


## Alteration of Right Ventricular-Pulmonary Arterial Coupling Before and After Decongestion in Non-Preserved Fraction Acute Heart Failure Patients at Adam Malik Hospital Medan

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### ABSTRACT

**Introduction:** Right ventricular-pulmonary arterial (RV-PA) coupling, represented by the ratio of end-systolic elastance ( $E_{es}$ ) to arterial elastance ( $E_a$ ), reflects the RV's contractility and its response to afterload. This study evaluates changes in RV-PA coupling, assessed by tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery systolic pressure (PASP), in acute heart failure (AHF) patients with non-preserved ejection fraction (non-HFpEF) before and after decongestion.

**Methods:** This study is an observational study with a prospective approach and consecutively collected, in patients AHF with non-HFpEF at Adam Malik Hospital Medan in the period from September 2023 until November 2024. The sample is an eligible population that meets the inclusion and exclusion criterias.

**Results:** Forty-four subjects participated, with a majority (75%) being male and an average age of 61. Hypertension was common (63.6%), and most patients had sinus rhythm (75%). Acute decompensated heart failure (ADHF) was the most prevalent phenotype (47.7%). Cardiogenic shock patients had the longest length of stay (median 9 days). Significant decreases in heart rate ( $p = 0.0001$ ), tricuspid valve gradient (TVG) ( $p = 0.0001$ ), and PASP ( $p = 0.0001$ ) were observed. RV-PA coupling significantly increased post-decongestion ( $p = 0.0001$ ), with a significant relationship between RV-PA coupling changes and decongestion ( $p = 0.005$ ).

**Conclusion:** RV-PA coupling showed a significant increase after decongestion in both complete and partial decongestion groups. A cut-off value of 0.65 for RV-PA coupling demonstrated sensitivity of 68.8% and specificity of 67.9%, suggesting its potential as a clinical indicator for decongestion outcomes.

Decongestion, AHF, non-HFpEF, RV-PA coupling

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## INTRODUCTION

Heart failure (HF) is a clinical syndrome characterized by symptoms such as shortness of breath, leg swelling, and fatigue, often accompanied by signs such as elevated jugular venous pressure, pulmonary rales, and peripheral edema.[1] Globally, HF affects approximately 64.34 million individuals, with an estimated incidence of 8.52 cases per 1,000 persons. Cases are categorized as mild (29%), moderate (19%), and severe (51%).<sup>2</sup> In Indonesia, the prevalence of HF based on physician diagnoses was 0.13%, and 0.3% when combining physician diagnoses and symptoms. According to the 2016 non-communicable disease profile, there were 50,010 HF-related hospitalizations in Indonesia, comprising 25,508 male and 24,507 female patients.[3,4]

Acute heart failure (AHF) is defined as the rapid or gradual onset of HF symptoms and/or signs that are severe enough to require immediate medical attention. This condition can either be the first manifestation of HF (new-onset) or, more commonly, the result of acute decompensation of chronic HF.[1] The right ventricle (RV) and left ventricle (LV) are closely related through shared myocardial fibers, a common septal wall, and the surrounding pericardium.[5] Given the increasing recognition of RV function in HF prognosis, the National Heart, Lung, and Blood Institute established a working group to explore the cellular and molecular mechanisms of right heart failure (RHF).[5]

RV-PA coupling, defined as the ratio of end-systolic elastance ( $E_{es}$ ) to arterial elastance ( $E_a$ ), reflects the intrinsic contractility of the RV and its response to afterload, which is represented by pulmonary arterial elastance.[6] The prevalence of right ventricular dysfunction (RVD) in HF patients with reduced ejection fraction (HFrEF) varies across populations but is universally linked to increased mortality. A meta-analysis conducted in Spain involving 2,234 HFrEF patients reported a prevalence of RVD of 48%.[7]

Right heart catheterization (RHC) is the gold standard for assessing RV-PA coupling through the  $E_{es}/E_a$  ratio. However, its invasiveness, high cost, and limited accessibility make its routine use challenging. Echocardiographic measures, such as the tricuspid annular plane systolic excursion/pulmonary artery systolic pressure (TAPSE/PASP) ratio, have shown good correlation with invasive methods and provide a non-invasive alternative for RV-PA coupling assessment.[6,7]

