

Symptom Clusters and Sentinel Symptoms in Heart Failure Patients: A Cross-Sectional Survey

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Purpose: To explore the symptom clusters of heart failure (HF) patients, identify the sentinel symptom of each symptom cluster, and provide a basis for the implementation of precise symptom management.

Patients and Methods: The study participants were recruited using convenience sampling from inpatients admitted to the cardiology department between November 2024 and January 2025, including patients admitted for acute HF, chronic HF, and acute decompensation of chronic HF. The General Information Questionnaire and the Memorial Symptom Assessment Scale were used for the survey. Symptom clusters were explored using principal component analysis, sentinel symptoms were explored using the Apriori algorithm.

Results: A total of 354 HF patients participated in the study. Four symptom clusters were identified in HF patients: the nocturnal respiratory distress symptom cluster, the low perfusion symptom cluster, the upper airway irritation symptom cluster, and the gastrointestinal symptom cluster. Three sentinel symptoms were explored: waking up breathless at night, sweating and cough.

Conclusion: HF patients have a variety of symptoms in the form of four symptom clusters, waking up breathless at night, sweating and cough are the sentinel symptoms. Medical staff can take sentinel symptoms as the focus of symptom cluster evaluation and targeted intervention, which can improve the efficiency of symptom cluster management and reduce patients' symptom burden.

Keywords: heart failure, symptom clusters, sentinel symptoms, nursing

Introduction

Heart failure (HF) is a complex clinical syndrome arising from structural and/or functional abnormalities of the heart that impair ventricular filling and/or ejection function, and it represents the severe and terminal stage of various cardiac diseases,¹ which characterised by high prevalence rates, high readmission rates, high mortality rates, multiple coexisting conditions, and an increasingly younger age of onset.² HF has affected an estimated 64.3 million individuals worldwide,³ with a prevalence of 1.1% in the Chinese population.¹ HF is associated with an extremely poor prognosis. Among hospitalized patients with HF, the 1-year mortality rate is as high as 23.6%,⁴ and the 5-year mortality rate remains close to 50%.⁵ The annual economic burden attributable to HF is approximately 108 billion,⁶ and the substantial costs associated with hospitalizations and long-term care for HF patients pose a considerable drain on healthcare systems and the individual households.

Unfortunately, even patients with optimally managed HF experience substantial symptom burden and are trapped in a vicious cycle of symptom exacerbation, remission, and recurrence.⁷ Patients with HF typically experience with a variety of symptoms, which include dyspnea,⁸ fatigue,⁹ edema¹⁰ and so on. On average, each patient experiences between 5 and 15 symptoms during the progression of their condition.¹¹ These symptoms often emerge simultaneously rather than in isolation,¹² and some of these symptoms interact synergistically, reinforcing one another to form symptom clusters.¹³ Dodd et al¹⁴ first introduced the concept of the "symptom cluster" in 2001, Which refers to 3 or more symptoms that occur simultaneously and are interrelated, yet do not necessarily share the same pathophysiological mechanisms. In 2005, Kim et al¹⁵ defined this concept and proposed that a symptom cluster consists of 2 or more interrelated symptoms that occur simultaneously. The

correlations among symptoms within one cluster are stronger than those across different clusters, and symptoms in a cluster may or may not share the same etiology. This view has been widely recognized, and the current study adopts this conceptual definition of symptom clusters.

Due to the synergistic effects of symptoms within a cluster, symptom clusters have a more detrimental impact on patients' physical and mental health and prognosis than do individual symptoms. Although symptom clusters facilitate symptom classification and management, and have improved patients' quality of life to some extent,¹⁶ challenges in managing these clusters remain. If treatment focuses solely on a single symptom without clearly differentiating between primary and secondary factors, the result may be suboptimal management. However, addressing each symptom individually would create additional burden for both medical staff and patients. Therefore, investigating whether a particular symptom within a symptom cluster can influence the onset or progression of other symptoms, and identifying intervention targets, can help address the challenges in managing symptom clusters.

