European Journal of Internal Medicine 144 (2026) 106540

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

Prognostic role of TAPSE/PASP ratio among older patients with acute heart failure and preserved ejection fraction

Giuseppe De Matteis [a], Amato Serra [a], Maria Livia Burzo [b,*], Francesco De Vito [a], Maria Anna Nicolazzi [c], Antonio Iaconelli [c], Antonio Gasbarrini [d,e], Francesco Franceschi [d,f], Giovanni Gambassi [d,e], Marcello Covino [d,f]

[a] Department of Internal Medicine, Fondazione Policlinico Universitario A.Gemelli IRCCS, Rome, Italy
[b] Division of Internal Medicine, Ospedale Santo Spirito in Sassia, Rome, Italy
[c] Department of Cardiovascular Medicine, Fondazione Policlinico Universitario A.Gemelli IRCCS, Rome, Italy
[d] Università Cattolica del Sacro Cuore, Rome, Italy
[e] Department of Medicine and Translational Surgery, Università Cattolica del Sacro Cuore, Rome, Italy
[f] Emergency Department, Fondazione Policlinico Universitario A.Gemelli IRCCS, Rome, Italy

ARTICLE INFO

Keywords:
Heart failure with preserved ejection fraction
Acute heart failure
TAPSE/PASP ratio
Right ventricular dysfunction

Objective: Right ventricular (RV)-pulmonary circulation (PC) uncoupling is associated with poor outcome in patients with Heart Failure with Preserved Ejection Fraction (HFpEF). Tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery systolic pressure (PASP) ratio is simple echo-derived indicator of RV-PC uncoupling. This study aimed to investigate the prognostic impact of TAPSE/PASP ratio among patients with HFpEF hospitalized for acute heart failure (AHF).

Methods: Single-centre, retrospective study including patients hospitalized for AHF over a 4-year period. Receiver operating character (ROC) curves for the TAPSE/PASP ratio were used to identify the cut-off value for the composite outcome of all-cause in-hospital mortality and hospital readmission.

Results: Overall, 398 patients were included (median age 83 years, 56.0% females). According to ROC curve analysis, we calculated an ideal cut-off of 0.36 mm/mmHg for TAPSE/PASP ratio. Patients were divided into two categories, preserved RV-PC coupling (TAPSE/PASP ratio $>$ 0.36) and RV-PC uncoupling (TAPSE/PASP ratio $\leq$ 0.36). Overall, both in-hospital mortality and readmission rate were higher among HFpEF patients with TAPSE/PASP ratio $\leq$ 0.36 compared to those with TAPSE/PASP ratio $>$ 0.36 (31.4 % vs 20.3%; $p = 0.008$). At multivariate analysis, TAPSE/PASP ratio $\leq$ 0.36 emerged as an independent risk factor both for death (HR 2.18 [1.08 – 4.42]; $p = 0.03$) and the composite outcome (HR 1.95 [1.22 – 3.12]; $p = 0.005$).

Conclusion: Among patients with HFpEF and hospitalized for AHF, the RV-PC uncoupling was associated with a more than two-fold increased risk of in-hospital mortality.

1. Introduction

Heart Failure with Preserved Ejection Fraction (HFpEF) is a growing health condition as patients experience poor quality of life and excess mortality [1,2]. The prevalence of HFpEF is increasing steadily, accounting for over 50 % of all HF cases [3].

A number of heterogeneous mechanisms are believed to be involved in the pathophysiology of HFpEF and this represents a challenge to the development of effective therapeutic strategies. The role of the right ventricle (RV) in HF, which has been largely neglected for many years, has increasingly been studied in the last decade. Since RV function has well established role in HF with reduced ejection fraction (HFrEF), recently, attention has been drawn to the role of RV in HFpEF [4].

It has been hypothesized that increased left ventricule (LV) filling pressures lead to progressive functional and structural changes in pulmonary arteries with consequent elevations in both postcapillary and precapillary pressure, driving RV dysfunction (RVD) [5]. Among patients with HFpEF it has been documented that RVD is associated with worse clinical symptoms and adverse prognosis, but it is also strongly predictive of Pulmonary Hypertension (pH) [6–9],.

An invasive measurement is necessary to determine the RV-pulmonary circulation accurately, but this approach is difficult to

* Corresponding author at: Division of Internal Medicine, Ospedale Santo Spirito in Sassia, Rome, Italy.
E-mail address: giuseppe.dematteis@policlinicogemelli.it (M.L. Burzo).

https://doi.org/10.1016/j.ejim.2025.106540
Received 10 June 2025; Received in revised form 28 September 2025; Accepted 3 October 2025
Available online 8 October 2025

implement in daily practice and especially in acute medical conditions [10,11],. In contrast, several echocardiographic parameters that are simple and highly reproducible can be used to assess RVD, such as fractional area change, tricuspid annular peak systolic velocity, and, specifically, reduction in tricuspid annular plane systolic excursion (TAPSE) [10]. TAPSE is measured as the displacement of the lateral tricuspid annulus toward the apex during systole and is an index of RV contractile function. Likewise, echocardiographically assessed pulmonary artery systolic pressure (PASP) is routinely used to estimate pH in clinical practice [12]. Recently, the TAPSE/PASP ratio has been introduced as a reliable and non-invasive index of RV-pulmonary circulation (RV-PC) coupling [13]. This ratio represents a more accurate indicator of disease severity and prognosis than TAPSE or PASP alone in patients with HFpEF, as also outlined in the Position Statement of the European Society of Cardiology (ESC) for HFpEF [4,7,13,14].

However, despite this promising evidence, measurement of the TAPSE/PASP ratio is not commonly used in clinical practice. Also, the in-hospital prognostic value of RVD among acutely deteriorated patients with preserved EF is still uncertain.

This study aims to investigate the prognostic role of TAPSE/PASP ratio among a cohort of patients with HFpEF hospitalized for AHF.

2. Methods

2.1. Study population

This is a single-center, retrospective cohort study conducted at "Fondazione Policlinico Universitario A. Gemelli IRCCS", a large medical center based in Rome, Italy.

We enrolled all patients consecutively admitted to the Emergency Department (ED) with a diagnosis of AHF and subsequently hospitalized. The study period considered was between January 1, 2016, and December 31, 2019.

