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Assessment of Bendopnea and Its Association With Clinical and Para-Clinical Findings in Systolic Heart Failure: A Cross-Sectional Study

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ABSTRACT

Background and Aims: Bendopnea is a symptom found in patients with heart failure (HF) defined as shortness of breath when bending forward. The present study examined the correlation between bendopnea with other cardiac symptoms, echocardiographic findings, and cardiac function parameters.

Methods: This was a single-center prospective cross-sectional study of patients diagnosed with systolic HF. Medical history, bending tests, laboratory tests, electrocardiography (ECG), echocardiography, and 6-min walking test (6-MWT) were evaluated. Patients with reduced ejection fraction were followed to assess the 2-year outcomes for cardiovascular death and rehospitalization.

Results: A total of 80 patients were included in this study, of whom 54 (67.5%) were male. Bendopnea was present in 34 (42.5%) and their mean age was 62.44 years (compared to group without bendopnea, $p = 0.869$). Symptoms of HF such as dyspnea of exertion (DOE) and orthopnea were significantly related to the presence of bendopnea ($p = 0.001$, odds ratio (OR): 6.87, and $p = 0.016$, OR: 3.18, respectively). The bendopnea-positive group had a higher New York Heart Association (NYHA) class ($p = 0.005$). ECG results showed no significant difference between the two groups. The echocardiographic findings showed that the inferior vena cava (IVC) respiratory collapse was significantly lower in the bendopnea-positive group ($p = 0.019$, OR: 0.339, 95% CI:0.13–0.85). Moreover, they had a substantially lower performance in 6-MWT (387.39 vs. 325.58 m, $p = 0.015$). Neither rehospitalization nor death was related to bendopnea after a 2-year follow-up ($p = 0.454$).

Conclusion: Bendopnea was associated with several signs and symptoms of HF, including orthopnea, DOE, NYHA class, lower IVC collapse, and impaired functional capacity measured via 6-MWT. However, there was no association between bendopnea and ECG findings, ejection fraction, and NT-proBNP levels. Further studies with larger sample sizes are needed to assess the associations with long-term outcomes and confirm our findings.

Elmira Javanmardi and Tara Reshadmanesh contributed equally to this study.

1 | Introduction

Prevalence and incidence of heart failure (HF) are dramatically growing due to increases in lifespan and advances in the treatment of cardiovascular diseases, especially acute myocardial infarction and long-standing hypertension, which ultimately lead to HF. Despite improved survival rates in patients with HF in recent decades, this condition results in a poor quality of life and a substantial economic burden on the healthcare system; therefore, it should be considered a global health priority [1, 2]. To date, several diagnostic and prognostic biomarkers and symptoms have been suggested for HF [3–6]. Considering the crucial role of clinical signs and symptoms in the diagnosis and evaluation of outcomes, several studies suggest the superiority of physical examination over ejection fraction (EF) in predicting clinical outcomes [7].

Bendopnea, also known as flexo-dyspnea, was first described by Thibodeau et al. [8] in 2014 as a novel respiratory symptom of HF. Later in 2016, The European Society of Cardiology [9] guidelines stated bendopnea as an HF symptom [10]. In the most recent guidelines by ESC (2021) and ACC/AHA (2022), bendopnea is described as one of the less common symptoms of HF [9, 11, 12]. Patients with bendopnea experience shortness of breath when bending forward within 30 s. Different types of dyspnea, such as orthopnea, paroxysmal nocturnal dyspnea, and exertional dyspnea, have also been attributed to other medical conditions besides HF; like chronic obstructive pulmonary disease, coronary artery disease, and the elderly; hence, they might have low specificity [13]. Therefore, discovering a more specific symptom in HF patients is beneficial in favor of having a more accurate diagnosis as well as a more precise estimation of hemodynamic status. Previous studies suggest that the presence of orthopnea and elevated jugular venous pressure (JVP) are associated with increased pulmonary capillary wedge pressure (PCWP) in advanced HF [14–16]. The underlying pathophysiology of bendopnea has been attributed to an increase in ventricular pressure, especially in patients with low cardiac index [8, 17]; however, its association with other signs and symptoms and prognostic value in patients with HF needs further investigation. Moreover, some studies suggest that bendopnea might have low specificity and might be observed in the general population [18], while some others suggest its use in differentiating HF from other medical conditions such as respiratory diseases or coronary artery disease [19].

Additionally, there is limited information about the association of bendopnea with quality of life in HF patients. Six-min walking test (6-MWT) is a simple exercise for assessing functional status in HF, and it can be considered as a substitute for cardiopulmonary exercise testing (CPET) [20]. So, it can be used to evaluate the association between functional ability and exercise tolerance with bendopnea. The present study was with the aim of assessing the relationship between the presence of bendopnea and walking ability using 6-MWT and cardiac function parameters including echocardiography, electrocardiography (ECG), and laboratory values.

