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Pulse Pressure and Proportional Pulse Pressure as Bedside Correlates of Left Ventricular Systolic Function in Chronic Heart Failure with Reduced Ejection Fraction - A Hospital-Based Cross-Sectional Study

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Abstract

Background: Heart failure with reduced ejection fraction (HFrEF) carries substantial mortality, and echocardiography is unavailable at many primary care facilities in India. Pulse pressure (PP) and proportional pulse pressure (PPP) are bedside indices of the arterial pressure waveform that reflect stroke volume.

Objectives: To correlate PPP with EF in chronic HFrEF and to assess its value as a bedside prognostic indicator.

Methods: A hospital-based cross-sectional study was conducted at a tertiary teaching hospital in Bangalore between February 2021 and August 2022. One hundred consecutive patients aged 18 to 75 years with clinical heart failure by Framingham criteria and EF below 40% were enrolled. PPP was calculated as PP divided by systolic blood pressure, expressed as a percentage. Patients were stratified into EF below 30% (n = 42) and EF 30% to 40% (n = 58). Chi-square, independent-samples t and Pearson correlation tests were applied.

Results: The cohort comprised 55 men and 45 women of mean age 54.12 years. Mean PP was 25.86 ± 6.11 versus 33.83 ± 7.92 mmHg in the two groups (p = 0.001) and mean PPP 27.31 ± 3.54% versus 29.08 ± 4.49% (p = 0.031). A PP of 30 mmHg or less occurred in 78.6% versus 36.2% (p = 0.01) and a PPP of 30% or less in 88.1% versus 51.7% (p = 0.01). EF correlated positively with PP (r = 0.639) and PPP (r = 0.635), both p < 0.001, but not with pulse rate (r = -0.024, p = 0.96).

Conclusion: PP and PPP correlated positively with EF and identified severely depressed systolic function. Both

are inexpensive bedside indices for risk stratification where echocardiography is unavailable.

Keywords: Heart Failure, Reduced Ejection Fraction, Pulse Pressure, Proportional Pulse Pressure, Echocardiography, Bedside Assessment

Introduction

Heart failure (HF) is the final common pathway of virtually every structural and functional disorder of the heart, and it remains among the most consequential chronic conditions in contemporary internal medicine. Contemporary estimates place the prevalence of HF at approximately 1% to 2% of the adult population in high-income countries, with a steep age gradient such that the condition affects only a small fraction of adults in the fifth decade but more than a tenth of those beyond the age of eighty.[1] Although age-adjusted incidence has plateaued or even declined in several Western populations because of improved control of hypertension, earlier revascularisation for acute coronary syndromes and wider use of disease-modifying pharmacotherapy, the absolute number of people living with HF continues to climb as populations grow older and as survival after myocardial infarction improves.[1,2] HF is now widely described as a global pandemic, and it accounts for a disproportionate share of hospital bed days, readmissions and health expenditure in every health system in which it has been formally costed.[2]

The Indian experience differs from the Western one in ways that are directly relevant to clinical practice. The Trivandrum Heart Failure Registry, which enrolled consecutive admissions across urban and rural hospitals in Kerala, reported that Indian patients hospitalised with HF were younger than their Western counterparts, were more often men, had a high prevalence of ischaemic heart disease as the underlying substrate, and received guideline-directed medical therapy in only a minority of instances.[3] A younger age at presentation implies a longer duration of disease burden and a greater number of productive years lost.

Superimposed on this are the structural realities of health care delivery across much of the country, in which patients frequently present first to a primary health centre or a taluk - level hospital where the diagnostic armamentarium may extend no further than a stethoscope, a sphygmomanometer, an electrocardio graph and a chest radiograph. The interval between the first clinical contact and the first echocardiogram may be measured in weeks. Any tool that allows a clinician at that first point of contact to estimate the severity of ventricular dysfunction, and thereby to triage referral, has obvious practical value. HF is defined by current consensus as a clinical syndrome comprising symptoms and signs caused by a structural or functional cardiac abnormality, corroborated by elevated natriuretic peptide concentrations or objective evidence of pulmonary or systemic congestion.[4] The universal definition and the major society guidelines classify the syndrome by left ventricular ejection fraction (EF), with HF with reduced ejection fraction (HFrEF) defined by an EF of 40% or less, HF with mildly reduced ejection fraction by an EF of 41% to 49%, and HF with preserved ejection fraction by an EF of 50% or above.[4,5] This taxonomy is not merely descriptive, because the therapies that reduce mortality have been demonstrated principally in the HFrEF phenotype, and accurate identification of that phenotype therefore carries direct therapeutic consequence.[5,6] EF is conventionally quantified by two-dimensional transthoracic echocardiography using the biplane method of discs, a technique that is safe, reproducible and inexpensive in absolute terms but that

nonetheless requires a machine, a trained operator and a patient who has reached a centre where both are present.

The pathophysiology of HFrEF provides the rationale for seeking haemodynamic surrogates at the bedside. An index injury to the myocardium, most commonly myocardial infarction in the Indian and Western contexts alike, initiates a programme of ventricular remodeling characterised by myocyte hypertrophy, interstitial fibrosis, chamber dilatation and progressive loss of contractile efficiency.

