

ORIGINAL RESEARCH ARTICLE

Proportional pulse pressure as a non-invasive predictor of cardiac index in heart failure with reduced ejection fraction: A pilot study

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Abstract

The primary objective of this pilot study is to examine the correlation between proportional pulse pressure (PPP) and cardiac index (CI) in patients with reduced ejection fraction (HFrEF) heart failure, and to assess the usability of PPP as a non-invasive, practical biomarker for predicting hemodynamic profiles. We enrolled 100 patients with HFrEF (EF $\leq$ 40%) from our cardiology clinic. Blood pressure was measured manually using a mercury sphygmomanometer, and CI was assessed via transthoracic echocardiography. Patients were stratified by CI (<2.2 L/min/m² vs. ≥ 2.2 L/min/m²), and PPP was calculated as pulse pressure divided by systolic blood pressure. The mean age was 67 years (77% male). PPP values were significantly diminished among patients with low CI ($p < 0.001$), while correlation analysis indicated a strong positive relationship between PPP and CI ($r = 0.584$, $p < 0.001$). A PPP threshold of $\geq 25.85\%$ identified CI ≥ 2.2 L/min/m² with 84% sensitivity and 89.2% specificity. PPP, readily derived from routine blood pressure measurements, strongly correlates with CI in patients with HFrEF. It can serve as a non-invasive hemodynamic assessment modality in primary care settings or healthcare facilities with limited resources where echocardiography is unavailable.

Keywords: Pulse pressure; Heart failure; Proportional pulse pressure; Cardiac index

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1. Introduction

Heart failure (HF), affecting over 20 million individuals globally, continues to be a health problem with increasing incidence. While its prevalence in the adult population is around 1–3% in high-income countries, this rate exceeds 10% among individuals aged 70 and over.¹ At least half of cases with HF, which has a multifactorial etiology, present with a decreased ejection fraction (HFrEF) phenotype. In this context, coronary artery disease (CAD) underlies approximately two-thirds of systolic HF cases. Before the 1990s, the five-year mortality rate was around 60–70%, and hospital admissions for HF often occurred in frequent and recurrent epidemics in many countries. In recent years, effective treatments have led to reductions in mortality and hospitalization rates.^{2–4} There are many invasive and non-invasive methods for determining cardiac index (CI) and cardiac output (CO). Transthoracic echocardiography (TTE) is the

preferred method due to its ease of use, widespread accessibility, and cost-effectiveness. These parameters, such as pulse pressure (PP) and proportional PP (PPP), obtained from non-invasive blood pressure (BP) data, can be complementary or alternative to TTE in predicting a patient's hemodynamic performance. PPP is a variable obtained by dividing PP by systolic BP (SBP). The 2021 European Society of Cardiology guidelines emphasize the critical importance of hemodynamic monitoring for determining treatment strategies in the management of HFrEF. Advanced diagnostic tools, such as TTE, which are expensive and technologically advanced, may not always be available in primary care facilities or centers with limited medical resources.⁵ PPP obtained from routine BP measurements is a simple, non-invasive option for estimating CI. Although there are studies in the literature examining the relationship between PPP and invasive CI measurements⁶, this pilot study is the first to investigate the interaction between echocardiographic CI and PPP in HFrEF cases; in this respect, it can address an important gap in the hemodynamic assessment process in outpatient settings. Indeed, Stevenson *et al.*⁶ documented a strong correlation between PPP and CI in patients with advanced chronic HF. On the other hand, data on the prognostic significance of PP changes in the chronic HF population are still limited in the literature. Research has revealed a substantial correlation between low PP and mortality in patients hospitalized due to decompensated chronic HF.^{7,8} The reduction in PP in this patient group is likely associated with cardiac dysfunction and, consequently, with mortality.⁹ A relationship has also been identified between cardiovascular morbidity and PP, which is influenced by factors including arterial elasticity, ventricular ejection fraction, and heart rate.¹⁰ In patients with left ventricular systolic dysfunction, decreased PP has been closely linked to adverse clinical outcomes.¹¹ Low PP was associated with increased mortality in patients hospitalized with cardiac failure, regardless of ejection fraction.¹² Interestingly, preserved PP in the context of severe decompensated systolic HF has been found to indicate preserved contractile reserve and a favorable prognosis.¹³ In patients with severe HF, the PPP value, which can be calculated from physical examination findings in outpatient settings, may provide valuable insights into the patient's hemodynamic status, tissue perfusion adequacy, and aid in treatment management decisions. In a prospective study conducted by Mercado and colleagues¹⁴, CO measurements were performed in mechanically ventilated patients in the intensive care unit using non-invasive TTE and an invasive method called pulmonary artery catheterization. In the comparison made, they showed that TTE yielded results

as precise and accurate as invasive pulmonary artery catheterization.¹⁴ In a prospective study conducted by Torchz and colleagues¹⁵, CO measurements obtained via pulmonary artery catheterization and TTE were found to be significantly correlated (Pearson correlation coefficients ranging from 0.57 to 0.64) and demonstrated a moderate level of agreement (intraclass correlation coefficient: 0.66–0.70).

