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Cardiac biomarkers predict mortality in emergency patients presenting with atrial fibrillation

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ABSTRACT

Objectives To assess the predictive value of N-terminal pro-brain natriuretic peptide (NT-proBNP) and high-sensitive troponin T (hs-TnT) serum levels for mid-term mortality in patients presenting with symptomatic atrial fibrillation (AF) to an emergency department.

Methods Non-interventional cohort/follow-up study, including consecutive patients presenting to a tertiary care university emergency department due to symptomatic AF between 2012 and 2016. Multivariable Cox proportional hazard regression models were used to estimate the mortality rates and hazards per 100 patient-years (pry) for NT-proBNP and hs-TnT serum levels in quintiles.

Results 2574 episodes of 1754 patients (age 68 (IQR 58–75) years, female gender 1199 (44%), CHA_2DS_2-VASc 3 (IQR 1–4)) were recorded. Following the exclusion of incomplete datasets, 1780 episodes were available for analysis. 162 patients deceased during the mid-term follow-up (median 23 (IQR 4–38) months); the mortality rate was 4.72/100 pry. Hazard for death increased with every quintile of NT-proBNP by 1.53 (HR; 95% CI 1.27 to 1.83; p<0.001) and by 1.31 (HR; 95% CI 1.10 to 1.55; p=0.002) with every quintile of hs-TnT in multivariate Cox-regression analysis. No interaction between NT-proBNP and hs-TnT levels could be observed.

Conclusion Elevated NT-proBNP and hs-TnT levels are independently associated with increased mid-term mortality in patients presenting to an emergency department due to symptomatic AF.

Trial registration number NCT03272620; Results.

INTRODUCTION

Atrial fibrillation (AF) as the primary symptom occurs in 3.3% to 10.0% of emergency department (ED) admissions.[1] As to the ongoing ED crowding worldwide, an effective management for patients with symptomatic AF is mandatory.[2 3] Ideally, optimisation of patient management and resource allocation should be based on a time and cost-effective risk stratification.[4] Up to now, the prognosis prediction is merely derived from established cardiovascular risk scores and thromboembolic risk prediction tools as the CHA_2DS_2-VASc score; a biomarker based approach might be then helpful for identification of patients at increased risk for mortality during mid-term follow-up.[3]

Brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT-proBNP) are established prognostic markers for outcome and mortality in various fields of cardiovascular (CV) disease.[5–8] Cardiac troponins are sensitive biomarkers for cardiac damage and already slight elevations are associated with adverse outcome in CV disease.[9–11]

It was recently proposed that the combination of a biomarker– approach might improve existing risk stratification tools in patients with AF.[8 12 13] The aim of the present study was then to evaluate the predictive value of both NT-proBNP and high-sensitive troponin T (hs-TnT) to predict mid-term mortality in symptomatic AF patients presenting to an ED.

METHODS

Design/Setting

In this single-centre cohort study, consecutive adult patients presenting with AF at the ED of the Medical University of Vienna from 2012 to 2016 were eligible for inclusion.

Data acquisition

Following written consent, demographic data, current prescriptions, relevant comorbidities and type of AF according to the current guidelines, duration and AF symptoms were recorded. As guideline definitions for paroxysmal and persistent AF evolved during the study period, both classes have been merged for analysis.

Laboratory values and measurements

Serum NT-proBNP and hs-TnT assays were processed on Cobas E602-Module (ECLIA, Roche Diagnostics GmbH, Mannheim, Germany) console with a coefficient of variation and the reference range of 5.7% and 0–14 ng/L for hs-TnT and 3.7% and 0–125 pg/mL for NT-proBNP. The limit of blank was 3 ng/L for hs-TnT, the limits of detection 5 ng/L for hs-TnT and 5 pg/mL for NT-proBNP (according to the CLSI EP17-A guideline).

Mortality data

Official 'all- cause death' data were provided by the Austrian death registry maintained by the national central statistical office (Statistik Austria, Guglgasse 13, A-1110 Vienna).