The main inclusion criteria for identifying cases was an admission diagnosis of AHF, defined as either *de novo* or acutely worsening HF. The diagnosis was made by ED physicians, and based on a set of standardized parameters including clinical symptoms, physical examination, laboratory parameters, biomarkers, and radiological findings. In addition, AHF needed to be coded as the primary diagnosis in the discharge record. Diagnoses at hospital discharge were based on ICD-10 codes [International Classification of Disease, 10th revision].

Among these patients, we included in our final study cohort all patients who were classified as HFpEF according to the European Society of Cardiology (ESC) guidelines [15]. Diagnosis of HFpEF was also confirmed by using H2FPEF score [*Supplementary materials*, Table S3]. Moreover, availability of both TAPSE and PASP was an inclusion criterion.

Furthermore, patients aged under 18 years, those with acute coronary syndromes at ED admission requiring catheter-based interventions, those with advanced atrioventricular blocks or cardiac tamponade, and those requiring admission to an intensive care unit (ICU) were excluded from the study.

2.2. Study variables

Data were extracted from a centralized hospital data repository searching for a diagnosis of AHF in each ED electronic health record. Each record contains all demographic and clinical characteristics, all information regarding symptoms at ED presentation, laboratory tests, and echocardiographic parameters, use of medications, and any event occurring during the hospital stay, including outcomes at discharge.

We included the following variables:

- Socio-demographic and anthropometric data such as age, sex, Body Mass Index (BMI); specifically, the sex of participants was defined based on self-report according to Sex and Gender Equity in Research (SAGER) guidelines [16].
- Vital parameters as heart rate (HR), systolic and diastolic blood pressure (SBP and DBP), peripheral oxygen saturation (spO2), body temperature (T°).
- Clinical characteristics and symptoms at ED admission such dyspnea, fatigue, syncope, chest pain and peripheral edema. Furthermore, patients were classified according to the severity of dyspnea using the New York Heart Association functional classification of heart failure (NYHA classes) [17];
- Laboratory tests results at ED admission, including NT-proBNP, Creatinine, Hemoglobin (Hb), Fibrinogen, White Blood Cells count (WBC), Platelets count (PLTs), Glucose, Procalcitonin, C-Reactive Protein, and High Sensitivity (HS) Troponin I;
- Cardiovascular Comorbidities including coronary artery disease (CAD), atrial fibrillation (AF), presence of pacemaker (PMK) and cerebrovascular disease;
- Systemic comorbidities including peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic liver disease, diabetes, chronic kidney disease (CKD) and malignancy.
- Medications prescribed at hospital discharge such as Loop diuretics (i.e. Furosemide), Beta-blockers, Mineralocorticoid Receptor Antagonists (MRA), ACE Inhibitors (ACEi) and Angiotensin Receptor Blockers (ARBs).

2.3. Echocardiographic variables

The following echocardiographic variables were measured in all patients:

- Left Ventricular Ejection Fraction (LVEF);
- interventricular septal thickness;
- Left Ventricular end-diastolic diameter (LVDd);
- Left Ventricular end-systolic diameter (LVSd);
- Tricuspid annular plane systolic excursion (TAPSE);
- Pulmonary Artery Systolic Pressure (PASP);
- Left Atrial dimension index (LAVi);
- E/A ratio;
- E/e' ratio;
- Right ventricular diastolic diameter (RVDD);
- Tricuspid regurgitation (TR) pression gradient;
- Severity of TR;
- Left Ventricular Diastolic Dysfunction (LVDD) ultrasound classification.

EF was calculated by the Simpson biplane method using apical 2-chamber and 4-chamber projection. The ratio of the mitral peak velocity of early filling E to the velocity of mitral annulus early diastolic motion e' (E/e') was estimated using the mean e' velocity obtained from the septal and lateral sides of the mitral annulus. TAPSE was tracked using apical 4-chamber projection in M-Mode. PASP was calculated by formula 4 x (velocity of tricuspid regurgitation)^2 + (estimated right atrial pressure), where the latter value was estimated by measuring the respiratory change in inferior vena cava diameter. The TR pression gradient was calculated by the modified Bernoulli equation. The severity of TR was graded as absent or mild (grade 1), moderate (grade 2) or severe (grade 3). Finally, LAVi was also calculated using the Simpson biplane method.

2.4. Outcome measures

The primary endpoint was the all-cause in-hospital mortality.

The secondary endpoint was a composite of in-hospital all-cause mortality and hospital readmission within 90 days after discharge.

Additional secondary endpoints were in-hospital mortality due to cardiovascular (CV) and non-cardiovascular causes and the length of

hospital stay (LOS). Causes of death were derived by reviewing the electronic medical records and the hospital-based death certificates.

We classified as CV deaths those occurring due to terminal HF and cardiogenic shock, acute myocardial infarction, arrhythmias, acute pulmonary embolism, cardiac tamponade, and acute cerebrovascular disease. Instead, non-CV related events were deaths occurring due to severe sepsis or septic shock, renal failure, respiratory failure due to primary pulmonary diseases, and major bleeding with hemorrhagic shock.

2.5. Statistical analysis

Categorical variables were presented as numbers and percentages. Continuous normally distributed variables were presented as mean ± standard deviation, non-normally distributed data were presented as median (inter-quartile range), and binary or ordinal variables were presented as absolute frequency (%). Parametric variables were compared by the Mann-Whitney U test, whereas categorical variables were compared by the Chi-square test (with Fisher test if indicated).

Significant variables at univariate analysis were entered into a multivariate Cox regression model to identify independent outcome predictors. To avoid overfitting and overestimating the parameters, the variables with high collinearity were excluded from the multivariate models, and categorical variables were preferred to continuous. To dichotomize the TAPSE/PAPS variables, we analyzed receiver operating characteristic (ROC) curves for the association of TAPSE/PASP ratio to in-hospital death, to identify the best cut-off values predicting survival. The other continuous variables entered into the uni- and multivariate Cox regression models were dichotomized using the median value.

The results of Cox regression models were expressed as Hazard Ratios (HR) with respective 95 % confidence intervals. Survival analysis was performed according to the Kaplan-Meier approach.

Time-dependent Brier scores were computed to compare the prediction error of survival models with and without TAPSE/PAPS, thus providing a dynamic assessment of model performance across follow-up time.

LOS was calculated as the time from ED admission to discharge or to the occurrence of the primary outcome. For follow-up time was extended to 90 days post- hospital discharge.

All data were analyzed by SPSS v26® (IBM, NY, USA). A two-sided p-value of 0.05 or less was considered statistically significant.