2 | Methods

2.1 | Study Design and Participants

This was a single-center, prospective cross-sectional study at the cardiovascular clinic of Mousavi Hospital in Zanjan, Iran, from August 2018 to August 2019. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the ethics committee of Zanjan University of Medical Sciences (IR.ZUMS.REC.1397.314). All the patients provided written informed consent. We included patients with a retrospective medical record of chronic systolic HF for enrollment in the study. The EF below 40% based on echocardiography at the clinical visit and the New York Heart Association (NYHA) functional class between I and III as primary symptoms were required for the diagnosis of patients [9, 11]. Exclusion criteria were as follows: the presence of HF exacerbation symptoms at the beginning of examinations, NYHA functional class IV (due to inability to perform 6MWT), history of decompensated HF within the last 6 months, uncontrolled high blood pressure, history of malignancy, liver cirrhosis, pregnancy, patients undergoing dialysis, chronic respiratory diseases and lung surgery, body mass index (BMI) $\geq 40\ kg/m^2$, and patients with obstructive sleep apnea.

2.2 | Variables and Outcomes

Patients underwent clinical history assessment and physical examination, together with ECG, echocardiogram, and 6-MWT. Demographic data, past medical and drug history, signs and symptoms of HF, including sleep apnea, snoring, dyspnea of exertion (DOE), orthopnea, angina, lung rale on auscultation, lower limb edema, night cough, NYHA class, and etiology of cardiomyopathy, were recorded in the checklist. To assess echocardiographic data, including cardiac chamber sizes, left and right ventricular function, tricuspid annular plane systolic excursion (TAPSE), pulmonary artery systolic pressure (PASP), and inferior vena cava (IVC) diameter and collapse, patients underwent standard 2-dimensional and doppler transthoracic echocardiography. Jugular vein pressure was determined for the patients in physical examination. For determining the presence of bendopnea, patients sat on a chair for about 10 min and then bent forward at the waist for 1 min; if they had shortness of breath, lightheadedness, or discomfort in the chest within 30 s, their test was considered positive [8]. Vital signs, including heart rate, blood pressure, and oxygen saturation, were recorded before and after bending. Then 6-MWT was performed according to protocol. In brief, this test is commonly used for objective assessment of functional exercise capacity in which the patient is asked to walk as far as 30 m for a period of 6 min [21]. According to protocols, 6-MWT was conducted indoors. The chosen route was about 30 m, flat and undeviating, and every 3 m was marked. Patients had taken their medications and were instructed to walk at a suitable rate to their condition. They could stop or slow down if they felt uncomfortable and resume walking whenever they felt better. Before and after the test, patients' heart rate, saturation oxygen, and brachial arterial pressure were recorded [1, 20]. In case of severe hemodynamic changes symptoms, such as dyspnea, palpitation, and dizziness, the patient was monitored again, and appropriate measures were taken. In case of hemodynamic alterations found in these measurements, we stopped the test. On completion of 6 min, patients were told to stop, and the total covered distance was calculated.

An antecubital venous blood sample was obtained for determining laboratory values such as cell blood count, C-reactive protein, erythrocyte sedimentation rate, N-terminal pro-brain natriuretic peptide (NT-pro BNP), thyroid-stimulating hormone, troponin, blood urea nitrogen, creatinine. Finally, all patients were followed by a phone call for 2 years after the initial assessment to collect data regarding cardiovascular rehospitalization and death. The cause of rehospitalization was determined by reviewing the patient records in the hospital.

2.3 | Study Size and Statistical Analysis

All statistical analyses were performed adhering to relevant recommendations for analysis, reporting, and interpretation of clinical research [22] and "Statistical Analyses and Methods in the Published Literature" (SAMPL) guidelines for reporting statistical analyses [23]. Since the frequency of bendopnea was estimated to be around 28% in the report by Thibodeau et al. [8], the minimum estimation of the required sample size for the reliable statistical analysis with an alpha error of 0.05 was considered for 80 patients, using the formula below.

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} \times P(1-P)}{d^2}.$$

In addition to the sample size calculation, post hoc power analysis was conducted to evaluate the power of the study to detect significant associations between bendopnea and clinical or para-clinical findings. Using an alpha error of 0.05, the study demonstrated adequate power (> 80%) for key comparisons. All statistical tests were two-tailed, with a significance threshold set at $p < 0.05$.

Continuous data were reported as mean (standard deviation [SD]). Data were analyzed using IBM SPSS Statistics software (version 24.0, SPSS, Chicago, Illinois). Data normality was assessed using Kolmogorov–Smirnov Test. The independent *t*-test was used to assess the relationship between normally distributed continuous variables, including changes in vital signs, laboratory values, 6-MWT parameters, and echocardiographic findings according to the presence of bendopnea. The Chi-square test was applied to determine the relationship between categorical variables, including clinical characteristics (signs and symptoms, medical history, HF etiology) and 2-year outcomes with the presence of bendopnea. For analyzing electrocardiographic findings, both independent *t*-test and chi-square test were used. The Spearman correlation coefficient was used to investigate the relationship between the NYHA class and the 6-MWT due to the non-parametric nature of these variables. Finally, logistic regression was performed to determine the predictor variables. A *p*-value less than 0.05 was considered statistically significant.

