Open Access Article

Ann. Acad. Med. Siles. (online) 2025; 79: 92–100
eISSN 1734-025X
DOI: 10.18794/aams/200441
www.annales.sum.edu.pl

PRACA ORYGINALNA
ORIGINAL PAPER

Analysis of echocardiographic parameters suggestive of pulmonary hypertension in patients with heart failure with preserved ejection fraction and assessment of clinical features favoring development of the PH-phenotype

Analiza parametrów echokardiograficznych wskazujących na nadciśnienie płucne u pacjentów z niewydolnością serca z zachowaną frakcją wyrzutową oraz ocena cech klinicznych sprzyjających rozwojowi fenotypu PH

Julia Dołęga, Katarzyna Ciekot, Aleksandra Owczarska, Gabriela Majta, Michał Macnar, Klaudia Marcinkiewicz, Katarzyna Mizia-Stec

1st Department of Cardiology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland; European Reference Network for Rare and Low Prevalence Complex Diseases of the Heart (ERN GUARD-Heart)

ABSTRACT

INTRODUCTION: Heart failure with preserved ejection fraction (HFpEF) is characterized by left ventricle (LV) diastolic dysfunction. Impaired diastolic function induces pulmonary congestion and leads to postcapillary pulmonary hypertension (PH), which is an important contributor to clinical deterioration and increased mortality.

MATERIAL AND METHODS: A retrospective one-centre analysis of 63 consecutive patients hospitalized due to HFpEF was performed. The study group was divided according to the echocardiographic probability of PH using tricuspid regurgitation peak velocity (TRV) into two groups: TRV ≥ 2.8 m/s – with an increased probability of PH (n = 15 (23.8%); females: 3 (20%); mean age 72.7 ± 10.8) and TRV < 2.8 m/s – with a low probability of PH (n = 48 (76.2%); females: 25 (52.1%); mean age 72.3 ± 13.7). The clinical data, transthoracic echocardiography (TTE) parameters and laboratory tests were analyzed.

RESULTS: The group of patients with an increased probability of PH was characterized by more severe HF symptoms, more frequent fatigue ($p = 0.03$) and the occurrence of ankle swelling ($p < 0.01$). Analysis of the baseline data revealed a trend towards a greater incidence of atrial fibrillation (AF; $p = 0.08$) in this group. The patients who had TRV ≥ 2.8 m/s had a larger left atrial area ($p < 0.001$), a higher E/A ratio ($p < 0.001$) with borderline differences in the left ventricular mass index (LVMI; $p = 0.06$) and left ventricular ejection fraction (LVEF; $p = 0.07$).

Received: 10.12.2024 **Revised:** 31.12.2024 **Accepted:** 24.01.2025 **Published online:** 22.04.2025

Address for correspondence: Julia Dołęga, Klinika Kardiologii I Katedry Kardiologii, Śląski Uniwersytet Medyczny w Katowicach, ul. Ziołowa 47, 40-635 Katowice, tel. +48 32 359 88 90, 359 87 29, e-mail: s81701@365.sum.edu.pl

Publisher: Medical University of Silesia, Katowice, Poland

CONCLUSIONS: About 25% of patients with HFpEF, mostly males, present with moderate features of PH that are associated with more advanced LV and left atrium (LA) remodeling and dysfunction. However, they are not reflected in the classic comorbidities, with the exception of AF.

KEYWORDS

heart failure, heart failure with preserved ejection fraction, postcapillary pulmonary hypertension, chronic atrial fibrillation

STRESZCZENIE

WPROWADZENIE: Niewydolność serca z zachowaną frakcją wyrzutową (*heart failure with preserved ejection fraction* – HFpEF) charakteryzuje się dysfunkcją rozkurczową lewej komory (*left ventricle* – LV). Zaburzenia funkcji rozkurczowej powodują zator płucny i prowadzą do zakapilarnego nadciśnienia płucnego (*pulmonary hypertension* – PH), które jest istotnym czynnikiem pogorszenia stanu klinicznego i zwiększonej śmiertelności.
MATERIAŁ I METODY: Przeprowadzono retrospektywną analizę jednoośrodkową, obejmującą 63 pacjentów hospitalizowanych z powodu HFpEF. Grupę badaną podzielono w zależności od echokardiograficznego prawdopodobieństwa PH na podstawie szczytowej prędkości niedomykalności zastawki trójdzielnej (*tricuspid regurgitation velocity* – TRV) na dwie grupy: TRV ≥ 2,8 m/s – zwiększone prawdopodobieństwo PH (n = 15 (23,8%); kobiety: 3 (20%); średni wiek 72,7 ± 10,8) oraz TRV < 2,8 m/s – niskie prawdopodobieństwo PH (n = 48 (76,2%); kobiety: 25 (52,1%); średni wiek 72,3 ± 13,7). Przeanalizowano dane kliniczne, parametry echokardiograficzne (*transthoracic echocardiography* – TTE) oraz wyniki badań laboratoryjnych.
WYNIKI: Grupa pacjentów ze zwiększonym prawdopodobieństwem PH cechowała się bardziej nasilonymi objawami HF, częstszym odczuwaniem zmęczenia (p = 0,03) oraz występowaniem obrzęków wokół kostek (p < 0,01). Analiza danych wyjściowych wskazała na tendencję do częstszego migotania przedsionków (*atrial fibrillation* – AF; p = 0,08) w tej grupie. U pacjentów z TRV ≥ 2,8 m/s obserwowano większą powierzchnię lewego przedsionka (p < 0,001), wyższy wskaźnik E/A (p < 0,001), a także graniczne różnice we wskaźniku masy lewej komory (*left ventricular mass index* – LVMI; p = 0,06) oraz frakcji wyrzutowej lewej komory (*left ventricular ejection fraction* – LVEF; p = 0,07).
WNIOSKI: U około 25% pacjentów z HFpEF, w większości mężczyzn, występują umiarkowane objawy PH, które wiążą się z bardziej zaawansowaną przebudową i dysfunkcją LV oraz lewego przedsionka (*left atrium* – LA). Nie znajdują one jednak odzwierciedlenia w typowych chorobach współistniejących, z wyjątkiem AF.

