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Cognitive Impairment in Heart Failure with Preserved Ejection Fraction: A Hospital-Based Case–Control Study

Dr. Sandeep Krishnarao Charde[1], Dr. Shreenivas Trivedi[2], Dr. Rakhee Joshi[3]

[1]Junior Resident, [3]Associate Professor, Department of General Medicine, Indira Gandhi Government Medical College & Hospital, Nagpur, India
[2]Intern, Datta Meghe Institute of Medical Sciences, Nagpur

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Corresponding Author:

Dr. Sandeep Krishnarao Charde
sandeepcharde10@gmail.com

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ABSTRACT

Background: Heart failure with preserved ejection fraction (HFpEF) accounts for nearly half of all heart failure cases and is associated with substantial morbidity. Cognitive impairment (CI) is an important yet under-recognized comorbidity in HFpEF, with limited data available from Indian populations. **Objectives:** To assess cognitive function in patients with HFpEF, compare it with patients having heart failure with reduced ejection fraction (HFrEF) and healthy controls, and evaluate the association of cognitive impairment with heart failure severity and cardiometabolic risk factors. **Methods:** This hospital-based case–control study included 92 patients with HFpEF, 92 patients with HFrEF, and 184 age- and sex-matched healthy controls. Heart failure was diagnosed using the Framingham criteria and classified according to the New York Heart Association (NYHA) functional class and echocardiographic ejection fraction. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA). Demographic data, anthropometric measurements, cardiometabolic risk factors, biochemical parameters including lipid profile and N-terminal pro–brain natriuretic peptide (Pro-BNP), and electrocardiographic and echocardiographic findings were recorded. Statistical analysis was performed using t-test, one-way analysis of variance, Chi-square test, and multivariate logistic regression. **Results:** Cognitive impairment was significantly more prevalent among heart failure patients compared to controls ($p < 0.001$). HFpEF patients demonstrated significantly lower mean MoCA scores than healthy controls. Cognitive impairment showed significant associations with higher NYHA functional class, hypertension, diabetes mellitus, obesity, dyslipidemia, and elevated Pro-BNP levels. On multivariate analysis, heart failure status and cardiometabolic risk factors emerged as independent predictors of cognitive impairment. **Conclusion:** Cognitive impairment is common in HFpEF and is closely associated with disease severity and cardiometabolic risk factors. Routine cognitive screening using simple tools such as MoCA may facilitate early identification and improve clinical management and outcomes in patients with HFpEF.

***Keywords**: Cognitive impairment; Heart failure; HFpEF; MoCA; NYHA classification.*

INTRODUCTION

Heart failure (HF) represents a major global public health challenge, affecting more than 64 million individuals worldwide and contributing substantially to morbidity, mortality, and healthcare expenditure.[1] With increasing life expectancy and a growing burden of cardiometabolic diseases, the prevalence of HF continues to rise, particularly in low- and middle-income countries such as India.[2] Beyond its cardiovascular manifestations, HF is increasingly recognized as a systemic condition with significant extra-cardiac complications, including cognitive impairment (CI), which adversely affects quality of life, self-care behavior, and clinical outcomes.[3]

Heart failure with preserved ejection fraction (HFpEF) accounts for nearly half of all HF cases and has emerged as a distinct clinical entity with unique epidemiological and pathophysiological characteristics.[4] HFpEF is more common among elderly individuals, females, and patients with multiple comorbidities such as hypertension, diabetes mellitus, obesity, dyslipidemia, chronic kidney disease, and atrial fibrillation.[5] Despite advances in the management of heart failure with reduced ejection fraction (HFrEF), therapeutic strategies for HFpEF remain limited, and its prognosis remains poor, with survival rates comparable to HFrEF.[6] The complex interplay of systemic inflammation, endothelial dysfunction, microvascular disease, and impaired ventricular-arterial coupling in HFpEF may predispose patients to multisystem involvement, including cerebral dysfunction.[7]

