-inflammatory drugs
Antiarrhythmic drugs
Anticoagulation therapy category: Non-vitamin K antagonist (NOAC)
Anticoagulation therapy category: Antiplatelet therapy only
Anticoagulation therapy category: Vitamin K antagonists only
Anticoagulation therapy category:Vitamin K antagonists & antiplatelet therapy
Anticoagulation therapy category:Heparin & fondaparinux
Anticoagulation therapy category: Other† or none

†Other: (vitamin K antagonists & antiplatelet therapy & NOAC) or (antiplatelet therapy & NOAC)
Systolic blood pressure and BMI were entered as continuous variables. Country was entered as dummy variables.

Supplementary Table 3 Symptoms according to European Heart Rhythm Association (EHRA) classification at baseline by gender in patients with new-onset AF (<90 days), N=847.

	Women				Men			
Symptom	**Never**	**Occasional**	**Intermediate**	**Frequent**	**Never**	**Occasional**	**Intermediate**	**Frequent**
Palpitations	97 (26.65)	160 (44.0)	74 (20.3)	33 (9.1)	189 (39.4)	190 (39.6)	75 (15.6)	26 (5.4)
Fatigue	90 (25.0)	135 (37.5)	92 (25.6)	43 (11.9)	158 (33.0)	172 (35.9)	103 (21.5)	46 (9.6)
Dizziness	201 (55.8)	107 (29.7)	43 (11.9)	9 (2.5)	320 (67.2)	122 (25.6)	26 (5.5)	8 (1.7)
Dyspnoea	122 (33.7)	116 (32.0)	75 (20.7)	49 (13.5)	201 (41.6)	146 (30.2)	82 (17.0)	54 (11.2)
Chest pain	262 (72.6)	80 (22.2)	17 (4.7)	2 (0.55)	337 (70.35)	103 (21.5)	33 (6.9)	6 (1.25)
Anxiety	140 (39.1)	132 (36.9)	50 (14.0)	36 (10.1)	265 (56.0)	150 (31.7)	43 (9.1)	15 (3.2)

Numbers and percent are provided.

Supplementary Table 4 Variables associated with one-year incidence of ischemic stroke/TIA/arterial thromboembolic events.

	Women Events=62/2,422		Men Events=73/3,697	
Variables selected*	**Odds ratio**	**95% confidence interval**	**Odds ratio**	**95%confidence interval**
Age	1.02	0.99, 1.05	1.04	1.00, 1.06
Lack of guideline compliance in anticoagulant therapy	4.32	1.92, 9.73	8.49	4.20, 17.16
Non-vitamin K antagonist	1.18	0.39, 3.53	4.36	2.00, 9.47
Previous ischemic stroke/TIA/ischemic-thromboembolic event	3.16	1.82, 5.47	2.78	1.62, 4.78
Pharmacological cardioversion	2.02	1.12, 3.67	2.49	1.45, 4.26
Antiplatelet agents, non-steroidal anti-inflammatory drugs intake**	1.28	0.70, 2.35	1.69	1.01, 2.84
Heart failure	1.88	1.08, 3.27	1.50	0.90, 2.52

*Sex, age and country (not shown) were forced into the model during the stepwise selection procedure which was done on the complete dataset and separate odds ratios for men and women were calculated subsequently. TIA, transient ischemic attack. **Medication as used in the HAS-BLED score.

Supplementary Table 5 Variables associated with one-year incidence of acute coronary syndrome events.

	Women Events=29/2,404		Men Events=61/3,654	
Variables selected*	**Odds ratio**	**95% confidence interval**	**Odds ratio**	**95% confidence interval**
Age	1.05	1.00, 1.10	1.02	0.99, 1.06
Previous cardiovascular disease (CHD, peripheral arterial disease, myocardial infarction)	3.26	1.47, 7.24	4.51	2.33, 8.72
Major bleeding	2.36	0.67, 8.33	2.19	0.95, 5.06
Dyslipidaemia	1.84	0.83, 4.11	2.14	1.15, 4.00
Chronic obstructive pulmonary disease	3.18	1.33, 7.60	1.36	0.71, 2.61
EHRA score	1.23	0.78, 1.95	1.34	0.99, 1.82
Vitamin K antagonists only	0.56	0.26, 1.19	0.58	0.34, 0.99

*Sex, age and country (not shown) were forced into the model during the stepwise selection procedure which was done on the complete dataset and separate odds ratios for men and women were calculated subsequently. CHD, coronary heart disease.