SŁOWA KLUCZOWE

niewydolność serca, niewydolność serca z zachowaną frakcją wyrzutową, postkapilarne nadciśnienie płucne, przewlekłe migotanie przedsionków

INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) is a complex condition characterized by left ventricular diastolic dysfunction with an left ventricular ejection fraction (LVEF) ≥ 50% [1]. Impaired LV diastolic function leads to inadequate ventricular filling. Prolonged elevation of pressure in the left of the heart and pulmonary veins as well as the presence of inflammation significantly impedes proper relaxation of vascular smooth muscles and leads to their stiffness [2,3]. Consequently, this progressive disturbance prompts pathological remodeling of the pulmonary arteries and leads to increased pulmonary vascular resistance. This cascade results in the development of pulmonary hypertension (PH), characterized by both pre- and sub-capillary features [3,4].
Furthermore, because of PH the right ventricle (RV) undergoes hypertrophy as an adaptive response to sustain normal ejection capability. Prolonged exposure to this increased workload can induce fibrotic alterations in the RV muscle, subsequently diminishing its contractile function, which in the long term may lead to RV failure. Together, these hemodynamic changes in HFpEF impede blood circulation, negatively impact cardiac function and eventually lead to clinical symptoms such as dyspnea, fatigue as well as an increased risk of cardiovascular complications [3,5].
Right heart catheterization (RHC) is the gold standard method for confirming the diagnosis of PH. However, by means of transthoracic echocardiography (TTE), we can assess in a non-invasive way the likelihood of PH and further determine if the patient needs RHC. There are numerous echocardiographic signs suggestive of PH. Considering the structural and functional remodeling of the myocardium, assessment of the peak tricuspid regurgitation volume (TRV) is recommended [6]. The presence of TRV ≥ 2.8 m/s indicates at least an intermediate probability of PH. Nonetheless, the presence or absence of PH cannot be reliably determined by TRV alone. TRV < 2.8 m/s without any additional echocardiographic signs suggests a low probability of PH. To alter the level of PH likelihood, the presence of signs from at least two echocardiographic categories regarding the ventricles, pulmonary artery, vena cava inferior (VCI) or right atrium (RA) is required [7]. A tricuspid regurgitation

(TR) peak velocity > 2.8 m/s is particularly relevant regarding the assessment of HFpEF patients because it also indicates increased pulmonary artery systolic pressure and is one of the major as well as the most commonly used indirect markers of LV diastolic dysfunction [8].

The majority of studies have investigated the connections between PH in patients with HF with reduced EF (HFrEF). Nevertheless, considering the possible alternative pathways contributing to the onset and development of PH in patients with HFpEF, further investigation and analysis of the clinical and echocardiographic features of PH among HFpEF patients is still limited, yet necessary.

The main objective of this study was to evaluate the prevalence of patients with at least an intermediate probability of PH in a group of patients with HFpEF, as well as assess the clinical and echocardiographic features in this group.

MATERIAL AND METHODS

Our analysis included 63 patients (aged 72 ± 13 years) on optimal medical therapy who were hospitalized in the 1st Department of Cardiology, Medical University of Silesia in Katowice European Reference Network for Rare and Low Prevalence Complex of the Heart (ERN GUARD Heart) between 02.2022–12.2022. A retrospective database was created from electronic medical records and included the assessment for HF symptoms and signs, typical clinical demographics, medications taken, in addition to the results of diagnostic laboratory tests and the available TTE parameters.

