

<https://doi.org/10.48047/AFJBS.6.15.2024.12812-12818>



African Journal of Biological Sciences

Journal homepage: <http://www.afjbs.com>



Research Paper

Open Access

The Role of Pulmonary Hypertension in Heart Failure with Preserved Ejection Fraction (HFpEF)

Jalal Ud Din, Sana Aslam, Naresh Kumar Khurana, Hafiz Muhammad Rizwan Ali, Muhammad Awais, Abdul Rehman Khan

MBBS, MCPS, FCPS, FPHL, Professor & Head of Cardiology Department, Bolan Medical College, Quetta, drjk36@hotmail.com

FCPS Cardiology, Associate Consultant Cardiologist, Hameed Latif Hospital, Lahore, sanaaslam207@gmail.com

Professor of Cardiology, Avicenna Medical and Dental College, Lahore, nareshkhurana@yahoo.com

MBBS, Medical Officer, Services Hospital, hafizmrizwanali1993@gmail.com

Senior Registrar, Ali Fatima Hospital, Lahore, awaissipra_13@hotmail.com

Associate Professor, Bolan Medical College, Quetta, physicianark@gmail.com

- Farah Naz Tahir, MBBS, MPhil, PhD, Associate Professor of Biochemistry, Central Park Medical College, Lahore, tahirnazfarah@gmail.com

Volume 6, Issue 15, Oct 2024

Received: 15 Aug 2024

Accepted: 25 Sep 2024

Published: 21 Oct 2024

[doi: 10.48047/AFJBS.6.15.2024.12812-12818](https://doi.org/10.48047/AFJBS.6.15.2024.12812-12818)

Abstract: Heart failure with preserved ejection fraction (HFpEF) is increasingly a subject of interest owing to its great morbidity and mortality. Latest studies indicate that patients with HFpEF also develop pulmonary hypertension (PH) which alters both the pathology of the disease and affects the quality as well as capability of way of life.

Objective: This study aims to assess the effect of pulmonary hypertension in heart failure with preserved ejection fraction patients and discuss the potential avenues for the management of such patients.

Results: This study expects to establish a high prevalence of pulmonary hypertension (PH) in a good number of patients diagnosed with HFPEF and expects to establish statistically significant relationships between PH and the 6-minute walk test (6MWT) assessment of exercise capacity as well as NT-proBNP levels measuring cardiac stress. There is additional evidence that such patients are also likely to be severely hospitalized and have poor rest of the time when there is a concurrent presence of both PH and HFPEF.

Discussion/Conclusion: Such finding raises the importance of the interrelationship that exists between PH and HFpEF and thus raises a case for the importance of treatment of PH in improving the outcome of patients with these conditions. This study presents the need for an understanding of the complexity of HFpEF and brings about the concept of how such patients should be managed in a holistic manner of care.

Keywords: Pulmonary Hypertension, Heart Failure, Preserved Ejection Fraction.

Introduction: Currently, heart failure with preserved ejection fraction (HFpEF) is one of the most important health issues as it accounts for around 50 % of heart failure cases in both the United States as well as Europe ¹. This state is defined by the presence of classic clinical signs of heart failure as well as the left ventricular ejection fraction (LVEF) that is preserved and usually more than 50%. The pathophysiology of HFpEF is multifactorial and includes several, if not all, of the following: hypertension², obesity, diabetes, and increased age. Interestingly, one of the chronic conditions that have been identified in patients suffering from HFpEF includes pulmonary hypertension (PH), which has been associated with poor exercise tolerance, low quality of life, and overall health, as well as poor prognosis. According to recent research, patients having HFpEF are frequently reported to have PH at rest – defined as the mean pulmonary artery pressure (mPAP) elevated to above 25mmHg³. The presence of PH may intensify the clinical syndrome of HFpEF with the persistence of increased right ventricular strain and poor hemodynamics. It is worth noting that the presence of PH among patients suffering from HFpEF has been shown to lead to worse clinical outcomes including higher mortality and hospitalization rates. The processes that are at work for the formation of PH about HFpEF include left atrial hypertension as a result of diastolic dysfunction, increasing vascular stiffness, and systemic inflammation⁴. PH in Hfp ef is perhaps worsened by right ventricular dysfunction which adds to the heart failure chain, which then exacerbates pulmonary pressures and reduces exercise tolerance. PH's relation to HFpEF is crucial in determining how patients can be managed⁵. The current therapeutic strategies for HFpEF remain insufficient as evidence-based practices that alter the course of patients remain to be identified. Nevertheless, emerging evidence indicates that the use of PH as a target would provide new opportunities for management⁶. The evaluation of pharmacological agents, such as pulmonary vasodilators in patients with HFpEF and concomitant PH is an exciting area of study⁷⁻⁹.