3 | Results

3.1 | Clinical Characteristics

A total of 80 patients were included in this study, of whom 54 (67.5%) were male. Bendopnea was present in 34 patients (42.5%). There were no statistical differences between the two groups in terms of gender ($p = 0.35$) and BMI ($p = 0.16$). The mean [10] age of patients was 62.67 (10.82) years, which was slightly lower in the bendopnea-positive group [62.44 (9.14) vs. 62.84 (12.01), $p = 0.87$]. Etiologies of HF included ischemic heart disease ($n = 57$, 71.3%), dilated cardiomyopathy ($n = 14$, 17.5%), and valvular heart disease ($n = 3$, 3.8%). Among these, bendopnea was higher in patients with dilated cardiomyopathy, although it was not significant ($p = 0.26$). There was no association between bendopnea and past medical and drug history (Table 1).

The prevalence of DOE was 88.2% ($n = 30$) and 53.3% ($n = 24$) in bendopnea positive group and bendopnea negative group, respectively ($p = 0.001$, OR: 6.87, 95% CI: 2.08–22.66). Also, the presence of orthopnea was significantly higher in patients with bendopnea ($p = 0.01$, OR: 3.18, 95% CI: 1.22–8.26).

Elevated JVP and advanced NYHA classes were higher in the bendopnea-positive group ($p = 0.007$ and $p = 0.005$, respectively). There was not any significant difference between the groups in terms of other signs and symptoms (Table 1 and Figure 1).

3.2 | Changes in Vital Signs With Position

The hemodynamic assessment showed that there were no changes in vital signs such as systolic blood pressure ($p = 0.48$), diastolic blood pressure ($p = 0.63$), pulse rate ($p = 0.80$), or oxygen saturation ($p = 0.46$), before and after bending in comparison of those with or without bendopnea. There was a slight increase in blood pressure and a decrease in oxygen saturation and pulse rate after bending in both groups, all insignificant (Table S1).

3.3 | Laboratory Values

Laboratory tests for assessing NT-pro BNP revealed no significant difference between the two groups ($p = 0.78$). None of the other laboratory findings were different either. The detailed information is presented in Table 2.

3.4 | ECG and Echocardiography Findings

Assessment of cardiac rhythm showed no remarkable difference between the two groups ($p = 0.30$). More information is summarized in Table 3. There was no difference between the two groups in terms of TAPSE, PASP, and TAPSE/PASP ratio.

The echocardiographic findings showed that the mean [10] IVC diameter was significantly higher in the bendopnea-positive

TABLE 1 | Patients' demographic characteristics.

Characteristic	Bendopnea (+) ($N = 34$)	Bendopnea (−) ($N = 46$)	p-value	OR (95% CI)
Age (years)	62.44 ± 9.14	62.84 ± 12.01	0.869	
BMI (kg/m^2)	30.05 ± 2.72	29.23 ± 2.41	0.160	
Male, n (%)	21 (61.8)	33 (71.7)	0.349	
Medical history				
Hypertension	27 (79.4)	31 (64.7)	0.234	
OAD	6 (17.6)	4 (8.7)	0.231	
CABG	6 (17.6)	12 (26.1)	0.372	
Cause of HF				
Ischemic	21 (34.4)	36 (48.0)	0.256	
Hypertension	27 (44.3)	31 (41.3)		
Valvular heart disease	1 (1.6)	2 (2.7)		
Dilated cardiomyopathy	10 (16.4)	4 (5.3)		
Congenital heart disease	0 (0.0)	1 (1.3)		
Anatomical	1 (1.6)	0 (0.0)		
History and physical examination findings				
Sleep apnea	2 (5.9)	3 (6.5)	0.907	
Snoring	11 (32.4)	14 (30.4)	0.855	
DOE	30 (88.2)	24 (53.3)	0.001	6.875 (2.08–22.66)
Orthopnea	17 (50.0)	11 (23.9)	0.016	3.182 (1.22–8.26)
Angina	3 (8.8)	2 (4.3)	0.668	
Prominent JVP	5 (14.7)	0 (0.0)	0.007	
Lung rale	4 (11.8)	3 (6.5)	0.412	
Lower limb edema	6 (17.6)	7 (15.2)	0.771	
Night cough	2 (5.9)	2 (4.3)	0.756	
NYHA			0.005	
Class I	4 (11.8)	23 (50.0)		
Class II	17 (50.0)	15 (32.6)		
Class III	13 (38.2)	8 (17.4)		

Note: Data are presented as mean ± SD or frequency (%).
Abbreviations: BMI, body mass index; CABG, coronary artery bypass graft; DOE, dyspnea on exertion; JVP, jugular vein pressure; NYHA, New York Heart Association; OAD, obstructive airway disease.

group [1.67 (0.47) vs. 1.41(0.49), $p = 0.019$]. The percentage of IVC collapse of > 50% was substantially lower in the presence of bendopnea (OR: 0.339, 95% CI: 0.13–0.85, $p = 0.01$). On the other hand, there was no association between bendopnea and right ventricle function indicators such as TAPSE, PASP, and fractional area change (FAC). Moreover, there was no difference between patients with and without bendopnea with respect to heart valve dysfunction, such as mitral valve regurgitation ($p = 0.48$) (Table 3).