All the patients satisfied the predefined inclusion criteria of HFpEF – the presence of symptoms and signs of HF, LVEF ≥ 50% and objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides [9]. We excluded from the study patients with HFrEF, heart failure with mildly reduced ejection fraction (HFmrEF) or heart failure with improved ejection fraction (HFimpEF), acute coronary syndrome, a congenital heart defect, infective endocarditis, known pericardial constriction, infiltrative or hypertrophic cardiomyopathy, a previous heart operation, as well as patients scheduled for valve surgery.

Subsequently, the patients were divided following their TTE results into two groups based on their TRV value: a group with an increased probability of PH – with TRV ≥ 2.8 m/s (n = 15; 23.8%), and a group with a low probability of PH – with TRV < 2.8 m/s without any additional TTE signs (n = 48, 76.2%) (Figure 1).

Fig. 1. Flowchart representing course of the study. HFpEF – heart failure with preserved ejection fraction; PH – pulmonary hypertension.

Then we collected, analyzed and compared the available data regarding additional echocardiographic signs suggestive of PH as proposed by the European Society of Cardiology (ESC) Guidelines [10].

Assessment of the additional TTE parameters in the group of patients with an increased likelihood of PH show that 4 patients (26.7%) had 1 additional TTE sign suggestive of PH, 5 (33%) had 2 TTE signs, and 2 patients (13.3%) had 3 additional TTE signs.

The patients from the group with TRV < 2.8 m/s did not exhibit any additional sign from the ≥ 2 echocardiographic categories that could alter the level of probability of PH; therefore, all of them presented a low echocardiographic probability of PH.

Definitions

- HFpEF was defined as the presence of HF symptoms and signs, with evidence of structural and/or functional cardiac abnormalities and/or raised natriuretic peptides with an LVEF ≥ 50%.
- Increased probability of PH was defined as the presence of TRV ≥ 2.8 m/s.
- Low probability of PH was determined by the presence of TRV < 2.8 m/s without any additional echocardiographic signs.
- Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2 documented or inferred for > 3 months.

- Chronic atrial fibrillation (AF) was defined as patients with persistent AF, which is AF persisting continuously for > 7 days, including episodes interrupted by cardioversion (pharmacological or electrical) after ≥ 7 days as well as permanent AF, which is AF that has been accepted by the patient and physician and no further attempts will be made to restore maintaining sinus rhythm [11].
- VCI dilatation was defined as a VCI diameter > 21 mm.
- Left ventricular end-diastolic pressure (LVEDP) was estimated non-invasively and calculated using an equation by Abd-El-Aziz [12], which employs the measurement of blood pressure and EF.

Statistics

To analyze the distribution for quantitative data, the Shapiro-Wilk test was used. Quantitative data with normal distribution were compared using Student's t-test and presented as the mean ± standard deviation (SD). On the other hand, quantitative data with a skewed distribution were compared by means of the Mann-Whitney U test and presented as medians. The statistical significance of the qualitative values was determined by Pearson's Chi-squared test. Statistical significance was considered for p-values < 0.05. The analysis was performed with STATISTICA 13.3 PL Software by StatSoft, Medical University of Silesia, Katowice, Poland.

RESULTS

The statistical analysis revealed no statistically significant differences between the groups in terms of age, height, weight, body mass index (BMI) or body surface area (BSA; Table I). However, the patients from the group with a low probability of PH had a tendency towards greater values of BMI, but it did not reach statistical significance (p = 0.06).

In terms of the clinical assessment, the patients from the group with the greater probability of PH exhibited a more pronounced severity of symptoms. Notably, this particular group displayed a statistically significantly greater prevalence of fatigue and ankle oedema compared to the group with the low likelihood of PH (Figure 2).

The baseline characteristics analysis revealed that the incidence of hypertension, diabetes mellitus, coronary artery disease, dyslipidemia, and chronic kidney disease exhibited no statistically significant differences between the studied groups. Nevertheless, it is noteworthy that the group with the increased probability of PH demonstrated a tendency towards a higher prevalence of AF (p = 0.08), without differences regarding its clinical types (Table II).

Considering pharmacological treatment, it was found that in the group with the increased likelihood of PH, loop diuretics (p = 0.001) and sodium glucose-linked transporter 2 (SGLT-2) inhibitors (p = 0.028) were prescribed more often in comparison to the group with the low probability of PH. Moreover, significant differences were found in the number of patients treated with novel oral anticoagulants (NOACs). Similarly, these medications were used more frequently in the group with the greater probability of PH (p = 0.017). None of the patients were taking drugs registered for the treatment of PH, such as phosphodiesterase-5--inhibitors, an endothelin receptor antagonist or prostanoids (Table III).