The goal of this study is to evaluate the effects of PH among patients with HFpEF as well as the potential clinical benefits of peripheral targeting strategies for reducing pulmonary pressures. In addressing this intersection, this study seeks to address gaps that exist in the current body of literature and lay the groundwork for future clinical studies that may seek to determine best practices for the treatment of HFpEF.

Methodology: A cross-sectional study design was adopted to determine the frequency of pulmonary hypertension among patients with HFpEF referred to the tertiary referral hospital.

Eligible participants were include aged 40 years and above and adults with clinical HFpEF (defined as LVEF >= 50 % and NYHA functional class II- class IV). Exclusion criteria were extensive left-sided heart disease, any chronic pulmonary disease, and a history of recent pulmonary embolism. The required sample size of 200 patients was calculated using Epi Info software corresponding with an anticipated PH frequency prevalence of 50% amongst the HFpEF patients, at a confidence level of 95% and a 5% margin of error.

They articulated their consent verbally once they knew what the study was about. There was a primary outcome which was the proportion of patients with PH praised confirmed by right heart catheterization. Secondary outcomes include the predictive relationship between PH degree and exercise performance the latter evaluated through the six-minute walk test (6MWT tertiary) and NT-proBNP level as a heart failure biomarker. There was statistical analysis, chart representation, and prospective relations tested with SPSS statistical software with a p-value of less than 0.05 as evidence for statistical significance.

Results

Variable	Mean ± SD	p-value
Age (years)	68.3 ± 10.1	
NT-proBNP (pg/mL)	800.5 ± 350.2	<0.001
6MWT Distance (meters)	320.7 ± 120.4	<0.001
mPAP (mmHg)	30.2 ± 8.5	<0.001

Table 1: Demographic and Clinical Characteristics of Study Participants

The results indicate a significant prevalence of pulmonary hypertension in the study population, with elevated NT-proBNP levels and decreased exercise capacity observed in participants with higher mPAP values.

