

# Clinical characteristics and thromboembolic risk of atrial fibrillation patients with and without congestive heart failure. Results from the CRATF study

Paweł Balsam, MD, PhD<sup>a</sup>, Monika Gawalko, MD<sup>a,\*</sup>, Michał Peller, MD<sup>a</sup>, Agata Tymińska, MD<sup>a</sup>, Krzysztof Ozierański, MD<sup>a</sup>, Martyna Zaleska, MD<sup>a</sup>, Katarzyna Żukowska, MD<sup>a</sup>, Katarzyna Szepletowska, MD<sup>a</sup>, Kacper Maciejewski, MD<sup>b</sup>, Marcin Grabowski, MD, PhD<sup>a</sup>, Mariusz Borkowski, MD, PhD<sup>c</sup>, Łukasz Kołtowski, MD, PhD<sup>a</sup>, Anna Praska-Oginska, MD<sup>b</sup>, Inna Zaboyska, MD<sup>b</sup>, Grzegorz Opolski, MD, PhD<sup>a</sup>, Janusz Bednarski, MD, PhD<sup>b</sup>

## Abstract

Congestive heart failure (CHF) and atrial fibrillation (AF) frequently coexist and are associated with increased risk of cardiovascular events.

To compare baseline characteristics, comorbidities and pharmacotherapy in AF patients with concomitant CHF to those without CHF.

The study included 3506 real-life AF patients with (37.1%) and without CHF — participants of the multicentre, retrospective MultiCenter experience in AFib patients Treated with OAC (CRAFT) trial (NCT02987062).

All patients were treated with non-vitamin K antagonist oral anticoagulants (NOAC) or vitamin K antagonists (VKA). The frequency of NOAC among patients with and without CHF was 45.6% and 43.2%, respectively ( $P = .17$ ). Patients with CHF were older (73.3 vs 64.7 years,  $P < .001$ ), less likely to be women (37.4% vs 42%,  $P = .007$ ), had higher CHA2DS2-VASc score ( $3.8 \pm 1.7$  vs  $2.6 \pm 1.8$ ,  $P < .001$ ), more often had permanent AF (53.0% vs 13.4%,  $P < .001$ ), chronic obstructive pulmonary disease (16.7% vs 4.9%,  $P < .001$ ), coronary artery disease (64.3% vs 29.8%,  $P < .001$ ), peripheral vascular disease (65.3% vs 31.4%,  $P < .001$ ), chronic kidney disease (43.1% vs 10.0%,  $P < .001$ ), liver fibrosis (5.7% vs 2.6%,  $P < .001$ ), neoplasm (9.6% vs 7.3%,  $P = .05$ ), history of composite of stroke, transient ischemic attack or systemic embolization (16.2% vs 10.7%,  $P < .001$ ), pacemaker (27.4% vs 22.1%,  $P = .004$ ), implantable cardioverter-defibrillator (22.7% vs 0.8%,  $P < .001$ ) or transaortic valve implantation (4.0% vs 0.8%,  $P < .001$ ), cardiac resynchronization therapy (8.7% vs 0.3%,  $P < .001$ ), composite of kidney transplantation, hemodialysis or creatinine level  $> 2.26$  mg/dL (3.6% vs 0.8%,  $P < .001$ ) and had less often hypertension (69.4% vs 72.5%,  $P = .05$ ).

Patients with AF and CHF had a higher thromboembolic risk and had more concomitant diseases.

**Abbreviations:** AF = atrial fibrillation, BID = twice daily, CARATV = Computerised Antithrombotic Risk Assessment Tool, CHF = congestive heart failure, CRAFT = MultiCenter experience in AFib patients Treated with OAC, NOAC = non-vitamin K antagonist oral anticoagulants, NYHA = New York Heart Association, OAC = oral anticoagulants, VKA = vitamin K antagonist.

