Profil godišnjeg rizika za ishemijski moždani udar/krvarenje određen CHA_2DS_2-VASc/HAS-BLED zbrojem te cirkulirajuće razine hs-troponina I i NT-proBNP-a kod prijema akutno dekompenziranih bolesnika sa zatajivanjem srca i fibrilacijom atrija

The annual risk profile for ischemic stroke/bleeding determined by CHA_2DS_2-VASc/HAS-BLED score and circulating levels of hs-troponin I and NT-proBNP at admission of patients with acutely decompensated heart failure and atrial fibrillation

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Uvod: Fibrilacija atrija (FA) je najčešća aritmija u zatajivanju srca (ZS).[1] Prethodna istraživanja su pokazala da su biljezi poput NT-proBNP-a i hs-Troponina I (hsTnI) povezani s povišenim rizicima za tromboembolijske i kardiovaskularne događaje u bolesnika s FA.[2] Ciljevi ovog istraživanja bili su procijeniti rizik za ishemijski moždani udar (IMU) i značajno krvarenje, prikazati kliničke i laboratorijske karakteristike te utvrditi potencijalni odnos NT-proBNP-a i hsTnI s navedenim rizicima u akutno dekompenziranih bolesnika sa ZS i FA.

Pacijenti i metode: Ova studija je uključila ukupno 47 bolesnika s akutnom dekompenzacijom ZS utvrđenom prema važećim dijagnostičkim kriterijima za Europskog kardiološkog društva[1] te klinički i elektrokardiografski potvrđenom dijagnozom FA, a koji su bili hospitalizirani u Kliničkom bolničkom centru Split tijekom 2018. godine (**tablica 1**). Bolesnici s akutnim koronarnim sindromom i infektivnim zbivanjem su isključeni.

Rezultati: Prosječni godišnji rizik za IMU bez terapije iznosio je 8,74% uz rizik krvarenja od 0,60% (p<0.001). Kada su rizici prilagođeni za individualnu antitrombotsku terapiju, prosječni rizik za IMU iznosio je 3,46%, a za krvarenje 3,10%, bez značajne razlike između navedenih rizika (p=0.430). Uporaba non-vitamin K oralnih antikoagulansa je gotovo izjednačena s uporabom varfarina (47,5% vs. 52,5%). Prosječna razina hsTnI pri prijemu je iznosila 56,7 ng/mL, a NT-proBNP-a 6550 pg/mL. Razine hsTnI iznad gornje granice referentnih vrijednosti prilagođenih za spol utvrđene su u 26 (55,3%) bolesnika. Razine hsTnI kod prijema su bile neznačajno (p=0.388), a NT-proBNP-a značajno (p=0.014) više u bolesnika s većim rizikom za IMU. Konačno, hsTnI je značajno pozitivno korelirao s NT-proBNP-om (r=0.545, p=0.010) i CRP-om (r=0.559, p<0.001) dok je NT-proBNP značajno pozitivno korelirao s prosječnim godišnjim rizikom za IMU (r=0.587, p=0.002) (**slika 1**).

Zaključci: Antitrombotska terapija je gotovo trostruko smanjila rizik za IMU uz prihvatljiv rizik krvarenja. hsTnI je povišen u velikog broja bolesnika što ukazuje da je većina akutnih dekompenzacija ZS s FA praćena oštećenjem miokarda. Izmjerena razina NT-proBNP-a pri prijemu u opisanoj populaciji mogla bi pomoći pri stratifikaciji godišnjeg rizika za IMU i tromboembolijski događaj.

Introduction: Atrial fibrillation (AF) is the most common arrhythmia associated with heart failure (HF).[1] Previous studies have shown correlation of cardiac markers such as NT-proBNP and high-sensitivity Troponin I (hsTnI) with increased risk for thromboembolic and adverse cardiovascular events in patients with AF.[2] Goals of this study were to evaluate the risk for ischemic stroke (IS) and significant bleeding, to examine clinical and laboratory characteristics, and to determine potential associations of NT-proBNP and hsTnI with aforementioned risks in patients with acute decompensated HF (ADHF) and AF.

Patients and Methods: This study included a total of 47 patients with ADHF and AF, diagnosed according to the current criteria of the European Society of Cardiology (ESC)1, which were hospitalized in University Hospital Centre Split during 2018 (**Table 1**). Patients with an acute coronary syndrome and/or infectious disease were excluded.

Results: Mean annual risk for IS without therapy was 8.74% while bleeding risk was 0.60% (p<0.001). After risk adjustment for individual antithrombotic therapy, mean risks for IS and bleeding were 3.46% and 3.10%, respectively, without significant difference between these risks (p=0.430). Use of non-vitamin K oral anticoagulants was almost equated with warfarin use (47.5% vs. 52.5%). Mean levels of hsTnI and NT-proBNP on admission were 56.7 ng/mL and 6550 pg/mL, respectively. Levels of hsTnI above the upper reference limit adjusted by sex were found in 26 (55.3%) patients. Levels of NT-proBNP on admission were significantly higher (p=0.014) in patients with higher risk for IS, as well as levels of hsTnI but without statistical significance (p=0.388). hsTnI showed positive correlation with NT-proBNP (r=0.545, p=0.010) and C-reactive protein (r=0.559, p<0.001), while NT-proBNP exhibited positive correlation with mean annual risk for IS (r=0.587, p=0.002) (**Figure 1**).

