

Supplement

Sex differences of vascular brain lesions in patients with atrial fibrillation

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Table e-1: Prevalence and volume of brain lesions in patients without history of stroke/TIA

Variable	Women (n=370)	Men (n=1023)
Large noncortical and cortical infarcts		
Prevalence, n (%)	47 (12.7)	164 (16.0)
Volume (mm ³), median (IQR)	417 (180, 1189)	554 (155, 3933)
Small noncortical infarcts		
Prevalence, n (%)	62 (16.8)	199 (19.5)
Volume (mm ³), median (IQR)	66 (33, 167)	57 (30, 155)
Any ischemic infarcts (LNCCI or SNCI)		
Prevalence, n (%)	100 (27.0)	315 (30.8)
Volume (mm ³), median (IQR)	191 (56, 460)	162 (51, 814)
Microbleeds		
Prevalence, n (%)	66 (18.3)	205 (20.7)
Counts (Number), median (IQR)	1 (1, 2)	1 (1, 2)
White matter hyperintensities		
Prevalence, Fazekas scale ≥ 2 , n (%)	204 (55.1)	494 (48.3)
Volume total (mm ³), median (IQR)	4287 (1603, 11263)	3309 (1242, 7956)

Values are median (interquartile range) or n (%). Only the volume of patients showing presence of lesions was taken into account. IQR = interquartile range; LNCCI = large noncortical and cortical infarcts (including acute lesions); SNCI = small noncortical infarcts (including acute lesions); TIA = transient ischemic attack. N=1393 patients without history of stroke or transient ischemic attack.

Table e-2: Association between female sex and the prevalence of brain lesions in patients without a history of stroke/TIA

	Univariable	Age adjusted model	Multivariable adjusted model
	All patients (n=1393)	All patients (n=1393)	All patients (n=1379)
Prevalence	OR (95% CI)	OR (95% CI)	OR (95% CI)
Large noncortical and cortical infarcts	0.76 (0.53; 1.07) p=0.13	0.69 (0.48; 0.98) p=0.04	0.81 (0.56; 1.18) p=0.29
Small noncortical infarcts	0.83 (0.61; 1.13) p=0.26	0.71 (0.51; 0.97) p=0.03	0.71 (0.50; 1.01) p=0.06
Ischemic infarcts (LNCCI and SNCI)	0.83 (0.64; 1.08) p=0.18	0.71 (0.54; 0.94) p=0.02	0.78 (0.58; 1.04) p=0.09
Microbleeds	0.86 (0.63; 1.17), p=0.34	0.77 (0.56; 1.05), p=0.10	0.86 (0.61; 1.20), p=0.38
White matter hyperintensities (Fazekas ≥ 2)	1.31 (1.03, 1.67), p=0.03	1.07 (0.82, 1.39), p=0.62	1.12 (0.85, 1.48), p=0.42

Data are presented as odds ratio and 95% confidence interval; Predictor of interest: Female sex; Multivariable adjusted model was adjusted for age, body mass index, smoking status, AF type (paroxysmal vs non-paroxysmal), systolic blood pressure, hypertension, diabetes mellitus, heart failure, coronary heart disease, sleep apnea, statin therapy, antihypertensive medication, oral anticoagulation, antiplatelet therapy. Missing values: microbleeds count (n=42); white matter hyperintensities (n=1); covariates (n=14). LNCCI = large noncortical and cortical infarcts (including acute lesions); SNCI = small noncortical infarcts (including acute lesions); CI = Confidence interval; OR = Odds Ratio; TIA = transient ischemic attack.

Table e-3: Association between female sex and the log-transformed volume of brain lesions in patients without a history of stroke/TIA

	Univariable	Age adjusted model	Multivariable adjusted model
	Multiplicative effect (95% CI)	Multiplicative effect (95% CI)	Multiplicative effect (95% CI)
Volume (log – transformed)			
Large noncortical and cortical infarcts	0.67 (0.37; 1.22) p=0.20	0.67 (0.37; 1.22) p=0.19	0.78 (0.37; 1.38), p=0.53
Small noncortical infarcts	1.12 (0.81; 1.54) p=0.49	1.12 (0.81; 1.55) p=0.48	1.24 (0.86; 1.79), p=0.25
Ischemic lesions (LNCCI and SNCI)	0.78 (0.51; 1.20) p=0.26	0.79 (0.51; 1.22) p=0.28	1.07 (0.65; 1.75), p=0.79
White matter hyperintensities	1.32 (1.12; 1.54), p<0.001	1.12 (0.97; 1.30), p=0.11	1.12 (0.95; 1.32), p=0.16