The study was conducted in accordance with the principles expressed in the Declaration of Helsinki and was approved by the local ethical committee (IRB #0051,814/19). Being a retrospective study performed on a database of anonymized patients, informed consent was not required.

3. Results

3.1. Study cohort and baseline characteristics

A total of 398 patients were included in the study, they were predominantly old [mean age 83 years, range 75 - 87], with a slight predominance of females (56.0 %). Patients were mainly hospitalized in Internal Medicine and Geriatrics wards (363 patients, 91.3 % of the whole sample), while 35 patients (8,7 %) were admitted to Cardiology wards.

The most common symptom at ED admission was dyspnea (58.8 %), followed by peripheral edema (27.1 %). Most patients (67.3 %) had a moderate functional limitation grade, as indicated by NYHA class III.

One-third of the patients was concomitantly affected by AF (33.4 %). Other frequent comorbidities were CKD (28.4 %), CAD (24.1 %), COPD (23.6 %), and diabetes (23.1 %).

Most patients (70.8 %) had left ventricular hypertrophy with a grade 2 diastolic dysfunction in 55.4 % of cases. Median TAPSE and PASP values were respectively 19 [17–22] and 40 [33–50], with a median TAPSE/PASP ratio of 0.50 [0.36 - 0.63].

3.2. Baseline characteristics of study subgroups according to TAPSE/PASP ratio

We used the ROC curve analysis [Fig. 1] to assess the cut-off value for the association of TAPSE/PASP ratio to in-hospital death. According to this method, a cut-off of 0.36 mm/mmHg was identified as the best predictor of the primary outcome.

The study population was subsequently divided into two groups, respectively patients with a preserved RV-PC coupling (TAPSE/PASP ratio > 0.36; $N = 296$) and those with an unpaired RV-PC coupling (TAPSE/PASP ratio ≤ 0.36; $N = 102$). Baseline characteristics of the two subgroups are reported in Table 1.

The two groups showed similar characteristics concerning age, sex, BMI, clinical presentation, and reported symptoms at ED admission. Dyspnea was more common in the TAPSE/PASP ≤ 0.36 group (65.7 % vs 56.4 %; $p = 0.063$) but NYHA classification did not differ between the two groups.

Patients in the TAPSE/PASP ≤ 0.36 group had significantly higher NTproBNP values at ED admission compared to the other group (5900 ng/mL vs 3644 ng/mL; $p = 0.001$).

Among patients with RV-PC uncoupling AF was more common (45.2 % vs 29.4 %) and, predictably, they showed significantly higher LAVI values (60 vs 56). Three times more patients in the group with a lower TAPSE/PASP ratio had a grade 3 diastolic dysfunction.

Other comorbidities were overlapped among the two groups.

Regarding medication at hospital discharge, we found that patients with RV-PC uncoupling were more frequently treated with diuretic therapies, either loop diuretics (95.3 % vs 83.3 %; $p = 0.003$) or MRA (67.1 % vs 46.9 %; $p = 0.001$), compared with the other group. Among the other medications recommended by clinical guidelines, there were no statistically significant differences between the two groups.

Overall, patients with a lower TAPSE/PASP ratio tended to have worse outcomes, both in terms of LOS, all-cause in-hospital mortality, and 90-day readmissions, although they did not reach statistical significance. However, CV mortality was 5-fold higher in the TAPSE/PASP ≤ 0.36 group (6.9 % vs 1.4 %).

3.3. Multivariate analysis for the whole sample

Over the study period, 34 patients (8.5 %) died and 191 patients

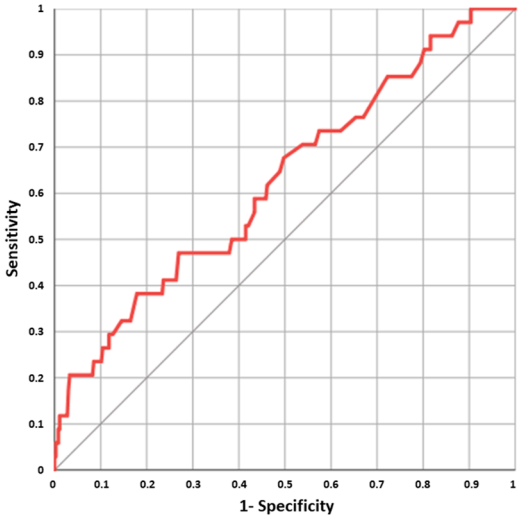

Fig. 1. Receiver operating characteristic (ROC) curve analysis for predicting the primary endpoint with tricuspid annular plane systolic excursion (TAPSE)/pulmonary artery systolic pressure (PASP) ratio.

Table 1
Baseline characteristics of the overall population and divided by TAPSE/PASP > 0.36 and TAPSE/PASP ≤ 0.36.