3.5 | 6-MWT

6-MWT was performed to assess functional capacity and exercise tolerance. The average walking distance was significantly lower in the bendopnea-positive group (325.58 vs. 387.39 m, $p = 0.15$) (Table 4 and Figure 2). Based on the contingency coefficient in the Chi-square test, the effect size of bendopnea-presence on walking distance was 0.22, which indicates a moderate effect (considering the distance of ≤ 300 m as a reliable prognostic marker for subsequent cardiac death in 6-MWT) [24].

In the bendopnea-positive group, 61.8% of the patients stopped during the 6-MWT, which was significantly higher ($p = 0.003$, OR: 4.10, 95% CI: 1.59–10.53). There was a moderate inverse correlation ($r = -0.437$ and $p < 0.001$) between NYHA functional class and average walking distance.

3.6 | Two-Year Outcome

Overall mortality was 3.8% during the follow-up period. Thirty-three (41%) patients were rehospitalized, and eight (10%) were

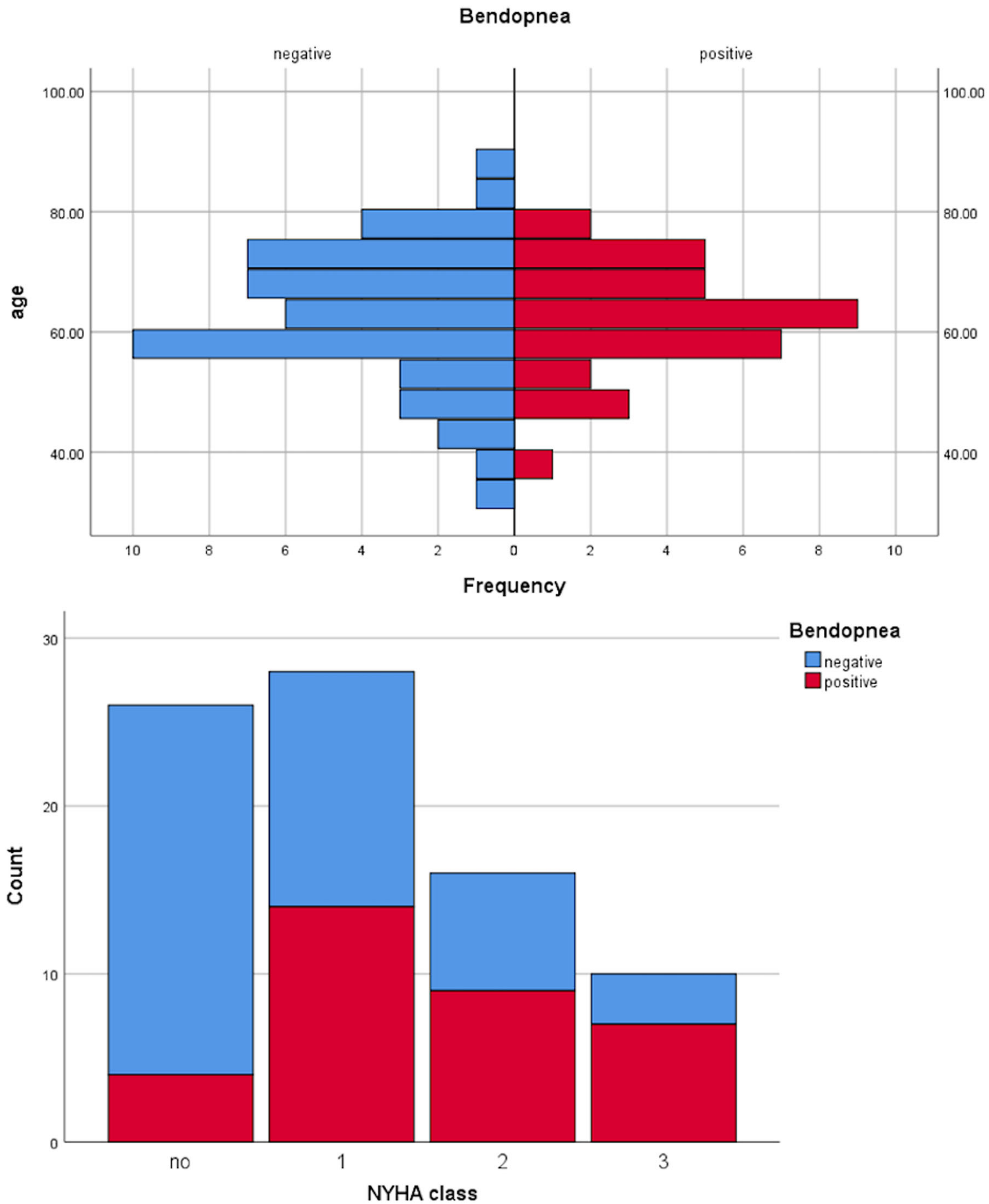

FIGURE 1 | Association of age and NYHA class with the presence of bendopnea.

lost to follow-up. Neither rehospitalization nor death was related to bendopnea ($p = 0.45$) (Table 4).

3.7 | Logistic Regression

Multivariable logistic regression showed that DOE ($p = 0.04$, OR: 7.42, 95% CI: 1.06–51.92) and IVC respiratory collapse ($p = 0.03$, OR: 0.25, 95% CI: 0.08–0.80) were predictive variables among the mentioned individually significant variables.