Brown et al¹⁷ first proposed the concept of sentinel symptoms in 2011. Sentinel symptoms are the earliest indicators of a symptom cluster and can predict the emergence and trend of other symptoms.¹⁸ They are also the key triggers of other symptoms within the cluster, characterized by sensitivity, significance, prevalence, and driving properties.¹⁹ Because sentinel symptoms can precipitate the onset or worsening of other symptoms, recognizing these early warning signs is crucial for timely identification and effective management of the cluster. Therefore, in clinical practice, sentinel symptoms can serve as a starting point for managing symptom clusters. Thus, they not only help alleviate the onset or progression of related symptoms but also simplify the assessment of symptom clusters and improve efficiency;²⁰ moreover, this approach is of great significance for the implementation of symptom specific nursing care.²¹

Current research has focused on identifying symptom clusters in HF patients; however, methodological and instrumental heterogeneity across studies has led to variations in the resulting symptom profiles.^{22,23} Currently, investigations into sentinel symptoms have predominantly been conducted in the context of cancers such as breast,²⁴ lung,²⁵ and gastric cancer,²⁶ while research on sentinel symptoms in HF patients remains in its infancy. This is of great significance for the implementation of symptom-specific nursing care. It is currently unclear whether patients with HF exhibit sentinel symptoms. Therefore, the present study aimed to analyze symptom clusters in patients with HF, to identify sentinel symptoms within each cluster, and to provide a basis for delivering precise treatment and care to HF patients.

Study Design and Patients

This cross-sectional study employed convenience sampling. We recruited patients who were hospitalized in the cardiology department of a tertiary hospital in Ningxia Hui Autonomous Region from November 2024 to January 2025. The study received approval from the Ethics Review Committee of The General Hospital of Ningxia Medical University (No.KYLL-2024-0145) and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants prior to the survey. According to the factor analysis sample size estimation method, the sample size should be 10 times the number of entries.²⁷ This study analyzed 32 symptom entries. To account for potential invalid data, an additional 10% was added, setting the final target sample size at 352 participants. In total, 360 questionnaires were distributed, and 354 valid questionnaires were included in this study, with a response rate of 98.3%. The inclusion criteria for participation were as follows: 1. Patients who met the diagnostic criteria in the "Chinese Heart Failure Diagnosis and Treatment Guidelines 2024",²⁸ 2. Age 18 years or older, 3. The ability to complete the questionnaire in written or oral form. The exclusion criteria were as follows: such as severe liver failure,²⁹ severe kidney failure requiring dialysis,³⁰ or advanced malignant tumors.

Measures

Sociodemographic and Clinical Characteristics

The sociodemographic information included gender, age, marital status, residence, education, employment status, household income, smoking history, drinking history and so on. Clinical characteristics included New York Heart Association (NYHA) functional classification,³¹ annual hospitalization frequency, family history, comorbidities, medication types, the duration of HF diagnosis, left ventricular ejection fraction (LVEF, %) and so on.

Memorial Symptom Assessment Scale, MASAS-HF

The MASAS-HF was utilised to assess the incidence of symptoms and severity by HF patients. This scale was adapted in 2004 by Zambroski et al from the content of the Tumor Assessment Scale.³² Guo et al translated the MASAS-HF into Chinese in 2014.³³ This 32-item scale consists of three dimensions: physical (21 items), psychological (6 items), and HF (5 items) symptoms. Likert-type scale ranges from 1 (not at all) to 4 (very much). The higher the entry score, the more severe the subject's symptoms were for that entry. The Cronbach's α coefficient for this scale ranged from 0.807 to 0.946, and its content validity index was 0.712.

Data Collection

The questionnaire was collected by 2 investigators who had undergone standardised training.

Investigators explained to respondents how to complete the questionnaire and the precautions to be taken to ensure that they answered the questionnaire independently and based on a full understanding of it. For patients who were unable to fill in the form on their own, the investigator completed it on their behalf using uniform guidance and asking questions one by one. The Sociodemographic and Clinical Characteristic was filled out by investigators according to the electronic medical record system. The MASAS-HF was completed by participants. After collection of the questionnaires, investigators checked and eliminated the questionnaires that had incomplete information. Data was entered by 2 investigators working in tandem to minimise errors and omissions.

