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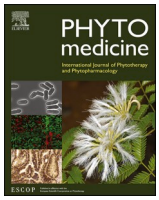

Original Article

Health and economic evaluation of herbal medicines for heart failure: A population-based cohort study

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ABSTRACT

Background: Heart failure (HF) represents an advanced stage of various cardiovascular disorders, with its elevated admission rates and resultant health economic burden posing an ongoing global concern.
Purpose: To evaluate the health and economic benefits of herbal medicine (HM) for patients with HF.
Study Design: Population-based cohort study.
Methods: A five-year retrospective cohort study was carried out at a nationally recognized hospital in China. The study utilized propensity score matching (PSM) to match patients with HF. Chi-square tests were used to analyze dichotomous variables, and *t*-tests were employed for continuous variables. Logistic regression was used to examine hospital readmission rates, while multiple linear regression was utilized to evaluate direct medical costs. Statistical significance was set at $p < 0.05$.
Results: After implementing PSM, 1924 HF patients were included in the analysis. The study identified two significant risk factors affecting the readmission rates: age over 65 years (adjusted odds ratio (OR) = 1.25, 95 % confidence interval (CI) [1.02, 1.53]) and smoking (adjusted OR = 1.31, 95 % CI [1.01, 1.70]). Additionally, patients who received adjunctive HM treatment exhibited a significantly lower readmission rate compared to those without HM treatment (adjusted OR = 0.76, 95 % CI [0.64, 0.92]). Furthermore, the use of HM during patient hospitalization did not significantly impact direct medical expenses but instead provided positive health economic benefits (incremental cost-effectiveness ratio (ICER) = 98.52). Factors influencing direct routine medical costs included over 65 years of age (Coef = 60.78, 95 % CI [36.25, 85.31]), and cardiac function classification (New York Heart Association (NYHA) III: Coef = 1979.92, 95 % CI [1401.82, 2558.03]; NYHA IV: Coef = 6052.48, 95 % CI [5166.59, 6938.38]).
Conclusions: The integration of HM in patients with HF reduced readmission rates without a notable increase in direct medical costs, and the expense of HM remains an economically range indicating positive health economic outcomes.

Abbreviations: HF, heart failure; HM, herbal medicine; PSM, propensity score matching; OR, odds ratio; Coef, coefficient; NYHA, New York Heart Association; ICER, incremental cost-effectiveness ratio; TCM, traditional Chinese medicine; CHD, coronary heart disease; CPM, Chinese patent medicine; SD, standard deviation; ROC, receiver operating characteristic.

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Introduction

Heart failure (HF) is a range of complex clinical syndromes caused by various cardiac structural and/or functional changes, leading to insufficient blood supply (McDonagh et al., 2023). It is the advanced stage of numerous cardiovascular diseases and is known to be associated with high morbidity, hospital admission rates, mortality, and healthcare costs (Savarese et al., 2023). Globally, >62 million patients suffer from the HF and resulting in a significant health burden (Benjamin et al., 2017), in which approximately 83 % of HF patients require hospitalization at least once a year and 43 % experiencing four or more hospitalizations annually (Benjamin et al., 2017). The total expenditure on HF in the United States is expected to increase from approximately $30.7 billion in 2012 to $69.8 billion by 2030 (Heidenreich et al., 2013; Virani et al., 2021). In China, there are estimated 12.1 million patients, with the mean inpatient cost of $4406.8 per-capita (Wang et al., 2021). The median length of hospital stay was 10 (range 7–15) days with an in-hospital mortality rate of 4.1 % (± 0.3 %) (Zhang et al., 2017).

Advancements in modern medical research on the pathophysiological mechanisms and pathogenic factors of HF have led to a transformation in the treatment paradigm from the initial focus on "cardiac, diuretic, and vasodilator" approaches to the current emphasis on "neuroendocrine and multi-targeted holistic regulation" (McDonagh et al., 2022). Building upon the established medical treatment foundation, individualized adjunctive therapies utilizing herbal medicine (HM) have gained acceptance. Previous studies have demonstrated the potential benefits of certain herbal medicines, such as Ginseng and Salvia miltiorrhiza, in enhancing myocardial contractility, vasodilation, diuresis, inhibition of ventricular remodeling, improvement of exercise tolerance, and symptom alleviation (Chow et al., 2010; Jiang et al., 2010; Meng et al., 2018; Zick et al., 2005). Chinese patent medicines (CPMs), including Qili Qiangxin capsules, Tongxinluo capsules and Shenmai injection have shown promise in improving cardiac function in clinical trials (Li et al., 2013; Xing et al., 2022; Yang et al., 2023; Zhou et al., 2014). In clinical practice, these herbal medicines are commonly used to treat HF.