Statistics

We present continuous data as median and 25% to 75% IQR, categorised data as absolute count

Table 1 Association of cardiac biomarkers and mortality

	NT-proBNP			hs-TnT		
	HR	95% CI	P values	HR	95% CI	P values
Model						
Unadjusted	1.97†	1.71 to 2.26	<0.001	1.99†	1.70 to 2.33	<0.001
Adjusted for clinical factors*	1.53†	1.27 to 1.83	<0.001	1.31†	1.10 to 1.55	0.002
Adjusted for CHA_2DS_2-VASc	1.70†	1.43 to 2.03	<0.001	1.52†	1.28 to 1.81	<0.001
Sensitivity analysis						
First episode only	1.68†	1.39 to 2.04	<0.001	1.91†	1.54 to 2.36	<0.001
Random effects models	2.34†	1.82 to 3.01	<0.001	2.98†	2.19 to 4.03	<0.001
Continuous scale‡	1.66	1.38 to 2.00	<0.001	1.26	1.07 to 1.49	0.006

*age, female gender, heart failure, chronic obstructive pulmonary disease, serum creatinine, arterial hypertension, coronary artery disease, hyperlipidaemia, diabetes mellitus, peripheral artery disease, history of stroke, history of transient ischemic attack, current smoking, pulmonary vein isolation, beta-blocker and diuretic therapy.
†HR for increase of biomarker quintile.
‡After natural log transformation.

and relative frequency (percentage, %). The entry time for the calculation of the observation period in patient-years (pry) was the first admission with AF at the study centre. Observation time was censored at the date of death or end of the follow-up. For the calculation of the prognostic value of NT-proBNP and hs-TnT, AF episodes with incomplete (only one or no biomarker value at the time of admission) cardiac biomarker information were excluded. To achieve appropriately sized groups including a centrally positioned one, we categorised NT-proBNP (Q_{bnp}) and hs-TnT (Q_{tnt}) into quintiles. To compare baseline data between NT-proBNP and hs-TnT quintiles, we used a χ^2 test for categorised variables. We used the Kruskal-Wallis test for continuous data to test the null hypothesis of no difference because the normality assumption was not met for all baseline data. The unit of analysis of our cohort were admissions (episodes) for AF and included 20% patients, who presented with more than one AF episode. We performed our analysis at the level of episodes, allowing for correlation within patients with multiple episodes using variance component estimates for clustered observations. We calculated mortality rates per 100 pry for NT-proBNP and hs-TnT quintiles and their combinations. We used Cox proportional hazards regression to estimate the hazards of death with NT-proBNP and hs-TnT quintiles simultaneously as the main covariates. We extended the models to assess the independent association of NT-proBNP and hs-TnT with other covariates (table 1).

We also calculated an alternative model with CHA_2DS_2-VASc as the summary integrative covariate of clinically relevant factors but did not model this covariable with the other factors to avoid multicollinearity. We used the Akaike information criterion for model comparison. We assessed first-order interactions of biomarkers by including interaction terms into the models and tested for deviation from linearity. We performed sensitivity analyses to assess the robustness of our multiepisode approach using the first episode only (ignoring other episodes of the same patients) or using random effects models. To assess the robustness of biomarker categorisation, we modelled biomarkers as covariables on a continuous scale after natural log transformation. We assumed that missing data were missing at random. Given the sample size, we decided not to use any methods of data imputation or replacement.

For data management and analysis, we used MS Excel and Stata 14 for Mac. Generally, a two-sided p value <0.05 was considered statistically significant.

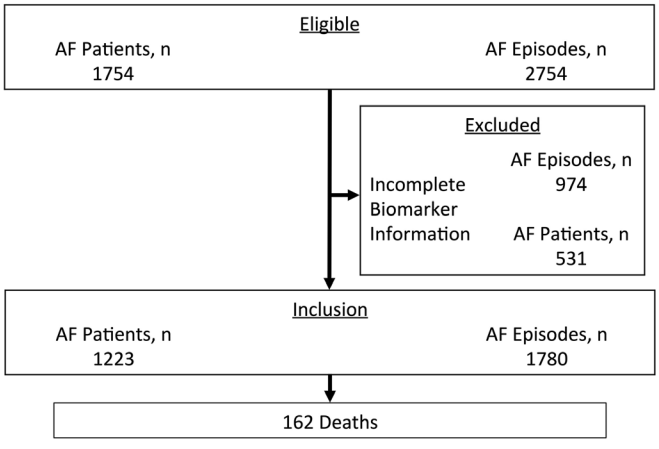

Figure 1 Flow chart of patient inclusion. AF, atrial fibrillation.