Some studies, mainly involving critically ill intensive care patients, demonstrated that echocardiographic findings were highly consistent with invasive hemodynamic monitoring data and that no significant differences were observed between the two groups.^{14,15} These data suggest that TTE is a reliable and valid modality for assessing cardiac hemodynamics. Indeed, current clinical guidelines also recommend echocardiography as a first-line approach for determining hemodynamic status, especially in critical cases.^{16,17} Based on current evidence, CI measurements were obtained using echocardiographic methods in this study. In the pathophysiology of HF, CI levels below the threshold of 2.2 L/min/m² are considered a major indicator that CO cannot meet systemic needs and that inadequate tissue perfusion is developing. This condition serves as an indication for initiating inotropic and/or vasodilator therapies aimed at improving tissue perfusion and is associated with poor prognosis in HF patients.¹⁸ Demonstrating the association between low CI values and reduced PP and PPP in HF patients has inspired studies investigating the relationship between these physical examination findings and patient prognosis. This study aims to investigate the relationships among CI, PP, and PPP in HF patients with reduced EF. Thus, in this study, we investigated the diagnostic power and clinical correlation of BP data obtained with a simple sphygmomanometer during physical examination in predicting cardiac hemodynamic status in HFrEF cases.

2. Materials and methods

2.1. Methods

This prospective study was conducted at the Department of Cardiology, Necmettin Erbakan University Meram Faculty of Medicine, following approval from the local ethics committee on December 1, 2017 (Approval No. 2017/1095). All study procedures were conducted in accordance with the updated Declaration of Helsinki and internationally accepted Good Clinical Practice standards. As a pilot study, no formal sample size calculation was performed; however, the sample size was deemed sufficient to detect significant correlations based on prior studies.⁶ However, the relatively small sample size may limit the generalizability of the findings.

2.2. Patient data

Between December 2, 2017, and April 10, 2018, a total of 220 patients previously diagnosed with HF with an EF $\leq$ 40% who consented to participate were included in the study. These patients were either outpatients presenting to our center or inpatients in the cardiology unit.

In this prospective pilot study, although 220 patients were enrolled within the specified time frame, 120 were excluded per the exclusion criteria. The reasons for exclusion included: atrial fibrillation in 55 patients; significant valvular pathology in 35 patients; prosthetic valve disease in 10 patients; operator variability in echocardiographically measured CO exceeding 5% in 10 patients; insufficient echocardiographic image quality in seven patients; and the presence of a pacemaker in three patients. Atrial fibrillation was excluded because it can introduce significant beat-to-beat variability in BP measurements, which could confound the accuracy of PPP calculations, as demonstrated in prior studies.¹⁹ This ensured the reliability of our hemodynamic assessments. All study participants underwent detailed evaluation for body surface area, age, gender, height, weight, diastolic BP, PP, SBP, PPP, heart rate, comorbidities (diabetes mellitus, hypertension, hyperlipidemia, atrial fibrillation, smoking, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular event), medications used (beta-blockers, acetylsalicylic acid, P2Y12 inhibitors, statins, oral anticoagulants, angiotensin-II receptor blockers or angiotensin-converting enzyme inhibitor, digitalis, aldosterone antagonists, nitrates, calcium channel blockers, diuretics), presence of dyspnea, peripheral edema, and rales, as well as physical examination findings and New York Heart Association (NYHA) classification.

Using TTE, the following parameters were assessed: Simpson-derived end-systolic volume, end-diastolic volume, left ventricular outflow tract (LVOT) diameter, ejection fraction, tissue Doppler-derived lateral isovolumetric contraction time, CO, myocardial performance index, LVOT velocity-time integral, ejection time, isovolumetric relaxation time, septal myocardial performance index, right ventricular myocardial performance index, tricuspid A velocity, tricuspid E velocity, systolic pulmonary artery pressure, mitral A velocity, and mitral E velocity.^{20,21}

The patients were divided into two groups based on CI: <2.2 L/min/m² and ≥ 2.2 L/min/m², and the groups were compared in terms of the aforementioned parameters. Patients with significant valvular pathology (stenosis or regurgitation), prosthetic valve disease, pacemaker presence, atrial fibrillation, insufficient echocardiographic image quality, or inter-operator variability exceeding 5% in

echocardiographically measured CO were excluded from the study cohort.

Patients who consented to participate were evaluated for demographic characteristics, comorbidities, medications used, and physical examination findings; their echocardiographic parameters were recorded.

2.3. Blood pressure measurement and cardiac output determination

Blood pressure of the patients was measured manually using a calibrated Erka mercury sphygmomanometer (Kallmeyer Medizintechnik GmbH & Co. KG, Germany). A mercury sphygmomanometer was preferred due to its proven accuracy and reliability in clinical settings.²² In this way, we minimized the variability of BP measurements. BP measurements were taken after patients rested in a chair for five minutes. Care was taken to ensure that the arm being measured was bare, that the patient remained silent and avoided crossing their legs, and that the cuff was wrapped around the arm at heart level with proper support. To ensure accurate results, the BP device's cuff size was selected to fit the patient's arm. Patients were instructed to abstain from smoking, tea or coffee consumption, and caffeine intake, and to avoid eating for 30 minutes prior to the measurement. Due to significant BP variability, six BP measurements were taken by two experienced doctors at five-minute intervals (three measurements from the right brachial artery and three from the left). If there was more than a 5% variation in measurements, they were excluded. The arithmetic mean of these six measurements was calculated to assess diastolic and SBP. From these routinely measured parameters, PP was calculated as SBP-DBP. PPP was derived using the formula: $PP \div SBP$.