However, it is unclear whether the use of herbal medicines in real clinical settings benefits patients with HF, particularly regarding long-term disease progression and health economics. This study aimed to investigate the impact of HM utilization on hospital readmission rates and health economics in HF patients through a cohort study in a nationally renowned hospital in China.

Material and methods

Study population and design

The diagnostic criteria for HF were determined according to the classification and diagnostic criteria for HF in the 2022 AHA/ACC/HFSA Guidelines for the Management of Heart Failure (Heidenreich et al., 2022). The inclusion criteria were as follows: (1) aged 20 to 80 years; (2) meeting the diagnostic criteria for HF; (3) patients with a New York Heart Association (NYHA) class of II, III, or IV; (4) currently receiving routine treatment, which includes diuretics, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta blockers, aldosterone receptor antagonists, digitalis, or vasodilators. The exclusion criteria included: (1) secondary cardiomyopathy (hyperthyroid heart disease, anemic heart disease and perinatal cardiomyopathy); (2) pulmonary heart disease; (3) active liver disease, or with unexplained persistent elevation of serum aminotransferases or upper limit of the normal reference value of glutamic-pyruvic transaminase; (4) severe renal dysfunction; (5) combination of severe primary diseases, including respiratory and hematological conditions, or malignant tumors; (6) pregnant or lactating women.

Ethics statement

This study was approved by the Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences (2023–145-KY). Patients with HF were admitted between December 1, 2016, and November 30, 2021, at Guang'anmen Hospital, a tertiary-level hospital with approximately 3.51 million annual visits. Patients admitted were diagnosed and treated by physicians who have the necessary qualifications to practice traditional Chinese medicine (TCM) and had undergone more than two years of standardized residency training. All routine and TCM-related treatments were further supervised by physicians who held the position of deputy director or above.

Variables of exposure

According to the guidelines for HF (Heidenreich et al., 2022), the non-exposed group of patients received routine treatment, which included pharmacological therapy (renin-angiotensin system inhibitors, β-blockers, salicylated corticosteroid receptor antagonists, sodium-glucose cotransporter protein 2 inhibitors, hydralazine, isosorbide nitrate, and others), device therapy (pacemakers, cardiac resynchronization therapy, implantable cardioverter-defibrillator), or surgical therapy (catheter ablation, coronary artery bypass grafting, valve repair or replacement, mechanical circulatory support, and heart transplantation). The exposure group received routine treatment combined with herbal medicine (patients received herbal medicines for at least one week in addition to routine treatment in accordance with the medication standards of the Chinese Pharmacopoeia (Committee, 2020)). The potential confounding factors studied included age, gender, smoking, drinking, cardiac function classification, hypertension, coronary heart disease (CHD), diabetes mellitus, hyperlipidemia, family history of hypertension, family history of CHD, and CPM treatment.

Outcome indicators

The main outcome was the readmission rate of patients with HF during the 1-year follow-up period, defining readmission as the occurrence of more than one hospitalization during the follow-up period. For patients with HF who had only one hospitalization in their records, a telephone survey was conducted to confirm whether the patient had HF-related hospitalization during the 1-year follow-up period. Cumulative readmission rate was used to compare trends in the proportion of readmission patients in the groups with/without HM during the follow-up period for patients who had accurate readmission dates recorded.

Health economic evaluation

The direct medical costs associated with each factor were statistically analyzed. The incremental cost-effectiveness ratio (ICER) was employed as a measure of health economics, representing the cost of each additional unit of utility. If ICER is within the acceptable threshold for decision makers, then the intervention is considered to have good cost effectiveness, and its economic impact is deemed acceptable. The patient's willingness to pay threshold is set at three times the GDP per capita recommended by the WHO. As of December 2023, China's GDP per capita was $12,621.721 US dollars. The data sources for calculating the ICER included the total hospitalization costs for patients receiving conventional treatment alone or in combination with HM, the mean difference calculated after discounted conversion at a 5 % annual conversion rate, and the results of the readmission rates for both groups.