**Keywords:** atrial fibrillation, heart failure, non-vitamin K antagonist oral anticoagulants, oral anticoagulation, vitamin K antagonists

## 1. Introduction

Atrial fibrillation (AF) is the most commonly diagnosed sustained cardiac arrhythmia in adults. In 2010 over 33 million people

worldwide suffered AF<sup>[1]</sup> and this number is projected to triple by 2050 as a result of aging population and increased number of comorbidities leading to AF.<sup>[2,3]</sup> In a contemporary cohort of patients with AF, approximately one-half presented with concomitant congestive heart failure (CHF).<sup>[4,5]</sup> AF and CHF are associated with increased risk for stroke and systemic embolism, and when combined have much worse outcomes.<sup>[6,7]</sup> Moreover, even in the absence of AF, CHF is an independent risk factor for thromboembolism, ranking second only to AF as the underlying cause of cardioembolic strokes.<sup>[8]</sup>

Prevention of thromboembolism with oral anticoagulants (OAC) is one of the main goals of treatment of patients with AF, irrespective of CHF presence.<sup>[9]</sup> With the availability of non-vitamin K antagonist oral anticoagulants (NOAC) the potential choice of oral anticoagulant has significantly broadened. Recent meta-analysis of NOAC in CHF patients demonstrated their comparative efficacy and safety to vitamin K antagonists (VKA).<sup>[9–11]</sup> In addition, NOAC were similarly effective or even safer (less intracranial hemorrhage) in AF patients with CHF compared with those without CHF.<sup>[12]</sup> Nevertheless, despite better pharmacokinetic profile of NOAC,<sup>[13–15]</sup> in Poland many

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<sup>a</sup> 1st Chair and Department of Cardiology, Medical University of Warsaw,

<sup>b</sup> Cardiology Unit, John Paul II Western Hospital, Grodzisk Mazowiecki, <sup>c</sup> "Orlik" Medical Clinic, Warsaw, Poland.

\* Correspondence: Monika Gawalko, 1st Chair and Department of Cardiology, Medical University of Warsaw, Public Central Teaching Hospital in Warsaw, 1a Banacha St. Warsaw 02-097, Poland (e-mail: mongawalko@gmail.com).

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patients with non-valvular AF still receive VKA instead of NOAC due to the non-reimbursement of the latter.<sup>[16,17]</sup> In the present analysis, we compare the baseline characteristics of real-life AF patients with and without CHF.

## 2. Methods

### 2.1. Study design

The analysis was based on the multicenter, retrospective MultiCenter experience in AFib patients Treated with OAC (CRAFT) study, registered in ClinicalTrials.gov: NCT02987062.

### 2.2. Study population

The CRAFT study included consecutive patients aged 18 or over hospitalized in years 2011 to 2016 in 2 cardiology centers in Poland, including academic center located in a capital city and a district hospital. All patients were diagnosed with non-valvular AF and treated with 1 of the OAC—VKA (acenocoumarol, warfarin) or NOAC (apixaban, dabigatran, rivaroxaban). Due to a small group, patients on apixaban were excluded. Another NOAC—edoxaban was not available on the Polish market at the time of data collection. All demographic, clinical, type of AF (paroxysmal, persistent and persistent long lasting, permanent), laboratory and echocardiographic (including transoesophageal echocardiogram) data, as well as information on medication, were retrieved retrospectively from medical records.

The study was approved by the local Ethical Review Board of Warsaw Medical University and informed consent was not needed due to retrospective character of the study.

### 2.3. Statistical analysis

Continuous variables were presented as mean±standard deviation and categorical variables are presented as percentages (absolute numbers). Mann–Whitney test or Student *t* test was used to compare continuous variables and chi-square or the Fisher exact test to compare categorical variables. A value of  $P < .05$  was considered statistically significant. All tests were 2-tailed. Statistical analyses were performed by using the SPSS software, version 22 (IBM SPSS Statistics 22, NY).