Table I. Baseline characteristics comparison between groups of patients with increased probability of pulmonary hypertension (PH) and low probability of PH

Demographic and anthropometric parameters	HFpEF (n = 63, F/M 40/23, mean age 72 ± 13)		p-value
	increased PH probability (n = 15/23.8%)	low probability of PH (n = 48/76.2%)	
Sex: females (n/%)	3/20	25/52	**0.029**
Age [y]	72.2 ± 10.8	72.3 ± 74.5	0.890
Height [cm]	166.8 ± 9.9	164.8 ± 164.0	0.340
Weight [kg]	75.0 ± 17.1	80.5 ± 80.0	0.169
BMI [kg/m^2]	26.7 ± 4.6	29.6 ± 28.7	**0.063**
BSA [m^2]	1.9 ± 0.3	1.9 ± 1.9	0.460

HFpEF – heart failure with preserved ejection fraction; F – female; M – male; BMI – body mass index; BSA – body surface area.

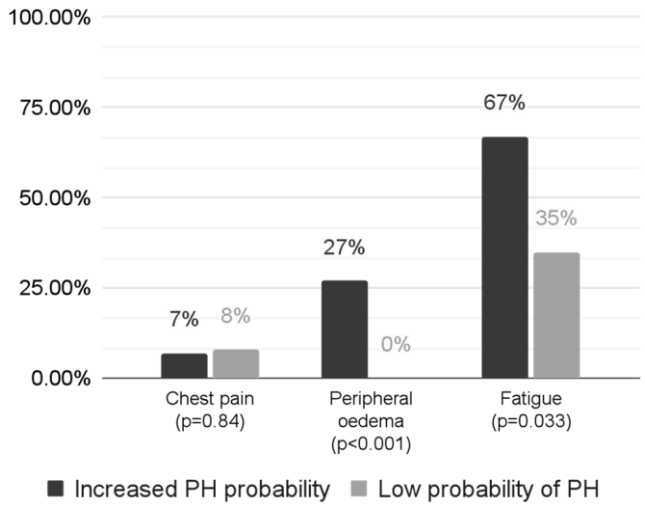

Fig. 2. Comparison of presented symptoms of heart failure in patients with increased pulmonary hypertension (PH) probability and low probability of PH.

Table II. Comparison of comorbidities and risk factors between groups of patients with increased pulmonary hypertension (PH) probability and low probability of PH

Clinical parameters	Increased PH probability (n = 15)	Low probability of PH (n = 48)	p-value
	n (%)	n (%)	
Hypertension	11 (73.3)	37 (77.1)	0.766
Diabetes mellitus	7 (46.7)	21 (43.8)	0.843
AF – any type	7 (46.7)	11 (22.9)	**0.076**
Paroxysmal AF	4 (26.7)	7 (14.6)	0.282
Chronic AF	3 (20)	4 (8.3)	0.209
Coronary artery disease	7 (46.7)	17 (35.4)	0.434
Dyslipidemia	7 (46.7)	32 (66.7)	0.164
Chronic kidney disease (eGFR < 60 mL/min/1.73 m^2)	7 (46.7)	16 (33.3)	0.349

AF – atrial fibrillation; eGFR – estimated glomerular filtration rate.

Table III. Comparison of selected medications taken between groups of patients with increased pulmonary hypertension (PH) probability and low probability of PH

Pharmacological treatment	Increased probability of PH (n = 15)	Low probability of PH (n = 48)	p-value
	n (%)	n (%)	
ACEI	9 (60)	26 (54.2)	0.691
ARB	0	5 (10.4)	0.193
Beta-blockers	7 (46.7)	23 (47.9)	0.933
Ca-blockers	3 (20)	14 (29.2)	0.485
MRA	8 (53.3)	12 (25)	0.141
ARNI	0	4 (8.3)	0.248
Loop diuretics	12 (80)	16 (33.3)	**0.001**
Thiazides	0	3 (6.3)	0.321
SGLT-2 inhibitors	4 (26.7)	3 (6.3)	**0.028**
Statins	11 (73.3)	37 (77.1)	0.766
Antiplatelet drugs	6 (40)	28 (58.3)	0.214
NOACs	7 (46.7)	8 (16.7)	**0.017**

ACEI – angiotensin-converting-enzyme inhibitors; ARB – angiotensin receptor blockers; Ca-blockers – calcium channel blockers; MRA – mineralocorticoid receptor antagonist; ARNI – angiotensin receptor-neprilysin inhibitor; SGLT-2 inhibitors – sodium glucose-linked transporter 2 inhibitors; NOACs – novel oral anticoagulants.

The mean values of the selected diagnostic laboratory tests were generally within the established reference ranges, except for N-terminal pro-B-type natriuretic peptide (NT-proBNP), which exceeded the threshold in both study groups. In the patients with an increased probability of PH, the NT-proBNP levels were 1435.9 ± 1404.2 pg/ml, compared to 1143.8 ± 1144 pg/ml in those with a low probability of PH ($p = 0.139$). The laboratory results were comparable in both groups.

