INTRODUCTION

Heart failure (HF) refers to cardiac function decline caused by various heart diseases, mainly manifested as shortness of breath, fatigue, palpitations, and lower extremity edema, which is extremely common in cardiovascular diseases in the elderly. According to statistics, the prevalence of HF in the global adult population is about 1-2%, and HF patients are around 6.50-8.75 million in China. Moreover, with age, the incidence of HF in people over 7 years of age has reached more than 10%. HF is a progressive condition that needs sustained management and treatment strategies to limit disease progression and protect patients' overall well-being and safety. Among the various forms of HF, heart failure with preserved ejection fraction (HFpEF) is a significantly prevalent subtype, accounting for half of all HF cases. HFpEF presents a distinctive HF variation characterized by impaired ventricular diastolic function or systolic dysfunction. Patients diagnosed with HFpEF typically contend with many underlying comorbidities, consequently increasing the predictive risk of mortality for these patients.

At present, the complete pathogenesis of HFpEF remains vague. Clinically, many factors, including pulmonary infections, hypertension, coronary heart disease, and diabetes mellitus, have been identified as potential contributors to the development of HFpEF. Moreover, the lack of standardized clinical guidelines has led to significant discrepancies in devising effective prevention strategies for this condition.

Identifying and exploring the potential associated factors is imperative to prevent and manage HFpEF efficiently. Therefore, this study aims to outline the prevailing clinical attributes of HFpEF through an in-depth analysis of these related factors. This study offers insight to guide future prevention and treatment strategies for HFpEF.

ABSTRACT

Objective • This study aims to identify the risk factors associated with heart failure with preserved ejection fraction (HFpEF) and to investigate the potential correlation between HFpEF and blood lipid metabolism.

Methods • A retrospective analysis was conducted on a cohort of 47 HFpEF cases (designated as the research group, RG) and 53 non-HF patients (referred to as the control group, CG) admitted to our hospital between December 2020 and December 2022. Clinical baseline data were carefully collected, and lipid profiles were assessed. Logistic regression analysis was used to examine the various factors influencing the onset of HFpEF. Furthermore, we investigated the differences in blood lipid metabolism markers between the two groups and explored the potential relationship between blood lipid metabolism and left ventricular ejection fraction (LVEF) in patients belonging to the RG.

Results • The outcomes of the logistic regression analysis revealed that age, sex, sarcopenia, and lipid levels were all independent factors influencing HFpEF (P<.05). Notably, the RG exhibited higher levels of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C), alongside lower levels of high-density lipoprotein cholesterol (HDL-C), compared to the CG (P<.05). The Pearson correlation coefficients unveiled negative correlations between TG, TC, LDL-C, and LVEF (P<.05), while a positive correlation was observed between HDL-C and LVEF (P<.05).

Conclusions • Age, sex, sarcopenia, and lipid levels emerge as independent factors contributing to the onset of HFpEF. Moreover, HFpEF patients manifest apparent irregularities in blood lipid metabolism. (Altern Ther Health Med. [E-pub ahead of print.])

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ALTERNATIVE THERAPIES, [E-PUB AHEAD OF PRINT]
MATERIALS AND METHODS

Study Design and Participants

The study employed a retrospective analysis approach to investigate the identified cohorts of HFrEF and non-HF patients. A total of 47 patients diagnosed with HFrEF (designated as the research group, RG) and 53 individuals without heart failure (referred to as the control group, CG) were enrolled as the subjects between December 2020 and December 2022. This study adhered rigorously to the principles outlined in the Declaration of Helsinki. Furthermore, all participants provided their informed consent before their inclusion in the study.

Inclusion and Exclusion Criteria

Research Group (RG). Inclusion criteria: (1) patients diagnosed with HFrEF at our hospital; (2) having complete case data; (3) and not presenting any of these medical conditions; recent acute myocardial infarction (AMI) within the last month, severe congenital heart disease or valve disorders, coma, significant infections, chronic conditions such as endocrine and immune disorders, malignancies, neuropsychiatric disorders, or cognitive impairment.

Control Group (CG). Encompassed patients with comprehensive medical records, confirmed as non-HF cases by our hospital, and without the above-mentioned medical conditions. Patients who did not meet the inclusion criteria were excluded from the study.