Activation of the sympathetic nervous system and of the rennin - angiotensin - aldosterone axis sustains perfusion pressure in the short term at the cost of afterload elevation, sodium and water retention, and accelerated remodelling in the long term.[5] The net haemodynamic consequence is a fall in stroke volume and cardiac index. Because the arterial pressure waveform is generated by the interaction of the ejected stroke volume with the mechanical properties of the aorta and the great vessels, a reduction in stroke volume is transmitted directly into the pulsatile component of the arterial pressure signal.

Pulse pressure (PP), the arithmetic difference between systolic and diastolic blood pressure, is the simplest available index of that pulsatile component. Its magnitude is governed principally by left ventricular stroke volume, by the compliance of the proximal aorta, and by the timing and amplitude of reflected pressure waves returning from the periphery.[7]

Mean arterial pressure, by contrast, represents the steady component of the pressure signal and is governed chiefly by cardiac output and systemic vascular resistance. The distinction matters because the two components carry different prognostic information. In older hypertensive populations, in whom progressive loss of aortic elastin and accumulation of collagen produce arterial stiffening, PP widens and has been shown to predict cardiovascular events more strongly than mean pressure.[7]

Analyses from the Framingham cohort demonstrated that for any given systolic pressure above 120 mmHg, coronary risk rose as diastolic pressure fell, which is to say that risk tracked with widening PP rather than with either component in isolation.[8]

This positive association between wide PP and incident disease extends specifically to the development of HF. In a prospective analysis of elderly participants, each incremental rise in PP was associated with a graded increase in the risk of subsequent HF, an effect attributed to the additional afterload imposed on the ventricle, the resultant increase in myocardial oxygen demand, the impairment of diastolic relaxation and the predisposition to subendocardial ischaemia that accompanies a stiff conduit system.[9] Similar findings emerged from community-based cohorts in which PP predicted both myocardial infarction and HF independently of conventional risk factors.[10]

The relationship inverts, however, once HFrEF is established. In a patient whose ventricle is already failing, a narrow PP no longer signifies a compliant aorta but rather an inability to generate an adequate stroke volume. Sphygmomanometrically determined PP was shown to carry independent prognostic information for survival in patients with left ventricular dysfunction, with lower values conferring higher mortality after adjustment for mean arterial pressure.[11]

The individual patient meta-analysis conducted by the Meta-Analysis Global Group in Chronic Heart Failure examined this question across a large pooled population and found that a lower PP, particularly below 53 mmHg, independently predicted mortality in HFrEF, with the gradient of risk most pronounced among patients whose

EF was below 30% and whose systolic pressure was below 140 mmHg; the same relationship was not consistently observed in HF with preserved ejection fraction.[12]

A subsequent analysis of a randomised HFrEF trial population, in which patients were stratified by PP tertile, confirmed that the association between PP and adverse cardiovascular outcome in this phenotype runs in the direction opposite to that seen in the general population.[13]

The apparent paradox resolves once it is recognised that PP is a composite signal whose dominant determinant shifts from arterial stiffness in the intact circulation to stroke volume in the failing one.

Because PP is measured in absolute millimetres of mercury, its interpretation is confounded by the prevailing level of systolic pressure. A PP of 30 mmHg carries different meaning in a patient whose systolic pressure is 150 mmHg than in one whose systolic pressure is 90 mmHg. Proportional pulse pressure (PPP), defined as PP divided by systolic blood pressure and expressed as a percentage, was introduced to normalise for this.

The index was popularised by the demonstration that conventional physical signs of congestion, including basal crepitations, pedal oedema and jugular venous distension, were frequently absent in patients with chronic HF and markedly elevated pulmonary capillary wedge pressures, whereas PPP correlated well with invasively measured cardiac index; a PPP below 25% identified a cardiac index below 2.2 L/min/m² with a sensitivity of 91% and a specificity of 83%.[14].

This observation underpinned the subsequent development of bedside haemodynamic profiling, in which patients admitted with HF are categorised as warm or cold and wet or dry on the basis of clinical assessment alone, with a narrow PPP among the few examination findings that independently predicted the hypoperfused profile and the associated adverse event-free survival.[15]

Despite this body of evidence, the majority of published data derive from Western referral populations with advanced HF, often assessed in the context of transplant evaluation or clinical trial enrolment. Data describing the behaviour of PP and PPP across the spectrum of EF in unselected Indian patients presenting to a public tertiary hospital are comparatively sparse, and the operational question of whether these indices can substitute, even approximately, for echocardiographic EF in a resource-constrained setting has not been extensively addressed in this population.

The present study was therefore designed to quantify the relationship between PP, PPP and EF in patients with chronic HFrEF attending a large government teaching hospital in Bangalore, and to determine whether these two bedside indices, alongside conventional symptoms and signs, discriminate patients with severe systolic impairment from those with moderate impairment.

Aims and Objectives

The objectives of the study were: firstly, to study the correlation between proportional pulse pressure and left ventricular ejection fraction in patients with chronic heart failure with reduced ejection fraction; and secondly, to study the prognostic value of proportional pulse pressure in patients with heart failure, assessed through its association with the severity of systolic dysfunction and with the clinical markers of congestion and hypoperfusion recognised to carry adverse prognostic weight.