RESULTS

Baseline characteristics

Patients and episodes

In total 2574 episodes of 1754 patients (age 68 (IQR 58–75) years, female gender 1199 (44%), CHA_2DS_2-VASc 3 (IQR 1–4)) with symptomatic AF were available for analysis (figure 1). Following exclusion of AF episodes with incomplete biomarker datasets, final analysis comprised 1780 episodes with both NT-proBNP and hs-TnT levels.

Median heart rate was at 122 (IQR 103–140) bpm. Paroxysmal/persistent AF was the most frequent type of AF in all biomarker subgroups. With increasing levels of NT-proBNP and hs-TnT, the hazard for permanent AF increased. The median duration of current AF episodes was 2 (IQR 1–4) and 3 (IQR 2–10) in the lowest, 20 (IQR 8–48) and 8 (IQR 3–48) hours in the highest respective NT-proBNP and hs-TnT quintiles. Duration of current AF correlated directly with biomarker levels. Cardiovascular risk factors were more prevalent in patients with higher biomarker levels (tables 2 and 3).

The total observed time was 3433 pry with a median follow-up duration of 23 (IQR 4–38) months. A total of 162 patients deceased during mid-term follow-up; mortality rate was 4.72 per 100 pry. Mortality rate increased linearly by biomarker levels (p<0.001).

NT-proBNP, hs-TnT and mortality

We could observe a significant crude association of mortality with both increasing NT-proBNP quintiles and increasing