2.4. Echocardiographic evaluation

All patients included in the study underwent TTE in the left lateral decubitus position using the Philips Epiq 7C ultrasound system (Bothell, United States) with a 5–1 MHz transducer. Echocardiographic measurements were performed by two experienced cardiologists who were blinded to the patients' demographic and clinical characteristics. If the inter-operator variability in echocardiographically measured CO exceeded 5%, the patient was excluded from the study. If the variability was less than 5%, the arithmetic mean of the two values was used. Measurements were performed in accordance with standard techniques and imaging protocols outlined in the American Society of Echocardiography guidelines. Apical two-chamber, apical four-chamber, apical long-axis views, parasternal short-axis, and parasternal long-axis views were obtained.

The LVOT velocity–time integral calculated from the apical long axis, using the LVOT diameter measured from the parasternal long axis, and heart rate, CO was determined using Equation 1²³:

$$\text{CO} = \text{Heart rate} \times \pi \times (\text{LVOT diameter}/2)^2 \times \text{LVOT VTI} \quad (1)$$

Cardiac index was determined as $\text{CI} = \text{CO}/\text{body surface area}$. In echocardiographic evaluation, ventricular volumes (end-diastolic volume, end-systolic volume) and ejection fraction measurements were performed from apical four-chamber windows based on the modified Simpson technique.²⁴ The pulsed wave Doppler technique was preferred for mitral inflow measurements; the measurement point was located 1 cm distal to the mitral leaflet tips. Deceleration time, late-diastolic wave, and early-diastolic wave were measured over 5–10 cardiac cycles, and their averages were calculated.²⁵

2.5. Statistical analysis

The data of the patients included in the study were analyzed using the Statistical Package for Social Sciences 22.0 program. The normality of distribution and homogeneity of variance of the demographic, clinical, and ultrasonographic data in the study groups were evaluated using the Shapiro–Wilk test. Data with normal distribution were presented as mean $\pm$ standard deviation, whereas data without normal distribution were presented as median and interquartile range. We compared groups using the Chi-square test. We presented categorical data

using frequencies and percentages. In the analysis of continuous variables, we used the independent-samples *t*-test for normally distributed data. For data that did not meet the parametric assumptions, we used the Mann–Whitney *U* test. Correlational relationships between variables were analyzed using Pearson or Spearman analyses, depending on the data distribution. To assess the diagnostic performance of PP and PPP parameters for predicting $\text{CI} \geq 2.2 \text{ L/min/m}^2$, we performed receiver operating characteristic (ROC) curve analysis to identify optimal cut-off values, sensitivity, and specificity. All analyses were performed at a 95% confidence level ($p < 0.05$).

3. Results

The study population consisted of 100 HFrEF patients with a mean age of 67 years; 77% of whom were male. Patients were divided into two groups based on hemodynamic assessment: those with a low CI ($< 2.2 \text{ L/min/m}^2$, $n = 75$) and those with a preserved CI ($\geq 2.2 \text{ L/min/m}^2$, $n = 25$). Comparison of the basic demographic and clinical profiles of these groups is summarized in Table 1. According to correlation analyses, a significant difference was observed in PP and PPP between groups with $\text{CI} < 2.2 \text{ L/min/m}^2$ and $\text{CI} \geq 2.2 \text{ L/min/m}^2$ ($p < 0.001$) (Figures 1 and 2). No significant correlation was found between PPP and body surface area or resting heart rate. For PPP, significant positive correlations were found between age ($r = 0.204$, $p = 0.043$), SBP ($r = 0.432$, $p < 0.001$), and CO ($r = 0.557$, $p < 0.001$). A strong positive correlation was found between PPP and CI ($r = 0.584$, $p < 0.001$) (Figure 3). In contrast,

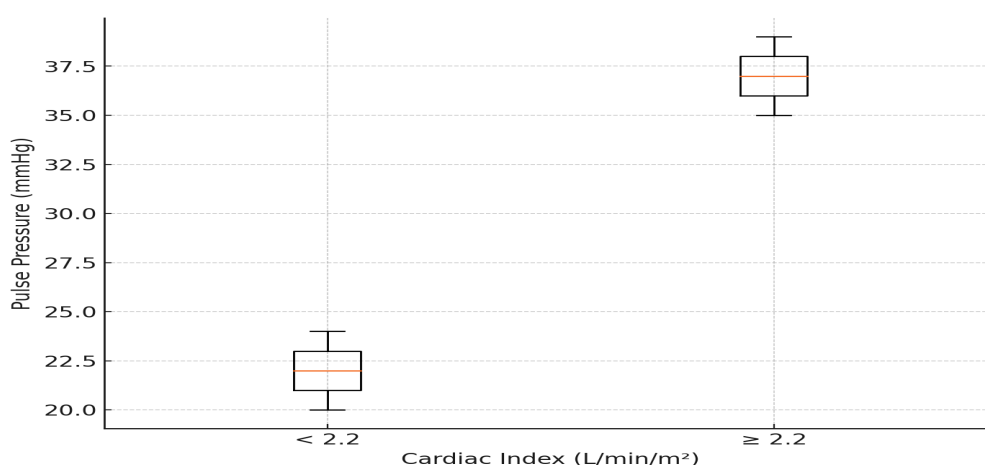


Figure 1. Comparison of pulse pressure by cardiac index groups. Box plot comparing pulse pressure (mmHg) between cardiac index groups ($< 2.2 \text{ L/min/m}^2$ and $\geq 2.2 \text{ L/min/m}^2$). A statistically significant difference was observed ($p < 0.001$).