Studies have highlighted the prognostic significance of RV-PA coupling. A cohort study involving 466 HFrEF patients demonstrated a strong association between ventricular-arterial coupling ( $E_a/E_{es}$ ) and New York Heart Association (NYHA) functional class, natriuretic peptide levels, and poor clinical outcomes.[8] Another study in Rochester, USA, involving 4,529 patients hospitalized in cardiovascular intensive care units (CICU) reported that the TAPSE/right ventricular systolic pressure (TAPSE/RVSP) ratio was inversely associated with in-hospital mortality and one-year post-discharge mortality.[9]

Complications such as pulmonary hypertension (PH) in AHF can lead to RVD, characterized by reduced RV  $E_{es}/E_a$  and RV dilation, which compromises stroke volume and RV ejection fraction. TAPSE/PASP, measured via Doppler echocardiography, serves as an independent echocardiographic predictor in PH patients.<sup>6</sup> A retrospective study in Korea involving 1,147 patients found a significant correlation between RV-PA coupling and left ventricular diastolic function and left atrial function.[10] Additionally, research in Spain involving 1,948 patients from 2007 to 2020 demonstrated that an RV-PA coupling ratio of less than 0.36, combined with significant functional tricuspid regurgitation, was associated with higher hospitalization rates and recurrent cardiovascular events in acute HF patients.[11]

A study by Hullin et al. (2022) showed that improvements in RV-PA coupling following decongestion therapy in AHF patients with reduced ejection fraction were associated with enhanced global longitudinal strain (GLS) as measured by transthoracic echocardiography (TTE).[12] Therefore, this study aims to investigate the changes in RV-PA coupling before and after decongestion therapy in AHF patients with non-heart failure with preserved ejection fraction (non-HFpEF) at Adam Malik Hospital, Medan.

## METHOD

This study employed an observational design with a retrospective approach involving patients with acute heart failure (AHF) and non-heart failure with preserved ejection fraction (non-HFpEF) at Adam Malik Hospital, Medan. The investigation was conducted at the Integrated Cardiac Center of Adam Malik Hospital, Medan, from September 2023 to November 2024. The target population comprised patients with AHF and non-HFpEF. The accessible population included patients meeting the inclusion and exclusion criteria at Adam Malik Hospital, Medan. The sample was selected consecutively, including all eligible subjects until the required sample size was achieved.

This study utilised an observational design with a retrospective approach involving patients diagnosed with acute heart failure (AHF) and non-heart failure with preserved ejection fraction (non-HFpEF) at Adam Malik Hospital, Medan. The investigation was conducted at the Integrated Cardiac Center of Adam Malik Hospital from September 2023 to November 2024. The study population included patients diagnosed with

AHF and non-HFpEF, with the sample collected consecutively until the required sample size of 35 participants was achieved. The sample size was calculated using the paired categorical-numerical analytic test formula, ensuring sufficient statistical power to detect significant changes in the variables of interest.

Participants were included if they were aged over 18 years, diagnosed with non-HFpEF, and underwent transthoracic echocardiography (TTE) within  $\leq 4$  hours of emergency admission, with results showing an ejection fraction (EF) of  $\leq 50\%$ . Additionally, TTE was required at discharge after decongestion therapy. Patients were excluded if they had congenital heart disease, significant valve stenosis, RV outflow tract obstruction, pulmonary hypertension (PH) due to other aetiologies, or pregnancy. Other exclusion criteria included acute pulmonary embolism, incomplete TTE data, prior high-dose diuretic or nitroglycerin therapy before TTE, or loss to follow-up due to discharge against medical advice or in-hospital mortality.

Acute heart failure (AHF) was defined as the rapid or gradual onset of symptoms or signs necessitating urgent medical intervention, either as an initial manifestation or due to decompensation of chronic HF. Right ventricular-pulmonary artery (RV-PA) coupling was assessed as the ratio of tricuspid annular plane systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP), measured via transthoracic echocardiography (TTE). Decongestion status was classified as complete when TTE demonstrated no elevated left ventricular filling pressure and an Everest score of  $\leq 2$ , or partial when TTE indicated reduced filling pressure and clinical improvement.

Ethical approval for the study was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara. Written informed consent was procured from all participants. Data collection encompassed recording demographic information, clinical history, and echocardiographic findings. The collected data were analysed using SPSS version 25, with statistical tests conducted to evaluate significant changes in RV-PA coupling before and after decongestion therapy.