Table 2 Baseline characteristics by NT-proBNP

	NT-proBNP Quintile 1 (5–241 pg/mL)	n	NT-proBNP Quintile 2 (242–628 pg/mL)	n	NT-proBNP Quintile 3 (629–1499 pg/mL)	n	NT-proBNP Quintile 4 (1500–3263 pg/mL)	n	NT-proBNP Quintile 5 (>3263 pg/mL)	n	P values
Clinical characteristics											
Age, years (IQR)	56 (48–66)	329	65 (57–73)	353	69 (61–75)	364	71 (66–77)	365	73 (67–81)	368	<0.001
Female gender, n (%)	74 (22)	329	136 (39)	353	152 (42)	365	188 (52)	365	178 (48)	368	<0.001
CHA_2DS_2-VASc (IQR)	1 (0–2)	275	2 (1–4)	330	3 (2–4)	346	3 (2–4)	357	3 (2–4)	360	<0.001
Laboratory											
hs-TnT, ng/L (IQR)	8.0 (5.0–14.0)	*329*	10.0 (6.0–17.0)	353	13.0 (8.0–25.0)	*365*	16.0 (10.0–29.0)	365	30.0 (19.0–57.0)	*368*	<0.001
Creatinine, mg/dL (IQR)	0.9 (0.8–1.1)	*326*	1.0 (0.8–1.1)	353	1.0 (0.9–1.2)	*363*	1.0 (0.8–1.2)	364	1.2 (1.0–1.6)	*366*	<0.001
Comorbidities											
Heart failure, n (%)	60 (18.2)	329	61 (17.3)	353	83 (22.7)	365	80 (21.9)	365	116 (31.5)	368	<0.001
Hypertension, n (%)	155 (47.1)	329	233 (66.0)	353	258 (70.7)	365	254 (69.6)	365	251 (68.2)	368	<0.001
DM, n (%)	30 (9.1)	329	61 (17.3)	353	64 (17.5)	365	52 (14.3)	365	75 (20.4)	368	0.001
TIA, n (%)	6 (2.0)	329	3 (0.9)	353	10 (2.7)	365	7 (1.9)	365	9 (2.5)	368	0.421
Stroke, n (%)	7 (2.1)	329	12 (3.4)	353	21 (5.8)	365	25 (6.9)	365	27 (7.3)	368	0.006
CAD, n (%)	20 (6.1)	329	44 (12.5)	353	65 (17.8)	365	82 (22.5)	365	115 (31.3)	368	<0.001
Previous MCI, n (%)	10 (3.0)	329	24 (6.8)	353	30 (8.2)	365	44 (12.1)	365	55 (15.0)	368	<0.001
PAD, n (%)	8 (2.4)	329	9 (2.6)	353	15 (4.1)	365	25 (6.9)	365	25 (6.8)	368	0.004
Hyperlipidaemia, n (%)	96 (29.2)	329	104 (29.5)	353	136 (37.3)	365	126 (34.5)	365	103 (28.0)	368	0.031
Current smoker, n (%)	20 (6.1)	329	16 (4.5)	353	16 (4.5)	365	21 (5.8)	365	20 (5.4)	368	0.17
COPD, n (%)	15 (4.6)	329	24 (6.8)	353	27 (7.4)	365	33 (9.0)	365	57 (15.5)	368	<0.001
Medication											
Beta-blockers, n (%)	90 (27.4)	329	146 (41.4)	353	159 (43.6)	365	182 (49.9)	365	206 (56.0)	368	<0.001
Amiodaron, n (%)	41 (12.5)	329	73 (20.7)	353	69 (18.9)	365	77 (21.1)	365	79 (21.5)	368	0.016
VKA, n (%)	57 (17.3)	329	102 (28.9)	353	133 (36.4)	365	113 (31.0)	365	112 (30.4)	368	<0.001
NOAC, n (%)	37 (11.3)	329	47 (13.3)	353	54 (14.8)	365	58 (15.9)	365	42 (11.4)	368	0.273
Diuretics, n (%)	26 (7.9)	329	54 (15.3)	353	89 (24.4)	365	84 (23.0)	365	136 (37.0)	368	<0.001

Baseline characteristics by all five quintiles of NT-proBNP .

CAD, coronary artery disease, COPD, chronic obstructive pulmonary disease, DM, diabetes mellitus, hs-TnT, high-sensitive troponin T, MCI, myocardial infarction, NOAC, new oral anticoagulant, NT-proBNP, N-terminal pro-brain natriuretic peptide, PAD, peripheral artery disease, VKA, vitamin K antagonist.