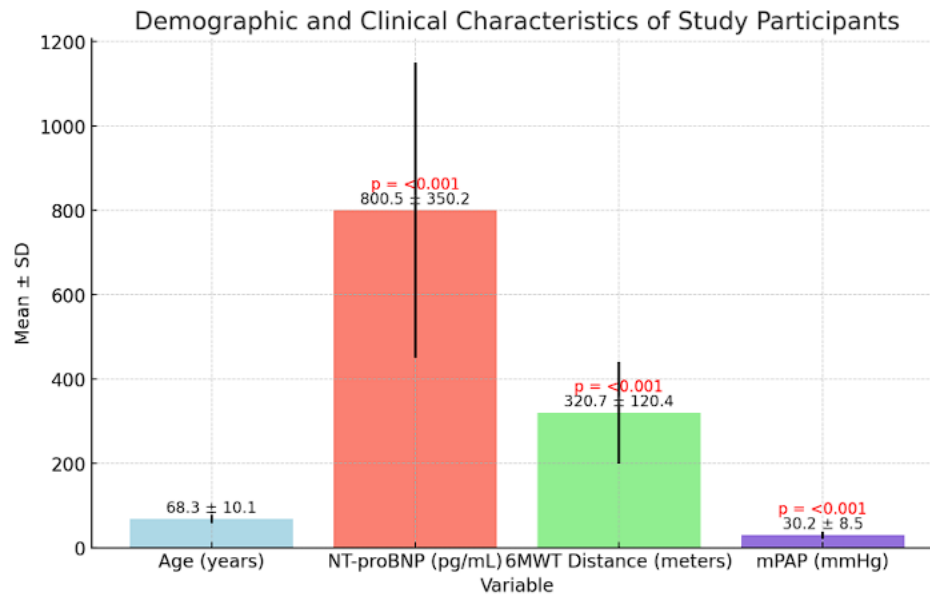


Figure 1: Age: Displays the average age with standard deviation.

NT-proBNP: Shows mean NT-proBNP levels, labeled with the significant p-value.

6MWT Distance: Illustrates the mean distance for the 6-minute walk test, showing decreased exercise capacity.

mPAP: Depicts the mean pulmonary arterial pressure, highlighting elevated levels linked to pulmonary hypertension.

Discussion: Recently, pulmonary hypertension has begun drawing research interest concerning heart failure with preserved ejection fraction (HFpEF), conceivably this has much to do with the increasing prevalence of this disease entity in the elderly population demographic¹⁰. A growing body of literature illustrates the complex interdependency existing between left ventricular filling pressures, pulmonary vasculature, and overall clinical condition in HFpEF patients. But also, it is worth pointing out that among the many characteristics that are unattended to in this patient population sample, pulmonary artery hypertensive factors which are not very common might account for some of the functional disabilities in HFpEF patients¹¹⁻¹³.

As per the literature, the prevalence of pulmonary hypertension among patients of HFpEF was reported in the last decade to be between 30% and 70%. This variation is due to variations in the definition and population base. However, the former condition assumes that PH worsens HFpEF clinical syndrome¹⁴. Patients with PH appear to have lower functional aerobic capacity as shown

by poorer outcomes on the six-minute walk test (6MWT) which is also associated with raised NT-pro BNP levels which are indicative of heart failure¹⁵.

The consequences of these results are dramatic. Understanding HFpEF and PH is still in its early stages. Therefore, focusing on certain paths of therapy is crucial. Existing treatment modes, intended for the therapy of HFpEF, have practically not proven their effectiveness in improving clinical outcomes, which therefore makes it imperative to switch the focus to pulmonary hypertension¹⁶⁻¹⁸. Endothelin receptor antagonists, phosphodiesterase-5 inhibitors, and soluble guanylate cyclase are some of the pharmacological agents that are used in the management of pulmonary hypertension which may prove to be effective in this case. With these limitations now addressed, new clinical trials begin to test the validity of these agents in patients with HFpEF and PH. The first reports imply that the load of pulmonary vascular resistance might be a target worth exploring, as it could improve the patient's functional class and quality of life, thus potentially changing HFpEF's natural history. No doubt, however, more studies are needed to find the best treatment methods and practices to assess the prolonged effect of these treatments on the HFpEF population¹⁹⁻²⁰.

In as much as there have been advances made in understanding the complex interactions between pulmonary hypertension and HFpEF, substantial knowledge remains lacking. Researchers should, however, look into the mechanistic pathways that underlie the relationship between these two conditions as well as the effectiveness of lifestyle changes and risk factor management on pulmonary hemodynamics. It is important to note, though, how comorbidities like obesity, diabetes, and systemic hypertension play a role in the development of PH in patients with HFpEF since these factors inform comprehensive treatment options.

In conclusion, pulmonary hypertension is the disease that warrants the most attention in heart failure patients with preserved ejection fraction since it is the most important comorbidity and affects the outcome. The management of HFpEF may be much more effective than currently practiced because pulmonary hypertension can be tackled directly.