Materials and Methods

Study design and setting

This was a hospital-based, observational, cross-sectional study conducted in the Department of General Medicine at Bangalore Medical College and Research Institute, Bangalore, and its attached teaching hospitals. Patients were recruited from both the medical outpatient department and the inpatient wards.

Study period

Recruitment and data collection were carried out between February 2021 and August 2022.

Study population and eligibility criteria

Consecutive patients presenting with symptoms and signs of heart failure were screened. Patients were included if they were aged between 18 and 75 years, satisfied the Framingham criteria for a clinical diagnosis of heart failure, had a left ventricular ejection fraction below 40% on transthoracic echocardiography, and provided written informed consent. Patients were excluded if they were unwilling to consent, were aged above 75 years, had heart failure secondary to primary pulmonary disease including corpulmonale, had significant valvular heart disease or pericardial disease, or were in a high-output state such as severe anaemia, thyrotoxicosis or arteriovenous fistula. These exclusions were applied because valvular lesions, pericardial constriction and high-output physiology each distort the arterial pressure waveform independently of left ventricular systolic performance and would therefore confound the interpretation of pulse pressure.

Sample size

The sample size was estimated from the study by Kothai et al, in which the mean pulse pressure and proportional pulse pressure among patients with chronic heart failure with reduced ejection fraction were reported as 30.1 ± 8.16 mmHg and 27.22 ± 3.91% respectively.[16] Using the formula $n = Z^2\sigma^2/d^2$, with Z taken as 1.96 for a 95% confidence level, σ as 8.16 and an absolute precision d of 2 mmHg, the minimum required sample was calculated. One hundred consecutive eligible patients were enrolled in order to improve the precision of the subgroup comparisons and to allow adequate representation within each ejection fraction stratum.

Ethical considerations

Approval was obtained from the Institutional Ethics Committee of Bangalore Medical College and Research Institute before commencement of the study. Written informed consent was obtained from every participant after explanation of the nature and purpose of the study in a language the patient understood. Participation was voluntary, refusal carried no consequence for clinical care, and all data were anonymised at the point of entry. The study was conducted in accordance with the Declaration of Helsinki.

Clinical evaluation

Each participant underwent a structured history and physical examination recorded on a predesigned proforma. Symptoms elicited included breathlessness on exertion, orthopnoea, paroxysmal nocturnal dyspnoea, chest pain, syncope and decreased urine output. Orthopnoea was recorded as present when the patient required two or more pillows to sleep comfortably. Functional status was graded according to the New York Heart Association (NYHA) classification. Physical examination gave particular attention to elevated jugular venous pressure, bilateral basal crepitations, pedal oedema and the presence of a third heart sound. Jugular venous pressure was assessed with the patient reclining at 45 degrees and was considered elevated when the top of the venous column lay more than 4 cm above the

sternal angle. The third heart sound was sought at the apex in the left lateral decubitus position using the bell of the stethoscope. A history of documented coronary artery disease was recorded from previous discharge summaries, angiographic reports or electrocardiographic evidence of prior infarction.

Blood pressure measurement and derivation of the pulsatile indices

Blood pressure was measured according to American Heart Association recommendations using a calibrated mercury sphygmomanometer with an appropriately sized cuff, with the patient seated and rested for at least five minutes, the arm supported at heart level and the back supported. Systolic blood pressure was taken at the first Korotkoff sound and diastolic blood pressure at the fifth. Two readings were taken at an interval of at least one minute and averaged. Pulse rate was counted at the radial artery over one full minute. Pulse pressure was calculated as the difference between systolic and diastolic blood pressure, expressed in millimetres of mercury. Proportional pulse pressure was calculated as pulse pressure divided by systolic blood pressure and multiplied by one hundred, expressed as a percentage.

Echocardiography and grouping

Transthoracic two-dimensional echocardiography was performed at rest by the institutional cardiology service. Left ventricular ejection fraction was derived using the biplane method of discs from apical four-chamber and two-chamber views. Only patients with an ejection fraction below 40% were retained in the study. For the purpose of analysis the cohort was divided into two groups on the basis of the severity of systolic impairment: Group 1 comprised patients with an ejection fraction below 30%, and Group 2 comprised patients with an ejection fraction of 30% to 40%. Pulse pressure and proportional pulse pressure were additionally dichotomised at 30 mmHg and 30% respectively for categorical analysis, and systolic blood pressure was dichotomised at 90 mmHg.

Statistical analysis

Data were entered into a Microsoft Excel spreadsheet and analysed using SPSS version 20 (IBM Corporation, Armonk, New York). Qualitative variables were summarised as frequencies and proportions, and quantitative variables as mean and standard deviation. The chi-square test was used to test the association of categorical variables with the ejection fraction groups. The independent-samples t test was used to compare continuous variables between the two groups. The Pearson correlation coefficient was computed to quantify the linear relationship between ejection fraction and each of pulse rate, systolic blood pressure, diastolic blood pressure, pulse pressure and proportional pulse pressure. A two-sided p value below 0.05 was taken to indicate statistical significance.