Cognitive impairment is a frequent but underdiagnosed comorbidity in patients with HF, with reported prevalence ranging from 20% to 80%, depending on the population studied and the assessment tools used.[3,8] Cognitive domains commonly affected include attention, executive function, memory, visuospatial abilities, and processing speed.[9] Several mechanisms have been proposed to explain CI in HF, including chronic cerebral hypoperfusion, impaired cerebrovascular autoregulation, neurohormonal activation, systemic inflammation, and silent cerebral ischemia.[10,11] Importantly, CI in HF is associated with poor medication adherence, impaired symptom recognition, increased hospital readmissions, and higher mortality.[12]

Although CI has been extensively studied in HFrEF, data focusing specifically on cognitive dysfunction in HFpEF remain limited and inconsistent. Emerging evidence suggests that HFpEF patients may exhibit a distinct cognitive profile, possibly related to a higher burden of vascular risk factors and microvascular disease, leading to vascular cognitive impairment rather than global cognitive decline.[9,13] Moreover, the severity of HF as assessed by New York Heart Association (NYHA) functional class and biomarkers such as N-terminal pro–brain natriuretic peptide (NT-proBNP) has been shown to correlate with the degree of cognitive dysfunction.[14] However, most available studies originate from Western populations, and data from Indian cohorts are scarce.

Early identification of CI in HFpEF is clinically important, as mild cognitive impairment represents a potentially reversible stage, and timely intervention may prevent progression to dementia.[15] Brief cognitive screening tools such as the Montreal Cognitive Assessment (MoCA) have demonstrated superior sensitivity in detecting mild cognitive deficits compared to the Mini-Mental State Examination (MMSE), particularly in patients with cardiovascular disease.[16] Routine cognitive screening in HF clinics may therefore offer an opportunity to improve patient-centered care and long-term outcomes.

In this context, the present study was undertaken to assess cognitive function in patients with HFpEF, compare it with patients having HFrEF and age- and sex-matched healthy controls, and evaluate the association of cognitive impairment with heart failure severity and cardiometabolic risk factors in an Indian tertiary care setting.

MATERIALS AND METHODS

This hospital-based case–control study was conducted at a tertiary care teaching hospital over a period of 18 months, from March 2023 to September 2024. The study population comprised patients diagnosed with heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF), and age- and sex-matched healthy controls. HF cases were diagnosed using the Framingham criteria for heart failure and further classified according to the New York Heart Association (NYHA) functional classification. Echocardiography was performed to categorize patients based on left ventricular ejection fraction (EF), with HFpEF defined as EF ≥50% and HFrEF as EF ≤40%. Controls were selected from healthy attendants or visitors without clinical evidence of heart failure. Adult participants aged ≥18 years who provided written informed consent were included. Patients with known causes of cognitive impairment such as dementia, Parkinson’s disease, hypothyroidism, vitamin B12 deficiency, chronic alcoholism, or those unable to communicate effectively were excluded.

Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), a validated screening tool for mild cognitive impairment. The MoCA evaluates multiple cognitive domains, including executive function, attention, memory, language, visuospatial abilities, abstraction, and orientation, with a total score ranging from 0 to 30. A score of ≥26 was considered normal cognition, while lower scores indicated varying degrees of cognitive impairment. An additional point was added for participants with ≤12 years of formal education, as per standard guidelines. Data collection included demographic characteristics, anthropometric measurements (body mass index and waist circumference), and cardiometabolic risk factors such as hypertension, diabetes mellitus, obesity, and dyslipidemia. Laboratory investigations included lipid profile parameters and N-terminal pro–brain natriuretic peptide (Pro-BNP) levels. Electrocardiographic and echocardiographic findings were recorded using standardized protocols.