Supplementary Table 6 Variables associated with one-year incidence of coronary revascularization events.

	Women Events=21/2,459		Men Events=82/3,752	
Variables selected*	**Odds ratio**	**95% confidence interval**	**Odds ratio**	**95% confidence interval**
Age	1.02	0.97, 1.07	1.03	1.00, 1.05
Previous cardiovascular disease (CHD, peripheral arterial disease, MI)	4.59	1.86, 11.32	4.45	2.72, 7.30
Vitamin K antagonists only	0.58	0.24, 1.40	0.77	0.49, 1.21
Previous ischemic stroke/TIA/ischemic-thromboembolic event	0.22	0.03, 1.64	0.45	0.20, 0.99

*Sex, age and country (not shown) were forced into the model during the stepwise selection procedure which was done on the complete dataset and separate odds ratios for men and women were calculated subsequently. CHD, coronary heart disease; TIA, transient ischemic attack.

Supplementary Table 7 Variables associated with one-year incidence of heart failure.

	Women Events=73/1,739		Men Events=82/2,536	
Variables selected*	**Odds ratio**	**95% confidence interval**	**Odds ratio**	**95%confidence interval**
Age	1.05	1.02, 1.08	1.03	1.00, 1.05
Lack of guideline compliance in anticoagulant therapy	1.02	0.23, 4.46	5.27	1.87, 14.84
Heart valve replaced	1.06	0.37, 3.04	3.74	1.84, 7.64
Chronic renal insufficiency	1.81	0.95, 3.46	1.88	1.03, 3.42
EHRA score	1.34	1.01, 1.77	1.29	1.00, 1.65

*Sex, age and country (not shown) were forced into the model during the stepwise selection procedure which was done on the complete dataset and separate odds ratios for men and women were calculated subsequently.

Supplementary Table 8 Variables associated with one-year incidence of major bleeding events.

	Women Events=71/2,440		Men Events=104/3,709	
Variables selected*	**Odds ratio**	**95% confidence interval**	**Odds ratio**	**95% confidence interval**
Age	1.05	1.01, 1.08	1.04	1.01, 1.06
Major bleeding	3.86	1.86, 8.03	4.51	2.58, 7.89
Chronic hepatic disease	3.41	1.24, 9.41	2.72	1.03, 7.17
Chronic renal insufficiency	1.90	1.08, 3.35	1.75	1.09, 2.82
Heart valve replaced	4.49	2.32, 8.69	1.25	0.59, 2.65
Vitamin K antagonists only	0.57	0.35, 0.95	0.70	0.47, 1.04

*sex, age and country (not shown) were forced into the model during the stepwise selection procedure which was done on the complete dataset and separate odds ratios for men and women were calculated subsequently.

Supplementary Table 9 Area under receiver operator curve (AUC) for one-year outcomes by gender.

	Women		Men	
Outcome	**AUC**	**95% Confidence interval**	**AUC**	**95% Confidence interval**
Stroke/TIA/arterial thromboembolism				
CHA_2DS_2-VASc	0.65	0.57, 0.73	0.65	0.58, 0.72
HAS-BLED	0.69	0.61, 0.77	0.69	0.62, 0.76
PREFER in AF model*	0.67	0.57, 0.76	0.75	0.68, 0.83
Major Bleeding				
HAS-BLED	0.65	0.58, 0.72	0.64	0.59, 0.70
CHA_2DS_2-VASc	0.58	0.52, 0.64	0.63	0.58, 0.69
PREFER in AF model*	0.66	0.58, 0.73	0.66	0.60, 0.72

AUC, area under the curve.

*PREFER in AF model refers to the combination of variables identified by stepwise regression in the current analyses (age, lack of guideline compliance in anticoagulant therapy, non-vitamin K antagonist, previous ischemic stroke/TIA/ischemic-thromboembolic event, pharmacological cardioversion, antiplatelet agents, non-steroidal anti-inflammatory drugs intake, heart failure for stroke; age, major bleeding, chronic hepatic disease, chronic renal insufficiency, heart valve replaced, vitamin K antagonists only for bleeding).

The AUCs of the PREFER in AF models were corrected for over-optimism as outlined in the methods.