4 | Discussion

In the current study, bendopnea was present in 34 out of 80 patients (42.5%). Our findings showed that DOE, orthopnea, and advanced NYHA classes were significantly higher in bendopnea-positive patients. The presence of bendopnea was also associated with a significant reduction in the average walking distance in 6MWT; meanwhile, it had no relation with NT-pro BNP levels and prognosis.

In a meta-analysis study, the prevalence of bendopnea mainly ranged from 18% to 48.8% in HF patients [25]. Thibodeau et al. [8]

TABLE 2 | Laboratory value associations with bendopnea.

Laboratory values	Bendopnea (+) ($N = 34$)	Bendopnea (−) ($N = 46$)	*p*-value
WBC (10^9 cells/L)	7.53 ± 2.51	6.84 ± 1.80	0.158
Hb (10^9 cells/L)	15.11 ± 1.64	14.72 ± 1.90	0.350
Hct (L/L)	44.34 ± 3.84	43.32 ± 4.58	0.296
Plt (10^9 cells/L)	213.52 ± 52.31	210.93 ± 50.12	0.823
CRP (mg/L)	9.53 ± 21.74	6.30 ± 10.60	0.383
ESR (mm/h)	18.61 ± 18.57	13.21 ± 11.14	0.138
NT-ProBNP (pg/mL)	521.17 ± 709.83	521.15 ± 649.78	0.782
TSH (mU/L)	2.11 ± 1.33	2.26 ± 2.08	0.707
Troponin (ng/mL)	12.34 ± 15.36	9.91 ± 10.84	0.410
BUN (mg/dL)	18.81 ± 7.23	17.76 ± 6.65	0.504
Cr (mg/dL)	1.15 ± 0.28	1.12 ± 0.23	0.587

Abbreviations: BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; NT pro-BNP, N-terminal pro-brain natriuretic peptide; Plt, platelet; TSH, thyroid stimulating hormone; WBC, white blood count.

TABLE 3 | Electrocardiographic and echocardiographic finding associations with bendopnea.

Variable	Bendopnea (+) ($N = 34$)	Bendopnea (−) ($N = 46$)	*p*-value	OR	95% Confidence interval
Electrocardiograph findings					
Sinus tachycardia	0 (0.0)	1 (2.2)	0.712		
Sinus bradycardia	3 (8.8)	3 (6.5)			
Sinus with PVC[1]	4 (11.8)	2 (4.3)			
Sinus with PAC[2]	1 (2.9)	0 (0.0)			
Atrial fibrillation	10 (29.4)	7 (15.2)			
ST-segment deviation					
Depression	9 (26.4)	8 (17.3)	0.615		
Elevation	5 (14.7)	8 (17.3)			
Poor R progression	10 (29.4)	12 (26.1)	0.742		
T wave alternance	3 (8.8)	1 (2.2)	0.177		
Echocardiograph findings					
LVEF-Simpson (%)	27.82 ± 8.98	27.23 ± 9.17	0.779		
TAPSE (mm)	18.2 ± 04.3	21.2 ± 27.2	0.530		
PASP (mmHg)	25.64 ± 11.45	26.10 ± 13.71	0.874		
TAPSE/PASP ratio	0.91 ± 0.56	0.93 ± 0.92	0.913		
IVC inspiratory diameter (cm)	1.67 ± 0.47	1.41 ± 0.49	0.019	0.26	0.04–0.48
IVC respiratory collapse					
< 50%	20 (58.8)	15 (32.6)	0.020	0.33	0.13–0.85
> 50%	14 (41.1)	31 (67.3)			

Note: Data is presented as mean ± SD or frequency (%).
Abbreviations: IVC, inferior vena cava; LVEF, left ventricular ejection fraction; OR, odds ratio; PAC, premature atrial contraction; PASP, pulmonary artery systolic pressure; PVC, premature ventricular contraction; TAPSE, tricuspid annular plane systolic excursion.

reported its prevalence as approximately 29% in a population with a mean age of 58 years and a mean left ventricular EF of 20%. In addition, in another study of decompensated HF patients with a mean age of 81.1 years, 48.8% presented with bendopnea [16]. A recent study conducted in Iran showed a prevalence of 44.2% for bendopnea in patients with decompensated systolic HF [26]. The diversity in the prevalence of bendopnea can be due to the differences in mean ages and clinical status of participants; however, it should be noted that the type of HF (e.g., HF with reduced EF and HF with preserved EF) varies in these studies.

TABLE 4 | 6-MWT finding and prognosis associations with bendopnea.

Variable	Bendopnea (+) ($N = 34$)	Bendopnea (−) ($N = 46$)	*p*-value	OR	95% Confidence interval
6-MWT					
Distance (m)	325.58 ± 113.60	387.39 ± 107.15	0.015		
Stopping	21 (61.8)	13 (28.2)	0.003	4.10	1.59–10.53
Two-year outcome					
Hospitalized	17 (50.0)	16 (34.75)	0.454		
Death	1 (2.9)	2 (4.3)			
Loss of follow-up	4 (11.8)	4 (8.7)			

Note: Data is presented as mean ± SD or frequency (%).
Abbreviation: 6MWT, 6-min walk test.