Ethical approval for the study was obtained from the Institutional Ethics Committee, and written informed consent was secured from all participants prior to enrollment. Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0. Continuous variables were summarized as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. Normality of data distribution was assessed using the Kolmogorov–Smirnov test. Depending on data distribution, comparisons between groups were performed using independent t-test, one-way analysis of variance (ANOVA), Chi-square test, or appropriate non-parametric tests. Multivariate logistic regression analysis was used to identify independent predictors of cognitive impairment. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 368 participants were included in the study, comprising 92 HFpEF patients, 92 HFrEF patients, and 184 age- and sex-matched controls. The majority of participants across all groups belonged to the middle-aged and elderly population. In both HFpEF and HFrEF groups, most patients were between 41 and 60 years of age. Female predominance was observed in the HFpEF group, whereas males constituted a higher proportion in the HFrEF group. The control group showed a relatively balanced gender distribution. The baseline demographic characteristics of the study population are summarized in **Table 1**.

Table 1. Baseline Demographic Characteristics of Study Participants

Variable	HFpEF (n=92)	HFrEF (n=92)	Controls (n=184)
Age group (years)	n (%)	n (%)	n (%)
21–30	8 (8.7)	2 (2.2)	15 (8.2)
31–40	23 (25.0)	7 (7.6)	13 (7.1)
41–50	30 (32.6)	31 (33.7)	51 (27.7)
51–60	18 (19.6)	35 (38.0)	66 (35.9)
>60	13 (14.1)	17 (18.5)	37 (20.1)
Gender			
Male	40 (43.5)	49 (53.3)	89 (48.4)
Female	52 (56.5)	43 (46.7)	95 (51.6)

Cognitive impairment was significantly more prevalent among heart failure patients compared to healthy controls. Among the 184 HF cases (HFpEF and HFrEF combined), cognitive impairment was observed in 59 patients (32.1%), whereas only 9 controls (4.9%) demonstrated cognitive impairment. The difference in prevalence between HF cases and controls was statistically significant ($p < 0.001$). These findings are detailed in **Table 2**.

Table 2. Prevalence of Cognitive Impairment in Heart Failure Patients and Controls

Cognitive Impairment	HF Cases (n=184)	Controls (n=184)	p-value
Present	59 (32.1%)	9 (4.9%)	<0.001
Absent	125 (67.9%)	175 (95.1%)	

When HFpEF patients were analyzed separately, cognitive impairment was observed in 26 out of 92 HFpEF patients (28.3%), compared to 5 out of 92 controls (5.4%). The mean MoCA score was significantly lower in the HFpEF group than in the control group, indicating poorer cognitive performance among HFpEF patients. This difference was statistically significant ($p < 0.001$). The comparison of MoCA scores between HFpEF patients and controls is presented in **Table 3**.

Table 3. Comparison of MoCA Scores Between HFpEF Patients and Controls

Group	n	Mean MoCA Score ± SD	p-value
HFpEF	92	18.43 ± 4.72	<0.001
Controls	92	28.64 ± 1.10	

Cognitive impairment was observed in both HF subtypes. Among HFrEF patients, 33 out of 92 (35.9%) exhibited cognitive impairment, compared to 26 out of 92 (28.3%) HFpEF patients. Although the prevalence of cognitive impairment was numerically higher in the HFrEF group, the difference between HFpEF and HFrEF patients was not statistically significant ($p > 0.05$). These findings are summarized in **Table 4**.

Table 4. Comparison of Cognitive Impairment Between HFpEF and HFrEF Patients

Cognitive Impairment	HFpEF (n=92)	HFrEF (n=92)	p-value
Present	26 (28.3%)	33 (35.9%)	0.34
Absent	66 (71.7%)	59 (64.1%)	

Hypertension was present in all HFpEF and HFrEF patients. Diabetes mellitus, generalized obesity, abdominal obesity, and dyslipidemia were highly prevalent in both HF groups, with a greater burden observed among HFpEF patients. Cognitive impairment was more frequently observed in patients with coexisting cardiometabolic risk factors compared to those without these conditions. The distribution of cognitive impairment according to hypertension, diabetes mellitus, obesity, and dyslipidemia is shown in **Table 5**.