Results

One hundred patients with chronic heart failure and an ejection fraction below 40% were studied. Forty-two patients (42.0%) had an ejection fraction below 30% and fifty-eight patients (58.0%) had an ejection fraction between 30% and 40%.

Demographic profile

The age of the participants ranged from 23 to 75 years, with an overall mean of 54.12 years. The largest single stratum was the 56 to 65 year band, which accounted for 36 patients (36.0%), followed by the 46 to 55 year band with 24 patients (24.0%). Seventeen patients (17.0%) were aged 66 years or above, and 23 patients (23.0%) were younger than 46 years, indicating that although the burden was concentrated in the sixth and seventh

decades, a substantial minority presented at a considerably younger age. Fifty - five participants (55.0 %) were men and 45 (45.0%) were women, giving a male to female ratio of approximately 11 to 9. The mean age of the group with an ejection fraction below 30% was 52.40 ± 13.49 years and that of the group with an ejection fraction of 30% to 40% was 55.36 ± 12.41 years, a mean difference of 2.95 years that did not reach statistical significance on independent-samples t testing (p = 0.26). The distribution across age bands likewise showed no significant association with the severity of systolic dysfunction (chi-square 4.05, p = 0.39), nor did sex (chi-square 0.201, p = 0.65). The demographic data are presented in Table 1 and the age band distribution by ejection fraction group in Table 2.

Table 1: Demographic characteristics of the study population (n = 100)

Variable	EF < 30% (n = 42)	EF 30–40% (n = 58)	Total (n = 100)	p value
Mean age, years (SD)	52.40 (13.49)	55.36 (12.41)	54.12	0.26
Age range, years	23–70	23–75	23–75	–
Male, n (%)	22 (52.4)	33 (56.9)	55 (55.0)	0.65
Female, n (%)	20 (47.6)	25 (43.1)	45 (45.0)	0.65

EF, ejection fraction; SD, standard deviation. Age compared using the independent-samples t test; sex compared using the chi-square test (chi-square 0.201).

Table 2: Distribution of age bands by ejection fraction group

Age band (years)	EF < 30%, n (%)	EF 30–40%, n (%)	Total, n (%)
23 to 35	7 (16.7)	5 (8.6)	12 (12.0)
36 to 45	6 (14.3)	5 (8.6)	11 (11.0)
46 to 55	7 (16.7)	17 (29.3)	24 (24.0)
56 to 65	16 (38.1)	20 (34.5)	36 (36.0)
66 to 75	6 (14.3)	11 (19.0)	17 (17.0)
Total	42 (100.0)	58 (100.0)	100 (100.0)

Chi-square 4.05, p = 0.39. EF, ejection fraction.

Symptom profile

Breathlessness on exertion was the dominant presenting symptom, reported by 90 patients (90.0%) overall, and its frequency was almost identical in the two groups at 90.5% and 89.7% respectively, so that it did not discriminate between them (chi-square 0.018, p = 0.89). Orthopnoea behaved very differently. It was present in 41 of 42 patients (97.6%) with an ejection fraction below 30% but in only 31 of 58 patients (53.4%) with an ejection fraction of 30% to 40%, a highly significant association (chi-square 20.996, p < 0.001). Paroxysmal nocturnal dyspnoea was reported by 41 patients (41.0%) overall, in 47.6% of the severely impaired group and 36.2% of the moderately impaired group, without reaching significance (chi-square 2.415, p = 0.25). Chest pain was reported by 34 patients (34.0%), with a comparable distribution across the two groups at 35.7% and 32.8% (p = 0.493). Decreased urine output was an infrequent complaint, recorded in 15 patients (15.0%), and although it was numerically more common in the

group with the lowest ejection fraction at 19.0% against 12.1%, the difference was not statistically significant (chi-square 2.426, p = 0.25). Syncope was reported by 11 patients (11.0%) and did not differ significantly between the groups (p = 0.07). The symptom data are set out in Table 3.

Table 3: Symptom profile by ejection fraction group

Symptom	EF < 30% (n = 42), n (%)	EF 30–40% (n = 58), n (%)	Total, n (%)	p value
Breathlessness on exertion	38 (90.5)	52 (89.7)	90 (90.0)	0.89
Orthopnoea	41 (97.6)	31 (53.4)	72 (72.0)	< 0.001
Paroxysmal nocturnal dyspnoea	20 (47.6)	21 (36.2)	41 (41.0)	0.25
Chest pain	15 (35.7)	19 (32.8)	34 (34.0)	0.493
Decreased urine output	8 (19.0)	7 (12.1)	15 (15.0)	0.25
Syncope	6 (14.3)	5 (8.6)	11 (11.0)	0.07

EF, ejection fraction. Chi-square test applied throughout.