Table 3 Baseline characteristics by hs-TnT

	hs-TnT Quintile 1 (1–5 ng/L)	n	hs-TnT Quintile 2 (6–8 ng/L)	n	hs-TnT Quintile 3 (9–15 ng/L)	n	hs-TnT Quintile 4 (16–28 ng/L)	n	hs-TnT Quintile 5 (>28 ng/L)	n	P values
Clinical characteristics											
Age, years (IQR)	58 (48–67)	210	62 (55–68)	284	69 (59–74)	456	72 (65–78)	405	73 (65–81)	424	<0.001
Female gender, n (%)	80 (38)	210	123 (43)	284	212 (46)	457	165 (41)	405	148 (35)	424	0.01
CHA_2DS_2-VASc (IQR)	2 (1–3)	185	2 (1–3)	260	3 (2–4)	434	3 (2–4)	389	3 (2–4)	400	<0.001
Laboratory											
hs-TnT, ng/L (IQR)	322 (112–720)	210	508 (182–1135)	284	789 (296–2044)	457	1441 (568–3249)	405	2946 (1195–6899)	424	<0.001
Creatinine, mg/dL (IQR)	0.9 (0.8–1.0)	208	0.9 (0.8–1.1)	283	1.0 (0.8–1.1)	453	1.1 (0.9–1.3)	404	1.2 (1.0–1.6)	424	<0.001
Comorbidities											
Heart failure, n (%)	36 (17.1)	210	55 (19.4)	284	90 (19.7)	457	90 (22.2)	405	129 (30.4)	424	<0.001
Hypertension, n (%)	105 (50.0)	210	180 (63.4)	284	309 (67.6)	457	281 (69.4)	405	276 (65.1)	424	<0.001
DM, n (%)	13 (6.2)	210	34 (12.0)	284	71 (15.5)	457	69 (17.0)	405	95 (22.4)	424	<0.001
TIA, n (%)	0 (0)	210	5 (1.8)	284	8 (1.8)	457	12 (3.0)	405	10 (2.4)	424	0.146
Stroke, n (%)	2 (1.0)	210	13 (4.6)	284	22 (4.8)	457	23 (5.7)	405	32 (7.6)	424	0.011
CAD, n (%)	9 (4.3)	210	24 (8.5)	284	60 (13.1)	457	101 (24.9)	405	132 ((31.1)	424	<0.001
Previous MCI, n (%)	5 (2.4)	210	13 (4.6)	284	32 (7.0)	457	47 (11.6)	405	66 (15.6)	424	<0.001
PAD, n (%)	1 (0.5)	210	6 (2.1)	284	17 (3.7)	457	25 (6.2)	405	33 (7.8)	424	<0.001
Hyperlipidaemia, n (%)	72 (34.3)	210	103 (36.3)	284	149 (32.6)	457	121 (29.9)	405	120 (28.3)	424	0.169
Current smoker, n (%)	11 (5.2)	210	13 (4.6)	284	21 (4.6)	457	23 (5.7)	405	25 (5.9)	424	0.198
COPD, n (%)	12 (5.7)	210	11 (3.9)	284	24 (5.3)	457	43 (10.6)	405	66 (15.6)	424	<0.001
Medication											
Beta-blockers, n (%)	85 (40.5)	210	115 (40.5)	284	210 (46.0)	457	184 (45.4)	405	189 (44.6)	424	0.466
Amiodaron, n (%)	32 (15.2)	210	46 (16.2)	284	88 (19.3)	457	88 (21.7)	405	85 (20.1)	424	0.227
VKA, n (%)	58 (27.6)	210	84 (29.6)	284	155 (33.9)	457	114 (28.2)	405	106 (25.0)	424	0.06
NOAC, n (%)	32 (15.2)	210	39 (13.7)	284	69 (15.1)	457	51 (12.6)	405	47 (11.1)	424	0.411
Diuretics, n (%)	14 (6.7)	210	41 (14.4)	284	97 (21.2)	457	107 (26.4)	405	130 (30.7)	424	<0.001

‡After natural log transformation. Baseline characteristics by all five quintiles of hs-TnT.

CAD, coronary artery disease, COPD, chronic obstructive pulmonary disease, DM, diabetes mellitus, hs-TnT, high-sensitive troponin T, MCI, myocardial infarction, NOAC, new oral anticoagulant, NT-proBNP, N-terminal pro-brain natriuretic peptide, PAD, peripheral artery disease, VKA, vitamin K antagonist.