	All cases N = 398	TAPSE/PASP > 0.36 N = 296	TAPSE/PASP ≤ 0.36 N = 102	P value
Age	83 [75 – 87]	82 [75 – 87]	83 [74 – 88]	0.429
Female	223 (56.0 %)	167 (56.4 %)	56 (54.9 %)	0.439
BMI (Kg/m^2)	26.1 [23.4 – 29.4]	26.0 [23.5 – 29.4]	26.6 [22.9 – 29.4]	0.953
Clinical presentation				
SBP (mmHg)	134 [114.25 – 153]	134 [115 – 155]	130 [110 – 147]	0.157
DBP (mmHg)	73 [61 – 84.75]	72 [62 – 85]	74 [60 – 84]	0.812
Heart Rate (beats/min)	80 [69 – 97]	81 [69 – 98]	78 [70 –91]	0.225
SpO2 (%)	95 [91 – 97]	95 [92 – 97]	94 [90 – 97]	0.116
T (°C)	36.5 [36 – 37.30]	36.5 [36 – 37]	36.7 [36.3 – 38.2]	0.235
Symptoms at ED admission				
Dyspnea	234 (58.8 %)	167 (56.4 %)	67 (65.7 %)	0.063
Chest pain	67 (16.8 %)	54 (18.2 %)	13 (12.7 %)	0.129
Syncope	25 (6.3 %)	20 (6.8 %)	5 (4.9 %)	0.345
Peripheral edema	108 (27.1 %)	86 (29.1 %)	22 (21.6 %)	0.089
Fatigue	43 (10.8 %)	32 (10.8 %)	11 (10.8 %)	0.579
NYHA Classification				
Class I and II	63 (15.8 %)	48 (16.2 %)	15 (14.7 %)	
Class III	268 (67.3 %)	197 (66.6 %)	71 (69.6 %)	0.850
Class IV	67 (16.8 %)	51 (17.2 %)	16 (15.7 %)	
Laboratory Findings at ED admission				
NT-proBNP (ng/L)	4510 [2184 – 9942]	3644 [1997 – 9236]	5900 [3633 – 12,134]	0.001
Creatinine (mg/dL)	1.21 [0.94 – 1.81]	1.21 [0.94 – 1.73]	1.25 [0.93 – 1.93]	0.527
Hemoglobin (g/dL)	11.1 [10.1 – 12.8]	11.3 [10.4 – 12.8]	10.5 [9.7 – 12.2]	0.017
Fibrinogen (mg/dL)	481 [388 – 589]	498 [398 – 622]	448 [377 – 547]	0.047
WBC (x10^9/L)	8.51 [6.83 – 10.86]	8.17 [6.83 – 11.10]	8.89 [6.97 – 10.09]	0.612
PLTs (x10^9/L)	226 [181 – 316]	239 [190 – 313]	212 [156 – 316]	0.497
Glucose (mg/dL)	123 [102 – 152]	124 [102 – 153]	118 [102 – 150]	0.839
Procalcitonin (ng/mL)	0.80 [0.05 – 0.33]	0.09 [0.05 – 0.20]	0.08 [0.05 – 1.32]	0.338
C-Reactive Protein (mg/L)	26.8 [11.3 – 83.5]	31.8 [11.3 – 86.5]	18.5 [8.9 – 73.6]	0.444
HS Troponine I	0.04 [0.01 – 0.11]	0.03 [0.01 – 0.12]	0.05 [0.02 – 0.10]	0.149
Cardiovascular Comorbidities				
CAD	96 (24.1 %)	70 (23.6 %)	26 (25.5 %)	0.401
Atrial Fibrillation	133 (33.4 %)	87 (29.4 %)	46 (45.1 %)	0.003
PMK	37 (9.3 %)	16 (5.4 %)	21 (20.6 %)	<0.001
Cerebrovascular disease	20 (5.0 %)	15 (5.1 %)	5 (4.9 %)	0.592
Systemic Comorbidities				
COPD	94 (23.6 %)	69 (23.3 %)	25 (24.5 %)	0.451
Chronic liver disease	9 (2.3 %)	5 (1.7 %)	4 (3.9 %)	0.175
Diabetes	92 (23.1 %)	71 (24.0 %)	21 (20.6 %)	0.289
Chronic kidney disease	113 (28.4 %)	81 (27.4 %)	32 (31.4 %)	0.257
Malignancy	46 (11.6 %)	35 (11.8 %)	11 (10.8 %)	0.468
Echocardiographic variables				
LVEF (%)	58 [55 – 62]	59 [55 –62]	57 [55 –62]	0.300
Left Ventricular Hypertrophy	259 (70.8 %)	190 (70.1 %)	69 (72.6 %)	0.372
LVDd (mm)	47 [42 – 52]	47 [41.2 – 51.0]	48 [43.5 – 53.0]	0.338
LVSd (mm)	31 [26 – 35]	30 [26 – 34]	32 [28.0 – 36.7]	0.006
TAPSE (mm)	19 [17 – 22]	20 [18 – 23]	16 [14 – 18]	< 0.001
PASP (mmHg)	40 [32.75 – 50]	35 [30 – 40]	60 [50 – 70]	< 0.001
TAPSE/PASP (mm/mmHg)	0.50 [0.36 – 0.63]	0.56 [0.47 – 0.68]	0.28 [0.23 – 0.32]	< 0.001
RVDD (mm)	27 [24 – 30]	27 [24 – 28]	32 [26 – 39]	0.003
TR gradient (mmHg)	2 [1 – 2]	1 [1 – 2]	2 [2 – 3]	<0.001
TR severity	34 [30 – 40]	33 [27 – 35]	47 [34 – 60]	<0.001
E/A	0.80 [0.64 – 1.16]	0.79 [0.63 – 1.15]	0.85 [0.65 – 1.30]	0.138
E/e'	12 [9 – 15]	12 [9 – 15]	12 [9 – 16]	0.471
LAVI (mL/m^2)	57 [48 – 62]	56 [45 – 62]	60 [52 – 66]	<0.001
Left Ventricular Diastolic Dysfunction (LVDD) Ultrasound Classification				
Normal	27 (14.7 %)	23 (14.3 %)	4 (17.4 %)	
Grade 1	39 (21.2 %)	34 (21.1 %)	5 (21.7 %)	
Grade 2	102 (55.4 %)	93 (57.8 %)	9 (39.1 %)	0.88
Grade 3	16 (8.7 %)	11 (6.8 %)	5 (21.7 %)	
Medication at discharge				
Loop diuretics	296 (86.3 %)	215 (83.3 %)	81 (95.3 %)	0.003
Beta-blockers	266 (77.6 %)	203 (78.7 %)	63 (74.1 %)	0.232
MRA	178 (51.9 %)	121 (46.9 %)	57 (67.1 %)	0.001
ACE inhibitors	90 (26.2 %)	64 (24.8 %)	26 (30.6 %)	0.181
ARB	69 (20.1 %)	57 (22.1 %)	12 (14.1 %)	0.073
Outcomes				
LOS (Days)	10.23 [6.41 – 15.53]	9.55 [6.34 – 15.65]	11.47 [6.98 – 15.61]	0.204
90-days Readmission	164 (41.2 %)	117 (39.5 %)	47 (46.1 %)	0.149
Death	34 (8.5 %)	20 (6.8 %)	14 (13.7 %)	0.028
Cardiovascular Death	11 (2.8 %)	4 (1.4 %)	7 (6.9 %)	0.008
Non-cardiovascular Death	23 (5.8 %)	16 (5.4 %)	7 (6.9 %)	0.371

Abbreviations: BMI, Body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO2; peripheral oxygen saturation; T, temperature; NYHA, New York Heart Association; NTproBNP, N-terminal pro-brain natriuretic peptide; WBC, white blood cells; PLT, platelets; HS, high sensivity; CAD, Coronary artery disease; PMK, pacemaker; COPD, Chronic Obstructive Pulmonary Disease; LVEF, left ventricular ejection fraction; LVDd, left ventricular enddiastolic diameter; LVSd, left ventricular end-systolic diameter; TAPSE, Tricuspid annular plane systolic excursion; PASP, pulmonary artery systolic pressure; RVDD, right ventricular diastolic diameter; TR, Tricuspid regurgitation; LAVI, left atrial dimension index; LVEF, left ventricular ejection fraction; LVDD, Left ventricular diastolic dysfunction; MRA, mineralocorticoid receptor antagonists; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; LOS, length of stay.