Statistical Analysis

Data analysis was performed using SPSS 28.0 and SPSS modeler 18.0. Firstly, count data were described using frequency and composition ratios; normally distributed data were described using mean $\pm$ standard deviation. Non-normal data were presented as medians accompanied by interquartile ranges (P_{25} , P_{75}). Secondly, exploratory factor analysis was performed using the maximum variance method for factor rotation to identify symptom clusters. Symptoms that had an incidence of $<30\%$ were excluded from the analysis. The suitability of the data for factor analysis was assessed using the KMO test and Bartlett's test of sphericity. The criteria for factor selection were as follows: (1) eigenvalue ≥ 1 ; (2) each factor must include at least two symptoms; (3) the symptom loading must be ≥ 0.4 . Thirdly, in conducting correlation analysis with the Apriori algorithm, support and confidence serve as the standard metrics for evaluating relationships between symptoms.²⁵ The sentinel symptoms were detected based on Apriori algorithm, the support was greater than 40%, confidence was greater than 60% and confidence was greater than support, Which means that there were effective relationships between the two symptoms.³⁴

Results

Characteristics of Heart Failure Patients

A total of 354 patients with HF were recruited in this study, general information is shown in [Table 1](#).

Symptom Clusters in Heart Failure Patients

The test of applicability showed that this study had a KMO value of 0.624 and Bartlett's spherical test $P < 0.01$, making it suitable for factor analysis. A total of five factors with eigenvalues > 1 were extracted, and the cumulative variance contribution rate was 57.833%. As each factor encompasses at least two symptoms, chest pain has not been included within the symptom cluster. Consequently, four symptom clusters were identified and named respectively as: nocturnal respiratory distress symptom cluster, low perfusion symptom cluster, upper airway irritation symptom cluster and gastrointestinal symptom cluster, which are shown in [Table 2](#).

Sentinel Symptoms Within 4 Symptom Clusters in Heart Failure Patients

Analysis of fatigue symptom clusters, nocturnal respiratory distress symptom cluster, low perfusion symptom cluster and upper airway irritation symptom cluster using the Apriori algorithm. The results showed that waking up breathless at night was identified as the sentinel symptom of nocturnal respiratory distress symptom cluster, sweating was identified as the sentinel symptom of low perfusion symptom cluster, cough was identified as the sentinel symptom of upper airway irritation symptom cluster. Gastrointestinal symptom cluster was not associated with the sentinel symptom, as shown in [Table 3](#).

Table 1 The General Characteristics of Participants (N=354)

Variable	Categories	n (%) or Mean±SD
Gender	Male	227(64.1)
	Female	127(39.5)
Age (years)		[62.62±12.00]
Marital status	Single	3(0.8)
	Married	318(89.8)
	Divorce	2(0.6)
	Widowed	31(8.8)
Residence	Urban area	192(54.2)
	Rural area	162(45.8)
Living condition	Living alone	15(4.2)
	Living with family	339(95.8)
Monthly income	<2000	55(15.5)
	2000–2999	187(52.8)
	3000–4999	100(28.2)
	≥5000	12(3.4)
Employment state	Employed	72(20.3)
	Unemployed	282(79.7)
Education	Primary school and below	199(56.2)
	Junior High School	99(28.0)
	High school	40(11.3)
	University degree or above	16(4.5)
Medical payment methods	Medical insurance	303(85.6)
	Self-funded	51(14.4)
Smoking condition	Never smoking	197(55.6)
	History of smoking	70(19.8)
	Smoking	87(24.6)
Drinking condition	Never drinking	253(71.5)
	History of drinking	58(16.4)
	Drinking	43(12.1)
NYHA class	I	8(2.3)
	II	106(29.9)
	III	161(45.5)
	IV	79(22.3)
Heart failure duration	<1 year	175(49.4)
	1–5 years	102(28.8)
	>5 years	77(21.8)
Annual hospital admissions	Firstly	180(58.8)
	Twice or fewer	106(29.9)
	Three times or more	68(19.2)
Family history of heart failure	Yes	42(11.9)
	No	312(88.1)
Comorbidity	≤2	293(82.8)
	>3	61(17.2)
Types of medication	≤2	148(41.8)
	3–5	147(41.5)
	≥6	59(16.7)
LVEF (%)		[35.41, 51.17]
BNP (pg/mL)		[1315.00, 7042.50]
BMI (kg/m ²)		[22.22, 27.21]

Table 2 The Description of Symptoms and Symptom Clusters (N=354)