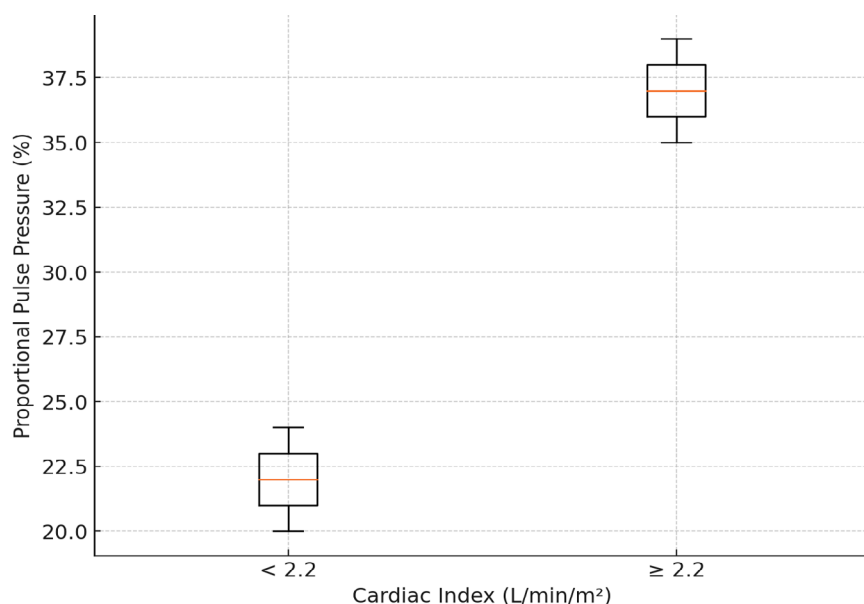


Figure 2. Comparison of proportional pulse pressure (PPP; %) by cardiac index groups. Box plot illustrating the comparison of PPP between cardiac index (CI) groups (<2.2 L/min/m² and ≥ 2.2 L/min/m²). The plot demonstrates a significant difference in PPP between the two groups.

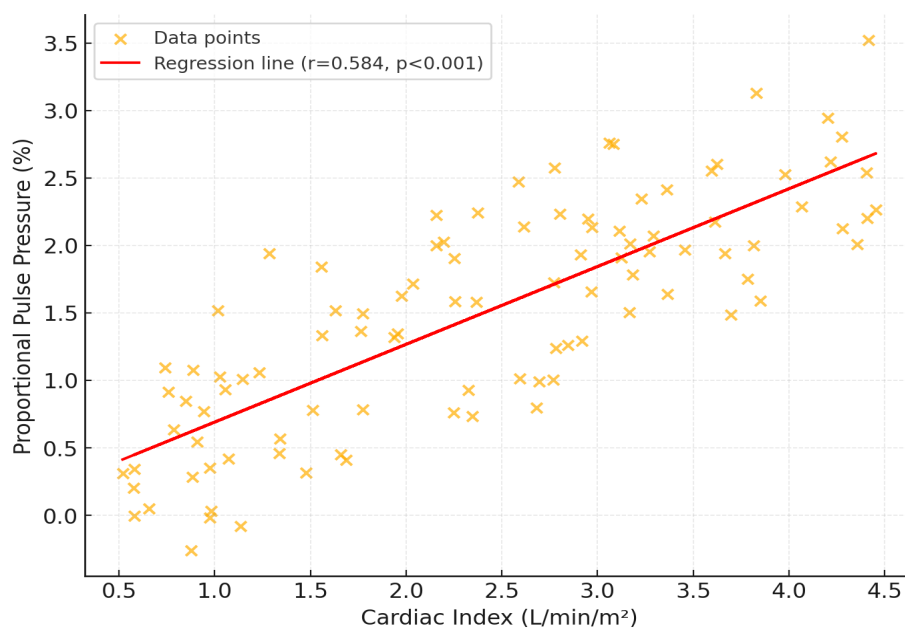


Figure 3. Correlation between proportional pulse pressure and cardiac index. This scatter plot illustrates the significant positive correlation between proportional pulse pressure (%) and cardiac index (L/min/m²). The regression line ($r = 0.584$, $p < 0.001$) demonstrates the trend of the relationship, where higher proportional pulse pressure values are associated with higher cardiac index values.