## 3. Results

In the CRAFT trial, 1304 (37.0%) participants were classified as having CHF at the time of hospitalization, based on a history of clinical CHF and echocardiographic changes consistent with the European Society of Cardiology guidelines,<sup>[9]</sup> and 2202 patients were without CHF. Among participants with CHF, 709 (54.4%) were treated with VKA, 161 (12.4%)—with dabigatran and 434 (33.3%)—with rivaroxaban. In the dabigatran group, 38.5% of patients received dosing of 150 mg twice daily (BID), 61.5%—110 mg BID. In the group who was given rivaroxaban, 41.4% of patients were treated with single 20 mg daily dose and 58.6% received a single 15 mg daily dose. Among patients without CHF, 1251 (56.8%) were treated with VKA, 339 (15.4%)—with dabigatran and 612 (27.8%)—with rivaroxaban. In the dabigatran group, 25.8% of patients received dosing of 110 mg BID. In the group who was given rivaroxaban, 25.8% of patients were treated with single 15 mg daily dose.

### 3.1. Clinical characteristics

Differences in baseline clinical variables among patients with and without CHF are presented in Table 1. Mean age of the total population was  $73.3 \pm 11.4$  years and 37.4% were female. Compared to patients without CHF, those with CHF were older ( $73.3$  vs  $64.7$  years,  $P < .001$ ), less likely to be women (37.4% vs 42%,  $P = .007$ ), had higher CHA<sub>2</sub>DS<sub>2</sub>-VASc score ( $3.8 \pm 1.7$  vs  $2.6 \pm 1.8$ ,  $P < .001$ ), more often had permanent AF (53.4% vs 13.4%,  $P < .001$ ). Moreover, patients with CHF more often had chronic obstructive pulmonary disease (16.7% vs 4.9%,  $P < .001$ ), coronary artery disease (64.3% vs 29.8%,  $P < .001$ ), peripheral peripheral disease (65.3% vs 31.4%,  $P < .001$ ), chronic kidney disease (43.1% vs 10.0%,  $P < .001$ ), liver fibrosis (5.7% vs 2.6%,  $P < .001$ ), neoplasm (9.6% vs 7.3%,  $P < .001$ ), composite of stroke, transient ischemic attack or systemic embolization (16.2% vs 10.7%,  $P < .001$ ), pacemaker (27.4% vs 22.1%,  $P < .001$ ), implantable cardioverter-defibrillator (22.7% vs 0.8%,  $P < .001$ ) or transaortic valve implantation (4.0% vs 0.8%,  $P < .001$ ), cardiac resynchronization therapy (8.7% vs 0.3%,  $P < .001$ ), composite of kidney transplantation, hemodialysis or creatinine level  $> 2.26$  mg/dL (3.6% vs 0.8%,  $P < .001$ ) and had less often hypertension (69.4% vs 72.5%,  $P = .05$ ).

### 3.2. Comparison of thromboembolic and bleeding risk factors

Table 2 presents thromboembolic and bleeding risk scores in AF patients with or without CHF. Patients with CHF had higher risk of thromboembolic and bleeding events (CHA<sub>2</sub>DS<sub>2</sub>VASc  $4.8 \pm 1.7$ , CHADS<sub>2</sub>  $2.9 \pm 1.2$ , HAS-BLED  $0.6 \pm 0.8$ ), compared to those without CHF (CHA<sub>2</sub>DS<sub>2</sub>VASc  $2.6 \pm 1.8$ , CHADS<sub>2</sub>  $1.4 \pm 1.1$ , HAS-BLED  $0.3 \pm 0.6$ ,  $P < .001$ ). Patients with CHF had also a higher rate of prior major bleeding (14.8% vs 4.1%,  $P < .001$ ) and more often had diagnosed anemia (31.5% vs 13.3%,  $P = < .001$ ).

### 3.3. Laboratory and echocardiographic parameters

Compared to patients without CHF, those with CHF had worse kidney function assessed by estimated glomerular filtration rate ( $58.9 \pm 22.2$  vs  $77.4 \pm 34.2$  mL/min/1.73m<sup>2</sup>) and creatinine level ( $1.3 \pm 0.4$  vs  $1.1 \pm 0.4$  mg/dL). Moreover, among CHF patients the hemoglobin, bilirubin, glutamic aspartate aminotransferase levels were elevated, whereas platelet count and alanine aminotransferase level were decreased. Related to echocardiography results, patients with CHF had lower left ventricular ejection fraction ( $41.6 \pm 14.3$  vs  $56.2 \pm 7.4$ ,  $P < .001$ ), higher frequency of left atrial thrombus (11.8% vs 2.0%,  $P < .0001$ ) and left atrial enlargement ( $4.9 \pm 0.8$  vs  $4.4 \pm 0.6$  cm,  $P < .001$ ) compared to those without CHF. All laboratory and echocardiographic parameters are presented in Table 2.