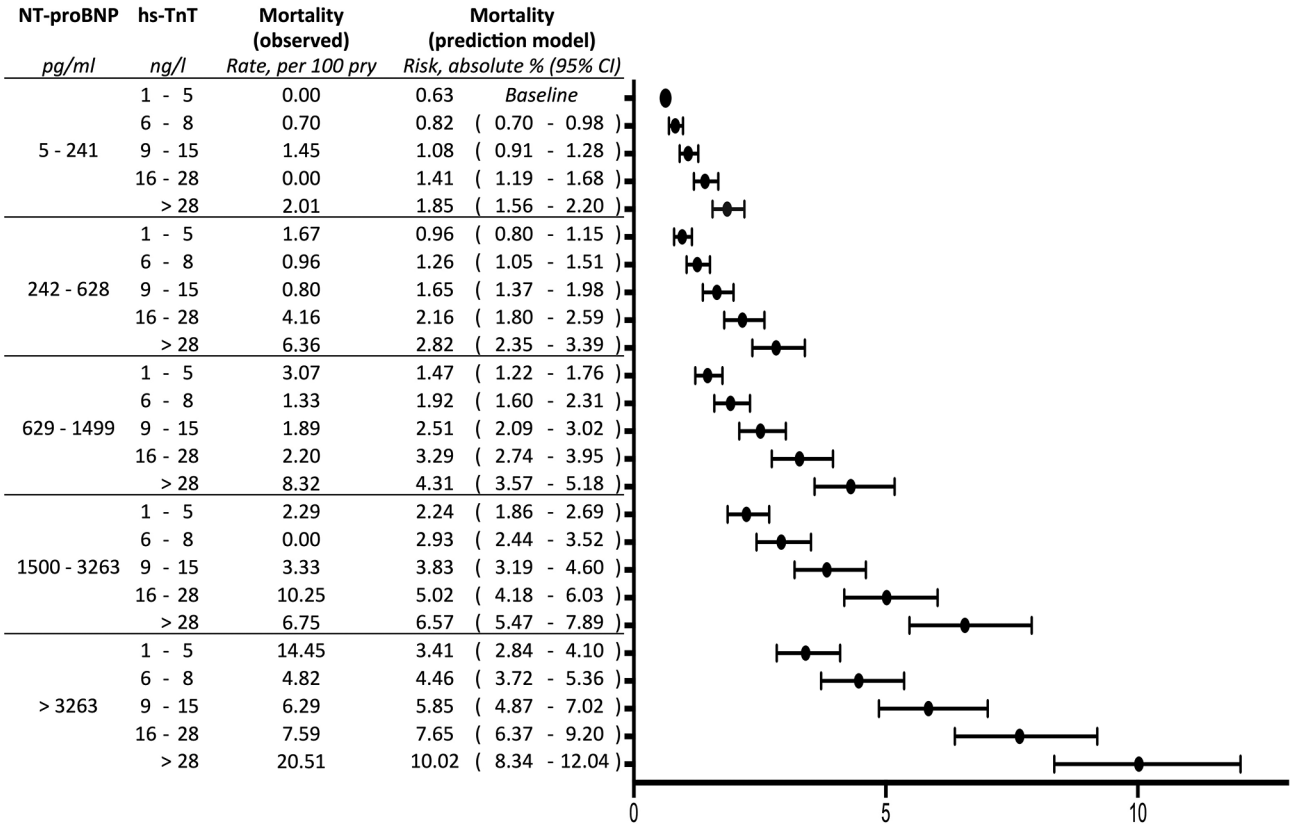

Figure 2 Mortality in patients presenting in an emergency department because of AF by NT-proBNP and hs-TnT (prediction model: Cox proportional-hazards regression; NT-proBNP and hs-TnT adjusted for the clinical risk factors age, female gender, heart failure, chronic obstructive pulmonary disease, serum creatinine, hypertension, coronary artery disease, hyperlipidaemia, diabetes mellitus, peripheral artery disease, stroke, current smoking, pulmonary vein isolation, beta-blocker therapy, diuretic therapy). AF, atrial fibrillation; NT-proBNP, N-terminal pro-brain natriuretic peptide; hs-TnT, high-sensitive troponin T.

hs-TnT quintiles. In multivariate analysis, adjusting for age, female gender, heart failure, COPD, serum creatinine, arterial hypertension, coronary artery disease, hyperlipidaemia, diabetes mellitus, peripheral artery disease, history of stroke, history of TIA, current smoking, pulmonary vein isolation, beta-blocker and diuretic therapy, hazard for death increased with every quintile of NT-proBNP by 1.53 and by 1.31 with every quintile of hs-TnT (table 3, figure 2). Adjustment for CHA_2DS_2-VASc resulted in an HR of 1.70 for each increase of NT-pro-BNP quintile and 1.52 for each increase of hs-TnT quintile for mortality (table 3).

There was no interaction between NT-pro-BNP and hs-TnT on their effect on outcome. Sensitivity analysis indicated robust estimates regarding handling of correlated data and biomarker categorisation (table 3).