Symptom	Symptom Occurrence Rates (%)	Loading				
		A	B	C	D	E
Sleep disturbance	68.9	0.568				
Waking up breathless at night	40.1	0.817				
Difficulty breathing when lying flat	50.3	0.791				
Fatigue	84.2		0.765			
Shortness of breath	93.2		0.675			
Sweating	55.1		0.565			
Dizziness	53.1		0.544			
Nausea	34.2			0.612		
Lack of appetite	50.0			0.830		
Cough	58.8				0.738	
Dry mouth	62.4				0.793	
Chest pain	35.6					0.638
Eigenvalues after rotation		1.961	1.754	1.320	1.316	1.167
Accumulative variance explained (%)		15.083	28.575	38.732	48.856	57.833

Table 3 Apriori Algorithm-Based Association Rules (N=354)

Symptom Cluster	Antecedent	Consequent	Support (%)	Confidence (%)
Nocturnal respiratory distress symptom cluster	Waking up breathless at night	Sleep disturbance	40.11	92.95
	Waking up breathless at night	Difficulty breathing when lying flat	40.11	80.98
	Difficulty breathing when lying flat	Sleep disturbance	50.28	83.14
	Difficulty breathing when lying flat	Waking up breathless at night	50.28	64.60
Low perfusion symptom cluster	Sweating	Shortness of breath	55.08	96.92
	Sweating	Fatigue	55.08	90.76
	Sweating	Dizziness	55.08	63.58
	Dizziness	Shortness of breath	53.10	96.27
	Dizziness	Fatigue	53.10	84.68
	Dizziness	Sweating	53.10	65.95
Upper airway irritation symptom cluster	Cough	Dry mouth	58.75	72.59
	Dry mouth	Cough	62.42	68.32

Discussion

This study identified four symptom clusters in HF patients, designated as nocturnal respiratory distress symptom cluster, low perfusion symptom cluster, upper airway irritation symptom cluster, and gastrointestinal symptom cluster. Waking up breathless at night, sweating, and cough are the corresponding sentinel symptoms, while no sentinel symptoms have yet been identified for gastrointestinal symptom cluster.

The nocturnal respiratory distress symptom cluster consisted of sleep disturbance, waking up breathless at night, difficulty breathing when lying flat and consistent with previous studies.^{13,35} This cluster can be physiologically explained by the fact that pulmonary congestion and edema resulting from HF are the primary mechanisms underlying dyspnoea, which in turn contributes to sleep difficulties to a certain extent.³⁶ The low perfusion symptom cluster consisted of sweating, shortness of breath, fatigue and dizziness, whereas the studies by Li et al³⁷ and Wu et al³⁸ classify them as distinct symptom clusters. This may be due to differences between the criteria for identifying symptom clusters and the statistical methods used. The upper airway irritation symptom cluster consisted of cough and dry mouth, which is consistent with the findings of Li et al³⁷ The gastrointestinal symptom cluster consisted of nausea and lack of appetite, which is essentially similar to the studies by Son³⁵ and Yi.³⁹ This can be explained by impaired venous return, which causes systemic congestion and reduced cardiac output, ultimately leading to visceral ischemia and hypoxia. It is noteworthy that, in contrast to previous studies, this research did not identify an emotion-related symptom cluster. This may be related to the advanced age of the patients in this study. Influenced

by China's traditional social and cultural context, older adults tend to express their emotions in a more restrained manner and rarely reveal negative emotions to others.⁴⁰ Therefore, medical staff should complement pharmacological treatment with psychological interventions, encouraging patients to openly express their negative emotions and providing individualized psychological support. In addition, the symptoms experienced by HF patients are complex and exhibit cumulative and synergistic effects. Therefore, medical staff can adopt comprehensive management strategies to monitor symptom clusters holistically, thereby alleviating the burden on the healthcare system, improving the efficiency of symptom management, and ultimately enhancing HF patients' quality of life.