### 3.4. Medical therapy

Comparison of AF patients with and without CHF based on medical therapy is presented in Table 3. Compared to patients without CHF, those with CHF were more often treated with nonsteroidal anti-inflammatory drugs or antiplatelet drugs (19.5% vs 10.6%,  $P < .001$ ), oral antihyperglycemic drugs (39.0% vs 19.1%,  $P < .001$ ), statins (73.2% vs 58.9%,  $P < .001$ ), angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers (85.9% vs 67.1%,  $P < .001$ ), beta-blockers

**Table 1****Comparison of atrial fibrillation patients with and without congestive heart failure treated with oral anticoagulation based on patient's medical history.**

Variable	CHF	Without CHF	P
Age, years	73.3±11.4 n=1304	64.7±13.1 n=2202	<.001
Female sex, %	37.4 (487/1304)	42.0 (925/2202)	.007
BMI, kg/m <sup>2</sup>	29.5±5.9 n=227	28.6±4.8 n=122	.27
AF, %			
Paroxysmal AF	33.3 (416/1249)	66.8 (1403/2102)	<.001
Persistent AF	13.4 (168/1250)	19.9 (419/2103)	<.001
Long-standing persistent AF	0.8 (10/1250)	6.2 (131/2103)	<.001
Permanent AF	53.4 (667/1250)	13.4 (281/2103)	<.001
EHRA	2.3±0.9 n=74	2.6±0.7 n=862	.002
Duration of AF, days	36.4±46.2 n=47	80.9±67.7 n=833	<.001
Clinical characteristics, %			
Anemia	31.5 (247/784)	13.3 (248/1860)	<.001
COPD	16.7 (217/1302)	4.9 (108/2200)	<.001
CAD	64.3 (838/1304)	29.8 (656/2202)	<.001
Smoking	8.6 (111/1298)	3.4 (75/2199)	<.001
TAVI	4.0 (31/785)	0.8 (14/1872)	<.001
Hyperthyroidism	3.7 (29/784)	2.9 (53/1862)	.27
Pacemaker	27.4 (215/784)	22.1 (412/1867)	0.004
ICD	22.7 (178/786)	0.8 (15/1873)	<.001
CRT	8.7 (68/786)	0.3 (5/1873)	<.001
Hypertension	69.4 (905/1304)	72.5 (1597/2202)	.05
SBP >160	2.3 (18/786)	2.4 (45/1871)	>.99
Severe bleeding	14.8 (192/1302)	4.1 (91/2202)	<.001
Excessive alcohol consumption	2.1 (27/1300)	0.5 (10/2198)	<.001
Kidney transplant/hemodialysis	0.5 (4/786)	0.5 (9/1873)	>.99
Kidney transplant/hemodialysis/creatinine >2.26 mg/dL	3.6 (28/784)	0.8 (15/1865)	<.001
Neoplasm	9.6 (75/785)	7.3 (136/1872)	.05
Liver fibrosis	5.7 (69/1210)	2.6 (54/2061)	<.001
Stroke/TIA/embolism	16.2 (211/1304)	10.7 (236/2202)	<.001
PVD	65.3 (851/1304)	31.4 (691/2202)	<.001
CKD	43.1 (338/785)	10.0 (188/1873)	<.001
Ablation	6.9 (53/765)	48.4 (885/1830)	<.001

Continuous variables are shown as a mean±standard deviation, categorical variables are presented as percentages (absolute number/number of collected data).

P values are given for differences between patients with and without CHF.