Clinical signs and functional class

Bilateral basal crepitations were audible in 72 patients (72.0%) overall and were far more frequent in the group with the lowest ejection fraction, being present in 41 of 42 patients (97.6%) compared with 31 of 58 patients (53.4%), a strongly significant association (chi-square 23.575, p < 0.01). A third heart sound was audible in 76 patients (76.0%) overall, in 41 of 42 patients (97.6%) with an ejection fraction below 30% and in 35 of 58 patients (60.3%) with an ejection fraction of 30% to 40% (chi-square 18.55, p < 0.001). Elevated jugular venous pressure was documented in 51 patients (51.0%) overall, in 29 of 42 patients (69.0%) in the severely impaired group and in 22 of 58 patients (37.9%) in the moderately impaired group (chi-square 9.43, p = 0.002). Pedal oedema, by contrast, was present in only 35 patients (35.0%) and showed no relationship whatever with the severity of systolic dysfunction, occurring in 33.3% and 36.2% of the two groups respectively (chi-square 0.088, p = 0.766).

Functional limitation tracked closely with systolic impairment. Forty patients (40.0%) were in NYHA class IV, 47 (47.0%) in class III and 13 (13.0%) in class II. Among patients with an ejection fraction below 30%, 22 of 42 (52.4%) were in class IV and only one (2.4%) was in class II, whereas among patients with an ejection fraction of 30% to 40%, 18 of 58 (31.0%) were in class IV and 12 (20.7%) were in class II (chi-square 9.1, p = 0.011). Coronary artery disease was documented in 46 patients (46.0%) overall, in 17 of 42 patients (40.5%) with an ejection fraction below 30% and in 29 of 58 patients (50.0%) with an ejection fraction of 30% to 40%. The clinical sign and functional class data are presented in Table 4.

Table 4: Clinical signs, functional class and comorbidity by ejection fraction group

Variable	EF < 30% (n = 42), n (%)	EF 30–40% (n = 58), n (%)	Total, n (%)	Chi-square	p value
Basal crepitations	41 (97.6)	31 (53.4)	72 (72.0)	23.575	< 0.01
Third heart sound	41 (97.6)	35 (60.3)	76 (76.0)	18.55	< 0.001
Elevated jugular venous pressure	29 (69.0)	22 (37.9)	51 (51.0)	9.43	0.002

Pedal oedema	14 (33.3)	21 (36.2)	35 (35.0)	0.088	0.766
NYHA class II	1 (2.4)	12 (20.7)	13 (13.0)	9.1	0.011
NYHA class III	19 (45.2)	28 (48.3)	47 (47.0)		
NYHA class IV	22 (52.4)	18 (31.0)	40 (40.0)		
Coronary artery disease	17 (40.5)	29 (50.0)	46 (46.0)	–	–

EF, ejection fraction; NYHA, New York Heart Association. The chi-square statistic for NYHA class refers to the full three-by-two table.

Haemodynamic parameters

The haemodynamic differences between the two groups were substantial and consistent. Mean systolic blood pressure was 99.12 ± 13.06 mmHg in patients with an ejection fraction below 30% and 113.53 ± 17.63 mmHg in those with an ejection fraction of 30% to 40%, a mean difference of 14.41 mmHg (p = 0.001). Mean diastolic blood pressure was 73.24 ± 8.17 mmHg and 78.55 ± 13.05 mmHg respectively, a mean difference of 5.31 mmHg (p = 0.022). Mean pulse pressure was 25.86 ± 6.11 mmHg in the group with the lowest ejection fraction against 33.83 ± 7.92 mmHg in the other group, a mean difference of 7.97 mmHg and the largest absolute separation observed among the pressure indices (p = 0.001). Mean proportional pulse pressure was 27.31 ± 3.54% against 29.08 ± 4.49%, a mean difference of 1.76 percentage points (p = 0.031). Pulse rate did not differ between the groups, at 87.48 ± 14.18 beats per minute and 87.33 ± 15.89 beats per minute respectively (p = 0.96). These comparisons are shown in Table 5.

Table 5: Comparison of haemodynamic parameters between ejection fraction groups (independent-samples t test)

Parameter	EF < 30% (n = 42), mean ± SD	EF 30–40% (n = 58), mean ± SD	Mean difference	p value
Pulse rate, beats/min	87.48 ± 14.18	87.33 ± 15.89	0.15	0.96
Systolic blood pressure, mmHg	99.12 ± 13.06	113.53 ± 17.63	-14.41	0.001
Diastolic blood pressure, mmHg	73.24 ± 8.17	78.55 ± 13.05	-5.31	0.022
Pulse pressure, mmHg	25.86 ± 6.11	33.83 ± 7.92	-7.97	0.001
Proportional pulse pressure, %	27.31 ± 3.54	29.08 ± 4.49	-1.76	0.031

EF, ejection fraction; SD, standard deviation. Mean difference expressed as EF < 30% minus EF 30–40%.

Categorical analysis of the pressure indices

When the pressure indices were dichotomised, the same relationships emerged in categorical form. A systolic blood pressure of 90 mmHg or less was recorded in 13 of 42 patients (31.0%) with an ejection fraction below 30% but in only 6 of 58 patients (10.3%) with an ejection fraction of 30% to 40% (chi-square 6.72, p = 0.01). A pulse pressure of 30 mmHg or less was present in 33 of 42 patients (78.6%) in the severely impaired group compared with 21 of 58 patients (36.2%) in the moderately impaired group, the strongest categorical association observed in the study (chi-square 17.60, p = 0.01). A proportional pulse pressure of 30% or less was present in 37 of 42 patients (88.1%) against 30 of 58 patients (51.7%), so that a normal or high proportional pulse pressure above 30% was recorded in only 5 patients (11.9%) with the most severely impaired ventricles compared with 28 patients (48.3%) in the

other group (chi-square 14.57, p = 0.01). These results are presented in Table 6.