Statistically significant differences were observed among the echocardiographic parameters, notably in the measurements of the right atrial (RA; $p < 0.001$) and left atrial (LA; $p < 0.001$) areas, as well as the left ventricular end-diastolic diameter (LVEDD; $p = 0.013$) and left ventricular end-systolic diameter (LVESD; $p = 0.01$).

There were also significant differences between the groups regarding TTE abnormalities consistent with the presence of HFpEF, such as the left ventricular mass index (LVMI; $p = 0.057$), the relative wall thickness (RWT; $p = 0.063$), E-wave ($p < 0.001$) and E/A ratio ($p < 0.001$) – it demonstrated greater values in the group with the increased probability of PH in comparison to the group with the low likelihood of PH.

Owing to the baseline structure and objectives of our study, there was a significant statistical difference regarding the measurements of TRV ($p < 0.001$). Furthermore, in the group with the increased probability of PH, the VCI was dilated more frequently than in the group with the low PH probability ($p = 0.01$). To estimate the right ventricular systolic pressure (RVSP) a simplified Bernoulli equation was used – it utilizes the TRV value and estimates right atrial pressure based on VCI measurements. Therefore, RVSP similarly demonstrated greater values in the group with the increased likelihood of PH ($p < 0.001$; Table IV).

The assessment of significant valvular defects in both the research groups revealed comparable results. Nonetheless, statistically significant differences were observed between these groups in terms of the presence of severe TR. It was more frequent in the group with the increased probability of PH in comparison to the group with the low likelihood of PH ($p < 0.001$).

Table IV. Comparison of echocardiographic parameters between patients with increased pulmonary hypertension (PH) probability and low probability of PH

Echocardiographic parameters	Increased PH probability (n = 15)	Low probability of PH (n = 48)	p-value
1	2	3	4
IVS thickness [mm]	13.8 ± 3.2	14.8 ± 15	0.085
PWT [mm]	11.3 ± 1.6	11.6 ± 11	0.928
LVEF [%]	55.1 ± 7	57.4 ± 55	**0.071**
LVESD [mm]	31.1 ± 6	26.5 ± 26	**0.010**
LVEDD [mm]	50 ± 5.1	45.8 ± 46	**0.013**
LVEDP [mmHg]	22.0 ± 4.1	23.7 ± 21.7	0.825
LVMI [g/m²]	138.4 ± 37.7	119.2 ± 115.3	**0.057**
LA area [cm2]	29.5 ± 5.7	22.4 ± 21.3	**< 0.001**
RA area [cm2]	26.8 ± 9.7	16.7 ± 15	**< 0.001**
RVOT in PLAX [mm]	32.5 ± 4.9	30 ± 30	0.083
RWT [g/m²]	0.5 ± 0.1	0.5 ± 0.5	**0.063**
Mitral valve			
Presence of severe MR	1 (6.7%)	0	0.071
E-wave [m/s]	1.2 ± 0.5	0.8 ± 0.8	**< 0.001**
IVS thickness [mm]	13.8 ± 3.2	14.8 ± 15	0.085
PWT [mm]	11.3 ± 1.6	11.6 ± 11	0.928
A-wave [m/s]	0.8 ± 0.4	1.0 ± 0.9	0.500
E/A ratio	2.0 ± 1.4	0.9 ± 0.8	**< 0.001**
Aortic valve			
Presence of severe AS	3 (20%)	19 (39.6%)	0.165
Ao Vmax [m/s]	3.0 ± 1.6	3.9 ± 4.1	**0.044**
PG mean [mmHg]	39.3 ± 21.1	40.4 ± 42.0	0.611
AVA [cm²]	0.8 ± 0.3	2.5 ± 0.8	0.524

cd. tab. IV

1	2	3	4
Tricuspid valve			
Presence of severe TR	8 (53.3%)	2 (4.2%)	**< 0.001**
TRV [m/s]	3.4 ± 0.4	0.5 ± 0.2	**< 0.001**
RVSP [mmHg]	53.5 ± 13.5	31.7 ± 31.5	**< 0.001**
Pulmonary valve			
PA Vmax [m/s]	0.8 ± 0.3	0.9 ± 26.5	0.412
AcT [ms]	106.3 ± 31.3	108.9 ± 110	0.439
VCI dilatation	4 (26.7%)	2 (4.2%)	**0.010**

IVS – interventricular septum; PWT – posterior wall thickness; LVEF – left ventricular ejection fraction; LVESD – left ventricular end-systolic diameter; LVEDD – left ventricular end-diastolic diameter; LVEDP – left ventricular end-diastolic pressure; LVMI – left ventricular mass index; LA – left atrium; RA – right atrium; RVOT – right ventricular outflow tract; PLAX – parasternal long axis; RWT – relative wall thickness; MR – mitral regurgitation; AS – aortic stenosis; Ao Vmax – maximum aortic velocity; PG mean – peak-to-mean pressure gradient; AVA – aortic valve area; TR – tricuspid regurgitation; TRV – tricuspid regurgitation peak velocity; RVSP – right ventricular systolic pressure; PA Vmax – pulmonary artery maximum velocity; AcT – acceleration time; VCI – vena cava inferior.