(47.9 %) met the criteria for the composite outcome [Table S2].

Fig. 2 Panel A illustrates the survival curve of the primary endpoint according to TAPSE/PASP ≤0.36 (HR 2.18 [95 % CI, 1.08 – 4.42], $p < 0.030$). NTproBNP values above the median at admission and, among comorbidities, CAD, diabetes, and CKD showed a significantly association with all-cause in-hospital death through a univariable Cox regression model [Table 2, *Supplementary material* Table S1].

Fig. 2 Panel B shows the survival curve of the secondary endpoint of all-cause death and AHF re-hospitalization according to TAPSE/PASP > 0.36 (HR 1.95 [95 % CI, 1.22 – 3.12], $p < 0.005$).

Time-dependent Brier score curves for the two Cox models (with and without TAPSE/PAPS) are shown in *Supplementary material* [Figure S1]. As expected, scores could be estimated only up to the last observed event (43.6 days), despite censoring extending to 68 days. The curves highlight that the difference between models is minimal in the first days after admission, but widens progressively from approximately two weeks

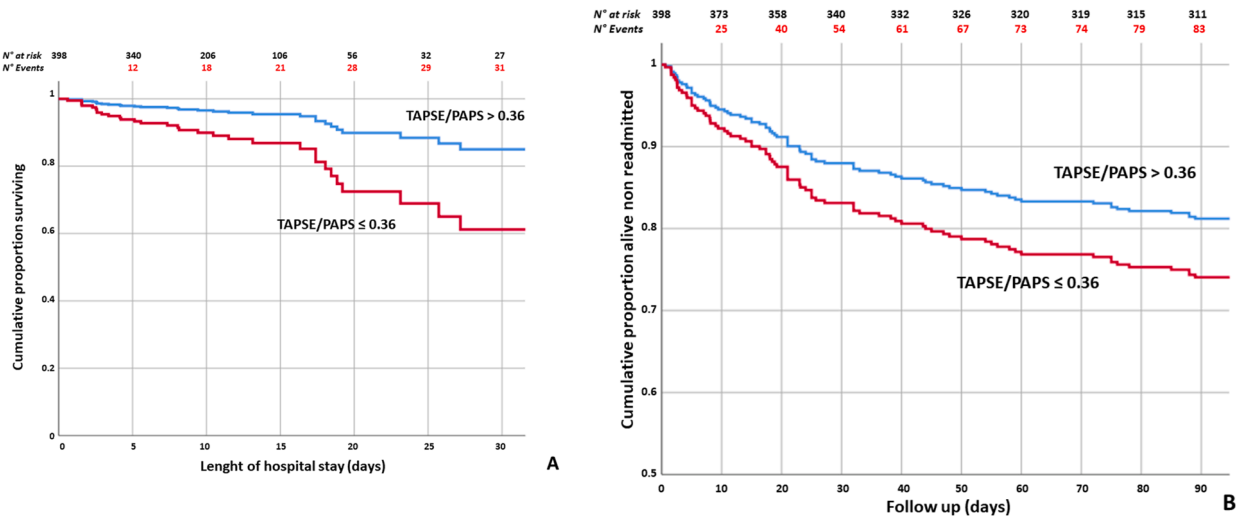

Fig. 2. Kaplan-Meier survival curves for prediction of the primary outcome (A) and the secondary outcome (B) based on the ideal cutoff (0.36) of the tricuspid annular plane systolic excursion (TAPSE)/pulmonary artery systolic pressure (PASP) threshold in this cohort.

Table 2
Multivariate analysis for the whole sample.

	Unadjusted HR [95 % CI]	p value	Adjusted HR [95 % CI]	p value
In-Hospital death				
TAPSE/PASP ≤ 0.36	2.53 [1.29 – 4.98]	0.007	2.18 [1.08 – 4.42]	0.030
NT-proBNP	6.28 [3.10 – 12.72]	<0.001	4.69 [1.89 – 11.65]	0.001
Creatinine	3.29 [1.64 – 6.57]	0.001	0.97 [0.47 – 2.03]	0.954
CAD	2.37 [1.18 – 4.75]	0.015	2.94 [1.39 – 6.20]	0.004
Diabetes	1.93 [0.96 – 3.88]	0.629	2.16 [1.04 – 4.52]	0.039
CKD	3.65 [1.82 – 7.23]	<0.001	2.97 [1.45 – 6.10]	0.004
In-Hospital death or Readmission at 90 days				
TAPSE/PASP ≤ 0.36	2.03 [1.29 – 3.18]	0.002	1.95 [1.22 – 3.12]	0.005
NT-proBNP	1.81 [0.99 – 3.30]	0.052	2.02 [1.10 – 3.73]	0.023
Hemoglobin	1.85 [1.22 – 2.81]	0.004	1.82 [1.18 – 2.82]	0.007
CKD	1.62 [1.05 – 2.52]	0.030	1.69 [1.06 – 2.68]	0.025

Abbreviations: TAPSE, Tricuspid annular plane systolic excursion; PASP, pulmonary artery systolic pressure; NTproBNP, N-terminal pro-brain natriuretic peptide; CAD, Coronary artery disease; CKD, chronic kidney disease.

onwards, confirming the added prognostic contribution of TAPSE/PAPS in the longer term.

Moreover, also patients with NTproBNP values above the median at admission (HR 2.02 [95 % CI, 1,10 – 3.73], $p = 0.023$) were at higher risk for the composite outcome. In addition, hemoglobin levels below the median at admission, and CKD were found to be independent risk factors for the composite outcome [Table 2, and *Supplementary material* Table S2].

4. Discussion

The present study demonstrated that RV-PC uncoupling, as measured by a low TAPSE/PASP ratio, is a negative prognostic factor among acutely hospitalized patients with HFpEF. Furthermore, we found that a TAPSE/PAPS ratio of 0.36 is associated with a five-fold increase in the risk of in-hospital CV death.

HFpEF is rapidly emerging as the predominant form of HF. Given the lack of a therapeutic strategies and the wide heterogeneity of patients affected by HFpEF [18], the identification of prognostic markers is of paramount importance.

