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Relationship between structural brain damage and cognitive function in patients with atrial fibrillation

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Background: Atrial fibrillation (AF) has been associated with dementia, but information on the association of structural brain lesions with cognitive function is scarce. The aim of this study was to investigate the relationship between structural brain lesions and neurocognitive function in a cohort of unselected AF patients.
Methods: Swiss-AF is an ongoing, prospective, multicentre, observational cohort study. Overall, 2,415 patients with documented AF were enrolled at 13 sites in Switzerland. All patients underwent neurocognitive testing using the Montreal Cognitive Assessment (MoCA) score, which is scaled from 0 (worst) to 30 (best). Cerebral magnetic resonance imaging (cMRI) was performed at baseline using a standardized protocol. Volumes of infarcts, microbleeds, lacunes and small vessel disease were measured. To assess the relationship between the log-transformed volume of brain lesions and the MoCA score linear regression analyses were performed.
Results: Overall, 1,736 study patients were included in this analysis. Mean age was 73±8 years and 1,261 (73%) were men. The mean CHA2DS2-VASc Score was 3.3±1.7 and 1,559 (90%) patients were on oral anticoagulation. Infarcts, lacunes, microbleeds and small vessel disease were found in 399 (23%), 331 (19%), 370 (21%) and 1709 (98%) patients, respectively. The mean MoCA score was 25.5±3.1. After multivariable adjustment, volume of infarct and volume of small vessel disease remained inversely associated with the MoCA score with β-coefficients (95% CI) of -0.26 [-0.41, -0.11], p<0.001 and -0.12 [-0.23, -0.01], p=0.03, respectively (Table). In a combined model including all brain lesions in one model, volume of infarcts and small vessel disease showed the strongest association with MoCA score (Table).

Brain damage and cognitive function

Model	β-coefficient (95% CI) Univariate	β-coefficient (95% CI) Multivariate*	β-coefficient (95% CI) Combined model**, Univariate
Infarct volume, mm^3	-0.27 [-0.43, -0.11], p<0.001	-0.26 [-0.41, -0.11], p<0.001	-0.56 [-0.85, -0.27], p<0.001
Small vessel disease, mm^3	-0.37 [-0.48, -0.27], p<0.001	-0.12 [-0.23, -0.01], p=0.03	-0.39 [-0.54, -0.23], p<0.001
Lacunes volume, mm^3	-0.28 [-0.62, 0.05], p=0.10	-0.13 [-0.45, 0.20], p=0.44	-0.29 [-0.60, 0.03], p=0.08
Microbleeds volume, mm^3	-0.12 [-0.44, 0.20], p=0.45	-0.17 [-0.48, 0.13], p=0.26	0.01 [-0.29, 0.31], p=0.97

*Multivariable adjusted model was adjusted for age, sex, BMI, education, smoking, hypertension, diabetes, oral anticoagulation, and type of atrial fibrillation. **All variables were added to the same model and brain damage variables are standardized. CI: confidence interval.

Conclusion: In this large cohort of unselected AF patients, there was a high prevalence of brain damage. Old infarcts and small vessel disease on cMRI were the strongest predictors for reduced cognitive function, while microbleeds did not show an association. These findings suggest a differential effect of the different brain lesions on cognitive function.
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Comparison of effectiveness, safety, and healthcare costs in non-valvular atrial fibrillation patients with heart failure prescribed direct oral anticoagulants