Echocardiographic Assessment

The echocardiographic evaluation involved the following observations: (1) Atrial and Ventricular Morphology: The left atrium measured 39 mm in diameter, while the dimensions of the other atrial cavities were within normal limits. Both the septum and the left ventricular free wall exhibited normal thickness. The motion of these structures was coordinated, and the systolic amplitude was within the normal range; (2) Aortic Root and Valve Morphology: The internal diameter of the aortic root was within the expected ranges. The valves demonstrated appropriate morphology, structure, and normal opening and closing motions. No significant abnormalities were detected in the aortic relationships; (3) Doppler Examinations: In the Doppler assessment, the diastolic mitral flow spectrum displayed an E/A ratio of less than 1, indicating altered diastolic function. Systolic mitral valve regurgitation was noted to be mild, while diastolic aortic valve regurgitation was of moderate degree. A slight systolic tricuspid valve regurgitation was observed, and the estimated pulmonary artery systolic pressure was approximately 26 mmHg. Additionally, minimal regurgitation of the diastolic pulmonary valve was detected.

Data Collection and Laboratory Analysis

General Data Collection. Primary clinical data, including age, gender, body mass index (BMI), and prevalent underlying medical conditions, were meticulously recorded for all enrolled subjects.

Assessment of Left Ventricular Function. The determination of left ventricular ejection fraction (LVEF) was executed using a Cardio Function Meter, providing insight into the cardiac pumping efficiency.

Laboratory Investigations. All participants underwent early morning fasting vein blood collection to facilitate comprehensive laboratory assessments upon admission. Routine examinations conducted at our facility included blood routine analysis using the BC5800 Automatic Blood Cell Analyzer (Myriad) and biochemical assessments employing the BS-600M Automatic Biochemistry Analyzer (Myriad). These analyses were instrumental in interpreting parameters such as total cholesterol (TC), triglycerides (TG), and the levels of low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C).

Study Endpoints

The study was designed to achieve the following endpoints: (1) Identification of Relevant Factors: The investigation aimed to identify the significant factors contributing to the development of HFrEF; (2) Inter-Group Differences in Blood Lipid Metabolism: Comparative analyses were conducted to explore variations in blood lipid metabolism between different subject groups; (3) Analysis of TC and TG Impact: The study explored the potential influence TC and TG on the onset of HFrEF; (4) Correlation Between Lipid Metabolism and LVEF: A comprehensive exploration was carried out to explain the correlation between blood lipid metabolism markers and LVEF among HFrEF patients.

Statistical Analysis

The data were analyzed using SPSS software version 25 (IBM) for comprehensive statistical analysis. Inter-group comparisons encompassing categorical variables, presented as [n (%)], and continuous variables, represented as (x̄ ± s), were carried out using the chi-square test and the independent samples t test, respectively. Logistic regression analysis was performed to identify relevant contributing factors, and Pearson correlation coefficients were utilized to explore potential associations. Throughout the study, a significance level of P <.05 was employed.

RESULTS

Univariate Analysis of HFrEF Incidence

The findings of comparative analysis of primary data between the RG and CG revealed no significant difference in terms of smoking, alcohol consumption, family history of diseases, body mass index (BMI), and other variables (P >.05). It suggests that these indicators exhibit no distinct association with the incidence of HFrEF. Conversely, patients in the RG in comparison to the CG have advanced age, coupled with a higher proportion of female patients, individuals with diabetes mellitus, and those with hypertension (P <.05). This observation strongly suggests that age, sex, diabetes mellitus, and hypertension stand as individual factors substantially influencing the occurrence of HFrEF; refer to Table 1.
Table 1. Univariate analysis of the occurrence of HFpEF