For a long time, HFpEF was universally regarded as a condition involving exclusively the left ventricle. Indeed, several recent studies have demonstrated that the right ventricle plays a role in the pathogenesis of HFpEF, and that RVD correlates with a worsening prognosis and a poor response to medical treatments [19,20],. However, a great challenge in studying the right ventricle is how to assess ventricular function without employing invasive techniques [21]. This is especially true when faced with pressure overload or filling volume, as common in AHF.

Among parameters that can be derived from ecocardiography, a lower TAPSE/PASP ratio has been linked to an excess risk of hospitalization for AHF among community-dwelling HFpEF patients, and that regardless of filling pressures, clinical characteristics, and natriuretic peptide levels [22]. The TAPSE/PASP ratio correlates with abnormal pulmonary capillary wedge pressure and mean pulmonary artery pressure at rest and during exercise [23].

The main finding of current study is that in HFpEF patients acutely hospitalized for AHF a TAPSE/PASP ≤0.36 was associated with more than two-fold increase of the risk of in-hospital mortality. Several studies, including the Position Statement of the ESC for right heart failure in HFpEF, are in accordance with our cut-off values [7,24],. A trial by Guazzi et al. which stratified a cohort of HFpEF patients using TAPSE/PASP ratio-based tertiles, showed that the tertile with $a < 0.36$ ratio had a lower pulmonary artery compliance, higher pulmonary vascular resistances, and worse clinical outcomes[25]. However, this study included patients with HFpEF selected in the outpatient setting. Similarly, another study in a cohort of patients with a lower median age, found that a TAPSE/PASP of 0.36 in patients with HFpEF admitted for AHF was associated with a higher mortality rate, further increased by the presence of severe functional tricuspid regurgitation [26]. Likewise, in a cohort of HFpEF patients hospitalized for AHF, a TAPSE/PASP ratio < 0.40 was independently associated with in-hospital major adverse cardiovascular events (MACEs) [27]. A more recent study performed by Palazzuoli et al. confirmed that the TAPSE/PASP ratio was an independent predictor of prognosis in patients hospitalized for AHF, with a reported median value of 0.37 in patients who underwent adverse events. Interestingly, the study showed that the RV longitudinal strain (RVLS) and RVLS/PASP ratio had greater accuracy in identifying patients at high risk of adverse events, mainly in the AHF with pEF

subgroups, supporting the development of new future studies to further investigate the use of this echocardiographic method in patients with HFpEF [28].

It should be noted that all of these studies were conducted on Western patients, and that it is reasonable to assume the existence of ethnic differences. A Japanese trial by *Nakagawa* et al., based on the large multicentric cohort study of the PURSUIT-HFpEF (Prospective Multicenter Observational Study of Patients with HFpEF), confirmed that RV-PC uncoupling was independently associated with all-cause mortality. However, the TAPSE/PASP ratio was 0.48, because of lower median values of TAPSE and PASP compared to western cohorts of patients. The authors speculated that the finding may be explained by the fact that Asian and Western populations have different prevalence of comorbidities that could affect precapillary pH, such as COPD, with Asians experiencing lower rates of COPD [12]. Consistently, two trials on HFpEF patients from China, considered as significant prognostic factors higher thresholds of TAPSE/PASP ratio compared to European population-based studies, <0.45 and <0.43 [29,30],. Thus, it seems reasonable that the TAPSE/PASP ratio cut-off should be adjusted according to ethnicity.

In our study cohort RV-PC uncoupling is significantly associated with the composite outcome of 90-day readmission and in-hospital mortality. Similarly, a previous study showed that a TAPSE/PASP ratio <0.36 was associated with a higher risk of all-cause and HF-related recurrent admissions, and that the risk was further increased in patients with the lowest ratio (TAPSE/PASP <0.28) [31]. In addition, *Palazzuoli* et al. showed that a lower TAPSE/PASP value tended to increase 180-day rehospitalizations, although the TAPSE/right ventricular end-diastolic diameter (RVEDD) ratio showed a stronger association with readmission rate [32].

We found that patients with RV-PC uncoupling had a higher median age, were more symptomatic, especially in terms of dyspnea, and had significantly higher NT-proBNP levels on admission, indicating a higher degree of congestion. This evidence also seemed to be confirmed by the analysis of medications at discharge, as a significantly higher proportion of patients on diuretic therapy, either with loop diuretics or MRA agents, was found in the group with TAPSE/PAPS <0.36. It has been extensively demonstrated that NT-proBNP is associated with mortality in HFpEF [33], as evidenced in the PARAGON—HF study where an elevated NT-proBNP value was associated with approximately a threefold higher risk of cardiovascular mortality and hospitalization for AHF. Furthermore, the increase in NT-proBNP levels was associated not only with significantly worse LV stiffness and left atrial function but also with the severity of diastolic dysfunction grades [34,35].

Moreover, among patients with a lower TAPSE/PASP ratio, we found a particularly high prevalence of concomitant CV comorbidities, primarily AF (45.1 %). Despite the well-established association between AF and adverse outcomes in patients with HFpEF [36,37], a reduced TAPSE/PASP ratio was associated with adverse outcomes in our study independently of AF. In addition to AF contributing to RVD, abnormal cardiac cycle length is known to reduce cardiac output by increasing left atrial pulsatile loading [25,38], suggesting RVD may play a prognostic role in HF, independent of its association with AF [39].

The characteristics found in our study in the group with RV-PC uncoupling, including the higher degree of congestion, the higher rates of associated cardiovascular comorbidities and chronic renal failure, along with the markedly worse prognosis, suggest these patients with HFpEF may be more closely resemble those with HFrEF [40], raising the question of what treatment is most appropriate for this subset of patients. It also indicates that HFpEF patients may further benefit from a more accurate phenotyping to appropriately prioritize therapeutic strategies.

4.1. Limitations

Some limitations of the study are worth mentioning. First, all diagnoses, clinical classifications, and symptoms were obtained from the hospital's electronic medical records and a possible misclassification cannot be rule-out. Likewise, the specific cause of death was derived from the hospital's death certificate, which may not always be accurate.

Secondly, due to the monocentric study design, the findings cannot be applicable to the entire HFpEF population. Information about the pharmacological treatment provided during hospitalization was incomplete. To mitigate this limitation, it should be noted that throughout the four year of the study, patients were admitted in internal medicine wards with permanent medical staff under the same coordinating chief, continuously reevaluating and implementing clinical guidelines. Moreover, the use of STGL-2 inhibitors for HFpEF treatment was later indicated [41] and this is not present in the current study.