Table 1. Baseline demographic and clinical characteristics of the study group ($n = 100$)

Parameters	Study group ($n = 100$)	Cardiac index < 2.2 L/min/ m^2 ($n = 75$)	Cardiac index ≥ 2.2 L/min/ m^2 ($n = 25$)	p -value
Age (years)	67 (15)	67 (16)	63 (14)	0.456
Gender: Male, n (%)	77 (77)	57 (76)	20 (80)	0.789
Body surface area(m^2)	1.87 (0.19)	1.88 (0.21)	1.86 (0.17)	0.177
Heart rate (bpm)	73 (15)	70 (18)	80 (22)	0.049*
Systolic BP (mmHg)	107 (9)	107 (9)	108 (16)	0.291
Diastolic BP (mmHg), median (IQR)	82 (9)	83 (5)	72 (11)	<0.001*
Mean BP (mmHg)	90 (7)	92 (7)	86 (11)	0.002*
Pulse pressure (mmHg), median (IQR)	22.50 (10)	22 (3)	37 (10)	<0.001*
Proportional pulse pressure (%)	20.80 (9.90)	20.20 (3.20)	33 (7.60)	<0.001*
PPP $\geq 25\%$, n (%)	29 (29)	8 (10.7)	21 (84)	<0.001*
Cardiac output (L/min), median (IQR)	2.96 (1.81)	2.75 (0.92)	5.12 (1.11)	<0.001*
Heart failure etiology: ischemic, n (%)	88 (88)	68 (90.7)	20 (80)	0.169
Symptoms, n (%)				
Pretibial edema	67 (67)	53 (70.7)	14 (56)	0.221
Rales	39 (39)	29 (38.7)	10 (40)	1.000
Dyspnea	92 (92)	69 (92)	23 (92)	1.000
NYHA functional class,				
Class 1	15 (15)	10 (13.3)	5 (20)	0.259
Class 2	62 (62)	46 (61.3)	16 (64)	
Class 3	23 (23)	19 (25.3)	4 (16)	
Comorbidities, n (%)				
Diabetes mellitus	53 (53)	41 (54.7)	12 (48)	0.646
Hypertension	65 (65)	49 (65.3)	16 (64)	1.000
Chronic kidney disease	23 (23)	17 (22.7)	6 (24)	1.000
Hyperlipidemia	32 (32)	23 (30.7)	9 (36)	0.628
Cerebrovascular event	12 (12)	9 (12.2)	3 (12)	1.000
Paroxysmal AF	6 (6)	5 (6.7)	1 (4)	1.000
COPD	34 (34)	27 (36)	7 (28)	0.627
Malignancy	5 (5)	3 (4)	2 (8)	0.596
Smoking status,				
Current smoker	22 (22)	18 (24)	4 (16)	0.942
Former smoker	33 (33)	22 (29.3)	11 (44)	
Never smoked	45 (45)	35 (46.7)	10 (40)	
Medications, n (%)				
Aspirin	91 (91)	70 (93.3)	21 (84)	0.222
P2Y12 inhibitors	50 (50)	42 (56)	8 (32)	0.063
Statins	77 (77)	57 (76)	20 (80)	0.789
Oral anticoagulants	5 (5)	4 (5.3)	1 (4)	1.000
ACEI/ARBs	92 (92)	71 (94.7)	21 (84)	0.105

(Cont'd...)

Table 1. (Continued)

Parameters	Study group (n = 100)	Cardiac index < 2.2 L/min/m ² (n = 75)	Cardiac index ≥ 2.2 L/min/m ² (n = 25)	p-value
Beta blockers	98 (98)	75 (100)	23 (92)	0.061
Calcium channel blockers	8 (8)	6 (8)	2 (8)	1.000
Aldosterone antagonists	42 (42)	27 (36)	15 (60)	0.060
Digitalis	5 (5)	3 (4)	2 (8)	0.596
Nitrates	23 (23)	18 (24)	5 (20)	0.789
Loop diuretics	51 (51)	39 (52)	12 (48)	0.819
Thiazide diuretics	13 (13)	9 (12)	4 (16)	0.732

Notes: Data presented as mean ± standard deviation, unless stated otherwise. A p-value < 0.05 indicates statistical significance.

Abbreviations: AF: Atrial fibrillation; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; BP: Blood pressure; bpm: Beats per minute; Cardiac index: Cardiac index; COPD: Chronic obstructive pulmonary disease; IQR: Interquartile range; NYHA: New York Heart Association; P2Y12: Purinergic receptor P2Y12; PPP: Proportional pulse pressure.

PPP showed a negative correlation with diastolic BP ($r = -0.334$, $p = 0.001$). ROC curve analyses were conducted to evaluate the effectiveness of PPP and PP in identifying patients with $CI \geq 2.2$ L/min/m².

For PP, a threshold value of ≥ 27.50 mmHg predicted $CI \geq 2.2$ L/min/m² with 84% sensitivity and 84% specificity (area under the curve [AUC]: 0.857; 95% confidence interval [CI]: 0.757–0.957, $p < 0.001$) (Figure 4). For PPP, a threshold value of $\geq 25.85\%$ PPP showed superior diagnostic accuracy by determining $CI \geq 2.2$ L/min/m² with 84% sensitivity and 89.2% specificity (AUC: 0.866; 95% CI: 0.767–0.964, $p < 0.001$) (Figure 5). Finally, we observed that both PP and PPP were strong, non-invasive predictors of CI and CO in patients with HFrEF.