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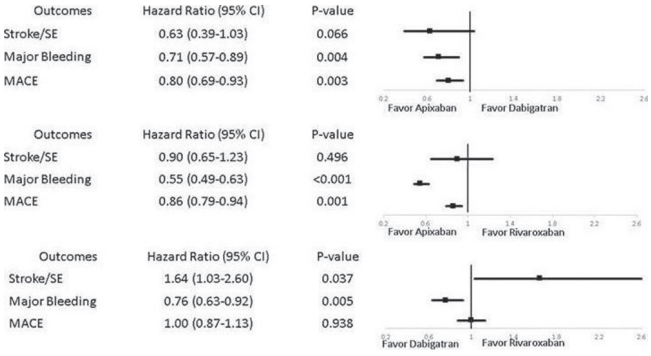
Background: Heart failure (HF) is common among non-valvular atrial fibrillation (NVAF) patients and associated with adverse outcomes. There is limited evidence regarding the effectiveness, safety, and healthcare costs associated with direct oral anticoagulants (DOACs) in NVAF patients with HF treated in clinical practice.
Purpose: Compare stroke/systemic embolism (S/SE), major bleeding (MB), major adverse cardiac events (MACE), and healthcare costs among NVAF patients with HF prescribed DOACs.
Methods: Elderly patients with NVAF and HF who initiated apixaban, dabigatran, or rivaroxaban from 01JAN2013–30SEP2015 in the US Medicare population were included. Propensity score matching was conducted between DOACs. Cox models were used to evaluate the risk of S/SE, MB, and MACE (composite of stroke, myocardial infarction and all-cause death). Generalized linear models were used to compare all-cause healthcare costs (sum of total medical and pharmacy costs); two-part models were used to compare S/SE- and MB-related medical costs.
Results: 4,263 apixaban-dabigatran, 10,477 apixaban-rivaroxaban, and 4,297 rivaroxaban-dabigatran matched pairs were included with a mean follow-up of 7–8 months. Apixaban patients had lower rates of MB and MACE vs. dabigatran and rivaroxaban. Dabigatran patients had a higher rate of S/SE, but a lower rate of MB vs. rivaroxaban (Figure). Apixaban patients had lower MB-related costs vs. dabigatran and rivaroxaban. Apixaban and dabigatran patients had lower total all-cause healthcare costs vs. rivaroxaban (Table).



Conclusions: In this retrospective observational study of NVAF patients with HF, apixaban and dabigatran were associated with lower risk of MB and lower all-cause healthcare costs vs. rivaroxaban. Rivaroxaban was associated with lower risk of S/SE vs dabigatran. This information may be useful in helping healthcare providers select appropriate DOAC treatment for NVAF patients with HF.
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Physical activity and outcome in patients with atrial fibrillation

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Abstract P979 – Table 1

	Apixaban vs Dabigatran N=4,263 N=4,263		Apixaban vs Rivaroxaban N=10,477 N=10,477		Dabigatran vs Rivaroxaban N=4,297 N=4,297	
	Cost PPPM	P-value	Cost PPPM	P-value	Cost PPPM	P-value
S/SE-related medical costs	$67 vs $118	0.075	$64 vs $83	0.243	$117 vs $66	0.064
MB-related medical costs	$194 vs $346	0.001	$248 vs $481	<0.001	$343 vs $424	0.186
Total medical costs	$3,031 vs $3,060	0.853	$3,127 vs $3,458	0.001	$3,075 vs $3,466	0.020
Total pharmacy costs	$526 vs $451	<0.001	$531 vs $485	<0.001	$450 vs $499	0.002
All-cause healthcare costs	$3,557 vs $3,510	0.765	$3,685 vs $3,943	0.004	$3,525 vs $3,965	0.009

PPPM: per patient per month.

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Background: Increased physical activity (PA) is associated with an improved prognosis in healthy individuals and patients with cardiovascular diseases. However, the benefits of PA and the amount needed are much less clear among patients with atrial fibrillation (AF).
Methods: The Basel Atrial Fibrillation Cohort study (BEAT-AF) is a prospective, multicenter cohort study that enrolled 1541 patients with documented AF. Patients reported whether they perform exercise on a regular basis. PA was quantified using the International Physical Activity Questionnaire (IPAQ). Three PA groups were defined: group 1: sedentary lifestyle; group 2: any moderate PA but no vigorous PA; group 3: any vigorous PA. The occurrence of all-cause death, cardiovascular death, major adverse cardiovascular events (MACE), major bleedings, heart failure hospitalization, stroke and myocardial infarction was assessed. To assess the relationships between PA and outcomes, Cox proportional hazards models were used to calculate hazard ratios (HR) and to adjust for clinically important confounders.
Results: The mean follow-up duration was 3.8±1.4years. Mean age was 69±12years, mean CHA2DS2-VASc score was 2.9±1.8. Exercise on a regular Basis was associated with a lower risk of all-cause death (HR 0.51, 95% CI 0.35–0.74), cardiovascular death (0.54, 0.33–0.90), MACE (0.66, 0.47–0.92), and major bleeding (0.45, 0.27–0.75). Vigorous PA conferred a lower risk of adverse events compared with moderate PA for most events, as shown in the table.