Statistical analysis and data processing were performed using SPSS software. Numerical variables were presented as mean  $\pm$  standard deviation (SD) for data with a normal distribution. For non-normally distributed data, numerical variables were presented as median and interquartile range (IQR). The normality of the data for all research subjects was assessed using the Kolmogorov-Smirnov test if the sample size exceeded 50, or the Shapiro-Wilk test for a sample size of less than 50. For paired data analysis, if the data were normally distributed, a paired t-test was employed. If the data did not meet the criteria for normal distribution, the Wilcoxon signed-rank test was utilised instead. Statistical significance was determined at a p-value threshold of less than 0.05, indicating meaningful differences or associations within the study variables.

This research adheres to ethical standards and received approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara. All procedures involving human participants were conducted in accordance with ethical guidelines, and informed consent was obtained from all study participants prior to their involvement.

## RESULTS

### Baseline Characteristics

This study included 44 patients with acute heart failure (AHF) and non-preserved ejection fraction (non-HFpEF) at Adam Malik Hospital, Medan. Among the subjects, 75% (n=33) were male, and 25% (n=11) were female, with a mean age of  $61.59 \pm 10.18$  years. The majority of patients presented with comorbidities, including hypertension (63.6%, n=28), diabetes mellitus (45.5%, n=20), and active smoking habits (29.5%, n=13). Dyslipidemia was reported in only 4.5% (n=2), while 13.6% (n=6) were classified as having de novo AHF. Most patients (75%, n=33) exhibited sinus rhythm, while atrial fibrillation was observed in 13.6% (n=6), and one patient had permanent ventricular pacing (PPM V-Pacing).

Echocardiographic findings revealed a mean TAPSE of  $16.45 \pm 3.55$  mm and a median PASP of 44.76 mmHg. The TAPSE/PASP ratio at admission was 0.365. Table 1 summarizes the baseline characteristics of the study population.

Table 1. Baseline Characteristics of Patients

Parameter	Value
Male (%)	75 (n=33)
Female (%)	25 (n=11)
Mean age (years)	61.59 ± 10.18
Hypertension (%)	63.6 (n=28)
Diabetes Mellitus (%)	45.5 (n=20)
Active Smoking (%)	29.5 (n=13)
Dyslipidemia (%)	4.5 (n=2)
Sinus Rhythm (%)	75 (n=33)
Atrial Fibrillation (%)	13.6 (n=6)
PPM V-Pacing (%)	2.3 (n=1)
Heart rate (bpm)	100.5 (range: 60–210)
TAPSE (mm)	16.45 ± 3.55
PASP (mmHg)	44.76 ± 12.66
TAPSE/PASP ratio	0.365 (range: 0.17–0.82)

Table 2. summarizes the supporting laboratory parameters of the study population.

Parameter	Value
Hb (g/L)	12.91 ± 2.57
Leucocytes (g/L)	12,197.93 ± 5,420.47
Thrombosis (g/L)	243,977.27 ± 8,6615.02
Sodium (mmol/L)	142 (124–152)
Potassium (mmol/L)	4 (3–6)
Creatinine (mg/dL)	2 (1–8)

### Phenotypes of Acute Heart Failure and Length of Hospital Stay

Patients were classified into three phenotypes of AHF, ADHF (47.7%, n=21), cardiogenic shock (25%, n=11), and acute pulmonary edema (ALO) (27.3%, n=12). Median hospital stay was longest for cardiogenic shock (9 days), followed by ALO (8 days) and ADHF (5 days). These findings are presented in Table 3.

Table 3. AHF Phenotypes and Length of Stay

Phenotype	Number (%)	Median Length of Stay (days)
ADHF	47.7 (n=21)	5 (range: 4–13)
Cardiogenic Shock	25 (n=11)	9 (range: 7–20)
ALO	27.3 (n=12)	8 (range: 6–14)

Table 4. Changes in Parameters from Admission to Discharge

Parameter	Admission	Discharge	p-value
Heart Rate (bpm)	100.5 (range: 60–210)	75.5 (range: 58–95)	<0.0001
TVG (mmHg)	31.36 ± 11.61	14.59 ± 14.17	<0.0001
PASP (mmHg)	44.77 ± 12.72	21.75 ± 15.32	<0.0001
TAPSE/PASP ratio	0.365 (range: 0.17–0.82)	0.96 (range: 0.11–4.03)	<0.0001
Ejection Fraction (%)	29.66 ± 10.01	30.27 ± 10.14	0.681
LVEDD (mm)	57 (range: 42–66)	54 (range: 33–78)	0.618
TAPSE (mm)	16.45 ± 3.53	17.43 ± 5.15	0.143

### Changes in Parameters from Admission to Discharge

Significant improvements were observed in key clinical and echocardiographic parameters from admission to discharge. Heart rate decreased significantly from 100.5 bpm to 75.5 bpm ( $p < 0.0001$ ). PASP and TAPSE/PASP ratio also improved significantly during hospitalization (Table 4).