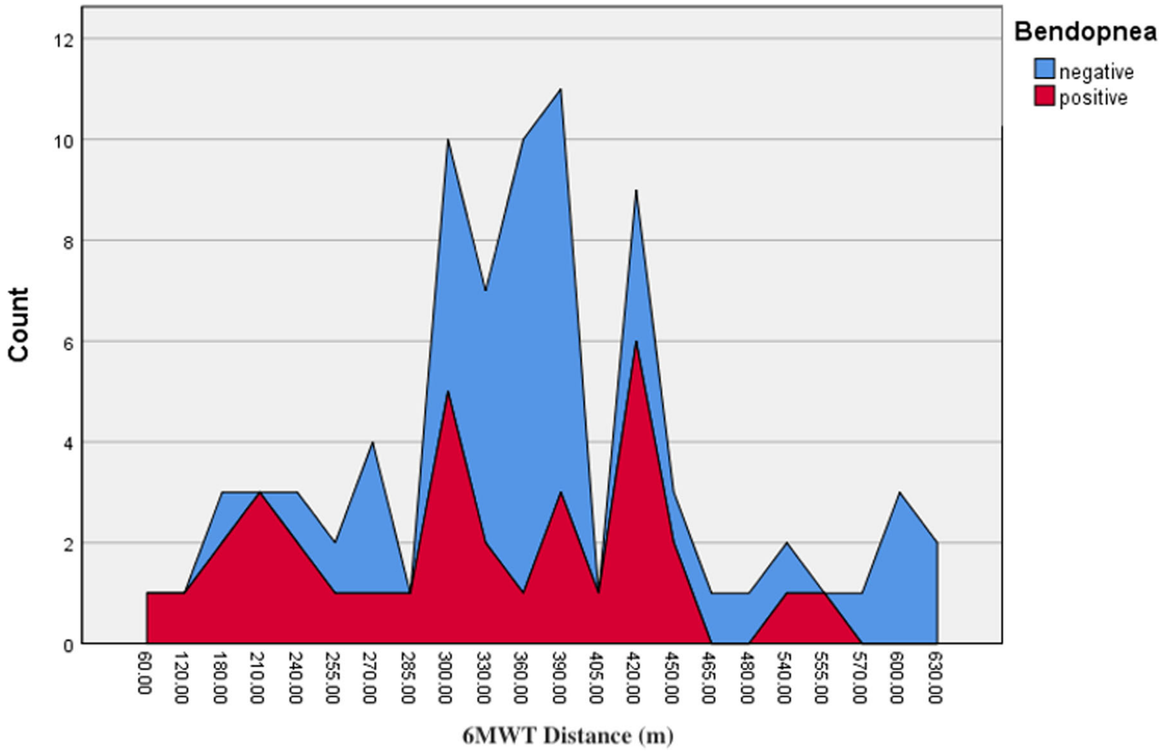

FIGURE 2 | The distance covered by patients with and without bendopnea in 6-MWT.

Previous studies have shown that bendopnea was common in those who had high PCWP and low cardiac index. Also, it was related to an increase in ventricular filling pressure when bending forward. Hence, given that orthopnea is a common symptom in HF patients, it is strongly associated with a high PCWP and elevated left ventricular filling pressure [8, 14, 27]. Therefore, an association between orthopnea and bendopnea is expected. Our findings showed that orthopnea and DOE were significantly higher in patients with bendopnea, consistent with previous studies that demonstrated the association of bendopnea with the presence of dyspnea, orthopnea, and paroxysmal nocturnal dyspnea [8, 16, 25, 28], our results revealed DOE as a predictor variable. A 2021 study also reported positive bendopnea in one-third of patients with severe obstructive sleep apnea and also found an association between the percentage of time spent at SaO2 below 90% (CT90) and bendopnea further emphasizing the involvement of pulmonary hypertension in the pathophysiology of bendopnea [29].

On physical examination, only elevated JVP was associated with bendopnea. This sign is present in several cardiac conditions, such as high right atrial pressure and PCWP, suggesting a marker of both elevated left or right-sided filling pressure [30]. Additionally, there was no relation between bendopnea and the presence of pulmonary rales, limb edema, and night cough. These findings may imply that bendopnea could be associated with increased left ventricular pressure and PCWP due to body position in patients whose baseline pressures are already elevated.

The 6-MWT is an easy method for the assessment of functional capacity as no special equipment is needed, and it is well-tolerated by the patients [20]. Previous studies have shown a correlation between performance in 6-MWD with peak VO2 and maximal power output in CPET [31]. In our study, patients had reduced EF, and 6-MWT was performed to evaluate their functional ability and exercise tolerance.

Our results demonstrated that the presence of bendopnea was accompanied by a reduction in the distance covered by patients (61.8% vs. 38.2%, $p = 0.003$) and an increase in the frequency of stops during the test. These findings suggest that the presence of bendopnea could be indicative of a decrease in functional capacity and daily activity performance. However, a randomized trial (Exercise Intolerance in Elderly Patients with Diastolic Heart Failure (SECRET)) in older patients with preserved EF showed no association between 6-MWD and parameters obtained from CPET [20]. These findings propose a possible association between bendopnea and low functional capacity in patients with low EF but not in patients with preserved EF. To understand the exact relationship between bendopnea and peak VO2, further studies are recommended. Considering NYHA functional class as another indicator of functional capacity status, we observed an association between advanced NYHA classes and bendopnea.