4. Discussion

Invasive hemodynamic monitoring methods are not always applicable in clinical practice due to their high cost and the associated risk of serious complications. TTE provides significant advantages over invasive procedures due to its cost-effectiveness, practicality, and non-invasive nature. However, physical examination methods, such as BP measurement with a sphygmomanometer, attracted our attention because they are simple, inexpensive, widely available, and non-invasive compared with both invasive hemodynamic monitoring and TTE. In this study, we aimed to demonstrate that PP and PPP parameters, which can be obtained using a standard sphygmomanometer, are simple, accessible clinical markers for predicting a patient's hemodynamic status. Similar to how TTE has replaced invasive pulmonary artery catheterization in certain indications in the past, we believe that PPP also has potential as a complementary diagnostic tool, especially in primary healthcare settings or low-resource clinical environments

where TTE facilities are limited. However, multicenter and large-scale validation studies are needed to standardize PPP as an independent assessment modality. Our findings demonstrated a strong positive correlation between PP and PPP values and the echocardiographically calculated CI. The threshold values, specifically 27.5 mmHg for PP and 25% for PPP, with sensitivities and specificities of 84.0% and 84.0% for PP, and 84.0% and 89.2% for PPP, respectively, are noteworthy for their high sensitivity and specificity in detecting cases with a $CI < 2.2$ L/min/m². However, the proposed PPP cut-off value should be considered preliminary and should be validated in larger multicenter cohorts before routine clinical implementation. Rapid identification of these patients in the early stages of clinical cardiac decompensation via PP and PPP can optimize treatment management and proactively prevent or alleviate potential decompensation scenarios. In cases where PPP is found to be high, PPP may help prioritize patients who require further echocardiographic evaluation, or in cases where PPP is found to be low, it may be recommended that patients undergo TTE.

Stevenson and colleagues⁶ compared hemodynamic parameters obtained from physical examination findings with hemodynamic parameters obtained via right heart catheterization in 50 HF patients. They found that measured PPP showed a strong positive correlation ($r = 0.82$) with CI values obtained via right-heart catheterization. Additionally, a PPP value below 25% was reported to have 91% sensitivity and 83% specificity in predicting patients with $CI < 2.2$ L/min/m². This finding aligns with the results of our study. Data from Stevenson and colleagues⁶ research demonstrated that PPP measurement is a reliable method for predicting CI in HF patients. The LURIC study showed that an increase in PP was associated with

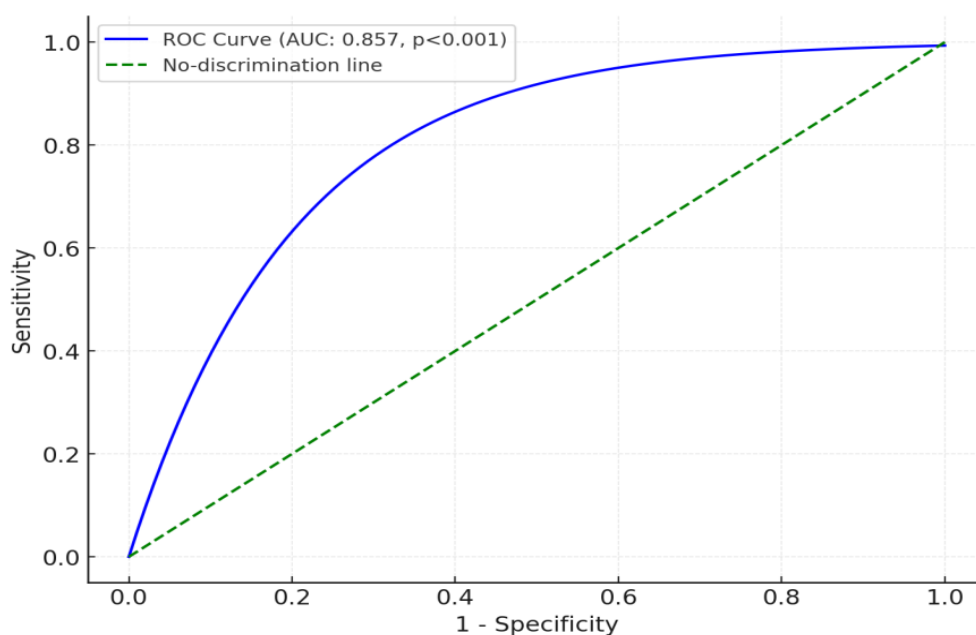


Figure 4. Receiver operating characteristic (ROC) curve for identification of cardiac index ≥ 2.2 L/min/m². This ROC curve illustrates the ability of pulse pressure (PP) to identify patients with a cardiac index (CI) ≥ 2.2 L/min/m². A threshold of PP ≥ 27.50 mmHg achieved a sensitivity of 84% and a specificity of 84% (area under the curve [AUC]: 0.857; 95% confidence interval: 0.757–0.957, $p < 0.001$).