**Correlation Between TAPSE/PASP Ratio Changes and Length of Stay**

The relationship between changes in the TAPSE/PASP ratio and the length of hospital stay was analyzed using Pearson correlation. No significant correlation was found between these variables ( $p = 0.829$ ,  $r = 0.033$ ). The results are shown in Table 5, and the scatter plot illustrating this relationship is presented in Figure 4.

Table 5. Correlation Between TAPSE/PASP Ratio Changes and Length of Stay

Variable	p-value	r
TAPSE/PASP Ratio Change	0.829	0.033

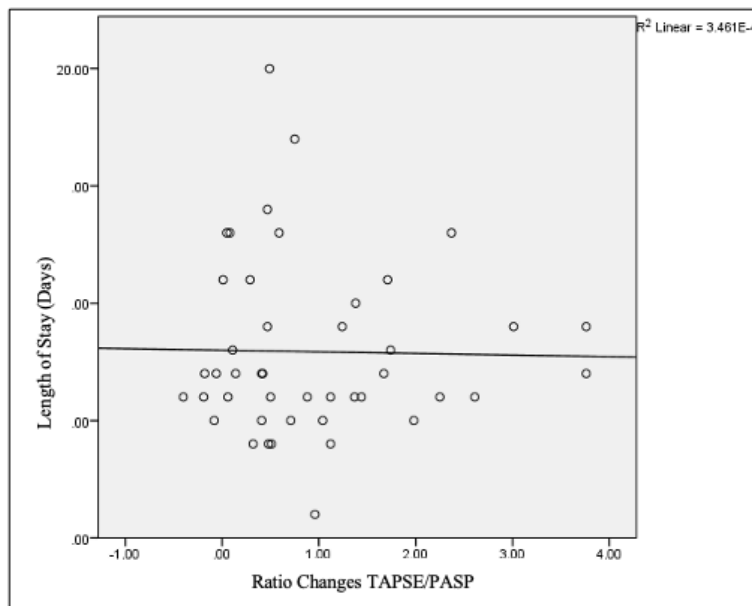


Figure 4. Scatter Plot of TAPSE/PASP Ratio Changes vs. Length of Stay

**Relationship Between TAPSE/PASP Ratio Changes and Decongestion in Acute Heart Failure**

The relationship between TAPSE/PASP ratio changes and acute heart failure phenotypes was evaluated using the Kruskal-Wallis’s test. No significant differences were found among the phenotypes ( $p = 0.497$ ). These results are presented in Table 6.

Table 6. TAPSE/PASP Ratio Changes by Acute Heart Failure Phenotype

Variable	Cardiogenic Shock	ADHF	ALO	p-value
TAPSE/PASP Ratio Change (n)	0.75 (0.08–3.76)	0.475 (-0.18–3.76)	0.51 (-0.4–2.61)	0.497

**TAPSE/PASP Ratio Changes and Decongestion**

A significant relationship was found between TAPSE/PASP ratio changes and the degree of decongestion ( $p = 0.005$ ). Patients with complete decongestion exhibited higher median TAPSE/PASP ratio changes (1.31 mmHg) compared to those with partial decongestion (0.445 mmHg). The results are summarized in Table 7.

Table 7. TAPSE/PASP Ratio Changes by Decongestion Status

Variable	Complete Decongestion	Partial Decongestion	p-value
TAPSE/PASP Ratio Change (mmHg)	1.31 (0.14–3.76)	0.445 (-0.20–3.76)	0.005

The Receiver Operating Characteristic (ROC) analysis for TAPSE/PASP ratio changes predicting complete decongestion showed an area under the curve (AUC) of 0.754 ( $p = 0.005$ ), indicating moderate

predictive accuracy. The sensitivity and specificity for predicting complete decongestion were 68.8% and 67.9%, respectively. These findings are illustrated in **Figure 6**