<table>
<thead>
<tr>
<th>Observed indicators</th>
<th>Control group (n = 53)</th>
<th>Research group (n = 47)</th>
<th>t and χ² value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.3 ± 13.33</td>
<td>75.5 ± 7.67</td>
<td>6.34 &lt; .01</td>
</tr>
<tr>
<td>Sex</td>
<td>Male/female</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>29(54.72)/24(45.28)</td>
<td>13/27 = 66/34</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>32(62.29)/23(47.71)</td>
<td>11/20 = 6/4</td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes/no</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>14(3.19)/27(69.81)</td>
<td>20/42 = 53/77</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>12(22.64)/41(77.36)</td>
<td>19/23 = 71/29</td>
</tr>
<tr>
<td>Drinking</td>
<td>Yes/no</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>12(22.64)/41(77.36)</td>
<td>19/23 = 71/29</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>12(22.64)/41(77.36)</td>
<td>19/23 = 71/29</td>
</tr>
<tr>
<td>Family History of Disease</td>
<td>Yes/no</td>
<td>8(1.55)/9(18.55)</td>
<td>3/17 = 5/9</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>Yes/no</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>13(28.30)/38(81.70)</td>
<td>26/35 = 21/44</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>26(55.32)/21(44.68)</td>
<td>14/13 = 12/37</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>Yes/no</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11(23.96)/35(66.04)</td>
<td>18/27 = 33/67</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>18(33.96)/35(66.04)</td>
<td>18/27 = 33/67</td>
</tr>
</tbody>
</table>

Note: This table presents the univariate analysis results comparing various indicators between the Control group (n = 53) and the Research group (n = 47). The t value for continuous variables and χ² value for categorical variables are shown along with corresponding P values for each indicator.

Abbreviations: HFpEF, Heart failure with preserved ejection fraction; BMI, Body mass index.

Table 2. Indicator Categorization

<table>
<thead>
<tr>
<th>Observed Indicators</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Measurement information does not need to be assigned</td>
</tr>
<tr>
<td>Sex</td>
<td>Male=0, female=1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>No=0, yes=1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>No=0, yes=1</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>No=0, yes=1</td>
</tr>
</tbody>
</table>

Note: This table delineates the categorization of observed indicators for the study.

Table 3. Multivariate analysis of the occurrence of HFpEF

<table>
<thead>
<tr>
<th>Observed Indicators</th>
<th>β</th>
<th>SE</th>
<th>Wald χ²</th>
<th>P value</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.53</td>
<td>1.22</td>
<td>8.27</td>
<td>&lt; .05</td>
<td>4.05</td>
<td>3.01-9.64</td>
</tr>
<tr>
<td>Sex</td>
<td>.87</td>
<td>.66</td>
<td>5.37</td>
<td>0.04</td>
<td>2.81</td>
<td>1.54-5.06</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.11</td>
<td>1.03</td>
<td>2.86</td>
<td>1.97</td>
<td>84-18.06</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>.92</td>
<td>.53</td>
<td>3.14</td>
<td>0.09</td>
<td>1.04-0.5</td>
<td></td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>2.63</td>
<td>1.72</td>
<td>1.81</td>
<td>0.05</td>
<td>4.73-1.35</td>
<td></td>
</tr>
</tbody>
</table>

Note: This table presents the outcomes of multivariate analysis for the occurrence of HFpEF. The table displays the estimated coefficients (β) along with their standard errors (SE), Wald chi-square (χ²) values, associated P values (P), odds ratios (OR), and their corresponding 95% confidence intervals (95%CI) for each observed indicator.

Abbreviations: HFpEF, Heart failure with preserved ejection fraction.

Table 4. Impact of Blood Lipid Metabolism on HFpEF Development

<table>
<thead>
<tr>
<th>Observed Indicators</th>
<th>β</th>
<th>SE</th>
<th>Wald χ²</th>
<th>P value</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>1.62</td>
<td>.95</td>
<td>12.14</td>
<td>0.00</td>
<td>4.74</td>
<td>3.06-5.99</td>
</tr>
<tr>
<td>TG</td>
<td>1.12</td>
<td>1.17</td>
<td>1.07</td>
<td>0.03</td>
<td>3.63</td>
<td>2.73-7.18</td>
</tr>
<tr>
<td>LDL-C</td>
<td>.86</td>
<td>.63</td>
<td>4.06</td>
<td>0.06</td>
<td>2.89</td>
<td>1.12-7.34</td>
</tr>
<tr>
<td>HDL-C</td>
<td>.78</td>
<td>1.18</td>
<td>1.59</td>
<td>0.02</td>
<td>4.72</td>
<td>2.6-9.99</td>
</tr>
</tbody>
</table>

Note: This table outlines the results of analyzing the influence of blood lipid metabolism on the pathogenesis of HFpEF. The table presents the estimated coefficients (β), their corresponding standard errors (SE), Wald chi-square (χ²) values, associated P values (P), odds ratios (OR), and their respective 95% confidence intervals (95%CI) for each observed indicator.