Statistical analysis

Initially, patients receiving convention or combination treatment were matched in a 1:1 ratio using the propensity score matching (PSM) method based on the factors of age, gender, smoking, drinking, cardiac

function classification, hypertension, CHD, diabetes mellitus, hyperlipidemia, family history of hypertension, family history of CHD, and CPM treatment. The distributions of demographic data, cardiac function classification, and comorbidities were expressed as frequencies (percentages) or mean ± standard deviation (SD). Categorical and continuous variables in baseline characteristics were assessed using the chi-square test and *t*-test, respectively. The Logistic regression analysis was employed to estimate the odds ratio (OR) and 95 % confidence interval (CI) of readmission rates. The Nelson-Aalen cumulative risk model was used to compare the cumulative readmission rate between the conventional treatment with/without HM (named, HM and non-HM groups respectively), which was expressed as a percentage over 365 days of follow-up. The coefficients (Coef) and 95 % CI were derived through multiple linear regression analyses for direct routine medical costs. ICER was calculated as the ratio between the mean difference of total hospitalization costs and the difference in the readmission rate. In the sensitivity analysis, the HM cost per patient was multiplied by 0.5 and 2, respectively, and compared with three times the GDP per capita (Bertram et al., 2016). Statistical analyses were performed using Stata 17.0 software (Stata Corp., College Station, TX, USA). A p - value <0.05 was considered statistically significant.

Results

Characteristics

A total of 987 patients in the routine treatment alone group (non-HM group) and 1819 patients in the combined HM and routine treatment group (HM group) were included. During the follow-up period, 340 patients lost follow-up, including 232 with NYHA II, 79 with NYHA III, and 29 with NYHA IV due to telephone disconnection, rejection, or refusal to communicate. A total of 2806 patients from both groups were used to match propensity scores. After PSM matching, a final sample of 962 patients was included in each group (Fig. 1). The mean age ± standard deviation (SD) in the non-HM group was 71.0 ± 11.4 years, including 296 patients between the ages of 20 and 65, and 666 patients