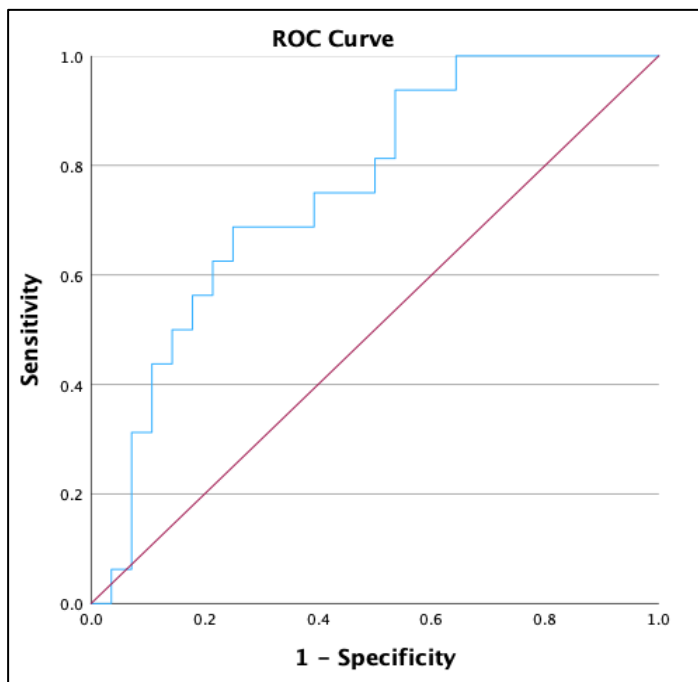


Figure 6. ROC Analysis of TAPSE/PASP Ratio Changes Predicting Complete Decongestion

The cut-off value for predicting complete decongestion was determined to be 0.652, with a sensitivity of 68.8% and specificity of 67.9%. This threshold is depicted in **Figure 7**.

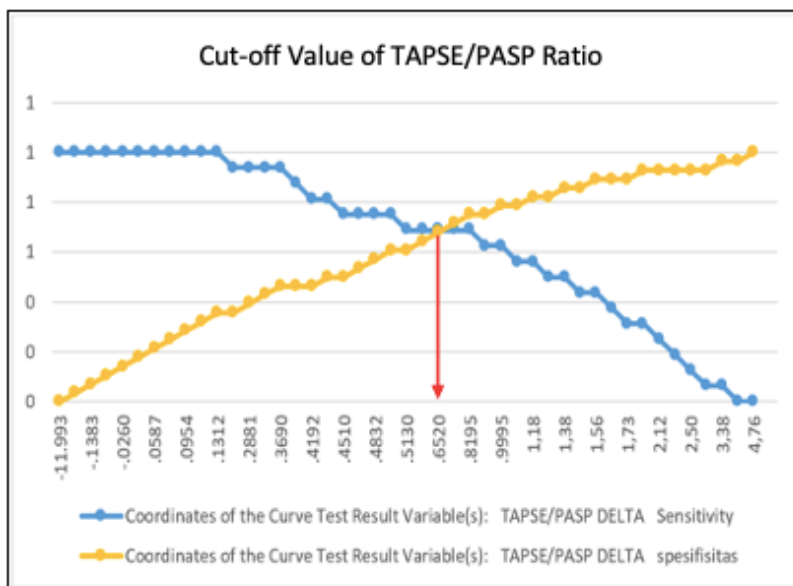


Figure 7. Cut-off Value of TAPSE/PASP Ratio Changes for Predicting Complete Decongestion

**DISCUSSION**

In this study, most patients were male (75%, n=37) with a median age of 61 years. This finding contrasts with the 2021 ESC guidelines on heart failure diagnosis and treatment, which reported a higher prevalence of heart failure among females across all types and an increasing prevalence with age, from approximately 1% in individuals under 55 years to more than 10% in those over 70 years. Hullin et al. (2022) similarly reported a higher prevalence of male patients, with a median age of 83 years in all acute heart failure (AHF) groups.