Abbreviations: HFpEF, Heart failure with preserved ejection fraction; TC, Total cholesterol; TG, Triglycerides; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol.

Multivariate Analysis of HFpEF Incidence

A logistic regression analysis was performed using the previously mentioned factors, presented in Table 2. The occurrence of HFpEF was employed as the independent variable, with the other factors serving as covariates. The results of this analysis, presented in Table 3, indicated that neither diabetes mellitus nor hypertension appeared as independent risk factors (P > .05). While the variables of age, sex, and sarcopenia demonstrated significant association as independent risk factors for HFpEF (P < .05).

Comparison of Blood Lipid Metabolism Between RG and CG

The levels of TG, TC, LDL-C, and HDL-C within the RG were determined as (5.91 ± 0.79) mmol/L, (2.88 ± 1.73) mmol/L, (3.06 ± 0.55) mmol/L, and (1.12 ± 0.43) mmol/L, respectively.
mmol/L, (3.29 ± 1.03) mmol/L, and (1.47 ± 0.81) mmol/L, respectively. The results revealed that TG, TC, and LDL-C demonstrated a significant increase when compared to the CG (P < .05), while HDL-C showcased a marked reduction (P < .05), as illustrated in Figure 2.

Impact of Blood Lipid Metabolism on HFpEF Pathogenesis

The results of the logistic regression analysis are presented in Table 3. The finding revealed that the occurrence of HFpEF among the study participants was an independent variable, whereas the blood lipid metabolism indices served as covariates. Notably, the data used in this analysis were of measurement nature and the original dataset. The results also suggest that as TG, TC, and LDL-C levels were increased and HDL-C decreased, the morbidity risk of developing HFpEF among patients exhibited a marked and statistically significant increase (P < .05).

Association Between Blood Lipid Metabolism and LVEF

The LVEF in RG was measured (68.43 ± 1.27) %. A Pearson correlation coefficient analysis was undertaken to explore the relationship between LVEF and blood lipid metabolism; results are presented in Figure 3. The results suggest that TG, TC, and LDL-C showed an inverse correlation with LVEF (P < .05), while HDL-C showed a positive association with LVEF (P < .05).

DISCUSSION

HF has emerged as a leading cause of mortality in older adults globally, and its incidence has been persistently rising in recent years.7 HFpEF is a common type of HF that poses a potential threat to patients and needs attention from clinicians and patients.10 While many studies have investigated HFpEF, there is no explicit agreement among them. A study by Savarese et al.6 suggests that HFpEF is linked with changes in body fluid movement. On the other hand, Omote et al.11 stated that HFpEF is a group of complications with symptoms mainly caused by inflammation that affects the small blood vessels and heart function. This lack of agreement makes deciding the best HFpEF prevention and treatment strategies hard.

In our study, logistic regression results revealed that age, sex, and sarcopenia act as independent factors influencing the onset of HFpEF. This finding is consistent with the results of several earlier research.7,10,13 Furthermore, a notable prevalence of female patients among those affected by HFpEF becomes evident, a pattern similar to that was observed in an epidemiological study focused on AMI.14

In clinical practice, most female patients diagnosed with AMI exhibit a high Killip cardiac function grade upon diagnosis and a limited probability of substantial post-treatment recovery.15 Studies centered around HF have uncovered similar distinct patterns. Notably, HF occurrences in men mainly stem from a decline in ejection fraction linked to ischemic conditions, whereas in women, factors like hypertension, diastolic dysfunction, and valvular abnormalities emerge as more prevalent contributors.16

Although the precise mechanism through which gender influences heart failure with HFpEF remains fully elucidated, physiological and structural variations between men and women could play an important role. Further exploration into this aspect holds promise for future research studies. Moreover, the influence of age on various cardiovascular diseases has been a long-term clinical consensus, and age-induced cardiac function degeneration and structural changes are the main reasons for HF.17

Furthermore, due to age-related compromised diastolic function and the development of left ventricular and left atrial hypertrophy while maintaining a relatively preserved ejection fraction, elderly patients become susceptible to HFpEF, which stands as a distinctive subtype of heart failure.18 Conversely, reduced muscle mass and weakened functional capacity are salient characteristics of frailty and integral to sarcopenia. While both frailty and sarcopenia encompass muscle degeneration that underlies physical dysfunction, the former encompasses a broader spectrum of factors in assessing the physical condition of the elderly compared to sarcopenia. It is widely recognized as a manifestation of physical vulnerability.19