Table 5. Association of Cardiometabolic Risk Factors with Cognitive Impairment in HF Patients

Risk Factor	HFpEF n (%)	HFrEF n (%)	Controls n (%)
Hypertension	92 (100)	92 (100)	136 (73.9)
Diabetes mellitus	62 (67.4)	45 (48.9)	114 (62.0)
Generalized obesity	49 (53.3)	46 (50.0)	93 (50.5)
Abdominal obesity	78 (84.8)	63 (68.5)	133 (72.3)
Dyslipidemia	55 (59.8)	41 (44.6)	96 (52.2)

Patients with heart failure demonstrated significantly higher levels of Pro-BNP and adverse lipid profiles compared to controls. Pro-BNP levels were markedly elevated in both HFpEF and HFrEF groups, with higher values observed in HFrEF patients. HFpEF patients showed higher mean total cholesterol, LDL cholesterol, and triglyceride levels, along with lower HDL cholesterol levels, compared to controls. Lower MoCA scores were associated with higher Pro-BNP levels and adverse lipid parameters. Detailed biochemical and echocardiographic comparisons are presented in **Table 6**.

Table 6. Comparison of Biochemical Parameters and Cognitive Scores Among Study Groups

Parameter	Group	Mean ± SD	p-value
LDL cholesterol (mg/dL)	HFpEF	145.03 ± 30.02	<0.001
	HFrEF	135.02 ± 28.31	
	Controls	125.23 ± 25.21	
Total cholesterol (mg/dL)	HFpEF	214.14 ± 35.23	<0.001
	HFrEF	198.73 ± 29.59	
	Controls	185.21 ± 27.42	
HDL cholesterol (mg/dL)	HFpEF	42.24 ± 7.86	<0.001
	HFrEF	45.15 ± 9.19	
	Controls	50.35 ± 8.34	
Triglycerides (mg/dL)	HFpEF	174.93 ± 40.32	<0.001
	HFrEF	173.76 ± 38.94	
	Controls	140.43 ± 35.42	
Pro-BNP (pg/mL)	HFpEF	490.54 ± 75.93	<0.001
	HFrEF	510.43 ± 69.32	
	Controls	110.23 ± 20.52	
MoCA score	HFpEF	18.43 ± 4.72	<0.001
	HFrEF	17.88 ± 3.78	
	Controls	28.64 ± 1.10	

On multivariate logistic regression analysis, heart failure status, higher NYHA functional class, elevated Pro-BNP levels, diabetes mellitus, obesity, and dyslipidemia emerged as independent predictors of cognitive impairment. After adjustment for age and sex, HFpEF remained significantly associated with cognitive impairment compared to controls. The results of the multivariate analysis identifying independent predictors of cognitive impairment are shown in **Table 7**.

Table 7. Multivariate Logistic Regression Analysis for Predictors of Cognitive Impairment

Variable	Adjusted OR	95% CI	p-value
Heart failure (vs controls)	4.12	2.01–8.43	<0.001
Higher NYHA class (III–IV)	2.86	1.45–5.63	0.002
Elevated Pro-BNP	1.02	1.01–1.03	<0.001
Diabetes mellitus	1.89	1.10–3.26	0.02
Obesity	1.67	1.01–2.75	0.04
Dyslipidemia	1.74	1.05–2.88	0.03

DISCUSSION

The present hospital-based case–control study demonstrates that cognitive impairment (CI) is significantly more prevalent among patients with heart failure compared to age- and sex-matched healthy controls, with a substantial burden observed in both HFpEF and HFrEF subgroups. Nearly one-third of HFpEF patients exhibited cognitive impairment, and mean MoCA scores were significantly lower in HFpEF patients than in controls. Although cognitive impairment was numerically more frequent in HFrEF than HFpEF, the difference between the two HF phenotypes was not statistically significant. Furthermore, cognitive impairment was associated with higher NYHA functional class, elevated Pro-BNP levels, and a greater burden of cardiometabolic risk factors including diabetes mellitus, obesity, and dyslipidemia. These findings underscore the clinical relevance of CI as a common comorbidity in HFpEF and support the concept that cognitive dysfunction is not limited to reduced ejection fraction heart failure but is also prominent in HFpEF patients.[3,17,18].