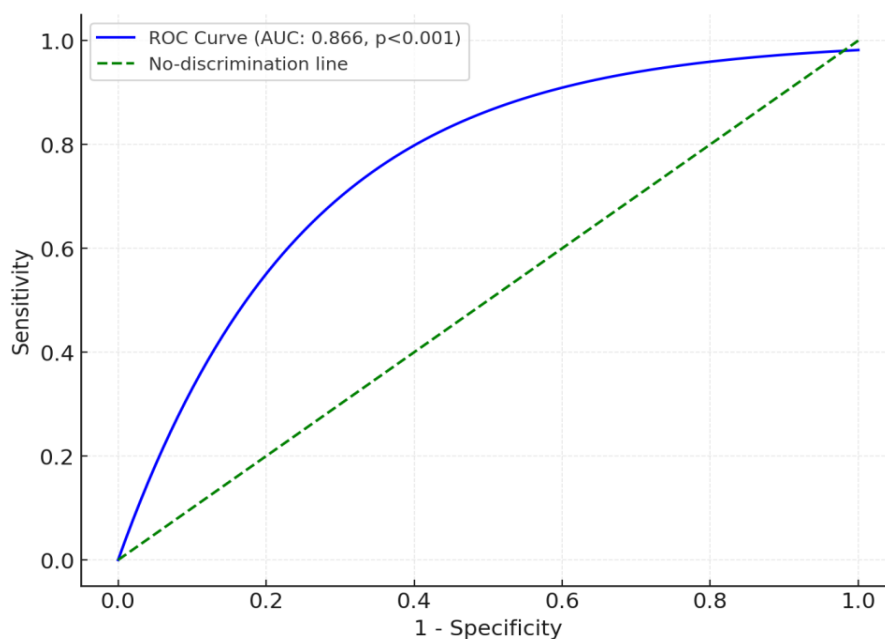


Figure 5. Receiver operating characteristic (ROC) curve for identification of cardiac index ≥ 2.2 L/min/m² (proportional pulse pressure). This ROC curve illustrates the ability of proportional pulse pressure (PPP) to identify patients with a cardiac index (CI) ≥ 2.2 L/min/m². A threshold of PPP $\geq 25.85\%$ achieved a sensitivity of 84% and a specificity of 89.2% (area under the curve [AUC]: 0.866; 95% confidence interval: 0.767–0.964, $p < 0.001$).

increases in both cardiovascular and all-cause mortality.²⁶ Furthermore, in HF with preserved ejection fraction, PPP has been associated with greater arterial stiffness and adverse cardiovascular outcomes.²⁷ In a prospective study conducted by Yildiran *et al.*²⁸, 225 HF patients (NYHA functional class, I–IV; mean age: 56.5 ± 12.3 years; 188 males) were followed for 670 ± 42 days. PP was calculated as the difference between diastolic and systolic BP values. The study population was divided into four quartiles according to PP (1st quartile PP <35 mmHg; 2nd quartile PP 35–45 mmHg; 3rd quartile PP 46–55 mmHg; and 4th quartile PP >55 mmHg). As the NYHA class increased, PP decreased ($p < 0.001$). Patients in the first quartile (PP <35 mmHg) had the lowest left ventricular ejection fraction and the highest left ventricular dimensions. According to Yildiran *et al.*²⁸, PP independently predicted death in patients with advanced HF and in the general population. According to ROC analysis, a PP threshold of 30 mmHg predicted death with 83.7% sensitivity and 79.7% specificity.²⁸ Jackson *et al.*²⁹ investigated the prognostic value of PP in HF patients, including 22,038 patients with HFrEF and 5,008 patients with HF with preserved ejection fraction, using data from 22 HF studies included in the Global Group of Meta-Analysis in Chronic Heart Failure. In HFrEF patients, compared with other PP groups, those in the fifth tier with the lowest PP had the highest adjusted HR for mortality (hazard ratio: 1.68; 95% CI: 1.53–1.84).²⁹ A retrospective study by Qiu *et al.*³⁰ found a J-shaped correlation between PP and all-cause mortality in patients with ischemic HF and left ventricular systolic dysfunction. The risk of death varied according to SBP status. Higher PP was associated with a worse prognosis in those with SBP > 110 mmHg, but this association was not statistically significant in those with low SBP.³⁰ Another study examining the relationship between PP and hemodynamic status in HF patients was conducted by Petrie and colleagues.³¹ Petrie and colleagues³¹ included a total of 1,897 patients in their study, all of whom underwent CI measurement via right heart catheterization and had either normal or impaired left ventricular function. Patients were divided into three groups based on their CI measurements. The analysis revealed a strong positive correlation between PP and CI in patients with CI <2 L/min/m² ($r = 0.414$). The same study also demonstrated that low PP was an independent predictor of low CI among patients with CI <3 L/min/m²[31]. The main difference between our study and the two studies mentioned above lies in the method used to determine CI values. In previous studies, CI values measured by right heart catheterization were compared with PPP values; however, in our study, CI values measured by echocardiography were compared with PPP values. Laskey *et al.*³² conducted a retrospective study with 40,421 HF patients. In patients