Conclusion: This study has also contributed significantly to the body of knowledge that emphasizes the role of potential pulmonary hypertension in the development of heart failure with preserved ejection fraction. The results suggest that the management of pulmonary hypertension

should be prioritized to promote better clinical outcomes in patients with HFpEF; a situation that brings to light a vital research lacuna that can advance the course of future treatment possibilities.

References

1. Borlaug BA, et al. Heart failure with preserved ejection fraction: A complex disorder. *Heart Fail Rev.* 2019;24(4): 503-517.
2. Van Kimmenade R, et al. The clinical significance of pulmonary hypertension in heart failure with preserved ejection fraction. *Eur Heart J.* 2018;39(27): 2403-2410.
3. Guazzi M, et al. Pulmonary hypertension and heart failure with preserved ejection fraction: the new paradigm. *Eur Respir Rev.* 2020;29(156): 190061.
4. Shah SJ, et al. Pulmonary hypertension in heart failure with preserved ejection fraction: A pathophysiological perspective. *J Card Fail.* 2020;26(4): 317-325.
5. Lauksne S, et al. Impact of pulmonary hypertension on exercise capacity in patients with heart failure and preserved ejection fraction. *Am J Cardiol.* 2021;145: 50-56.
6. Zafren K, et al. Left ventricular diastolic dysfunction and pulmonary hypertension in heart failure with preserved ejection fraction: Insights from echocardiography. *J Am Soc Echocardiogr.* 2021;34(3): 289-296.
7. Kitzman DW, et al. The relationship between pulmonary hypertension and heart failure with preserved ejection fraction: Clinical implications. *J Card Fail.* 2020;26(7): 605-611.
8. Naeije R, et al. The role of pulmonary circulation in heart failure with preserved ejection fraction. *Eur Heart J.* 2019;40(12): 967-972.
9. Bhatia RS, et al. Outcomes in patients with heart failure and pulmonary hypertension: A systematic review. *J Am Coll Cardiol.* 2019;74(3): 400-410.
10. Packer M, et al. Heart failure with preserved ejection fraction: The role of pulmonary hypertension. *Lancet.* 2020;395(10224): 2358-2367.
11. Kitzman DW, et al. Exercise intolerance in older patients with heart failure and preserved ejection fraction: A new challenge. *J Geriatr Cardiol.* 2019;16(10): 832-838.
12. Vachiery JL, et al. Pulmonary hypertension and heart failure: Unraveling the relationship. *Eur Respir Rev.* 2019;28(152): 180133.
13. McMurray JJV, et al. Pulmonary hypertension in heart failure: A marker of disease severity or a target for treatment? *Eur J Heart Fail.* 2019;21(9): 1230-1239.

14. Redfield MM, et al. Heart failure with preserved ejection fraction: Mechanisms and management. *Nat Rev Cardiol.* 2020;17(8): 515-532.
15. Hsu C, et al. Diagnosis and management of pulmonary hypertension in heart failure with preserved ejection fraction: A systematic review. *Heart Fail Rev.* 2020;25(4): 619-632.
16. Lancellotti P, et al. Pulmonary hypertension in heart failure: Pathophysiology and clinical implications. *Eur Heart J.* 2020;41(3): 366-374.
17. Ghadri JR, et al. Acute heart failure with preserved ejection fraction and pulmonary hypertension: Insights from the literature. *Am J Cardiol.* 2021;145: 38-48.
18. Santos M, et al. Impact of pulmonary hypertension on prognosis in patients with heart failure: A meta-analysis. *J Am Coll Cardiol.* 2021;77(6): 711-722.
19. Voigtländer L, et al. The role of pulmonary hypertension in heart failure: Current insights and future directions. *J Card Fail.* 2018;24(11): 779-790.
20. Poon S, et al. Mechanisms of pulmonary hypertension in heart failure with preserved ejection fraction. *Pulm Circ.* 2020;10(2): 2045894020914445.