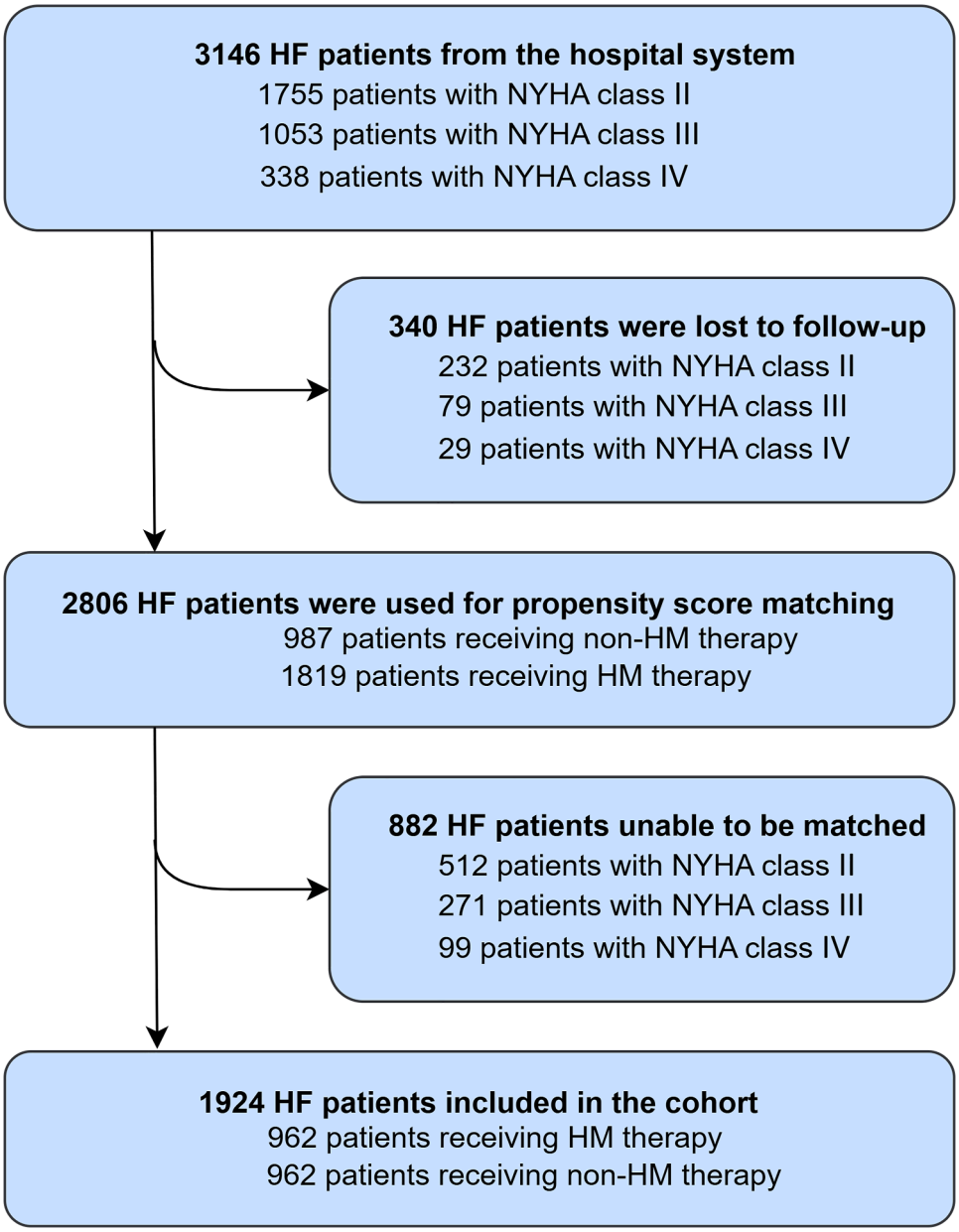

Fig. 1. Flow chart of inclusion of patients with heart failure. Note: HF, heart failure; NYHA, New York Heart Association; HM, herbal medicine.

over the age of 65. The mean age ± SD in the HM group was 71.1 ± 11.4 years, with 291 patients between the ages of 20 and 65, and 671 patients over the age of 65. No statistically significant differences were found in demographic characteristics, comorbidities, family history of CHD, or CPM treatment between the two matched groups ($p > 0.05$) (Table 1). Names and species of Chinese medicines used by the patients are listed in the **Supplementary Table S1**.

Readmission rate

The univariate and multivariate logistic regression analyses demonstrated a significant correlation between HM use and lower readmission rate in patients with HF (Table 2, Fig. 2(a)). Patients in the HM group had a 23 % lower readmission rate compared to patients who did not receive HM (OR = 0.77, 95 % CI [0.64, 0.92]). After adjusting for confounding factors including age, gender, smoking, drinking, NYHA, hypertension, CHD, diabetes, hyperlipemia, family history of hypertension, family history of CHD, and CPM treatment, patients using HM had a 24 % lower readmission rate compared to those not using HM (adjusted OR = 0.76, 95 % CI [0.64, 0.92]). Furthermore, the readmission rate was significantly higher in patients over the age of 65 compared to patients aged 20 to 65 (OR = 1.31, 95 % CI [1.08, 1.60], adjusted OR = 1.25, 95 % CI [1.02, 1.53]). Smoking significantly increased the readmission rate in the adjusted analysis (OR = 1.31, 95 % CI [1.01, 1.70]). There were no significant differences in HM treatment time, CPM treatment, gender, alcohol consumption, cardiac function, hypertension, CHD, diabetes, hyperlipidemia, family history of hypertension, and family history of CHD on the readmission rate ($p > 0.05$). The receiver operating characteristic (ROC) curve demonstrated that the analytical model had predictive value (area under ROC curve = 0.57) (Fig. 2(b)).

A total of 611 HF patients in the HM group and 587 patients in the non-HM group were recorded for specific lengths of re-hospitalization or non-hospitalization during follow-up. By the 365-day follow-up, patients in the HM group had a cumulative readmission rate of nearly 15 %, with 84 rehospitalizations, compared with nearly 25 %, with 122 patients rehospitalization, in the non-HM group (Fig. 3).

Table 1
Characteristics of HM and non-HM groups in HF patients.