Our findings are consistent with previous studies reporting a high prevalence of cognitive impairment in HF populations. Cannon et al. reported a pooled prevalence of CI of approximately 43% among HF patients and demonstrated a significantly increased risk of CI compared to non-HF controls.[10] Sterling et al., in the REGARDS cohort, observed that cognitive impairment may not always be present at the time of HF diagnosis but often develops during disease progression, emphasizing the importance of ongoing cognitive assessment.[3] Huynh et al. demonstrated that even mild cognitive impairment detected using MoCA independently predicted early readmission and mortality in HF patients.[19] While most prior studies have focused predominantly on HFrEF, emerging evidence suggests that HFpEF patients may have a distinct cognitive profile characterized by vascular cognitive impairment rather than global cognitive decline.[9] Our observation of a strong association between cardiometabolic risk factors and CI in HFpEF aligns with this hypothesis and supports findings from studies linking diabetes, obesity, dyslipidemia, anemia, and renal dysfunction to cognitive decline in HF patients.[12,20] The present study adds to the limited Indian data on this subject and highlights that the burden of CI in HFpEF in low- and middle-income settings is comparable to that reported in Western cohorts.

Several pathophysiological mechanisms may explain the high prevalence of cognitive impairment observed in HFpEF patients. Chronic cerebral hypoperfusion due to impaired cardiac output and abnormal cerebrovascular autoregulation has been proposed as a central mechanism linking HF to brain dysfunction.[20] HFpEF is characterized by systemic inflammation, endothelial dysfunction, and microvascular disease, which may contribute to silent cerebral ischemia and white matter changes, leading to vascular cognitive impairment.[9] Elevated Pro-BNP levels, reflecting HF severity, have been shown to correlate with cognitive decline, further supporting a hemodynamic and neurohormonal link between cardiac dysfunction and brain injury.[19] From a clinical perspective, the high prevalence of CI in HFpEF has important implications. Cognitive impairment adversely affects self-care behaviors, medication adherence, and symptom recognition, thereby increasing the risk of hospitalization and mortality.[10,13] Routine cognitive screening using sensitive tools such as the MoCA may facilitate early identification of at-risk patients and allow for timely multidisciplinary interventions. The strengths of this study include a well-defined case–control design, inclusion of both HFpEF and HFrEF groups, use of a validated cognitive assessment tool, and comprehensive evaluation of cardiometabolic and biochemical correlates. However, certain limitations must be acknowledged. The cross-sectional nature of the study limits causal inference, and the single-center design may affect generalizability. Neuroimaging and detailed neuropsychological testing were not performed, which may have underestimated subtle cognitive deficits. Despite these limitations, the study provides important insights into the burden and determinants of cognitive impairment in HFpEF and supports the incorporation of cognitive assessment into routine HF care.

CONCLUSION

Cognitive impairment is common among patients with heart failure with preserved ejection fraction and shows a significant association with disease severity and cardiometabolic risk factors. The findings highlight that cognitive dysfunction is not limited to heart failure with reduced ejection fraction but represents an important comorbidity in HFpEF as well. Early identification of cognitive impairment using simple and sensitive screening tools such as the Montreal Cognitive Assessment may facilitate timely intervention, improve patient self-care, and potentially enhance clinical outcomes in this population.

RECOMMENDATIONS

Based on the study findings, the following recommendations are proposed:

- Routine cognitive screening should be incorporated into heart failure clinics, particularly for patients with HFpEF.
- A multidisciplinary approach involving cardiologists, physicians, neurologists, and allied healthcare professionals is essential for optimal management of cognitive impairment in heart failure patients.
- Longitudinal follow-up of cognitive function should be undertaken to monitor progression and assess the impact of therapeutic interventions.