Laboratory tests showed no significant difference between the two groups. NT-Pro BNP and BNP levels are among the most influential independent predictors of mortality in patients with HF and thus can provide prognostic information [32, 33]. No relationship between the levels of NT-Pro BNP and bendopnea was observed, which was similar to previous studies [8, 16].

ECG findings showed no relationship between cardiac rhythm and bendopnea. To our knowledge, the relationship between ECG findings and bendopnea has not previously been investigated. The absence of new ischemic changes in the ECG would pronounce the specificity of bendopnea in HF and show its discriminatory ability, as proposed [19]. No relationship between EF and bendopnea was found, which was consistent with previous studies [25]. In addition, no association was observed between right ventricular function indicators such as TAPSE, PASP, FAC, and so forth, with bendopnea, which was in contrast to the study of Baeza-Trinidad, Mosquera-Lozano, and El Bikri [16], where patients with bendopnea had significantly higher PASP.

Our study made a novel comparison of the TAPSE/PASP ratio in patients with and without bendopnea. This ratio has been demonstrated to have potency as an independent predictor of precapillary pulmonary hypertension and to have an association with HF prognosis [34, 35]. Previous evidence suggests that it can serve as an independent predictor of mortality, specifically in patients with HF with HFrEF [36]. Pathophysiologically, this ratio reflects the RV response to changes in afterload [37]. A higher TAPSE/PASP ratio indicates better RV function [34], with suggested thresholds of < 0.31 and < 0.36 as indicators of RV-PA uncoupling [38, 39]. While our study did not reveal any significant differences between the two groups, it is noteworthy that both groups exhibited TAPSE/PASP ratios exceeding 0.36 mm/mmHg.

On the other hand, hemodynamic congestion can be considered a hallmark of HF, measured via the distention of great veins such as IVC [40]. There was a significant relationship between a lower percentage of IVC respiratory collapse and higher IVC diameter as indicators of hemodynamic congestion in the right or biventricular HF [41], with the presence of bendopnea, which would indicate higher hemodynamic congestion in these patients [42]. In other words, based on our findings, patients with bendopnea had higher IVC inspiratory diameter and lower IVC collapse, which in turn shows higher right atrium pressure and right-sided failure. Since there is still limited data on the association between echocardiographic findings and bendopnea, further investigations are recommended.

Neither mortality nor hospitalization was associated with the presence of bendopnea in our study ($p = 0.45$). Other studies with an average of 12 months follow-up, reported no relationship between bendopnea and mortality as well [25, 43]. Similarly, a recent study assessing 6-month mortality did not find any difference between patients with and without bendopnea [26]. On the other hand, a study by Baeza-Trinidad, Mosquera-Lozano, and El Bikri [16] reported higher mortality in elderly patients with decompensated HF and bendopnea. Thibodeau et al. [44] also found an increased risk of death and other composite endpoints in univariate but not multivariable analysis. This was similar in a retrospective study of 4644 patients with HF in which bendopnea was associated with worse clinical outcomes [45]. A pooled meta-analysis reported increased mortality in patients with bendopnea ($p = 0.002$, OR: 2.21) [25]. These contradictory findings are explained through the different mean age and the type of HF patients enrolled in these studies, plus, the fact that our study had a relatively small number of participants and did not include patients with NYHA class of IV. Additional studies with larger sample sizes and more extended follow-up periods are required to determine a more accurate association between the presence of bendopnea and prognosis.

While showing the rate of bendopnea and associated features in patients with systolic HF, our investigation has several limitations worth mentioning. Our study consisted of patients with reduced EF, and those with HFpEF were not examined, which limited our conclusions concerning the role of bendopnea in HF patients with normal left ventricular systolic function. Assessment of daily activity performance and functional capacity was via 6-MWT. We did not perform other tests, such as CPET, that directly measure peak VO2, which is a determinant of functional capacity. In addition, we assessed stable outpatients, and hospitalized patients or those with acute HF were not evaluated, which may have influenced the results. Then, while we assessed 2-year outcomes by phone call follow-up, we were not able to perform survival analysis and this signifies the need for further studies on this. Then, in 6-MWT, we only measured vital signs before and after the test and in cases of symptomatic hemodynamic alterations, and hence, slight changes in the vital signs could not be measured, preventing us from performing additional analyses. Finally, while we showed the association between bendopnea and other clinical, imaging, and laboratory markers, there was no intervention assessed for patients with bendopnea, which is clearly a clue for future research on this topic. Randomized trials assessing the novel HF therapies might consider those with