Variable	Before PSM matched		*p* - value	After PSM matched		*p* - value
	HM (*N* = 1819) n (%)	Non-HM (*N* = 987) n (%)		HM (*N* = 962) n (%)	Non-HM (*N* = 962) n (%)	
Age, yr			0.263			0.804
20 - 65	529	307	0.697	291	296	0.252
> 65	(29.1)	(31.1)		(30.3)	(30.8)	
Mean ± SD	1290 (70.9)	680 (68.9)		671 (69.8)	666 (69.2)	
	71.4 ± 11.2	71.2 ± 11.4		71.1 ± 11.4	71.0 ± 11.4	
Gender			0.248			0.050
Female	963	500		437	481	
Male	(52.9)	(50.7)		(45.4)	(50.0)	
	856 (47.1)	487 (49.3)		525 (54.6)	481 (50.0)	
Smoking	712 (39.1)	402 (40.7)	0.412	403 (41.9)	377 (39.2)	0.227
Drinking	653 (35.9)	303 (30.7)	0.006	330 (34.3)	303 (31.5)	0.190
Cardiac function			0.007			0.023
NYHA II	1000	523		503	508	
NYHA III	(55.0)	(53.0)		(52.3)	(52.8)	
NYHA IV	600 (33.0)	374 (37.9)		336 (34.9)	367 (38.2)	
	219 (12.0)	90 (9.1)		123 (12.8)	87 (9.0)	
Hypertension	960 (52.8)	542 (54.9)	0.278	501 (52.1)	523 (54.4)	0.315
CHD	309 (17.0)	149 (15.1)	0.196	157 (16.3)	147 (15.3)	0.532
Diabetes	647 (35.6)	344 (34.9)	0.705	343 (35.7)	335 (34.8)	0.703
Hyperlipemia	1246 (68.5)	644 (65.3)	0.079	657 (68.3)	632 (65.7)	0.225
Family history of hypertension	600 (33.0)	325 (32.9)	0.975	306 (31.8)	317 (33.0)	0.592
Family history of CHD	212 (11.7)	103 (10.4)	0.329	120 (12.5)	103 (10.7)	0.226
CPM	1326 (72.9)	554 (56.1)	< 0.001	579 (60.2)	554 (57.6)	0.247

Note: HM, herbal medicine; PSM, Propensity score matching; NYHA, New York Heart Association; CHD, Coronary heart disease; CPM, Chinese patent medicine treatment.

Table 2
Logistic regression of readmission in HF patients.

Variable	Crude		Adjusted†	
	OR	95 % CI	OR	95 % CI
HM				
No	1	Reference	1	Reference
Yes	**0.77**	**(0.64, 0.92)**	**0.76**	**(0.64, 0.92)**
HM time, day				
< 7	1	Reference	1	Reference
7 - 14	0.88	(0.63, 1.23)	0.86	(0.61, 1.21)
> 14	0.84	(0.65, 1.08)	0.83	(0.64, 1.07)
CPM	1.14	(0.95, 1.37)	1.06	(0.86, 1.33)
Age, yr				
20 - 65	1	Reference	1	Reference
> 65	**1.31**	**(1.08, 1.60)**	**1.25**	**(1.02, 1.53)**
Gender				
Female	1	Reference	1	Reference
Male	**0.82**	**(0.68, 0.98)**	0.83	(0.67, 1.04)
Smoking	0.99	(0.83, 1.19)	**1.31**	**(1.01, 1.70)**
Drinking	0.83	(0.68, 1.00)	0.82	(0.63, 1.07)
Cardiac function				
NYHA II	1	Reference	1	Reference
NYHA III	1.16	(0.96, 1.41)	1.11	(0.91, 1.35)
NYHA IV	1.17	(0.87, 1.57)	1.16	(0.86, 1.57)
Hypertension	1.05	(0.88, 1.25)	1.02	(0.85, 1.23)
CHD	0.99	(0.78, 1.27)	0.98	(0.76, 1.26)
Diabetes	1.04	(0.87, 1.26)	1.05	(0.86, 1.27)
Hyperlipemia	1.05	(0.87, 1.27)	1.04	(0.85, 1.26)
Family history of hypertension	1.04	(0.86, 1.26)	1.03	(0.85, 1.25)
Family history of CHD	0.98	(0.74, 1.30)	0.99	(0.72, 1.37)

Note: HF, heart failure; OR, odd ratio; CI, confidence interval; HM, herbal medicine; NYHA, New York heart association functional class; CHD, coronary heart disease; CPM, Chinese patent medicine; Bold font indicates statistical significance ($p < 0.05$); †Adjusted for age, gender, smoking, drinking, heart function grade of NYHA, coronary heart disease, hypertension, diabetes, hyperlipemia, family history of hypertension, and family history of coronary heart disease.