DISCUSSION

Our study showed that among patients with HFpEF, nearly 24% present with at least an intermediate probability of PH. Studies have reported a wide range of prevalence rates, which often depend on various factors including the study population, diagnostic criteria or the specific methods used to identify PH. In the trial PARAGON-HF [13], which tested the efficacy of sacubitril-valsartan on patients with HFpEF, the prevalence of PH based on echocardiographic criteria reached 31%. Similarly, in the TOPCAT study [14] among patients with HFpEF and a measurable TR jet, the peak velocity was elevated over 2.9 m/s in 36% of patients. However, the estimated prevalence can be even greater and reach up to 80% of patients with HFpEF when employing echocardiographic estimates of pulmonary artery systolic pressure (PASP) ≥ 35 mmHg to define PH [15]. Nevertheless, it is noteworthy that Leung et al. [16] conducted a study among patients with HFpEF who underwent RHC – the prevalence of PH, defined as a mean pulmonary artery pressure > 25 mmHg, reached 52.5%.

The prevalence of comorbidities in our research was comparable in both groups. The results are similar to other studies [15]. However, we found a tendency towards a greater BMI in the group of patients with HFpEF and a low probability of PH in comparison to the group with the increased likelihood of PH ($p = 0.063$). In a study by Lam et al. [15], the mean BMI was also greater in the HFpEF group without PH than in the group with PH, nonetheless, it did not reach statistical significance. Nevertheless, studies indicate the presence of an obesity-related HFpEF phenotype – obese patients with HFpEF exhibited greater values of pulmonary capillary wedge pressure (PCWP) than in the non-obese group with HFpEF [17].

In our study the individuals with the increased likelihood of PH were more commonly diagnosed with AF, irrespective of its type, compared to the group with the low probability of PH although it did not attain statistical significance ($p = 0.076$). In HFpEF, because of the diastolic dysfunction of the LV and an increased LV filling pressure, the LA undergoes stiffening, dilation and remodeling, increasing its susceptibility to fostering the development of AF [18]. Therefore, it was not surprising that while analyzing the TTE parameters in the patients with the greater probability of PH, we observed a larger LA area ($p < 0.001$), as well as RA area ($p < 0.001$) compared to the group with the low likelihood of PH. These alterations in patients with HFpEF often result in an exacerbation of symptoms, the development of pulmonary vascular dysfunction, a more pronounced RV dysfunction, a reduced exercise tolerance and finally adverse outcomes [19,20]. Hence, the conclusion is that the development of AF may be an indicator of a more advanced stage of HFpEF in the group with the increased probability of PH.

Furthermore, a meta-analysis of 10 studies regarding different phenotypes of HFpEF showed that, among others, the presence of AF and a high BMI were related to phenotypes with adverse outcomes [21].

In our study, the patients with the greater probability of PH more frequently exhibited HF symptoms – especially fatigue ($p = 0.033$), ankle swelling ($p < 0.001$) and dyspnea ($p = 0.091$), compared to the group with the low probability of PH. Scientific evidence suggests that in patients with HFpEF, despite slight differences at rest and a normal LVEF, systolic and diastolic function dramatically deteriorates during exercise, which is manifested by a decreased exercise capacity [22]. What is more, in the meta-analysis mentioned previously, a worse symptom severity was one of the key factors in identifying HFpEF phenotypes associated with adverse outcomes [21].

In accordance with the inclusion criteria, all the participants had an LVEF ≥ 50%; however, upon comparing the mean values at the threshold of statistical significance, we observed that the value of

LVEF in the group of patients with the greater probability of PH was slightly lower than in the group with the low likelihood (p = 0.071). In HFpEF, despite having a normal EF, patients display impairments beyond diastolic dysfunction and evidence suggests abnormal LV systolic performance, which subtly impacts cardiac output and LV filling pressures [22].

Despite the lack of statistical significance, the group with the greater probability of PH had higher values of LVMI (p = 0.057), RWT (p = 0.063). The mean values of these parameters surpass the threshold values in both the examined groups, which also points to the presence of concentric LV hypertrophy related to HFpEF. Nonetheless, in the group of patients with HFpEF and the greater likelihood of PH, the mean values of LVEDD (p = 0.013) and LVESD (p = 0.01) were statistically significantly greater compared to the patients in the group without PH. This might suggest a more severe state of dysfunction and remodeling of the heart among patients with HFpEF and an increased probability of PH.