The incomplete characterization of the etiologies of HFpEF is another limitation of our study. In particular, no systematic evaluation with bone scintigraphy, cardiac MRI, or serum free light-chain assay was performed to exclude transthyretin cardiac amyloidosis (ATTR-CM), which is increasingly recognized as a prevalent and prognostically relevant cause of HFpEF, especially in older patients [42].

Since only patients with HFpEF who underwent echocardiography were included, very early deaths and ICU admissions were not assessed. Therefore, our findings pertain to patients who were clinically stable and eligible for echocardiographic evaluation.

The TAPSE/PASP values were retrieved from electronic chart records, which may have introduced inter-observer variability into our analysis. However, all scans were performed at the same centre with standardized acquisition protocols.

In addition, we acknowledge that both TAPSE and PASP are load-dependent measures, and that the proposed 0.36 cut-off was derived from a single-centre cohort with uniform imaging protocols. Therefore, its generalizability across different ultrasound vendors, operators, and treatment settings remains uncertain, and external validation in independent populations will be necessary to confirm its robustness.

Finally, follow up was limited to only at the first 90 days following discharge, and long-term outcomes were not considered.

4.2. Conclusions

Among patients with HFpEF hospitalized for AHF, the TAPSE/PASP ratio appears to be a reliable parameter for detecting RV-PC uncoupling not invasively. We found that a TAPSE/PAPS ratio $\leq$ 0.36 was associated with a more than two-fold increase of in-hospital mortality risk, independently from age and comorbidities burden, confirming that RV-PC uncoupling negatively impacts the prognosis of HFpEF patients admitted for AHF.

Since there are limited treatment options available for patients with HFpEF, a more routinely measurement of the TAPSE/PAPS ratio in clinical practice, can serve both as a prognostic indicator as well as a measure of RV-PC coupling, providing a useful tool for advanced phenotyping of HFpEF patients and improved treatment outcomes. Indeed, it can be envisaged that phenotype-specific therapies targeting pulmonary vascular dysfunction and RV-PC uncoupling may be helpful for patients with poorest outcomes.

Further studies are required to clarify the relationship between TAPSE/PASP ratio and long-term survival, and to integrate this ratio into HFpEF treatment guidelines.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

None declared.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2025.106540.

References

[1] Redfield MM, Borlaug BA. Heart failure with preserved ejection fraction. JAMA 2023;329:827. https://doi.org/10.1001/jama.2023.2020.

[2] Forsyth F, Brimicombe J, Cheriyan J, et al. Characteristics of patients with heart failure with preserved ejection fraction in primary care: a cross-sectional analysis. BJGP Open 2021;5. https://doi.org/10.3399/BJGPO.2021.0094.

[3] Dunlay SM, Roger VL, Redfield MM. Epidemiology of heart failure with preserved ejection fraction. Nat Rev Cardiol 2017;14:591–602. https://doi.org/10.1038/nrcardio.2017.65.

[4] Ghio S, Guazzi M, Scardovi AB, et al. Different correlates but similar prognostic implications for right ventricular dysfunction in heart failure patients with reduced or preserved ejection fraction. Eur J Heart Fail 2017;19:873–9. https://doi.org/10.1002/EJHF.664.

[5] Inciardi RM, Abanda M, Shah AM, et al. Right ventricular function and pulmonary coupling in patients with heart failure and preserved ejection fraction. J Am Coll Cardiol 2023;82:489–99. https://doi.org/10.1016/j.jacc.2023.05.010.

[6] Ghio S, Gavazzi A, Campana C, et al. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. J Am Coll Cardiol 2001;37:183–8. https://doi.org/10.1016/S0735-1097(00)01102-5.

[7] Gorter TM, van Veldhuisen DJ, Bauersachs J, et al. Right heart dysfunction and failure in heart failure with preserved ejection fraction: mechanisms and management. Position statement on behalf of the Heart failure association of the European society of cardiology. Eur J Heart Fail 2018;20:16–37. https://doi.org/10.1002/ejhf.1029.

[8] Ansari Ramandi MM, van Melle JP, Gorter TM, et al. Right ventricular dysfunction in patients with new-onset heart failure: longitudinal follow-up during guideline-directed medical therapy. Eur J Heart Fail 2022;24:2226–34. https://doi.org/10.1002/ejhf.2721.

[9] Palazzuoli A, Cartocci A, Pirrotta F, et al. Different right ventricular dysfunction and pulmonary coupling in acute heart failure according to the left ventricular ejection fraction. Prog Cardiovasc Dis 2023;81:89–97. https://doi.org/10.1016/j.pcad.2023.07.008.

[10] Hameed A, Condliffe R, Swift AJ, et al. Assessment of right ventricular function—a state of the art. Curr Heart Fail Rep 2023;20:194–207. https://doi.org/10.1007/s11897-023-00600-6.

[11] Guazzi M. Right ventricular to pulmonary circulation coupling comes to the front line in acute heart failure with preserved ejection fraction. Circ Cardiovasc Imaging 2020;13. https://doi.org/10.1161/CIRCIMAGING.120.012001.

[12] Nakagawa A, Yasumura Y, Yoshida C, et al. Prognostic importance of right ventricular-vascular uncoupling in acute decompensated heart failure with preserved ejection fraction. Circ Cardiovasc Imaging 2020;13. https://doi.org/10.1161/CIRCIMAGING.120.011430.

[13] Guazzi M, Bandera F, Pelissero G, et al. Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. Am J Physiol-Heart Circ Physiol 2013;305:H1373–81. https://doi.org/10.1152/ajpheart.00157.2013.

[14] Bosch L, Lam CSP, Gong L, et al. Right ventricular dysfunction in left-sided heart failure with preserved versus reduced ejection fraction. Eur J Heart Fail 2017;19:1664–71. https://doi.org/10.1002/ejhf.873.

[15] McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599–726. https://doi.org/10.1093/eurheartj/ehab368.

[16] Heidari S, Babor TF, De Castro P, et al. Sex and gender equity in research: rationale for the SAGER guidelines and recommended use. Res Integr Peer Rev 2016;1(2). https://doi.org/10.1186/s41073-016-0007-6.

[17] Russell SD, Saval MA, Robbins JL, et al. New York heart association functional class predicts exercise parameters in the current era. Am Heart J 2009;158:S24–30. https://doi.org/10.1016/j.ahj.2009.07.017.

[18] Cohen JB, Schrauben SJ, Zhao L, et al. Clinical phenogroups in heart failure with preserved ejection fraction. JACC Heart Fail 2020;8:172–84. https://doi.org/10.1016/j.jchf.2019.09.009.