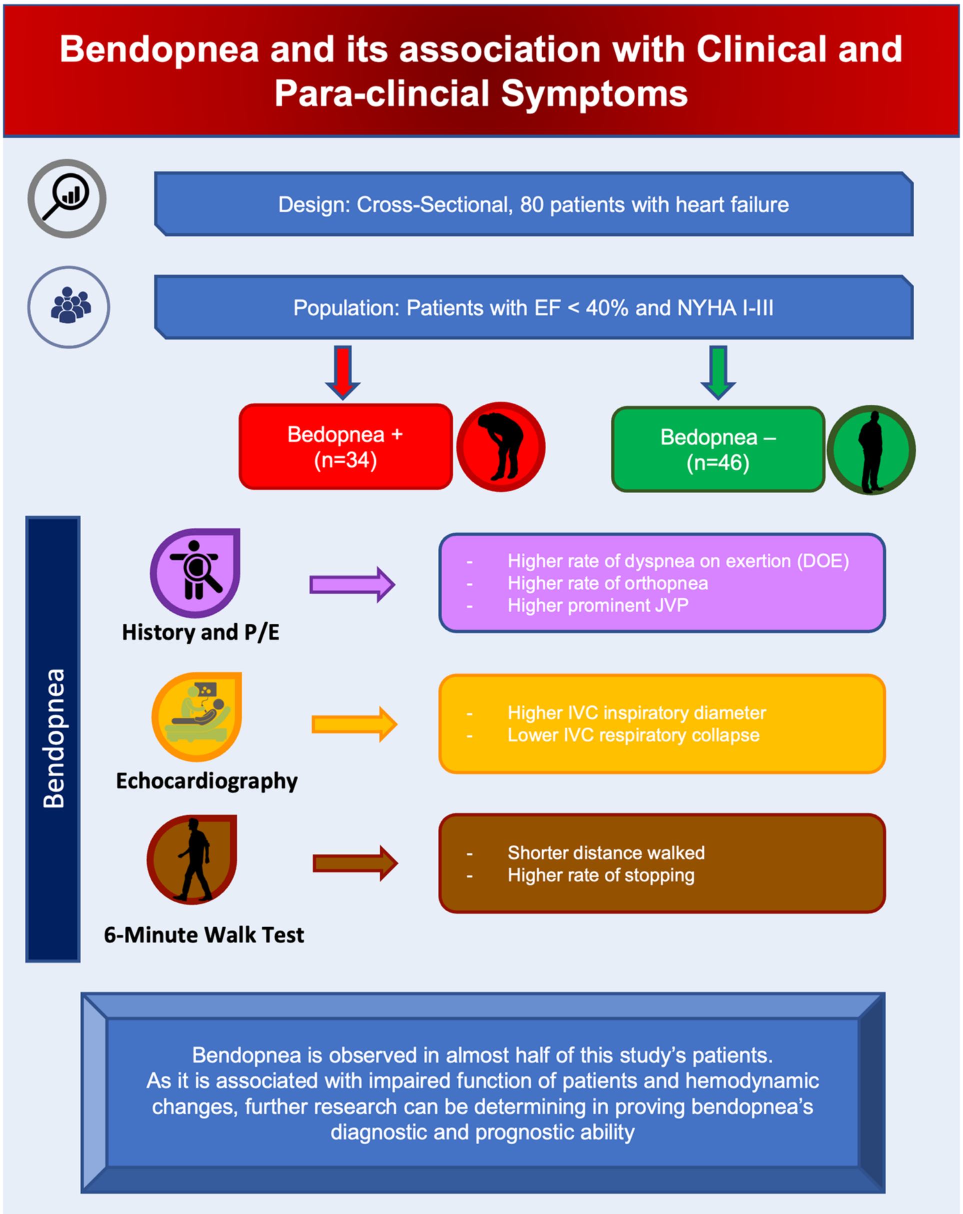

FIGURE 3 | Summary of findings of the current study. EF, ejection fraction; IVC, inferior vena cava; NYHA, New-York Heart Association; P/E, physical examination.

bendopnea as a separate group and assess the change in this symptom as well.

5 | Conclusion

In conclusion, the incidence rate of bendopnea was 42.5% in patients with systolic HF who were in a stable state. Moreover, this symptom was associated with orthopnea, DOE, elevated JVP, higher NYHA functional class, higher IVC diameter, lower collapse, and impaired functional capacity (Figure 3). No association was seen between bendopnea and myocardial wall stress biomarker (NT-Pro BNP) and outcome. Consequently, the presence of this symptom may indicate a higher hemodynamic congestion state in these patients. Further studies aiming at investigating bendopnea diagnostic and prognostic ability, in addition to assessing its effect on long-term outcomes such as mortality in patients with HF, are warranted to confirm the role of this less-investigated symptom.

Author Contributions

H.A. and E.J. contributed to the study's conception and design. Clinical section and data acquisition was performed by E.J. and S.G. The literature search, data analysis, and interpretation were performed by T.R. The first draft of the manuscript was written by T.R., and all authors commented on previous versions of the manuscript. Final revision, supervision, and manuscript editing were performed by H.A. and A.H.B. All authors have read and approved the final version of the manuscript. H.A. had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

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Ethics Statement

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Zanjan University of Medical Science (Code: IR.ZUMS.REC.1397.314).

Consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data/information supporting this study is available from the corresponding author upon reasonable request.

Transparency Statement

The corresponding author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.