In our study, the patients with the increased probability of PH statistically more frequently exhibited severe TR (p < 0.001). It might be associated with the development of the atrial functional type of this regurgitation, which in our study was reflected by an enlarged RA and the greater prevalence of AF in this group. However, in HFpEF the presence of a diastolic dysfunction of LV, improper relaxation and remodeling of the left of the heart with further pulmonary vascular disease consequently leads to pressure overload of the RV, affects its geometry and function, thereby contributing to the development of TR [3,5].

In comparison to the group with a low probability of PH, the patients in the group with an increased likelihood of PH used loop diuretics (p = 0.001) and SGLT-2 inhibitors (p = 0.028) statistically more frequently. This inclination is probably connected to the heightened symptomatology and signs of pulmonary congestion within this subset. Additionally, a more prevalent use of NOACs (p = 0.017) is likely linked to more frequent occurrences of AF in this group, as mentioned previously.

Limitations

There are numerous echocardiographic signs suggestive of PH. Considering the functional and structural remodeling of the myocardium, we applied the simplification associated with the definition of HFpEF; hence, the idea of evaluating patients with an elevated TRV that present with features of HF. The current study was conducted using a retrospective analysis with all the inherent limitations of a single center. Because of the retrospective nature of the study, we did not have all the available parameters regarding TTE. Therefore, we were unable to compare every given value and create detailed cut-off points because of the limited amount of data. Furthermore, some of the TTE signs may be dependent on the patient's state of hydration.

To determine the presence of PH, it is necessary to perform RHC – it would be intriguing to examine these findings within the context of our study to see if they align with echocardiographic data or yield different outcomes.

CONCLUSIONS

About 25% of HFpEF patients exhibit intermediate echocardiographic features of PH that are associated with more severe remodeling and dysfunction of the LV and LA. Features of PH are associated with AF and are not reflected in the classic comorbidities.

Authors' contribution

Study design – J. Dołęga, K. Ciekot, K. Mizia-Stec
Data collection – J. Dołęga, K. Ciekot, A. Owczarska, G. Majta, M. Macnar, K. Marcinkiewicz
Data interpretation – J. Dołęga, K. Ciekot, A. Owczarska, G. Majta, M. Macnar, K. Marcinkiewicz
Statistical analysis – K. Ciekot, J. Dołęga
Manuscript preparation – J. Dołęga, K. Ciekot, A. Owczarska, G. Majta, M. Macnar, K. Marcinkiewicz
Literature research – J. Dołęga, K. Ciekot
Final approval of the version to be published – K. Mizia-Stec

REFERENCES

1. Eltelbany M., Shah P., deFilippi C. Biomarkers in HFpEF for diagnosis, prognosis, and biological phenotyping. Curr. Heart Fail. Rep. 2022; 19(6): 412–424, doi: 10.1007/s11897-022-00578-7.

2. Chen Y., Guo H., Xu D., Xu X., Wang H., Hu X. et al. Left ventricular failure produces profound lung remodeling and pulmonary hypertension in mice: heart failure causes severe lung disease. Hypertension 2012; 59(6): 1170–1178, doi: 10.1161/HYPERTENSIONAHA.111.186072.

3. Karasek D., Sinkiewicz W. Nadciśnienie płucne w przebiegu chorób lewego serca — aktualne leczenie i kierunki rozwoju terapii. Folia Cardiol. 2017; 12(3): 317–325, doi: 10.5603/FC.2017.0061.

4. Rosenkranz S., Gibbs J.S.R., Wachter R., De Marco T., Vonk-Noordegraaf A., Vachiéry J.L. Left ventricular heart failure and pulmonary hypertension. Eur. Heart J. 2016; 37(12): 942–954, doi: 10.1093/eurheartj/ehv512.

