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Clinical and Metabolic Predictors of Ventricular Arrhythmias in Heart Failure with Preserved Ejection Fraction: A Nationwide Inpatient Study

—Predictors of Ventricular Arrhythmias in Heart Failure with Preserved Ejection Fraction

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Abstract

Introduction: Ventricular arrhythmias (VAs) are a well-recognized cause of morbidity and sudden cardiac death in patients with heart failure with reduced ejection fraction (HFrEF). In contrast, the epidemiology and predictors of VAs in heart failure with preserved ejection fraction (HFpEF) remain incompletely characterized. We evaluated the prevalence of VAs and identified independent clinical, metabolic, renal, and electrolyte predictors among hospitalized patients with HFpEF using a nationally representative database. Methods: We performed a retrospective analysis of the National Inpatient Sample (2016-2018). Adult hospitalizations with HFpEF and HFrEF were identified using ICD-10-CM codes. Ventricular arrhythmias included ventricular tachycardia, ventricular fibrillation, and ventricular flutter. Hospitalizations with combined systolic and diastolic heart failure were excluded. Survey-weighted multivariable logistic regression was used to identify independent predictors of VAs in HFpEF after adjustment for demographic characteristics, comorbidities, and electrolyte abnormalities. Results: Among 1,289,705 heart failure hospitalizations, VAs occurred significantly less frequently in HFpEF than in HFrEF (1.89% vs. 6.48%; $p < 0.001$). Despite the lower prevalence, VAs in HFpEF were independently associated with male sex (OR 1.71), older age, Black race, diabetes mellitus, obesity, hypothyroidism, chronic obstructive

pulmonary disease, chronic kidney disease, acute kidney injury, liver cirrhosis, alcohol use, obstructive sleep apnea, hypokalemia, hypocalcemia, and hypomagnesemia, whereas hypertension and hyperkalemia were not independently associated. Patients with HFrEF had higher in-hospital mortality than those with HFpEF (4.46% vs. 3.64%; $p < 0.001$). Conclusion: Although ventricular arrhythmias occur less frequently in HFpEF than in HFrEF, they are associated with distinct demographic, cardiometabolic, renal, and electrolyte risk profiles. These readily identifiable clinical factors may facilitate early risk stratification, closer rhythm surveillance, and timely electrophysiology evaluation in hospitalized patients with HFpEF. Prospective studies are needed to validate these findings and determine whether targeted management of modifiable risk factors reduces ventricular arrhythmia burden.

Keywords

Heart Failure with Preserved Ejection Fraction, HfpEF, Ventricular Arrhythmias, Ventricular Tachycardia, National Inpatient Sample

1. Introduction

Heart failure with preserved ejection fraction (HFpEF) is characterized by a left ventricular ejection fraction (LVEF) of 50% or greater, with evidence of spontaneous or provoked increased LV filling pressures (LVFP), as evidenced by elevated brain natriuretic peptides or hemodynamic measurements [1] [2]. HFpEF is a heterogeneous clinical syndrome; pathophysiology differs from heart failure with reduced ejection fraction (HFrEF, EF ≤ 40%) [1] [2]. Obesity and diabetes are important risk factors and predictors of HFpEF [3]. High blood pressure is a significant risk factor for the development of HFpEF in all populations; obesity is a particularly pronounced risk factor for patients who identify as African American or Hispanic [4]. Other risk factors for the development of HFpEF include: increased age, female sex, type 2 diabetes, sleep apnea, hypertension, pulmonary hypertension, chronic obstructive pulmonary disease, iron deficiency, coronary artery disease, atrial fibrillation, and dysrhythmias, where the exact pathogenic role of each risk factor is poorly understood [5]. The lifetime risk of HFpEF approximates 19.3%, exceeding the approximate 11.4% lifetime risk of HFrEF, as per data from the second 25-year epoch of the Framingham Heart Study (1990-2014) [6]. The incidence and prevalence of HFpEF are increasing overall, partially due to improved diagnostic capabilities and more uniform diagnostic parameters [1]. Tsao *et al.* reported an increase of 53% in HFpEF diagnoses among participants in the Framingham Heart Study and Cardiovascular Health Study between 2000 and 2009 [7]. Chang *et al.* reported an 8.2% increase in HFpEF diagnoses among black women compared to a 5.9% increase for white women, and demonstrated a rise in HFpEF diagnoses for black men with 5.7% and white men with 6.3% [8]. In contrast to this, data from Olmstead County in Minnesota demonstrated a de-

