Identification of novel biomarkers for predicting atrial fibrillation outcomes in patients with cardiovascular risk factors

Khashaba A.[1]; Brady P.[1]; Nehaj F.[1]; Schnabel RB.[2]; Kirchhof P.[2]; Fabritz L.[1]; Chua W.[1]

[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom of Great Britain & Northern Ireland
[2]University Medical Center Hamburg Eppendorf, Hamburg, Germany

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Background: Several novel blood biomarkers were recently found to reflect underlying pathophysiology implicated in atrial fibrillation (AF). These biomarkers could be used for stratifying patients at risk of developing AF or AF-related adverse events.

Purpose: We combined 9 clinical risk factors and 12 biomarkers to model composite outcomes of 1) incident AF, hospitalisation for arrhythmias, and cardiovascular death in sinus rhythm patients at risk of AF, and 2) recurrent AF, hospitalisation for arrhythmias, and cardiovascular death in patients with AF.

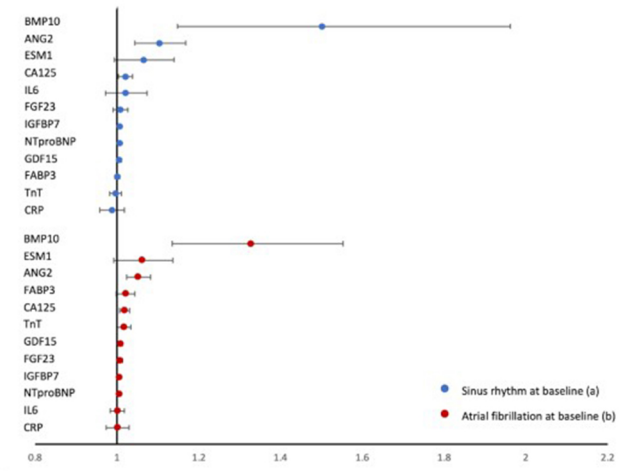
Methods: 1455 patients presenting acutely to hospital with either diagnosed AF (n = 648) or sinus rhythm and ≥2 CHA2DS2-VASc risk factors (n = 807, silent AF ruled out by 7-day ECG monitoring) were followed up for two years. Outcomes were collected from linked hospital episode statistics (HES) and Office of National Statistics (ONS) data from NHS Digital. We univariately evaluated 12 cardiovascular biomarkers quantified from EDTA plasma collected at baseline (ANG2, BMP10, CA125, CRP, ESM1, FABP3, FGF23, GDF15, IGFBP7, IL6, NTproBNP, Troponin T). Two predictive models combining clinical characteristics and biomarkers were developed for each patient group, using Cox regression with backward elimination and considering non-cardiovascular death as a competing risk.

Results: In sinus rhythm patients (n = 117/807 with outcome), elevated BMP10, ANG2, CA125, IGFBP7, NTproBNP univariately predicted the composite outcome (adjusted for age, sex, body mass index (BMI), eGFR, heart failure, stroke/TIA, hypertension, diabetes, coronary artery disease – see Figure part A). In the combined model, age, prior stroke/TIA, coronary artery disease, ANG2, IGFBP7 and NTproBNP predicted the outcome (C-statistic [95% confidence interval (CI)] 0.733 [0.683, 0.784]).

In patients with AF (n = 193/648 with outcome), elevated BMP10, ANG2, CA125, troponin T, GDF15, IGFBP7, NTproBNP univariately predicted the composite outcome (adjusted for same variables as above – see Figure part B). In the combined model, high BMI, low eGFR, hypertension, IGFBP7, NTproBNP and troponin T were predictive of the composite outcome (C-statistic [95% CI]: 0.643 [0.596, 0.689]).

Conclusion: Combinations of clinical risk factors and biomarkers were predictive of two-year AF-related adverse events in sinus rhythm patients at risk of AF and in patients with AF. These markers could be used to identify patients for more intensive follow-up or therapy. IGFBP7 and NTproBNP were present in both models, implicating pathways involved with cardiac overload, inflammation, and oxidative stress. These findings call for external validation of these markers and prospective evaluation in at-risk populations.

Abstract Figure. Biomarkers predicting 2-year AF outcomes



	Biomarker	Hazard ratio	95% CI Lower	95% CI Upper
Sinus rhythm at baseline	BMP10	1.501	1.148	1.962
	ANG2	1.104	1.044	1.168
	ESM1	1.065	0.994	1.140
	CA125	1.021	1.003	1.038
	IL6	1.021	0.972	1.073
	FGF23	1.008	0.990	1.026
	IGFBP7	1.007	1.004	1.011
	NTproBNP	1.006	1.003	1.009
	GDF15	1.005	0.999	1.010
	FABP3	1.001	0.995	1.007
	TnT	0.996	0.982	1.010
	CRP	0.987	0.958	1.018
Atrial fibrillation at baseline	BMP10	1.327	1.135	1.552
	ESM1	1.061	0.992	1.136
	ANG2	1.052	1.023	1.082
	FABP3	1.021	0.998	1.044
	CA125	1.018	1.006	1.031
	TnT	1.017	1.001	1.033
	GDF15	1.009	1.004	1.014
	FGF23	1.007	1.000	1.014
	IGFBP7	1.006	1.004	1.009
	NTproBNP	1.005	1.003	1.008
	IL6	1.001	0.983	1.018
	CRP	1.001	0.974	1.029