5. Melenovsky V., Hwang S.J., Lin G., Redfield M.M., Borlaug B.A. Right heart dysfunction in heart failure with preserved ejection fraction. Eur. Heart J. 2014; 35(48): 3452–3462, doi: 10.1093/eurheartj/ehu193.
6. Humbert M., Kovacs G., Hoeper M.M., Badagliacca R., Berger R.M.F., Brida M. et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur. Heart J. 2022; 43(38): 3618–3731, doi: 10.1093/eurheartj/ehac237. Erratum in: Eur. Heart J. 2023; 44(15): 1312, doi: 10.1093/eurheartj/ehad005.
7. Corrigendum to: 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG). Eur. Heart J. 2023; 44(15): 1312, doi: 10.1093/eurheartj/ehad005. Erratum for: Eur. Heart J. 2022; 43(38): 3618–3731, doi: 10.1093/eurheartj/ehac237.
8. Pieske B., Tschöpe C., de Boer R.A., Fraser A.G., Anker S.D., Donal E. et al. How to diagnose heart failure with preserved ejection fraction: the HFA--PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur. Heart J. 2019; 40(40): 3297–3317, doi: 10.1093/eurheartj/ehz641. Erratum in: Eur. Heart J. 2021; 42(13): 1274, doi: 10.1093/eurheartj/ehaa1016.
9. McDonagh T.A., Metra M., Adamo M., Gardner R.S., Baumbach A., Böhm M. et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. Eur. J. Heart Fail. 2024; 26(1): 5–17, doi: 10.1002/ejhf.3024.
10. Humbert M., Kovacs G., Hoeper M.M., Badagliacca R., Berger R.M.F., Brida M. et al. Wytyczne ESC/ERS 2022 dotyczące rozpoznawania i leczenia nadciśnienia płucnego. Polskie Towarzystwo Kardiologiczne, 2023-06-13 [online] https://ptkardio.pl/wytyczne/49-wytyczne_escers_2022_dotyczace_rozpoznawania_i_leczenia_nadcisnienia_plucnego [accessed on 3 December 2024].
11. Hindricks G., Potpara T., Dagres N., Arbelo E., Bax J.J., Blomström-Lundqvist C. et al. Wytyczne ESC 2020 dotyczące diagnostyki i leczenia migotania przedsionków opracowane we współpracy z European Association of Cardio-Thoracic Surgery (EACTS). Polskie Towarzystwo Kardiologiczne, 2021-03-04 [online] https://ptkardio.pl/resources/data/wytyczne/-1/wytyczne_migotanie_przedsionkow_2020_final.pdf?download=true [accessed on 3 December 2024].
12. Abd-El-Aziz T.A. Noninvasive prediction of left ventricular end-diastolic pressure in patients with coronary artery disease and preserved ejection fraction. Can. J. Cardiol. 2012; 28(1): 80–86, doi: 10.1016/j.cjca.2011.02.001.
13. Shah A.M., Cikes M., Prasad N., Li G., Getchevski S., Claggett B. et al. Echocardiographic features of patients with heart failure and preserved left ventricular ejection fraction. J. Am. Coll. Cardiol. 2019; 74(23): 2858–2873, doi: 10.1016/j.jacc.2019.09.063.
14. Shah A.M., Shah S.J., Anand I.S., Sweitzer N.K., O'Meara E., Heitner J.F. et al. Cardiac structure and function in heart failure with preserved ejection fraction: baseline findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist trial. Circ. Heart Fail. 2014; 7(1): 104–115, doi: 10.1161/CIRCHEARTFAILURE.113.000887.
15. Lam C.S., Roger V.L., Rodeheffer R.J., Borlaug B.A., Enders F.T., Redfield M.M. Pulmonary hypertension in heart failure with preserved ejection fraction: a community-based study. J. Am. Coll. Cardiol. 2009; 53(13): 1119––1126, doi: 10.1016/j.jacc.2008.11.051.
16. Leung C.C., Moondra V., Catherwood E., Andrus B.W. Prevalence and risk factors of pulmonary hypertension in patients with elevated pulmonary venous pressure and preserved ejection fraction. Am. J. Cardiol. 2010; 106(2): 284–286, doi: 10.1016/j.amjcard.2010.02.039.
17. Obokata M., Reddy Y.N.V., Pislaru S.V., Melenovsky V., Borlaug B.A. Evidence supporting the existence of a distinct obese phenotype of heart failure with preserved ejection fraction. Circulation 2017; 136(1): 6–19, doi: 10.1161/CIRCULATIONAHA.116.026807.
18. Shah A.M. Ventricular remodeling in heart failure with preserved ejection fraction. Curr. Heart Fail. Rep. 2013; 10(4): 341–349, doi: 10.1007/s11897-013-0166-4.
19. Santos A.B., Kraigher-Krainer E., Gupta D.K., Claggett B., Zile M.R., Pieske B. et al. Impaired left atrial function in heart failure with preserved ejection fraction. Eur. J. Heart Fail. 2014; 16(10): 1096–1103, doi: 10.1002/ejhf.147.
20. Freed B.H., Daruwalla V., Cheng J.Y., Aguilar F.G., Beussink L., Choi A. et al. Prognostic utility and clinical significance of cardiac mechanics in heart failure with preserved ejection fraction: importance of left atrial strain. Circ. Cardiovasc. Imaging 2016; 9(3), doi: 10.1161/CIRCIMAGING.115.003754.
21. Rabkin S.W. Evaluating the adverse outcome of subtypes of heart failure with preserved ejection fraction defined by machine learning: A systematic review focused on defining high risk phenogroups. EXCLI J. 2022; 21: 487–518, doi: 10.17179/excli2021-4572.
22. Tan Y.T., Wenzelburger F., Lee E., Heatlie G., Leyva F., Patel K. et al. The pathophysiology of heart failure with normal ejection fraction: exercise echocardiography reveals complex abnormalities of both systolic and diastolic ventricular function involving torsion, untwist, and longitudinal motion. J. Am. Coll. Cardiol. 2009; 54(1): 36–46, doi: 10.1016/j.jacc.2009.03.037.