DISCUSSION

Presentation and symptoms vary widely for patients with AF admitted to an ED; the demand for an improved risk stratification seems reasonable to facilitate optimal and cost-effective care.[14 15] The present study evaluated the value of cardiac biomarkers in predicting mortality in patients and we could clearly demonstrate that both elevated NT-proBNP and hs-Troponin T levels at the time of admission were strongly and independently associated with increased mid-term mortality.

NT-proBNP, hs-TnT and mortality in AF

NT-proBNP and cardiac troponins have been successfully evaluated to predict prognosis in various fields of cardiovascular medicine.[8 12 13] To our best knowledge, this is the first study investigating the predictive value of both NT-proBNP and hs-TnT for all-cause mortality in patients presenting because of symptomatic AF to an ED. We found that both elevated NT-proBNP and high hs-TnT levels at the time of admission are independently associated with increased mortality in patients presenting because of AF in an ED. Following adjustment for clinical factors, the hazard for death increases with every quintile of NT-proBNP by 1.53 and by 1.31 with every quintile of hs-TnT.

Comparing our findings to previous reports, some specifics have to be considered: the RELY study comprised symptomatic and asymptomatic patients with rather long-lasting AF with a well-controlled median heart rate of 72 (IQR 62–82) per minute[8] In contrast, in our present cohort, all patients were symptomatic, median heart rate exceeded 100 beats per minute and duration of AF episodes was short in general; these characteristics are typical for patients with symptomatic AF presenting to an ED, thus fostering the robustness of our findings for application as a risk stratification tool.[16] Second, Stoyanov *et al* have reported recently hs-TnT levels of patients with AF in a similar setting; in line with our observation, a direct association between symptomatic AF, biomarker levels and mortality has been observed. As this particular study did not focus primarily on symptomatic AF as the primary diagnosis as patients with other reasons for hs-TnT level elevations have been included, residual confounding cannot be excluded, however.[17] In contrast, our study comprised unselected patients seeking help because of symptoms primary due to AF reducing this potential risk of confounding significantly. Last, we could demonstrate a clear biological gradient as

Table 4 Baseline characteristics by biomarker availability

	All episodes	Incomplete information	Both biomarkers available
	n = 2754	n = 974	n = 1780
Clinical presentation			
Age, years (IQR)	68 (58–75)	67 (56–75)	68 (59–75)
Female gender, n (%)	1199 (44)	472 (48)	728 (41)
CHA_2DS_2-VASc (IQR)	3 (1–4)	2 (1–4)	3 (2–4)
Comorbidities			
Heart failure, n (%)	628 (22.8)	228 (23.4)	400 (22.5)
Hypertension, n (%)	1696 (61.6)	548 (56.3)	1151 (64.7)
DM, n (%)	401 (14.6)	120 (12.3)	282 (15.8)
TIA, n (%)	46 (1.7)	11 (1.1)	35 (2.0)
Stroke, n (%)	141 (5.1)	49 (5.0)	92 (5.2)
CAD, n (%)	458 (16.6)	132 (13.6)	326 (18.3)
Previous MCI, n (%)	219 (8.0)	56 (5.7)	163 (9.2)
PAD, n (%)	107 (3.9)	25 (2.6)	82 (4.6)
Hyperlipidaemia(%)	840 (30.5)	277 (28.4)	565 (31.7)
Current smoker, n (%)	130 (4.7)	37 (3.8)	93 (5.2)
COPD, n (%)	256 (9.3)	100 (10.3)	156 (8.8)
Medication			
Beta-blockers, n (%)	1133 (41.1)	382 (39.2)	751 (42.2)
Amiodaron)	477 (17.3)	138 (14.2)	339 (19.0)
VKA, n (%)	766 (27.8)	249 (25.6)	517 (29.0)
NOAC, n (%)	355 (12.9)	120 (12.3)	237 (13.3)
Diuretics, n (%)	567 (20.6)	180 (18.5)	389 (21.9)

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; hs-TnT-sensitive troponin t, MCI, myocardial infarction;NOAC, new oral anticoagulant; NT-proBNP, N-terminal pro-brain natriuretic peptide ; PAD, peripheral artery disease; VKA, vitamin K antagonist.

the hazard for death increases independently with every quintile of hs-TnT and NT-proBNP.