Conclusion: The antithrombotic management reduced the risk for IS by nearly threefold, with an acceptable bleeding risk. Levels of hsTnI were increased in a large number of patients suggesting that myocardial injury is common during the hospitalization event of ADHF with AF. Levels of NT-proBNP on admission, in presented population, may aid in annual risk stratification for IS and thromboembolic event.

TABLE 1. Baseline characteristics of heart failure patients with atrial fibrillation.

Variable	Mean ± SD or N(%) or Median (IQR)	Variable	Mean ± SD or N(%) or Median (IQR)
Age (years)	73.3 ± 9.9	LAVI (mL/m^2)	41.3 ± 15.7
BMI (kg/m^2)	30.1 ± 4.1	Hemoglobin (g/L)	142 ± 17
Male sex	32 (68.1%)	PT-INR	3.2 ± 2.4
Positive history of a prior ACS event	18 (38.3%)	APTT (s)	30.6 ± 13.4
Prior stroke, TIA or thromboembolism	7 (14.9%)	NT-proBNP at index admission (pg/mL)	6550 ± 3381
Prior CABG	8 (17.0%)	hs-cTnI at index admission (ng/mL)	56.7 ± 40.6
Arterial hypertension	42 (89.4%)	CRP at index admission (mg/L)	27.3 ± 29.2
Dyslipidemia	27 (57.4%)	Mean HR at admission (bpm)	100 ± 27
Diabetes mellitus	16 (34.0%)	Mean QRS duration (msec)	115 ± 33
Smoking (ex or current)	13 (26.5%)	Mean QTc (msec)	433 ± 47
PAD	12 (25.5%)	Prolonged QT interval	17 (36.2%)
Vascular disease (PAD, AMI, aortic plaque)	27 (57.4%)	Oral anticoagulants	40 (85.1%)
CHA_2DS_2-VASc score	5 (4-5)	Warfarin	21/40 (52.5%)
0-4% stroke or thromboembolism risk	17 (36.2%)	NOAC	19/40 (47.5%)
4-8% stroke or thromboembolism risk	16 (34.0%)	Antiplatelet agent	10 (21.3%)
>8% stroke or thromboembolism risk	14 (29.8%)	ACE inhibitor or ARB	38 (80.9%)
HAS-BLED score	2 (1-2)	Beta-blocker	38 (80.9%)
NYHA functional class	3 (2-4)	Loop and/or thiazide and/or thiazide-like diuretics	39 (82.9%)
SBP (mmHg)	132 ± 20	ARNi	8 (17.0%)
DBP (mmHg)	81 ± 11	Mineralocorticoid antagonist	14 (29.8%)
eGFR (mL/min/1.73 m^2)	57.1 ± 22.5	Calcium channel blocker	10 (21.3%)
LVEF (%)	37 ± 14	Digoxin	15 (31.9%)
LA diameter (mm)	52 ± 10	Statin	18 (38.3%)
LA volume (mL)	72 ± 31	Allopurinol	7 (14.9%)

Abbreviations: ACE-angiotensin-converting enzyme; **ACS**-acute coronary syndrome; **AMI**-acute myocardial infarction; **APTT**-activated partial thromboplastin time; **ARB**-angiotensin II receptor blocker, **ARNi**-angiotensin receptor-neprilysin inhibitor; **BMI**-body mass index, **CABG**-coronary artery bypass grafting; **CRP**-C-reactive protein; **DBP**-diastolic blood pressure; **eGFR**-estimated glomerular filtration rate; **HR**-heart rate; **hs-cTnI**-high-sensitivity cardiac troponin I; **LA**-left atrium; **LAVI**-left atrial volume indexed by body surface; **NT-proBNP**-N-terminal prohormone of brain natriuretic peptide; **NYHA**-New York Heart Association functional classification of heart failure; **PAD**-peripheral artery disease; **PT-INR**-prothrombin time international standardized ratio; **SBP**-systolic blood pressure; **TIA**-transient ischemic attack.

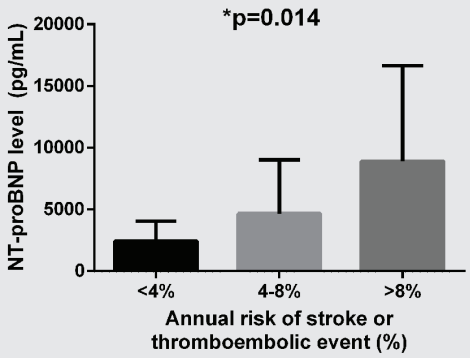

FIGURE 1. Mean NT-proBNP plasma levels (pg/mL) according to the annual risk of stroke or thromboembolic event divided in three categories of risk (<4%, 4-8%, >8%).

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