Data are presented as multiplicative effect and 95% confidence interval; multiplicative effect = e^{β} -coefficient (due to log-transformed outcome variable); Only the volume of patients showing presence of lesions was taken into account; Predictor of interest: Female sex; Multivariable adjusted model was adjusted for age, body mass index, smoking status, AF type (paroxysmal vs non-paroxysmal), systolic blood pressure, hypertension, diabetes mellitus, heart failure, coronary heart disease, sleep apnea, statin therapy, antihypertensive medication, oral anticoagulation, antiplatelet therapy and normalized brain volume. Missing values multivariable adjusted models: covariates (n=3). LNCCI = large noncortical and cortical infarcts (including acute lesions); SNCI = small noncortical infarcts (including acute lesions); CI = Confidence interval; TIA = transient ischemic attack. Multivariable adjusted model (including brain volume): LNCCI: n=177 ; SNCI: n=239 ; Ischemic lesions: n=365 ; white matter hyperintensities: n= 1201.

Table e-4: Sex differentiated percentage of voxels affected by ischemic lesions and white matter lesions within different brain regions

Ischemic lesions	Percentage % Median (interquartile range)					
(LNCCI and SNCI)						
<i>n</i> = 588	<i>Women Left</i>	<i>Men Left</i>	<i>p-Value</i>	<i>Women Right</i>	<i>Men Right</i>	<i>p-Value</i>
ACA	0.02 (0.01; 0.14)	0.04 (0.01; 0.23)	0.09	0.02 (0.01; 0.07)	0.04 (0.01; 0.29)	0.36
MCA	0.03 (0.01; 0.24)	0.04 (0.01; 0.28)	0.18	0.07 (0.01; 0.44)	0.04 (0.01; 0.38)	0.39
PCA	0.13 (0.02; 0.50)	0.12 (0.02; 1.01)	0.19	0.07 (0.01; 1.40)	0.13 (0.01; 0.90)	0.56
Brainstem	1.34 (0.80; 1.88)	0.56 (0.08; 1.48)	0.49	0.09 (0.04; 0.10)	0.82 (0.45; 1.18)	0.90
Cerebellum	0.31 (0.09; 0.64)	0.23 (0.08; 0.64)	0.06	0.16 (0.11; 0.36)	0.24 (0.10; 0.77)	0.18

WMH	Percentage % Median (interquartile range)					
<i>n</i> = 1698	<i>Women Left</i>	<i>Men Left</i>	<i>p-Value</i>	<i>Women Right</i>	<i>Men Right</i>	<i>p-Value</i>
ACA	0.29 (0.07; 0.80)	0.18 (0.06; 0.55)	< 0.001	0.30 (0.10; 0.87)	0.23 (0.07; 0.62)	< 0.001
MCA	0.69 (0.23; 1.67)	0.45 (0.14; 1.12)	< 0.001	0.68 (0.27; 1.61)	0.48 (0.15; 1.13)	< 0.001
PCA	0.22 (0.10; 0.49)	0.22 (0.10; 0.45)	0.24	0.17 (0.07; 0.32)	0.18 (0.07; 0.33)	0.76
Brainstem	0.42 (0.24; 1.17)	0.48 (0.22; 0.88)	< 0.001	0.63 (0.30; 1.41)	0.37 (0.16; 0.98)	< 0.001
Cerebellum	0.09 (0.07; 0.14)	0.08 (0.05; 0.16)	0.53	0.06 (0.05; 0.22)	0.06 (0.04; 0.13)	0.97

Values are median percentage % (interquartile range). The p-value compares women and male patients. Only patients with presence of ischemic lesions were taken into account. Ischemic lesions n=588, Women n=154 (26%), Men n=434 (74%); WML n=1698, Women n=470 (28%), Men n=1228 (72%); LNCCI = large noncortical and cortical infarcts; SNCI = small noncortical infarcts; ACA = anterior cerebral artery; MCA = middle cerebral artery; PCA = posterior cerebral artery; WMH = white matter hyperintensities

Figure e-1: Localization of white matter hyperintensities stratified by sex

The figure shows the distribution of white matter hyperintensities in the SWISS-AF patients with successful co-registration (n=1716) compared between men (n=1245) and women (n=471) in a standard space. The color indicates that a voxel is affected by a white matter hyperintensity in this percentage (%) of patients.

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