crease of 28% in the incidence of HFpEF diagnoses between 2000 and 2010 [9]. There are also geographical differences in the worldwide incidence and prevalence of HFpEF. Shiga *et al.* reported a prevalence of 43% in 1245 patients with HF hospitalized in Japan between 2013-2014 [10], while Wang *et al.* evaluated 5236 patients in Australia and reported a prevalence of 37.4% [11]. The prevalence of HFpEF was only 16% in the European Society of Cardiology long-term registry and the Asian Sudden Cardiac Death in Heart Failure Registry [12].

A constellation of changes that occur at the cellular, tissue, and organ levels that lead to the pathogenesis of HFpEF. These include structural remodelling of the LV, reduced LV reserve, abnormal hemodynamics, and secondary organ dysfunction [13]. Obesity causes a chronic systemic inflammatory state that induces hemodynamic derangements and hormonal abnormalities, produces subclinical changes in the structure and function of the LV, even in the presence of normal LVEF [14] [15]. The most significant hemodynamic finding in HFpEF is elevated LVFP, resulting from LV diastolic dysfunction secondary to incomplete myocardial relaxation, increased ventricular stiffness with subsequent decreased ventricular distensibility, and a shift in the Frank-Starling mechanism [13]. These elevated filling pressures cause remodelling of the left atrium, which is further exacerbated by atrial fibrillation, increasing the risk of pulmonary hypertension, which then induces right ventricular dysfunction, ultimately leading to a spectrum of signs and symptoms seen in HFpEF [16] [17].

Although the underlying mechanisms are unknown, sudden cardiac death (SCD) is the most common mode of death in HFpEF [18]. Ventricular arrhythmias (VAs) are commonly reported in HFpEF; however, their burden and mechanisms have not been established [19]. Various randomized controlled trials (RCTs) and prospective registries have investigated the mode of death in HFpEF, where cardiovascular (CV) deaths were responsible for 60% of all deaths in HFpEF, and 30% of all deaths were from non-CV causes [20]. There was a lesser burden of CV deaths and reduced sudden deaths in HFpEF compared to HFrEF [20]. Adabag *et al.* developed a multivariate Cox regression model, which was based on age, male gender, history of diabetes mellitus and myocardial infarction, left bundle branch block on ECG, and the natural logarithm of N-terminal pro brain natriuretic peptide (NT-pro BNP), and identified patients with HFpEF who had a risk of sudden death over 5 years [21]. Vaduganathan *et al.* used the TOPCAT trial data to investigate predictors of sudden death in HFpEF; male sex and insulin-treated diabetes mellitus independently predicted risk of sudden death in HFpEF [22]. There were 282 patients with HFpEF in a study by Woolcott *et al.*, who investigated the prevalence of shockable rhythms (ventricular tachycardia/VT or ventricular fibrillation/VF at the time of cardiac arrest), 27% had shockable rhythms, asystole in 43.3% of cases, and pulseless electrical activity in 28.7%. These findings suggested that VAs are the major cause of death in HFrEF, while VAs might play a less significant role in sudden death in HFpEF patients [23]. Several studies investigated the burden of VA in HFpEF. Gutierrez *et al.* performed ambulatory ECG monitoring or pacemaker interrogations, and non-sus-