Outcomes according physical activity

Endpoint	Risk factor	Adjusted HR (95% CI)
All-cause death	moderate PA	0.75 (0.51, 1.11)
	vigorous PA	0.38 (0.24, 0.60)
Cardiovascular death	moderate PA	0.77 (0.46, 1.27)
	vigorous PA	0.29 (0.15, 0.56)
MACE	moderate PA	0.74 (0.50, 1.10)
	vigorous PA	0.53 (0.34, 0.81)
Major bleeding	moderate PA	0.56 (0.32, 0.99)
	vigorous PA	0.38 (0.21, 0.69)
Heart failure hospitalization	moderate PA	0.78 (0.50, 1.23)
	vigorous PA	0.53 (0.32, 0.86)

Reference group is the sedentary lifestyle group. PA: physical activity.

Conclusions: Our study shows that regular PA is strongly associated with a reduced risk of death, cardiovascular death and major bleeding in patients with AF, and there was an inverse dose-response relationship for most outcomes. Regular PA may be beneficial in patients with AF.

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Long-term clinical impact of sinus rhythm restoration in atrial fibrillation patients with heart failure with mid-ranged ejection fraction

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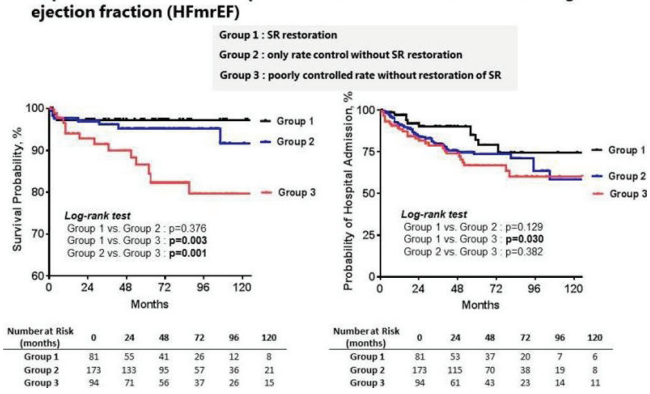
Background: It has been recently reported that a lowering atrial fibrillation (AF) burden in patients coexisting atrial fibrillation and heart failure with reduced ejection fraction was associated with lower rates of death from any cause and lower rates of hospitalization for heart failure. However, it is unclear whether sinus rhythm restoration is associated with all-cause mortality or hospital admission in AF patients with heart failure with mid-ranged ejection fraction (HFmrEF).
Purpose: The aim of our study was to determine the impact of sinus rhythm (SR) restoration by antiarrhythmic drugs (AADs) on mortality or hospitalization in AF patients with HFmrEF during long-term follow-up.
Methods: We enrolled 5,585 consecutive AF patients (≥19 years, mean age 66±13 years, 41.1% female) in a tertiary hospital from 2007 to January 2017. Patients with a left ventricular ejection fraction (LVEF) in the range of 40–49% were defined as HFmrEF. AF patients with HFmrEF were divided into three groups according to history of SR conversion and rate control (heart rate target <100 bpm): group 1 (81 patients with history of SR restoration by AAD with rate control), group 2 (173 patients who had an only rate control (heart rate<100 bpm) without restoration of SR) and group 3 (94 patients who had a poorly controlled rate without restoration of SR).
Results: There were no significant differences in age (p=0.305), female (p=0.930), LVEF (p=0.709) and the proportions of comorbidities including hypertension (p=0.679), diabetes mellitus (p=0.466) and prior stroke (p=0.284) among three each groups. The use of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (p=0.591), oral anticoagulation (p=0.329) and antiplatelet agent (p=0.807) were similar among three groups. During 77±42 months follow-up, 2 (2.5%) patients in group 1 died from any cause compared with other groups [9 (5.2%) in group 2 and 19 (20.2%) in group 3, p<0.001). Significantly fewer patients in group 1 were hospitalized for worsening HF (12 (14.8%) in group 1, 43 (24.9%) in group 2, and 29 (30.9%) in group 3; p=0.038). Kaplan-Meier estimates showed a significant difference in any cause death or hospitalization between group 1 and group 3 (p<0.001). In Cox proportional-hazards models, after adjusting relevant risk factors, chronic kidney disease (hazards ratio [HR] 1.98, 95% confidence interval [CI] 1.24–3.17, p=0.004) and SR restoration (HR 0.44, 95% CI 0.25–0.80, p=0.007) were independently associated with mortality or hospitalization for worsening HF.