with HFrEF, increasing PP to 50 mmHg was associated with a significant reduction in mortality risk. However, the same study showed that PP values above 50 mmHg were associated with an increased risk of death.³² Interestingly, some studies have also observed an almost linear inverse relationship between mortality and PP in acute HFrEF.³³ Supporting these findings, Shah *et al.*³⁴ found that low PP values (<40 mmHg) were an independent indicator of poor prognosis in the cohort with advanced systolic dysfunction (ejection fraction < 30%), whereas relatively high PP values (>50 mmHg) correlated with better clinical outcomes.³⁴ The aforementioned studies show a correlation between PP and mortality, indicating that PP is predictive of mortality. On the other hand, in our study, PP and the relationship between PPP and patient prognosis/mortality were not evaluated because there were no long-term follow-up data for the patients. In 2020, Kothai and colleagues³⁵ suggested that patients with low socioeconomic status in India often lack access to echocardiographic evaluation. They proposed that inexpensive clinical parameters such as PP and PPP, which correlate with ejection fraction measured by TTE, could aid in HF risk stratification, treatment intensity, and hospitalization decisions in such populations. Consequently, a linear correlation was observed in regression analysis between EF value determined by TTE and PPP in patients with HF ($r = 0.667$, $p < 0.001$). However, this study did not investigate the relationship between PP or PPP and CI.³⁵ In a 2017 study by Petrie and colleagues³⁶ involving patients with acute HF, it was found that CI measurements obtained both before treatment and after stabilization of acute HF showed a positive correlation with PP product. The authors stated that PPP was the non-invasive parameter most closely associated with CI.³⁶ In primary care settings, where TTE is often unavailable, PPP can serve as a rapid screening tool to identify HFrEF patients at low CI risk and guide referrals for further evaluation or treatment optimization. While most similar studies to date have used invasive methods, our study used non-invasive techniques and is therefore the first of its kind. This finding demonstrates that in this patient group, hemodynamic status can be assessed in outpatient settings using a parameter measured during physical examination without the need for invasive methods. PPP, particularly in outpatient settings, can provide information for decisions regarding inotropic treatment or diuretic titration in HFrEF, subject to further validation. We believe that the results obtained in a simple and practical way will assist clinicians in the management of HF (e.g., patient triage, treatment optimization).

Cardiovascular outcomes in HFrEF are influenced by a complex interplay of hemodynamic impairment, arrhythmic burden, neurohormonal activation, and

structural cardiac abnormalities. Therefore, PPP should be interpreted as a surrogate marker reflecting only one aspect of cardiovascular risk. Emerging evidence also suggests that improvements in hemodynamic status may interact with modulation of arrhythmic risk, including susceptibility to atrial fibrillation, highlighting the multifactorial nature of prognosis in patients with HFrEF.³⁷

Comorbid conditions commonly encountered in HFrEF patients, including hypertension, diabetes mellitus, chronic kidney disease, and chronic obstructive pulmonary disease, may independently influence arterial stiffness, vascular compliance, and PP characteristics. Therefore, PPP values may partially reflect systemic vascular alterations in addition to cardiac performance. This highlights the importance of interpreting PPP within the broader clinical context of multimorbidity.

Invasive measurements carry significant risks of complications and are expensive and impractical. Echocardiography is more practical and cost-effective than invasive methods. In this context, PP and PPP obtained from routine BP measurements with a BP monitor are simple methods for estimating the patient's hemodynamic status. PPP is particularly promising as a complementary tool to TTE in primary healthcare settings where TTE is not available or in resource-constrained environments.

There are several limitations to this study. This cross-sectional pilot study was unable to evaluate the prognostic role of physical examination findings due to the lack of long-term follow-up data. A significant limitation is the lack of follow-up data to evaluate the prognostic value of PP and PPP and their relationship to clinical outcomes such as mortality and morbidity. The small number of patients and the single-center nature of the study are also important limitations. The pilot design and relatively small sample size constitute important limitations, and therefore the findings should be interpreted cautiously.

Another important limitation is the absence of invasive hemodynamic validation using right heart catheterization. Therefore, PPP was compared with another non-invasive modality rather than with a gold-standard invasive technique. Furthermore, the homogeneous study population is a limitation. The exclusion of a considerable number of initially screened patients may have introduced selection bias and limited the external validity of the study. However, strict exclusion criteria were applied to minimize hemodynamic heterogeneity and improve measurement reliability. Because of the limited sample size and pilot design, multivariable regression analysis adjusting for potential confounders was not performed.

Future larger-scale studies should evaluate whether PPP

remains independently associated with CI after adjustment for demographic and clinical variables (HF including conditions such as atrial fibrillation, heart valve disease, prosthetic heart valves or pacemakers, peripartum kmp, dilated HF, idiopathic HF, ischemic HF, etc.). Whether PPP retains similar diagnostic performance across different comorbidity profiles remains uncertain and warrants evaluation in larger multicenter studies.

5. Conclusion

Proportional PP can facilitate the management of HFrEF in primary healthcare by quickly identifying patients who may benefit from enhanced monitoring and therapeutic intensification. PPP can serve as a practical complementary bedside screening tool in settings where echocardiographic assessment is not readily available.

Abbreviations

Abbreviations	Full form
CO	Cardiac output
HFrEF	Heart Failure with reduced ejection fraction
LVOT	Left ventricular outflow tract
NYHA	New York Heart Association
SBP	Systolic blood pressure
TTE	Transthoracic echocardiography

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Conflict of interest

The authors declare no competing interests.

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Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Necmettin Erbakan University Meram Faculty of Medicine (Approval No. 2017/1095). Written informed consent was obtained from all participants before participation in the study.

Consent for publication

Participants provided consent to the publication of their data.

Availability of data

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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