Table 6: Categorical distribution of pressure indices by ejection fraction group

Index	Category	EF < 30% (n = 42), n (%)	EF 30–40% (n = 58), n (%)	Chi-square	p value
Systolic blood pressure	> 90 mmHg	29 (69.0)	52 (89.7)	6.72	0.01
	≤ 90 mmHg	13 (31.0)	6 (10.3)		
Pulse pressure	> 30 mmHg	9 (21.4)	37 (63.8)	17.60	0.01
	≤ 30 mmHg	33 (78.6)	21 (36.2)		
Proportional pulse pressure	> 30%	5 (11.9)	28 (48.3)	14.57	0.01
	≤ 30%	37 (88.1)	30 (51.7)		

EF, ejection fraction.

Correlation between ejection fraction and the bedside indices

Pearson correlation analysis across the whole cohort of 100 patients demonstrated a statistically significant positive linear relationship between ejection fraction and each of the pressure-derived indices. The strongest correlation was with pulse pressure (r = 0.639, p < 0.001), followed closely by proportional pulse pressure (r = 0.635, p < 0.001) and by systolic blood pressure (r = 0.532, p = 0.001). Diastolic blood pressure showed a weak but statistically significant positive correlation (r = 0.254, p = 0.022). Pulse rate showed no correlation with ejection fraction whatever (r = -0.024, p = 0.96). The direction of these coefficients indicates that as ejection fraction falls, pulse pressure and proportional pulse pressure fall in parallel, and that the pulsatile indices track systolic function more closely than either the steady component of the pressure signal or the chronotropic response. The correlation data are given in Table 7.

Table 7: Pearson correlation of clinical parameters with left ventricular ejection fraction (n = 100)

Parameter	Correlation coefficient (r)	p value	Interpretation
Pulse rate	-0.024	0.96	No correlation
Systolic blood pressure	0.532	0.001	Moderate positive correlation
Diastolic blood pressure	0.254	0.022	Weak positive correlation
Pulse pressure	0.639	< 0.001	Moderate to strong positive correlation
Proportional pulse pressure	0.635	< 0.001	Moderate to strong positive correlation

Summary of discriminating variables

Taken together, the variables that discriminated significantly between the two ejection fraction strata were orthopnoea, basal crepitations, the third heart sound, elevated jugular venous pressure, NYHA functional class, systolic blood pressure, pulse pressure and proportional pulse pressure. Variables that did not discriminate were age, sex, breathlessness on exertion, paroxysmal nocturnal dyspnoea, chest pain, syncope, decreased urine output, pedal oedema and pulse rate. Table 8 summarises the discriminatory performance of the variables studied.

Table 8: Summary of variables tested for association with severity of systolic dysfunction

Variable	p value	Statistically significant
Age group	0.39	No
Sex	0.65	No
Breathlessness on exertion	0.89	No
Orthopnoea	< 0.001	Yes
Paroxysmal nocturnal dyspnoea	0.25	No
Chest pain	0.493	No
Syncope	0.07	No
Decreased urine output	0.25	No
Pedal oedema	0.766	No
Basal crepitations	< 0.01	Yes
Third heart sound	< 0.001	Yes
Elevated jugular venous pressure	0.002	Yes
NYHA functional class	0.011	Yes
Systolic blood pressure (≤ 90 mmHg)	0.01	Yes
Pulse pressure (≤ 30 mmHg)	0.01	Yes
Proportional pulse pressure (≤ 30%)	0.01	Yes

NYHA, New York Heart Association.

Discussion

The central finding of this study is that both pulse pressure and proportional pulse pressure fall as left ventricular ejection fraction falls in patients with chronic heart failure with reduced ejection fraction, and that they do so with sufficient consistency to separate patients with severe systolic impairment from those with moderate impairment at the bedside. Pulse pressure correlated with ejection fraction at r = 0.639 and proportional pulse pressure at r = 0.635, both with p values below 0.001, whereas pulse rate showed no relationship at all. A pulse pressure of 30 mmHg or less was found in 78.6% of patients with an ejection fraction below 30% compared with 36.2% of those with an ejection fraction of 30% to 40%, and a proportional pulse pressure of 30% or less in 88.1% against 51.7%.

These findings sit comfortably within the established literature.