Hypertension was the most prevalent comorbidity, affecting 63.6% of patients, aligning with the ESC 2021 guidelines, which cited hypertension in nearly two-thirds of heart failure cases. Hullin et al. (2022) also identified hypertension as the predominant comorbidity, affecting 81% of patients. Right ventricular dysfunction in heart failure was noted in the ESC 2021 guidelines as diagnosable through transthoracic echocardiographic parameters such as TAPSE, fractional area change (FAC), or tissue Doppler-derived systolic S' velocity. This study similarly observed reduced TAPSE values, with a mean of 16.45, consistent with Hullin et al.'s findings of an average TAPSE of 15 at admission across all AHF groups.[13,14]

Laboratory findings revealed elevated leukocyte and creatinine levels, alongside haemoglobin levels that were within the low-normal range. These findings contrast with Hullin et al. (2022), where patients with heart failure with reduced ejection fraction (HFrEF) had higher haemoglobin levels and lower leukocyte counts than those with mildly reduced ejection fraction (HFmrEF), with only haemoglobin differences being statistically significant ( $p < 0.05$ ).

Among AHF phenotypes, acute decompensated heart failure (ADHF) was the most prevalent, followed by cardiogenic shock, which exhibited the longest hospital stay. Previous studies, including Hullin et al. (2022), found no significant differences in length of stay among AHF phenotypes, though left heart failure was the most common type reported. The absence of a significant correlation between TAPSE/PASP changes and length of stay in this study ( $p = 0.829$ ) may reflect the influence of other clinical factors, such as the severity of congestion and response to decongestion therapy.

Significant improvements were observed in several parameters from admission to discharge, including heart rate, tricuspid valve gradient (TVG), E/e' ratio, PASP, and the TAPSE/PASP ratio. While TAPSE, LVEDD, and ejection fraction improved at discharge compared to admission, these changes were not statistically significant. The reduction in heart rate from admission to discharge was significant and consistent with findings from Hullin et al. (2022). Vollmert et al. (2020) reported that a reduction in heart rate was associated with lower mortality in HF patients, with heart rates  $\geq 77$  bpm linked to nearly double the mortality risk compared to rates below 77 bpm. The significant changes in TVG and PASP observed in this study align with prior findings by Hullin et al. (2022), which attributed these improvements to effective decongestion therapy. Mutlak et al. (2018) also highlighted the association between tricuspid valve regurgitation severity and right ventricular function, with significant tricuspid regurgitation being linked to pulmonary hypertension and RV dysfunction. However, RV dysfunction alone was not identified as a risk factor for heart failure readmission or mortality.

The improvement in RV-PA coupling was significant in patients with complete or partial decongestion. While no significant association was found between RV-PA coupling changes and AHF phenotypes, the coupling demonstrated moderate accuracy in predicting complete decongestion (sensitivity: 68.8%, specificity: 67.9%), with a cut-off value of 0.65. Hullin et al. (2022) similarly reported improvements in TAPSE/PASP associated with reduced rehospitalisation and mortality ( $p = 0.02$ ). Bok et al. (2023) identified a lower TAPSE/PASP cut-off of 0.33, associating lower values with worse outcomes in AHF patients. Palazzuoli et al. (2023) further emphasised the prognostic value of RV-PA coupling in both HFrEF and HFmrEF populations, linking TAPSE/PASP values below 0.49 with poor clinical outcomes within 180 days. Theoretical explanations suggest that reduced left atrial elasticity, diastolic dysfunction, and increased pulmonary artery pressures contribute to RV decompensation.

The observed improvements in RV-PA coupling, heart rate, TVG, and PASP demonstrate the efficacy of decongestion in restoring RV function. However, patients with incomplete decongestion did not experience similar improvements, emphasising the necessity for individualised treatment approaches. In conclusion, this study underscores the clinical utility of RV-PA coupling, particularly TAPSE/PASP, as a non-invasive marker for evaluating decongestion in AHF patients with non-HFpEF. Future research should focus on validating these findings in larger, multi-centre cohorts and incorporating TAPSE/PASP into routine clinical practice to enhance heart failure management.

## CONCLUSION

This study concluded that significant improvements in RV-PA coupling were observed in AHF patients with non-HFpEF following decongestion therapy, particularly in those achieving complete decongestion. The majority of patients were male, with a median age of 61 years, and hypertension as the most common comorbidity. Significant reductions in heart rate, E/e', TVG, and PASP were noted from admission to discharge, although no significant association was found between RV-PA coupling changes and hospital length of stay or AHF phenotypes. The identified TAPSE/PASP cut-off value of 0.65 demonstrated moderate predictive accuracy for successful decongestion, highlighting its potential utility as a non-invasive marker for guiding heart failure management.

## DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara / Adam Malik General Hospital Medan.

## CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

## FUNDING

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## COMPETING INTERESTS

The authors declare that there is no conflict of interest in this report.

## AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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