Sarcopenia can also contribute to HFpEF through limb-skeletal and respiratory muscle alterations.20 Dual-energy X-ray and contrast-enhanced MRI examinations have confirmed a notable reduction in limb muscle mass among HFpEF patients, alongside increased fat infiltration. This phenomenon is observed concomitantly with a decline in physical function, evidenced by the correlation between increased thigh skeletal muscle fat infiltration and decreased exercise capacity.21 Moreover, patients diagnosed with HFpEF exhibit a more substantial reduction in skeletal muscle mass compared to the effects of normal aging. This reduction directly results in a decreased maximum oxygen consumption during exercise, ultimately leading to limitations in physical activity.22

Furthermore, around 30% of individuals diagnosed with HFpEF encounter inspiratory muscle weakness. Notably, HFpEF patients with reduced exercise endurance display diaphragm atrophy alongside inspiratory muscle weakness.23,24 Sarcopenia plays a pivotal role in prompting cardiovascular remodeling and dysfunction, ultimately resulting in the development of HFpEF and frailty. These processes may be interconnected with pathways involving inflammation, insulin resistance, and cytokine imbalance.

Several studies highlighted that underlying conditions like diabetes mellitus, hypertension, renal dysfunction, smoking, and other factors contribute primarily to HFpEF.25,26 The present study acknowledges the possibility of multiple explanations for the disparities in the abovementioned indicators. Our findings could potentially be attributed to factors such as the limited sample size, unintended statistical calculations, or regional distinctions within the study population (including variations in lifestyle and dietary practices). In future, we aim to conduct a more comprehensive analysis to address these aspects.

Our study suggests that sarcopenia could potentially emerge as a key modifiable factor in the prospective
prevention and treatment of HFpEF. To further confirm the connection between bodily function and HFpEF, our study explored the interrelation between HFpEF and blood lipid metabolism. Notably, TG, TC, and LDL-C exhibited significantly higher levels within the RG compared to the CG, while HDL-C demonstrated a visible decrease. These alterations in blood lipid metabolism emphasize the definite irregularities within HFpEF patients. Furthermore, our regression analysis revealed that unexpected blood lipid metabolism might increase susceptibility to HFpEF. Intriguingly, TG, TC, LDL-C, and HDL-C exhibited strong correlations with LVEF among patients.

It is projected that focusing on patients’ lipid metabolism could emerge as a novel avenue for both the prevention and treatment of HFpEF in the coming years. We believed that the complicated relationship between blood lipid metabolism and HFpEF could encompass a range of factors, including alterations in dietary intake, insulin sensitivity, inflammation within adipose tissue, cardiorespiratory function, and overall mobility. Studies focused on lipid-modifying interventions could potentially yield promising prognostic outcomes. However, the precise mechanisms underlying these interventions and their target patient populations require clarification through detailed, high-quality, and prolonged investigations.

Study Limitations

It is important to acknowledge a few limitations that might affect the results of our study. First, our research focused on a specific group of patients, so the findings might not apply to the entire patient population. Also, we collected data at one point, limiting interpretations to cause-and-effect relationships. Additionally, there might be other biases that could influence the results. Despite these limitations, our study offers valuable insights into the factors linked to HFpEF.

CONCLUSION

In conclusion, our study highlighted the complex relationship between various factors influencing the onset of HFpEF. Age, sex, and sarcopenia stand out as independent factors that play a role in triggering HFpEF. Notably, HFpEF patients exhibit evident irregularities in their blood lipid metabolism. These findings align with previous research, underscoring the significance of these factors in influencing cardiac health. In future, the prospect of treatments aimed at lowering lipid levels holds potential as a dependable way to enhance prognoses for HFpEF patients. While our study has limitations, such as its focus on a specific patient group and its cross-sectional nature, the insights gained contribute to a deeper understanding of HFpEF’s underlying mechanisms. This understanding could pave the way for future targeted prevention and treatment strategies.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Ethics Committee of The First peoples Hospital of Chuzhou approved the study.

DATA AVAILABILITY STATEMENT

The data used in the article is obtained from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The authors declare to have no conflict of interest.

FUNDING

No funding was received for this study.

REFERENCES


Li—Heart Failure Risk Factors and Lipid Metabolism