The conceptual foundation was laid by Stevenson and Perloff, who demonstrated that the classical physical signs of congestion are unreliable indicators of haemodynamic status in chronic heart failure; among 43 patients with a pulmonary capillary wedge pressure of 22 mmHg or above, 18 had neither crepitations nor oedema nor jugular venous distension, giving these signs a sensitivity of only 58% despite a specificity of 100%. Proportional pulse pressure, by contrast, correlated well with cardiac index, and a value below 25% identified a cardiac index below 2.2 L/min/m² with a sensitivity of 91% and a specificity of 83%.[14] Our cohort reproduces the essential asymmetry described in that work. Pedal oedema, the most familiar sign of heart failure to the

general practitioner, was present in only 35% of our patients and showed no relationship with the severity of systolic dysfunction (p = 0.766), whereas the pulsatile indices discriminated clearly. Basal crepitations and the third heart sound performed better in our series than in the original description, being present in 97.6% of patients with an ejection fraction below 30%, which probably reflects the fact that our patients were recruited largely at the point of symptomatic decompensation rather than in a stable ambulatory transplant clinic.

The prognostic literature on bedside haemodynamic profiling supports the same conclusion. Shah and colleagues found that proportional pulse pressure was the only multivariable predictor of a pulmonary capillary wedge pressure above 18 mmHg and a cardiac index below 2.2 L/min/m², and Nohria and colleagues subsequently demonstrated that event-free survival was significantly lower in patients classified as wet and cold than in those classified as dry and warm, with a narrow proportional pulse pressure among the examination findings that identified the hypoperfused state.[15,17] If a narrow proportional pulse pressure marks the cold profile, and the cold profile predicts adverse outcome, then the association we observed between a low proportional pulse pressure and a severely depressed ejection fraction carries prognostic as well as diagnostic implication.

The most directly comparable Indian work is that of Kothai and colleagues, who studied 150 patients with reduced ejection fraction and reported a mean age of 58.99 ± 11.03 years, with 57.33% of participants aged between 45 and 65 years and coronary heart disease as the underlying aetiology in 76%.[16] Their finding that proportional pulse pressure showed a significant association with ejection fraction, and that the specificity for detecting heart failure was highest for proportional pulse pressure and systolic blood pressure, is reproduced in our data. Our cohort was somewhat younger, with a mean age of 54.12 years, and had a lower documented prevalence of coronary artery disease at 46%, a difference that may reflect the case mix of a government tertiary hospital in which a proportion of patients with dilated cardiomyopathy of non-ischaemic origin present without prior angiographic characterisation. The mean proportional pulse pressure in their series was 27.22 ± 3.91%, which is almost identical to the 27.31 ± 3.54% observed in our most severely impaired group.

Voors and colleagues reported that a low pulse pressure was independently related both to elevated natriuretic peptide concentrations and to increased mortality in advanced chronic heart failure, providing a mechanistic bridge between the bedside index and the neurohormonal severity of disease.[18] Schillaci and colleagues, analysing a large national cardiology registry, concluded that for any given level of mean arterial pressure a low pulse pressure independently predicted cardiovascular death in heart failure.[19]

Petrie and colleagues extended the observation by showing that low pulse pressure independently predicted mortality and morbidity in patients with non-ischaemic advanced heart failure, while mean arterial pressure carried the greater weight among those whose heart failure was of ischaemic aetiology.[20]Yildiran and colleagues similarly identified low pulse pressure as a predictor of death across the spectrum from mild to advanced heart failure.[21] The most robust evidence comes from the MAGGIC individual patient meta-analysis, in which a pulse pressure below 53 mmHg independently predicted mortality in heart failure with reduced ejection fraction, with the effect most

pronounced in patients whose ejection fraction was below 30% and whose systolic pressure was below 140 mmHg, and in which no consistent relationship was demonstrable in heart failure with preserved ejection fraction.[12] That the gradient of risk in MAGGIC was steepest precisely in the subgroup corresponding to our Group 1 lends external support to the pattern we observed.

A subsequent analysis of a randomised trial population with an ejection fraction of 35% or less, in which pulse pressure was divided into tertiles at 42 and 54 mmHg, confirmed that the direction of association between pulse pressure and adverse cardiovascular outcome in this phenotype is the reverse of that seen in the general population.[13] Laskey and colleagues, examining long-term outcomes in a large heart failure registry, described a comparable relationship with the risk nadir at a pulse pressure of approximately 50 mmHg.[22]

It is worth noting that the absolute pulse pressures in our cohort, with means of 25.86 and 33.83 mmHg, were considerably lower than the thresholds used in these Western cohorts. This is consistent with the lower absolute systolic pressures in our population, means of 99.12 and 113.53 mmHg, and reinforces the argument for normalising pulse pressure to systolic pressure rather than applying an absolute millimetre-of-mercury threshold uncritically across populations. It also explains why a proportional pulse pressure cut-off of 30% rather than the classical 25% was informative in our data, since a cut-off set at 25% would have classified too few patients as abnormal to be discriminating in a cohort whose mean proportional pulse pressure was already below 30% in both strata.