[19] Rieth AJ, Richter MJ, Tello K, et al. Exercise hemodynamics in heart failure patients with preserved and mid-range ejection fraction: key role of the right heart. Clin Res Cardiol 2022;111:393–405. https://doi.org/10.1007/s00392-021-01884-1.

[20] Astengo M, Bobbio E, Polte CL, et al. Multiparametric right ventricular assessment improves risk stratification in patients with new-onset acute heart failure. ESC Heart Fail 2024;11:3378–87. https://doi.org/10.1002/ehf2.14954.

[21] Steffen J, Lux M, Stocker TJ, et al. Right ventricular to pulmonary artery coupling in patients with different types of aortic stenosis undergoing TAVI. Clin Res Cardiol 2025;114:227–38. https://doi.org/10.1007/s00392-024-02457-8.

[22] Wang N, Rueter P, Ng M, et al. Echocardiographic predictors of cardiovascular outcome in heart failure with preserved ejection fraction. Eur J Heart Fail 2024;26:1778–87. https://doi.org/10.1002/ejhf.3271.

[23] Chen Z, Chung Y, Cheng J, et al. Right ventricular-vascular uncoupling predicts pulmonary hypertension in clinically diagnosed heart failure with preserved ejection fraction. J Am Heart Assoc 2024;13. https://doi.org/10.1161/JAHA.123.030025.

[24] Anastasiou V, Papazoglou AS, Moysidis DV, et al. The prognostic impact of right ventricular-pulmonary arterial coupling in heart failure: a systematic review and meta-analysis. Heart Fail Rev 2023;29:13–26. https://doi.org/10.1007/s10741-023-10341-2.

[25] Guazzi M, Dixon D, Labate V, et al. RV Contractile function and its coupling to pulmonary circulation in heart failure with preserved ejection fraction. JACC Cardiovasc Imaging 2017;10:1211–21. https://doi.org/10.1016/j.jcmg.2016.12.024.

[26] Santas E, De la Espriella R, Chorro FJ, et al. Right ventricular dysfunction staging system for mortality risk stratification in heart failure with preserved ejection fraction. J Clin Med 2020;9:831. https://doi.org/10.3390/jcm9030831.

[27] Fauvel C, Dillinger J-G, Rossanaly Vasram R, et al. In-hospital prognostic value of TAPSE/sPAP in patients hospitalized for acute heart failure. Eur Heart J Cardiovasc Imaging 2024;25:1099–108. https://doi.org/10.1093/ehjci/jeae059.

[28] Palazzuoli A, Dini FL, Pugliese NR, et al. Right ventricular–pulmonary artery uncoupling and strain in acute heart failure. J Am Heart Assoc 2025;14. https://doi.org/10.1161/JAHA.124.039858.

[29] Wang J, Li X, Jiang J, et al. Right ventricular–pulmonary arterial coupling and outcome in heart failure with preserved ejection fraction. Clin Cardiol 2024;47. https://doi.org/10.1002/clc.24308.

[30] Jia H, Liu L, Bi X, et al. Right ventricular-arterial uncoupling as an independent prognostic factor in acute heart failure with preserved ejection fraction accompanied with coronary artery disease. Chin Med J (Engl) 2023. https://doi.org/10.1097/CM9.0000000000002637.

[31] Santas E, Palau P, Guazzi M, et al. Usefulness of right ventricular to pulmonary circulation coupling as an indicator of risk for recurrent admissions in heart failure with preserved ejection fraction. Am J Cardiol 2019;124:567–72. https://doi.org/10.1016/j.amjcard.2019.05.024.

[32] Palazzuoli A, Ruocco G, Evangelista I, et al. Prognostic significance of an early echocardiographic evaluation of right ventricular dimension and function in acute heart failure. J Card Fail 2020;26:813–20. https://doi.org/10.1016/j.cardfail.2020.01.002.

[33] Morfino P, Aimo A, Castiglione V, et al. Biomarkers of HFpEF: natriuretic peptides, high-sensitivity troponins and beyond. J Cardiovasc Dev Dis 2022;9:256. https://doi.org/10.3390/jcdd9080256.

[34] Islam MN, Chowdhury MS, Paul GK, et al. Association of diastolic dysfunction with n-terminal pro-b-type natriuretic peptide level in heart failure patients with preserved ejection fraction. Mymensingh Med J 2019;28:333–46.

[35] Dal Canto E, Scheffer M, Kortekaas K, et al. Natriuretic peptide levels and stages of left ventricular dysfunction in heart failure with preserved ejection fraction. Biomedicines 2023;11:867. https://doi.org/10.3390/biomedicines11030867.

[36] Liu G, Long M, Hu X, et al. Meta-analysis of atrial fibrillation and outcomes in patients with heart failure and preserved ejection fraction. Heart Lung Circ 2021;30:698–706. https://doi.org/10.1016/j.hlc.2020.10.010.

[37] De Matteis G, Burzo ML, Serra A, et al. Clinical characteristics and prognostic impact of atrial fibrillation among older patients with heart failure with preserved ejection fraction hospitalized for acute heart failure. Intern Emerg Med 2025;20:95–104. https://doi.org/10.1007/s11739-024-03754-w.

[38] Vijan A, Daha IC, Delcea C, Dan G-A. The complex interplay between right ventricular dysfunction and atrial fibrillation – a narrative review. Rom J Intern Med 2023;61:77–83. https://doi.org/10.2478/rjim-2023-0004.

[39] Nakagawa A, Yasumura Y, Yoshida C, et al. Right Ventricular Dimension for Heart Failure With Preserved Ejection Fraction Involving Right Ventricular-Vascular Uncoupling. CJC Open 2022;4:929–38. https://doi.org/10.1016/j.cjco.2022.07.014.

[40] Nouraei H, Rabkin SW. A new approach to the clinical subclassification of heart failure with preserved ejection fraction. Int J Cardiol 2021;331:138–43. https://doi.org/10.1016/j.ijcard.2021.01.052.

[41] McDonagh TA, Metra M, Adamo M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2023;44:3627–39. https://doi.org/10.1093/eurheartj/ehad195.

[42] Tomasoni D, Adamo M, Porcari A, et al. Right ventricular to pulmonary artery coupling and outcome in patients with cardiac amyloidosis. Eur Heart J Cardiovasc Imaging 2023;24:1405–14. https://doi.org/10.1093/ehjci/jead145.