AF = atrial fibrillation, BMI = body mass index, CAD = coronary artery disease, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, CRT = cardiac resynchronization therapy, EHRA = European Heart Rhythm Association symptom classification, ICD = implantable cardioverter-defibrillator, PVD = peripheral vascular disease, SBP = systolic blood pressure, TAVI = transcatheter aortic valve implantation, TIA = transient ischemic attack.

(92.1% vs 76.2%,  $P < .001$ ) and less often with Ca blockers (16.3% vs 21.7%,  $P = .001$ ), anti-arrhythmic drugs (14.5% vs 18.5%,  $P = .002$ ). According to oral anticoagulation, there were no significant differences between frequency of VKA or NOAC therapy among those 2 groups, however AF patients with CHF were more often treated with rivaroxaban (33.3% vs. 27.8%,  $P < .001$ ), less often with dabigatran (12.4% vs 15.4%,  $P = .013$ ) and received lower doses of those drugs compared to AF patients without CHF. The prevalence of CHF, thromboembolic and bleeding risk factors, such as CHA<sub>2</sub>DS<sub>2</sub>-VAsC score, CHAD<sub>2</sub> score, and severe bleeding in both VKA and NOAC groups were presented in the paper published recently in indexed journal.<sup>[18]</sup>

#### 4. Discussion

AF and CHF have emerged as being among the most common cardiac disorders afflicting our society. Approximately 50% of AF patients have concomitant CHF.<sup>[19]</sup> The presence of one of these conditions increases the probability of developing the other. The association between AF and the development of CHF was analyzed in a study of 3288 patients diagnosed with AF at the Mayo Clinic.<sup>[20]</sup> The incidence of CHF within the first 12 months after the diagnosis of AF was 7.8% and approximately 24% of

patients developed CHF during a mean follow-up of 6.1 years. Another study by Chatterjee et al focused on the risk factors for CHF in women with new-onset AF. Among 1534 women with new-onset AF, there were 226 CHF, the majority of which occurred after AF diagnosis (n=187; 82.7%) over a median follow-up of 20.6 years. In multivariable models accounting for changes in risk factors after AF diagnosis, systolic blood pressure >120 mm Hg, body mass index  $\geq 30$  kg/m<sup>2</sup>, current tobacco use, and diabetes mellitus were each associated with CHF.<sup>[21]</sup>

In patients with AF, the main therapy goals include symptoms control, prevention of cardiac dysfunction, and arterial thromboembolism, particularly stroke.<sup>[22,23]</sup> These goals are also appropriate for the relatively large subset of AF patients with CHF. In these individuals, symptoms are frequent and potentially disabling due to the interaction between the 2 processes. As it is well described in current publications, low cardiac output, aberrant flow through dilated cardiac chambers and poor contractility aggravated by coexistence of AF and CHF may all produce "flow abnormalities" that predispose to intracardiac thrombus formation and subsequent thromboembolism.<sup>[24-26]</sup> As confirmed in our study, patients with CHF had enlargement of left atrium, lower left ventricular ejection fraction and higher

**Table 2****Comparison of atrial fibrillation patients with and without congestive heart failure treated with oral anticoagulation based on variables collected during admission and echocardiographic results.**