The contrast with the general population literature deserves explicit statement, because it is a frequent source of confusion. In older hypertensive subjects, a wide pulse pressure rather than mean pressure determines cardiovascular risk.[7]

In the Framingham cohort, coronary risk rose as diastolic pressure fell at any systolic pressure of 120 mmHg or above, implicating widening pulse pressure.[8] In the elderly, an increased pulse pressure predicted incident heart failure.[9] Vaccarino and colleagues found pulse pressure to be an independent predictor of both myocardial infarction and heart failure among community-dwelling elderly.[10] In the PROCAM cohort, each 10 mmHg increment in pulse pressure was associated with an increased risk of coronary heart disease, with risk in men whose pulse pressure exceeded 70 mmHg more than three times that in men whose pulse pressure was below 50 mmHg.[23]

The REGARDS analysis likewise reported an independent positive association between pulse pressure and incident coronary heart disease events.[24] These findings do not contradict ours. In an intact circulation, pulse pressure is dominated by aortic stiffness and wave reflection, and a wide value signals vascular ageing. In a failing ventricle, pulse pressure is dominated by stroke volume, and a narrow value signals pump failure. Domanski and colleagues captured this duality by demonstrating that sphygmomanometrically determined pulse pressure and mean arterial pressure carry independent prognostic information in patients with left ventricular dysfunction.[11]

Our findings on the conventional physical signs also merit comment. Elevated jugular venous pressure was significantly associated with the severity of systolic dysfunction (69.0% versus 37.9%, $p = 0.002$), consistent with the work of Butman and colleagues, who reported that resting or inducible jugular venous distension

identified a pulmonary capillary wedge pressure of 18 mmHg or above with a sensitivity of 81%, a specificity of 80% and a predictive accuracy of 81%.[25]Drazner and colleagues demonstrated that an elevated jugular venous pressure and a third heart sound in patients with asymptomatic left ventricular dysfunction predicted the subsequent development of heart failure and adverse outcome.[26] Both signs performed well in our cohort. Breathlessness on exertion, present in 90% of patients, was too ubiquitous to discriminate, and pedal oedema was neither sensitive nor specific, findings that reinforce the case for supplementing the traditional examination with the pulsatile indices rather than relying on it alone. The association between NYHA class and ejection fraction ($p = 0.011$) confirms that functional limitation broadly tracks systolic impairment, although the presence of 18 patients in class IV within the group whose ejection fraction exceeded 30% illustrates the well-recognised imperfection of that relationship. The practical implication of these data is straightforward. In a patient who satisfies the Framingham criteria for heart failure, a proportional pulse pressure of 30% or less should raise the probability of severe systolic impairment sufficiently to justify expedited referral for echocardiography and early institution of guideline-directed medical therapy, even where the ejection fraction cannot immediately be measured. Conversely, a proportional pulse pressure comfortably above 30% in a symptomatic patient argues against the most severe grades of systolic dysfunction. The index requires nothing beyond a sphygmomanometer and simple arithmetic, is reproducible, costs nothing, and can be repeated at every follow-up visit to track the haemodynamic response to treatment. In a country in which a large proportion of first contacts for heart failure occur at facilities without echocardiography, that combination of properties is not trivial.

Limitations

Several limitations should be acknowledged. The sample size of 100 patients drawn from a single centre limits the precision of the subgroup estimates and the generalisability of the findings. The cross-sectional design permits statements about association but not about causation, and although the literature establishes the prognostic weight of a low pulse pressure, the present study did not follow patients longitudinally and therefore cannot report mortality or rehospitalisation outcomes directly. No healthy control group was included, so the discriminatory performance of the indices was assessed only within a heart failure population and not against normal subjects. Blood pressure was recorded by brachial cuff, which measures peripheral rather than central pulse pressure and is subject to amplification along the arterial tree.

Cardiac index was not measured invasively, so the mechanistic assumption that a narrow proportional pulse pressure reflects a low cardiac index was inferred from published work rather than confirmed directly in our patients. The influence of ongoing pharmacotherapy, particularly vasodilators, diuretics and beta-blockers, on the measured pressure indices was not modelled. Finally, formal receiver operating characteristic analysis with derivation of sensitivity, specificity and predictive values at the 30% threshold was not undertaken, and would strengthen a future study.

Conclusion

In this cross-sectional study of 100 patients with chronic heart failure and an ejection fraction below 40%, both pulse pressure and proportional pulse pressure showed a moderate to strong positive correlation with left

ventricular ejection fraction, with correlation coefficients of 0.639 and 0.635 respectively and p values below 0.001. Patients with an ejection fraction below 30% had significantly lower systolic blood pressure, pulse pressure and proportional pulse pressure than patients with an ejection fraction of 30% to 40%, and a proportional pulse pressure of 30% or less was present in 88.1% of the former group compared with 51.7% of the latter.

Among the conventional bedside findings, orthopnoea, basal crepitations, the third heart sound, elevated jugular venous pressure and NYHA functional class discriminated significantly between the two strata, whereas breathlessness on exertion, pedal oedema, chest pain, syncope, pulse rate, age and sex did not. Proportional pulse pressure therefore behaves as a simple, inexpensive and reproducible bedside surrogate for the severity of left ventricular systolic dysfunction. It is well suited to use by physicians in primary and secondary care settings where echocardiography is not readily accessible, both for initial risk stratification at the time of presentation and for serial assessment of the haemodynamic response during follow-up.

Longitudinal studies with larger samples, invasive haemodynamic correlation and formal receiver operating characteristic analysis are warranted to define the optimal threshold and to confirm the prognostic value of the index in the Indian population.

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