Health and economic evaluation

In health economics, the multiple linear regression analyses revealed no significant correlation between the use of HM and the direct routine medical costs incurred by HF patients during hospitalization (Coef = 300.08, 95 % CI [−228.58, 828.74]). There was a statistically significant increase in direct medical costs for patients over 65 years of age (60.78, 95 % CI [36.25, 85.31]). Furthermore, patients with cardiac function classified as NYHA III (Coef = 1979.92, 95 % CI [1401.82, 2558.03]) and NYHA IV (Coef = 6052.48, 95 % CI [5166.59, 6938.38]) experienced a statistically significant increase in direct medical costs compared to patients with cardiac function classified as NYHA II (Table 3). There were no significant correlations in CPM treatment, gender, age, alcohol consumption, hypertension, CHD, diabetes, hyperlipidemia, family history of hypertension, and family history of

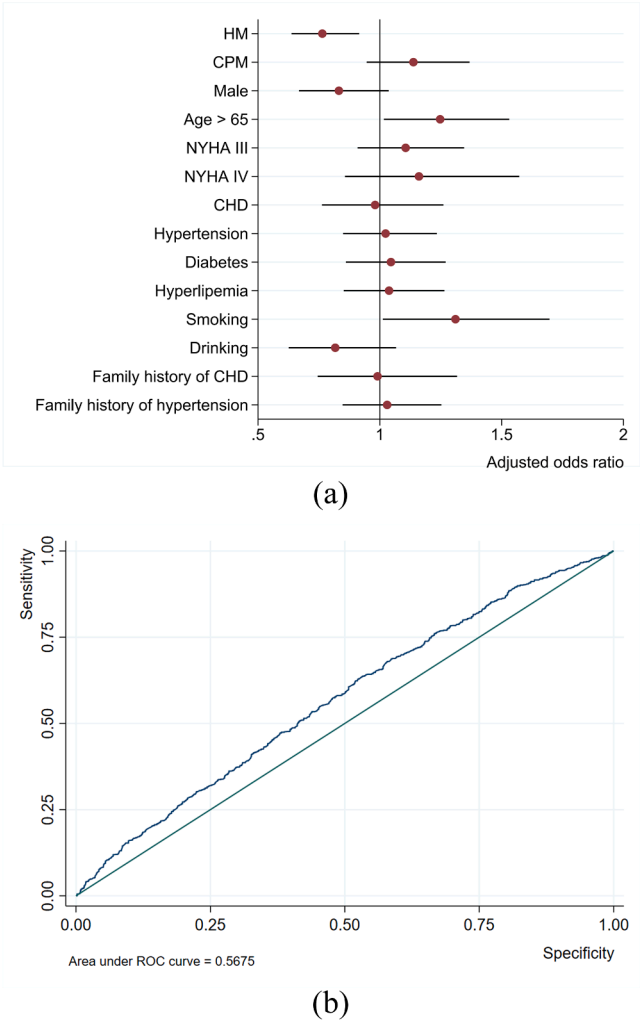

Fig. 2. Logistic regression of multivariable factors and readmission in patients with heart failure. Note: HM, herbal medicine; CPM, Chinese patent medicine; NYHA, New York Heart Association; CHD, coronary heart disease.

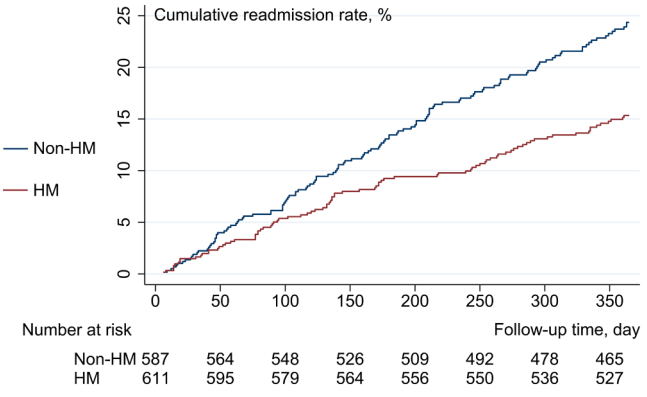

Fig. 3. Cumulative readmission rate between herbal medicine and non-herbal medicine groups in patients with heart failure. Note: HM, herbal medicine.