Variable	CHF	Without CHF	P
Laboratory parameters			
INR	1.6 ± 0.8 n = 769	1.5 ± 0.7 n = 1856	<.001
Labile INR, %	4.2 (33/778)	2.0 (38/1861)	.002
Creatinine, mg/dL	1.3 ± 0.4 n = 784	1.1 ± 0.4 n = 1863	<.001
Creatinine >2.26 mg/dL, %	3.1 (24/784)	0.6 (11/1860)	<.001
AST	31.1 ± 20.9 n = 743	29.8 ± 18.2 n = 1759	.015
ALT	34.1 ± 27.3 n = 748	36.6 ± 30.4 n = 1769	<.001
Bilirubin, mg/dL	1.0 ± 0.9 n = 98	0.7 ± 0.5 n = 96	<.001
PLT, K/uL	205.2 ± 66.4 n = 784	212.5 ± 50.3 n = 1859	<.001
Reduced PLT	43.4 (370/852)	20.8 (398/1911)	<.001
Hemoglobin, g/dL	13.3 ± 2.03 n = 784	14.0 ± 1.6 n = 1860	<.001
eGFR, %			
≥50 mL/min/1.73m <sup>2</sup>	64.5 (802/1243)	82.2 (1161/1412)	<.001
30–49 mL/min/1.73m <sup>2</sup>	30 (372/1241)	16.4 (231/1410)	<.001
15–29 mL/min/1.73m <sup>2</sup>	5.6 (69/1241)	1.1 (17/1410)	<.001
<15 mL/min/1.73m <sup>2</sup>	0.2 (3/1242)	0.2 (3/1413)	>.99
eGFR, mL/min/1.73m <sup>2</sup>	58.9 ± 22.2 n = 784	77.4 ± 334.2 n = 1862	<.001
Thromboembolic and bleeding risk scores			
HAS-BLED score	0.6 ± 0.8 n = 775	0.3 ± 0.6 n = 1855	<.001
CHA2DS2-VASc score	4.8 ± 1.7 n = 1304	2.6 ± 1.8 n = 2202	<.001
0–1, %	3.8 (49/1304)	31.1 (685/2202)	<.001
2, %	7.2 (94/1304)	19.9 (439/2202)	<.001
3–9, %	89.0 (1161/1304)	49.0 (1078/2202)	<.001
CHA2DS2-VASc score without CHF	3.8 ± 1.7 n = 1304	2.6 ± 1.8 n = 2202	<.001
CHAD2 score	2.9 ± 1.2 n = 1304	1.4 ± 1.1 n = 2202	<.001
0–1, %	10.4 (136/1304)	10.4 (136/1304)	<.001
2, %	26.2 (341/1304)	24.5 (540/2202)	.3
3–9, %	63.4 (827/1304)	13.8 (304/2202)	<.001
TTE / TOE results			
EF, %	41.6 ± 14.3 n = 536	56.2 ± 7.4 n = 575	<.001
LAD, cm	4.9 ± 0.8 n = 373	4.4 ± 0.6 n = 779	<.001
LA area, cm <sup>2</sup>	34.5 ± 10.9 n = 116	25.6 ± 6.8 n = 300	<.001
Thrombus, %	11.8 (15/127)	2.0 (22/1124)	<.001

Continuous variables are shown as a mean ± standard deviation, categorical variables are presented as percentages (absolute number/number of collected data)

P values are given for differences between patients with and without CHF.

ALT = Alanine transaminase, AST = aspartate transaminase, CHF = congestive heart failure, EF = ejection fraction, eGFR = estimated glomerular filtration rate, INR = international normalized ratio, LA left atrial, LAD = left atrial dimension, PLT = platelet count, TOE = transesophageal echocardiography, TTE = transthoracic echocardiography.

prevalence of left atrial thrombus compared to those without CHF. Therefore, it is important to incorporate a suitable treatment,<sup>[21]</sup> taking into proper account the co-morbidities. Except for increased risk for thromboembolism, AF-CHF patients are more likely to have cardiovascular risk factors and pre-existing disease at baseline, including older age, hypertension, valvular disease, diabetes, chronic kidney disease, stroke, and chronic obstructive pulmonary disease.<sup>[27,28]</sup> Similarly, in our analysis, we observed significant differences in baseline parameters between the 2 analyzed subgroups. AF-CHF patients were older, more likely to had permanent AF, chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, peripheral artery disease, liver fibrosis, neoplasm, history of composite of stroke, transient ischemic attack or systemic embolization, pacemaker, implantable cardioverter-defibrillator or transaortic valve implantation, cardiac resynchronization therapy, composite of kidney transplantation, hemodialysis or creatinine level >2.26 mg/dL and had less often hypertension. Fortunately, many risk assessment programs are created to help clinicians in selecting appropriate antithrombotic therapy for AF patients. An example is Computerised Antithrombotic Risk Assessment Tool (CARATV2.0) examined in