Kaplan–Meier Curves in AF patients with heart failure with mid-ranged ejection fraction (HFmrEF)



Number at Risk (months)	0	24	48	72	96	120
Group 1	81	55	41	26	12	8
Group 2	173	133	95	57	36	21
Group 3	94	71	56	37	26	15

Number at Risk (months)	0	24	48	72	96	120
Group 1	81	53	37	20	7	6
Group 2	173	115	70	38	19	8
Group 3	94	61	43	23	14	11

Conclusion: Sinus restoration in AF patients with HFmrEF was associated with a significantly lower rate of death from any cause or hospitalization for worsening heart failure.

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Is there an obesity paradox for adverse outcomes in patients with atrial fibrillation? insights from the FANTASIIA registry

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Background: Both obesity and atrial fibrillation (AF) are increasing in epidemic proportions. Prior studies have demonstrated an obesity paradox, where overweight and obese patients with AF appear to have a better prognosis than do leaner patients with the same degree of cardiovascular diseases.
Purpose: To investigate the characteristics and incidence of adverse events in "real-world" AF patients taking oral anticoagulants (OACs) enrolled in the FANTASIIA registry according to the body mass index (BMI, kg/m^2) comparing patients with normal BMI (18.5 to <25kg/m^2), overweight (25 to<30kg/m^2) and obese (≥30kg/m^2).
Methods: We analyzed anticoagulated AF patients who were prospectively recruited into the multicentre FANTASIIA registry. We calculated the BMI and analyzed baseline characteristics according to the three groups. After 3 years follow-up, all adverse outcomes were recorded.
Results: We analyzed 1,956 patients (56% male, mean 73.8±9.4 years). Of these, 358 (18.3%) had normal BMI, 871 (44.5%) were overweight and 727 (37.6%) were obese. Obese patients were younger (72.1±9.2 vs 74.5±9.5 vs 75.3±9.5 years, p<0.001) and had more comorbidities compared to overweight and obesity patients, eg. hypertension (obese 86.5% vs overweight 79.6% vs normal 69.8%; P<0.001), diabetes (36.5% vs 25.9% vs 24.3%; p<0.001), prior heart failure (32.8% vs 25.8% vs 28.2%; p=0.008). There were no differences in the quality of anticoagulation control with VKA according to BMI, as assessed by time in therapeutic range (61.2% vs 61.5% vs 63.2%, respectively).After 1,070 (750–1110) days of follow-up, we did not observe differences in adverse outcomes according to BMI (table). On multivariable Cox analysis, BMI was not independently associated with all-cause mortality, cardiovascular mortality, stroke, major bleeding nor MACE.

	Normal weight (n=358)	Overweight (n=871)	Obesity (n=727)	p value
Stroke (%/year)	9 (0.85)	19 (0.74)	17 (0.79)	0.903
Major Bleeding (%/year)	23 (2.18)	75 (2.91)	48 (2.24)	0.223
Acute Myocardial Infarction (%/year)	6 (0.56)	28 (1.09)	19 (0.86)	0.314
Cardiovascular Mortality (%/year)	16 (1.51)	56 (2.18)	35 (1.63)	0.263
MACE (%/year)	24 (2.27)	84 (3.27)	60 (2.79)	0.237

Conclusion: In a real-world anticoagulated cohort of AF patients from the FANTASIIA registry, overweight and obesity patients had more concomitant cardiovascular risk factors. No significant differences in adverse events were observed between normal and obese patients and on multivariate analysis, increasing BMI was not independently associated with mortality and adverse outcomes.
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