Pathophysiological considerations

Cardiac troponins have been primarily introduced as sensitive biomarkers for the inclusion and exclusion of acute myocardial infarction; however, it has been previously shown that elevation of cardiac troponins might also indicate the severity of other non-cardiac-related conditions; as symptomatic AF is an abnormal physiological state, elevated levels of troponins might reflect an oxygen demand/delivery mismatch and changes in microvascular blood flow thus indicating the urgency or emergency of disease.[18–21] This hypothesis might further be strengthened by the fact that BNPs are mainly released in response to high wall tension during states of haemodynamic stress.[22]

Clinical implications

EDs play a key role in the management of the inhomogeneous group of patients with AF[3 23 24]; the use of risk stratification tools is mandatory for a time-effective and cost-effective treatment and easily accessible biomarkers might assist in this goal-oriented and risk-oriented approach.[8 13] As to our observations, NT-proBNP and hs-TnT may serve as those ideal biomarkers for identification of patients with symptomatic AF at risk; due to the increased risk of all-cause mortality, an extensive screening and more aggressive treatment stratified should be considered in all patients with AF with elevated NT-proBNP or/and hs-TnT levels presenting to an ED.

Strengths and limitations

The present study inherits all known limitations of a prospective observational study design that have to be acknowledged; those limitations are not limited to individual patient profiles, management at the ED and in further care only. However, this study covers a large cohort of consecutive patients within a limited and short time frame that decreases the potential negative impact on our conclusions. Due to the nature of an ED setting, only 1780 of a total 2574 episodes were available for analysis as to missing biomarker data; however, baseline characteristics between those included and excluded showed no significant differences lowering the potential impact of this limitation (table 4). Besides the clear demonstration of a biological gradient between biomarker levels and mid-term mortality, the probably greatest strength of our study is all-cause mortality being the primary outcome measure; as the issuance of death certificates is mandatory in Austria and registered by a central, state-controlled office, information bias can be nearly excluded. Due to our single-centre design, however, our results will not be fully generalisable to other settings and populations; our results ideally need confirmation in larger populations and this might allow then to estimate conceivable cut-off values for risk estimation and stratification that we were not able to due to sample size limitations.

CONCLUSION

Indicating substantially increased mid-term mortality in patients with symptomatic AF, NT-proBNP and hs-TnT could help deciding whether hospitalisation and/or specific long-term management are expedient in high-risk patients. Due to the

Key messages

What was already known on this subject?

- It is common knowledge that atrial fibrillation (AF) is regarded as a risk factor for increased mortality but information on specific patient subgroups at risk is scarce. N-terminal pro-brain natriunatriureticde (NT-proBNP) and cardiactroponins are known, powerful predictors of prognosis in various fields of cardiovascular medicine. It was recently proposed that cardiac troponins and NT-proBNP improve existing risk stratification in patients with AF.

What might this study add?

- Patients with symptomatic AF are at a substantial risk for increased mortality (4.72/100 pry) during follow-up. Elevated NT-proBNP and high-sensitive troponin T (hs-TnT) levels are capable to predict mid-term outcome independently: following adjustment for established risk factors, hazards for death increases with every quintile of NT-proBNP by 1.53 - (HR; 95% CI 1.27 to 1.83; p<0.001) and by 1.31 (HR; 95% CI 1.10 to 1.55; p=0.002) with every quintile of hs-TnT).

How might this impact on clinical practice?

- Indicating substantially increased mid-term mortality in patients with symptomatic AF, NT-proBNP and hs-TnT could help to decide whether hospitalisation and/or specific long-term management are expedient in high-risk patients. Due to the increased risk of all-cause mortality, an extensive screening and more aggressive treatment stratified by elevated NT-proBNP and hs-TnT might be considered in patients with AF presenting to an emergency department.

increased risk of all-cause mortality, an extensive screening and more aggressive treatment stratified by elevated NT-proBNP or/and hs-TnT might be considered in AF-patients presenting to an ED.

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