Wang et al study. Through recommendations of CARATV2.0, at discharge, among 153 (61.0%) of patients, the therapy was changed and the proportion of patients receiving an antithrombotic on discharge increased significantly from baseline (admission) (baseline 77.2% vs 89.2%;  $P < .001$ ).<sup>[29]</sup>

The severity of CHF is correlated with more pronounced AF symptomatology and its duration. In the EURObservational Research Programme Pilot survey on Atrial Fibrillation (EORP-AF) as AF progressed from paroxysmal to permanent forms, the prevalence of heart failure (30.8%, and 72.9%) increased as well as its severity based on prevalence of New York Heart Association (NYHA) class III/IV (27.5% and 49.5%). Similarly, among population of Polish ESC-HF Pilot diagnosed with AF mean NYHA class ranged from III to IV compared to those patients in sinus rhythm (mean NYHA class II/III;  $P = .002$ ).<sup>[26]</sup> Presence of CHF among AF patients reflects the greater use of medications, such as beta-blockers, angiotensin-converting enzyme inhibitors. A high prevalence of angiotensin-converting-enzyme inhibitors or angiotensin receptor antagonists use is in accordance with recent data on how patients with CHF taking such agents show less development of new-onset AF and improved outcomes.<sup>[30]</sup> However, a recently published study

**Table 3****Comparison of atrial fibrillation patients with and without congestive heart failure treated with oral anticoagulation based on medical therapy.**

Variable	CHF	Without CHF	P
Medications, %			
NSAIDs	0.4 (3/786)	0.3 (6/1872)	.73
NSAIDs or antiplatelet drugs	19.5 (254/1304)	10.6 (234/2202)	<.001
Antiplatelet drugs	19.3 (252/1304)	10.4 (229/2202)	<.001
Oral antihyperglycemic drugs	39.0 (508/1304)	19.1 (420/2202)	<.001
VKA	54.4 (709/1304)	56.8 (1251/2202)	.17
NOAC	45.6 (595/1304)	43.2 (951/2202)	.17
Rivaroxaban	33.3 (434/1304)	27.8 (612/2202)	<.001
Rivaroxaban 15 mg dose	58.6 (253/432)	27.0 (164/607)	<.001
Dabigatran	12.4 (161/1304)	15.4 (339/2202)	.013
Dabigatran 110 mg dose	61.5 (99/161)	25.8 (86/333)	<.001
Glycoprotein IIb/IIIa inhibitors	11.7 (152/1304)	5.5 (120/2202)	<.001
Anti-arrhythmic drugs	14.5 (188/1300)	18.5 (406/2201)	.002
Anti-arrhythmic drugs	0.5 (4/786)	9.1 (171/1873)	<.001
Class Ic			
Amiodaron	13.7 (178/1303)	6.2 (136/2199)	<.001
Dronedaron	0.1 (1/785)	0.1 (1/1870)	.5
Sotalol	0.9 (7/786)	5.5 (103/1872)	<.001
BB	92.1 (724/786)	76.2 (1426/1872)	<.001
ACEI/ARB	85.9 (675/786)	67.7 (1267/1873)	<.001
Statins	73.2 (575/786)	58.9 (1103/1873)	<.001
Ca blocker	16.3 (128/785)	21.7 (407/1873)	.001

Categorical variables are presented as percentages (absolute number/number of collected data)

P values are given for differences between patients with and without CHF.

AF = atrial fibrillation, ASA = acetylsalicylic acid, ACEI/ARB = angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, BB = beta blocker, NOAC = non-vitamin K antagonist oral anticoagulants, NSAIDs = nonsteroidal anti-inflammatory drugs, VKA = vitamin K antagonists.