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REFERENCES
1. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Card. Fail. Rev. 2017;3:7–11.
2. Prabhakaran D, Jeemon P, Roy A. Cardiovascular Diseases in India: Current Epidemiology and Future Directions. Circulation 2016;133:1605–20.
3. Cannon JA, Moffitt P, Perez-Moreno AC, Walters MR, Broomfield NM, McMurray JJV, et al. Cognitive Impairment and Heart Failure: Systematic Review and Meta-Analysis. J. Card. Fail. 2017;23:464–75.
4. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N. Engl. J. Med. 2006;355:251–9.
5. Borlaug BA. The pathophysiology of heart failure with preserved ejection fraction. Nat. Rev. Cardiol. 2014;11:507–15.
6. Lam CSP, Carson PE, Anand IS, Rector TS, Kuskowski M, Komajda M, et al. Sex Differences in Clinical Characteristics and Outcomes in Elderly Patients With Heart Failure and Preserved Ejection Fraction. Circ. Heart Fail. 2012;5:571–8.
7. Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. J. Am. Coll. Cardiol. 2013;62:263–71.
8. Pressler SJ, Subramanian U, Kareken D, Perkins SM, Gradus-Pizlo I, Sauve MJ, et al. Cognitive Deficits in Chronic Heart Failure. Nurs. Res. 2010;59:127–39.
9. Alosco ML, Spitznagel MB, Cohen R, Sweet LH, Hayes SM, Josephson R, et al. Decreases in daily physical activity predict acute decline in attention and executive function in heart failure. J. Card. Fail. 2015;21:339–46.
10. Havakuk O, King KS, Grazette L, Yoon AJ, Fong M, Bregman N, et al. Heart Failure-Induced Brain Injury. J. Am. Coll. Cardiol. 2017;69:1609–16.
11. Jefferson AL, Poppas A, Paul RH, Cohen RA. Systemic hypoperfusion is associated with executive dysfunction in geriatric cardiac patients. Neurobiol. Aging 2007;28:477–83.
12. ameron J, Worrall-Carter L, Page K, Riegel B, Lo SK, Stewart S. Does cognitive impairment predict poor self-care in patients with heart failure? Eur. J. Heart Fail. 2010;12:508–15.
13. Huynh QL, Negishi K, Blizzard L, Saito M, De Pasquale CG, Hare JL, et al. Mild cognitive impairment predicts death and readmission within 30days of discharge for heart failure. Int. J. Cardiol. 2016;221:212–7.
14. Pulignano G, Del Sindaco D, Di Lenarda A, Tinti MD, Tarantini L, Cioffi G, et al. Chronic renal dysfunction and anaemia are associated with cognitive impairment in older patients with heart failure. J. Cardiovasc. Med. Hagerstown Md 2014;15:481–90.
15. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. J. Alzheimers Assoc. 2011;7:270–9.
16. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J. Am. Geriatr. Soc. 2005;53:695–9.
17. Pressler SJ. Cognitive functioning and chronic heart failure: a review of the literature (2002-July 2007). J. Cardiovasc. Nurs. 2008;23:239–49.
18. Sterling MR, Jannat-Khah D, Bryan J, Banerjee S, McClure LA, Wadley VG, et al. The Prevalence of Cognitive Impairment Among Adults With Incident Heart Failure: The 'Reasons for Geographic and Racial Differences in Stroke' (REGARDS) Study. J. Card. Fail. 2019;25:130–6.
19. Ampadu J, Morley JE. Heart failure and cognitive dysfunction. Int. J. Cardiol. 2015;178:12–23.
20. Ghanbari A, Moaddab F, Salari A, Kazemnezhad Leyli E, Sedghi Sabet M, Paryad E. The study of cognitive function and related factors in patients with heart failure. Nurs. Midwifery Stud. 2013;2:34–8.