CHD with the direct routine medical costs ($p > 0.05$). Compared with non-HM patients, HM treatment cost 98.52 RMB (approximately $13.59 US dollars) for each 1 % reduction in the rate of readmission, which is much lower than $12,621.72 US dollars (China's GDP per capita), reflecting good economic acceptance. Sensitivity analysis showed that the ICER obtained by 0.5 times HM cost and 2 times HM cost were 69.20 RMB (approximately 9.55 US dollars) and 157.16 RMB (approximately 21.69 US dollars) respectively, which still reflects good economic acceptance (Table 4).

Table 3
Multiple linear regression of direct medical costs in HF patients.

Variable	Coef	95 % CI
HM	300.08	(−228.58, 828.74)
CPM	37.30	(−501.80, 576.41)
Male	297.04	(−344.69, 938.78)
Age > 65	**60.78**	**(36.25, 85.31)**
Smoking	623.78	(−125.10, 1372.67)
Drinking	−242.86	(−1020.33, 534.61)
Cardiac function		
NYHA III	**1979.92**	**(1401.82, 2558.03)**
NYHA IV	**6052.48**	**(5166.59, 6938.38)**
Hypertension	210.51	(−355.05, 756.07)
CHD	231.70	(−499.72, 963.13)
Diabetes	−133.13	(−701.21, 434.96)
Hyperlipemia	25.11	(−551.22, 601.44)
Family history of hypertension	−45.92	(−618.27, 526.44)
Family history of CHD	−88.33	(−924.41, 747.76)

Note: HF, heart failure; Coef., coefficient; CI, confidence interval; HM, herbal medicine; CPM, Chinese patent medicine; NYHA, New York heart association functional class; CHD, coronary heart disease; ICER: incremental cost-effectiveness ratio; Bold font indicates statistical significance ($p < 0.05$).

Discussion

In the study, we retrospectively analyzed the adjuvant efficacy and health economics of HM treatment for patients with HF. We applied the readmission rate as a measure of adjuvant efficacy through patient follow-up. The results indicated that HM significantly reduced the readmission rate of patients with HF. Previous evidence has consistently shown the efficacy of TCM for treating cardiovascular disease. For instance, Qili Qiangxin capsules adjunctive to the treatment of HF reduced the readmission rate and levels of NT-proBNP in patients with HF (Li et al., 2013; Xing et al., 2022). For assessing the prognosis, NT-proBNP levels are positively correlated with HF severity, accompanied by deterioration in cardiac function class and hemodynamic data, which also influences the readmission of patients (McDonagh et al., 2023). Moreover, a recent randomized, double-blind, placebo-controlled trial based on 124 clinical centers found that the Tongxinluo capsules, as an adjunct to guideline-directed therapy, significantly improved major adverse cardiovascular and cerebrovascular events at 30 days and 1 year in patients with acute myocardial infarction (Yang et al., 2023). These CPMs are derived from HM based on TCM theories. Furthermore, previous systematic evaluations have indicated that TCM could be used as a complementary and alternative approach for primary and secondary prevention of cardiovascular disease (Hao et al., 2017).

Among the factors influencing the readmission rate of patients with HF, our analysis revealed a notable association between age and readmission. Specifically, we observed that HF patients aged 65 years and older had a higher likelihood of being readmitted for treatment. Previous studies found that age played a crucial role in the development, diagnosis and treatment of HF. HF usually affects individuals of

Table 4
Incremental cost-effectiveness ratio of HM and sensitivity analysis in HF patients.