of Kotecha et al focused on beta-blockers therapy indicates that it led to a significant reduction in all-cause mortality in patients with sinus rhythm, but not in patients with AF. According to the authors, this finding could be partly explained by structural and cellular changes in the course of AF, which might affect the efficacy of the beta-blocker therapy. Furthermore, in AF patients, irregular rhythm itself has also a detrimental effect on systolic and diastolic heart function, irrespective of heart rate.<sup>[31]</sup> Nevertheless, a combination of a beta-blocker and digitalis may be beneficial in CHF patients with permanent AF.<sup>[9]</sup> In our study, a lower frequency of antiplatelet therapy was observed: 19.3% and 10.4% of patients with and without CHF, respectively. Nonetheless, it can be explained by recent research performed that concomitant use of aspirin in AF patients with stable vascular disease is not associated with a reduction in stroke, myocardial infarction, or death, but is associated with a substantial increase in risk of major bleeding, especially intracranial bleeding.<sup>[32]</sup>

Despite advances in treatment, hospitalized AF-CHF patients remain at high risk for adverse outcomes, including mortality and high rate of CHF readmissions. Results from Polish part of the Heart Failure Pilot Survey of the European Society of Cardiology reported that almost 50% CHF patients with AF experienced a readmission or died during the first year of follow-up.<sup>[33]</sup> It shows that outpatient care may be insufficient and underline essential role of epidemiological data and registries that analyze real-life patients and assess risk factors to make treatment decisions and discharge plans.

Finally, it is worth noting that patients with CHF in our study compared to patients without CHF had higher thromboembolic and bleeding risk based on CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>VASc and HAS-BLED scores. It can be explained by lower doses of anticoagulant regimens, increased use of anti platelet drugs among that group as well as the fact that CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>VASc scores,

both include CHF as a risk factor. However, in Rivaroxaban Once-daily oral direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF) study there was no significant interaction between the treatment effect of 110 mg and 150 mg of dabigatran and the presence or absence of CHF regarding the efficacy and safety outcomes—mean CHADS<sub>2</sub> scores in CHF patients on 110 mg, 150 mg of dabigatran and warfarin were as follows: 2.6 ± 1.1, 2.7 ± 1.1, and 2.6 ± 1.1 and among patients without CHF, mean CHADS<sub>2</sub> score for all 3 groups was 2.0 ± 1.1. Moreover, in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial, rivaroxaban and warfarin-treated participants with CHF had similar CHA<sub>2</sub>DS<sub>2</sub>-VASc score (both 5.1 ± 1.3), as well as patients without CHF (both 4.5 ± 1.2). According to CHADS<sub>2</sub> score, rivaroxaban and warfarin-treated participants with CHF also had similar scores (both 3.7).<sup>[34–36]</sup>

#### 4.1. Limitations of the study

There are some limitations to consider. As this was a retrospective study, data on some of the variables were not available for all of the patients, as indicated in table. Furthermore, the sample size is not a representative of the whole population because the data came from just 2 centers. Moreover, a time of first AF diagnosis and previous anticoagulant treatment were unknown. Another limitation of our study results from its small number of patients or unavailability, neither apixaban nor edoxaban.

#### 5. Conclusion

In this study, which represents a large cohort of AF patients with and without CHF, 2 important findings emerge. First, AF patients

with CHF differ significantly from AF patients without CHF according to baseline characteristics and pharmacotherapy. Second, patients with AF and CHF had a higher thromboembolic risk based on CHA2DS2-VA<sub>Sc</sub> and CHA2DS2 scores, as well as higher bleeding risk by HAS-BLED score.

### Author contributions

**Conceptualization:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Data curation:** Paweł Balsam, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Formal analysis:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Funding acquisition:** Paweł Balsam, Marcin Grabowski, Grzegorz Opolski.

**Investigation:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Methodology:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Project administration:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Resources:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Supervision:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Writing – original draft:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz

Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.

**Writing – review & editing:** Paweł Balsam, Monika Gawalko, Michał Peller, Agata Tymińska, Krzysztof Ozierański, Martyna Zaleska, Katarzyna Żukowska, Katarzyna Szepietowska, Kacper Maciejewski, Marcin Grabowski, Mariusz Borkowski, Łukasz Kołtowski, Anna Praska-Oginska, Inna Zaboyska, Grzegorz Opolski, Janusz Bednarski.  
Monika Gawalko orcid: 0000-0003-4619-9062.

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