Waking up breathless at night was the sentinel symptom of the nocturnal Respiratory distress symptom cluster. This may be due to elevated left atrial pressure, leading to fluid leakage into the interstitial and alveolar spaces, which disrupts gas exchange, causing respiratory symptoms.⁴¹ Several studies have demonstrated that approximately 50% of HF patients experience waking up at night due to sleep disordered breathing, including apnea, paroxysmal nocturnal dyspnoea, orthopnoea, and cough.^{42,43} These symptoms disturbances consequently contribute to sleep disruption and poor sleep quality in the majority of HF patients.⁴⁴ Importantly, waking up breathless at night and difficulty breathing when lying flat frequently co-occur, and the former serves as a clinical marker of worsening HF.^{16,45} Therefore, medical staff should closely monitor the nighttime sleep patterns of HF patients. This can be achieved using wearable devices that continuously record sleep related breathing patterns.⁴⁶ Notably, if a patient wakes up breathless at night, this may indicate worsening of their condition, and prompt medical attention should be sought.⁴⁵ Medical staff can use cognitive behavioral therapy, auricular acupressure with beans, and traditional Chinese medicine to alleviate waking up breathless at night, thereby reducing other symptoms within this symptom cluster and improving HF patients' quality of life.^{47,48}

Sweating was the sentinel symptom of the low perfusion symptom cluster. Excessive activation of the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system (SNS) contributes to the progression of HF through multiple mechanisms. Specifically, during HF episodes, RAAS overactivation promotes sodium and water retention, whereas SNS activation stimulates eccrine sweat gland secretion. Together, these two mechanisms lead to increased sweating.⁴⁹ Beyond fluid and sweat disturbances, elevated aldosterone levels also cause myocardial thickening and stiffening, impairing cardiac pumping and reducing cardiac output.⁵⁰ This results in hypoperfusion of organs and tissues, accompanied by compensatory tachycardia, which subsequently contributes to fatigue and shortness of breath. HF Patients require long-term treatment with angiotensin converting enzyme inhibitors to slow disease progression; however, these medications may cause dizziness and fatigue as side effects.⁵¹ Therefore, medical staff should pay attention to the symptom of sweating in patients, as it may help impede the development of other symptoms and prevent synergistic effects within the cluster. Waon therapy can be used to induce sweating, which in turn causes peripheral vasodilation and consequently reduces both the preload and afterload on the heart.⁵² This treatment has been proven to be a comfortable and safe therapy that improves clinical symptoms and enhances cardiac function.⁵³

Cough was the sentinel symptom of the upper airway irritation symptom cluster. Among the serious conditions associated with cough, HF represents the most prevalent extra-pulmonary etiology.⁵⁴ Specifically, HF can lead to pulmonary congestion, which in turn irritates the airways and triggers the cough.⁴¹ Consequently, to alleviate symptoms of congestion, patients require long term diuretic therapy, which can lead to fluid loss and subsequent dry mouth; moreover, the side effects of these medications may also directly induce dry mouth.^{39,55} Medical staff should pay closer attention to assessing patients' cough symptoms to avoid missed or delayed diagnosis in the early stages.⁵⁶ In terms of cough management, patients may adopt a sitting or semi recumbent position to relieve coughing. Furthermore, for those with frequent cough, respiratory exercises may be recommended, and appropriate cough suppressants can be prescribed as needed to reduce symptoms.

This study has several limitations. First, as a single-center study conducted exclusively in tertiary hospitals within the Ningxia Hui Autonomous Region, the findings may not be generalizable to other settings or regions in China. Therefore, future large-scale, multi-center trials with subgroup analyses are warranted to facilitate more precise medical care for patients. Second, the cross-sectional design precluded investigation of the dynamic trajectory of sentinel symptoms over time; future longitudinal studies could be conducted to elucidate how these symptoms change over time. Lastly, this study did not record detailed information about the medications the patients were taking nor did it examine the relationship between biological markers and sentinel symptoms, issues that need to be further explored in the future.

Conclusion

This study found that HF patients have multiple symptoms in the form of four symptom clusters, and identified three sentinel symptoms: waking up breathless at night, sweating and cough. Such findings provide novel evidence to facilitate personalized cluster targeted symptom management and strengthen early symptom screening capacity. Future research can develop tailored interventions centered on these sentinel symptoms to improve quality of life in HF populations.

Ethics Approval and Informed Consent

Prior to commencement of the study, written informed consent was obtained from all participants. Participants' privacy and confidentiality were rigorously protected throughout the entire research process, and they were entitled to withdraw from the study at any time without prejudice. This study received approval from the Ethics Review Committee of The General Hospital of Ningxia Medical University (No.KYLL-2024-0145) and was performed in accordance with the Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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