Hospitalization costs, RMB	HM	Non-HM	ICER
Total costs per capita	10,514.59	8,012.24	98.52
0.5 times HM in total costs per capita	9,769.82	8,012.24	69.20
2 times HM in total costs per capita	12,004.14	8,012.24	157.16

Note: HF, heart failure; HM, herbal medicine; ICER, incremental cost-effectiveness ratio.

advanced age more (Harvey et al., 2021). An etiologic study demonstrated that frailty was associated with age and HF (McAlister, 2023). In addition, exercise is emphasized as a valuable intervention for preventing age-related decline and discovering new therapeutic targets for HF (Li et al., 2020). Besides, we discovered that smoking, as a confounding factor, significantly increased the readmission rate for HF patients, echoing the findings of a previous systematic review that reported a 44.8 % increase in readmission rates associated with smoking (Son and Lee, 2020). Smoking is a well-established risk factor for various cardiovascular diseases, including HF (Banks et al., 2019). A Mendelian randomization study found that individuals with a genetic predisposition to smoking and a higher lifetime burden of smoking had a heightened risk of developing HF (Lu et al., 2021). Notably, smoking is particularly associated with an increased occurrence of adverse cardiovascular events in older adults with HF (Gottdiener et al., 2022).

Furthermore, our analysis identified several factors contributing to health economic impact for patients with HF. (1) A previous observational study demonstrated that TCM significantly reduced the utilization of medical resources among asthma patients (Liao et al., 2022), but evidence on the health economic benefits of TCM in the treatment of HF is still lacking. The cost-effectiveness analysis results from this study revealed that the incremental cost in the reduction of readmission rate by adjuvant HM therapy fell significantly below the willing-to-pay threshold. This finding suggests that the routine treatment combined with the HM approach for HF has favorable health economic impact. (2) Notably, the worsening cardiac function in classification significantly increases the direct routine medical costs attributing to more treatment needs. Therefore, the early HM intervention adjunctive to the standard treatment for patients with HF is preferred to reduce the medical cost. (3) Additionally, an increase in the readmission rate of older patients over 65 years of age could lead to an increase in direct medical costs. Previous study found that the smoking burden of former smokers is significantly associated with the incidence of admission for HF compared to never smokers (Kamimura et al., 2018). We found that smoking as an important factor influenced readmission in patients with HF after adjusting for the confounding factors. However, we did not find that smoking increases direct medical costs. It may be resulted from the low smoking intensity in our study. A previous study demonstrated a dose-dependent association between smoking intensity and the incidence of HF (Gopal et al., 2012). In addition, the risk of HF in people who quit smoking for >15 years was similar to that of nonsmokers (Ahmed et al., 2015). Therefore, variations in smoking cessation and smoking density among patients with HF may influence the health economics evaluation.

The study has several limitations that should be acknowledged. Firstly, the number of patients included for observation was not large, and the follow-up time was limited, which hindered our ability to analyze the effect of HM on mortality. Secondly, we only matched HM as the primary exposure factor, while CPM was considered a confounding factor due to its predominant use in treating comorbidities other than HF. Thirdly, in terms of smoking history, we did not differentiate between individuals before and after the diagnosis of HF, so we were unable to further investigate the effects of smoking cessation on disease progression after the diagnosis of HF. Finally, the study only considered direct medical costs, and in fact there are indirect costs in the diagnosis and treatment of heart failure, such as transportation costs, lost wages, etc. Further combined with the analysis of ICER, it was found that based on the reduction of hospitalization rates, the analysis suggests that the use of HM has a positive health economics benefit.

Future studies could focus on analyzing the efficacy of HF patients with preserved ejection fraction, taking into consideration the specifications outlined in the latest guidelines (McDonagh et al., 2023). Additionally, the inclusion of patients from multiple centers and the extension of follow-up duration should be conducted to address current limitations.

Conclusions

The adjunctive therapy of HM decreases the hospital readmission rate among patients with HF with positive health economic outcomes. Advanced age and smoking increase the risk of readmission in patients with HF, while advanced age and worsening cardiac function contribute to higher direct medical costs.

CRediT authorship contribution statement

Jianbo Guo: Writing – original draft, Visualization, Software, Methodology, Formal analysis. **Xinyu Lu:** Writing – original draft, Validation, Methodology, Investigation, Data curation. **Pei Zhang:** Validation, Methodology, Investigation, Data curation. **Ruolin Du:** Validation, Methodology, Investigation, Data curation. **Chen Liu:** Software, Formal analysis. **Guang Chen:** Software, Formal analysis. **Xiangjun Yin:** Writing – review & editing, Validation. **Tiantian Meng:** Writing – review & editing, Validation. **Anqi Li:** Writing – review & editing, Validation. **Haiyong Chen:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Qingyong He:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

All authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.phymed.2024.156310.

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