tained VT (NSVT) was found in 32.5%, which was associated with a 3.4-fold increased risk of death in HFpEF [24]. Cho *et al.* found NSVT in 37% of patients with HFpEF, sustained VT in 1/110 HFpEF patients, and covariate-adjusted logistic regression showed HFpEF was associated with increased risk of NSVT [25]. Veldhuisen *et al.* found that 18% of HFpEF patients had NSVT, and 1/113 developed sustained VT [26]. The mechanisms underlying VAs in HFpEF include the following: 1) Reduced conduction velocity, primarily due to ventricular hypertrophy, which affects the heart's electrical conduction; 2) Delayed repolarization occurs due to down-regulation of potassium currents in HFpEF hearts, creating a potential for early afterdepolarizations that can trigger arrhythmias, 3) Calcium leakage and altered excitation-contraction coupling in HFpEF can lead to delayed afterdepolarizations, and 4) Increased ventricular fibrosis due to systemic inflammation provides substrates for functional re-entry and further contributes to arrhythmias. Hypertension and the resulting ventricular hypertrophy decrease conduction velocity in HFpEF hearts through a heterogeneous distribution of connexin 43. Collectively, these factors contribute to the development of VAs in patients with HFpEF [20].

It is crucial to understand the predictors of VAs in HFpEF, given that these patients are older, have a high burden of metabolic and systemic comorbidities, and are typically excluded from device trials. It will enable physicians to identify independent risk factors for better prognostication, arrhythmia monitoring, and timely electrophysiologic evaluation in this underrecognized population. Despite increasing recognition of HFpEF, predictors of VAs in this population remain poorly defined, particularly in large real-world datasets. To our knowledge, few large nationwide studies have systematically evaluated predictors of VAs specifically among hospitalized patients with HFpEF. Therefore, we analyzed a large nationally representative cohort from the National Inpatient Sample (NIS) to determine the prevalence of VAs among hospitalized patients with HFpEF, identify independent demographic, cardiometabolic, renal, and electrolyte predictors, and compare inpatient outcomes with patients hospitalized with HFrEF.

2. Methods

We conducted a retrospective cross-sectional study using the NIS database from 2016 through 2018, developed as part of the Healthcare Cost and Utilization Project (HCUP). The NIS represents approximately 20% of all hospital discharges in the United States and incorporates a stratified sampling design that allows for the generation of nationally representative estimates through the application of discharge weights. As the dataset is de-identified and publicly available, institutional review board approval was not required.

We identified adult hospitalizations (≥18 years) with a diagnosis of heart failure using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes. Patients were categorized into two groups:

Heart failure with preserved ejection fraction (HFpEF): I50.3, I50.30, I50.31,

I50.32, I50.33.

Heart failure with reduced ejection fraction (HFrEF): I50.2, I50.20, I50.21, I50.22, I50.23.

Hospitalizations with combined systolic and diastolic heart failure (I50.4, I50.40, I50.41, I50.42, I50.43) were excluded to avoid overlap between phenotypes. Because the NIS is a hospitalization-level database, each admission was treated as an independent observation.

VAs were identified using ICD-10-CM codes in any diagnosis field and included: Ventricular tachycardia (I47.2), Ventricular fibrillation (I49.01), Ventricular flutter (I49.02).

Heart failure diagnoses (HFpEF and HFrEF), VAs, comorbidities, and electrolyte abnormalities were each identified using ICD-10-CM codes present in any diagnosis field of the discharge record, without restriction to the principal (primary) diagnosis position. Consequently, the HFpEF and HFrEF cohorts include both hospitalizations in which heart failure was the primary reason for admission and hospitalizations in which heart failure was a co-existing condition, and VAs were similarly captured regardless of whether they precipitated the admission or developed during hospitalization. This any-position approach maximizes the sensitivity of case ascertainment but does not distinguish the clinical context in which each diagnosis arose; this should be considered when interpreting the composition of the study population and the generalizability of our findings to admissions specifically triggered by decompensated HFpEF or by a VA.

Because HFpEF and HFrEF were defined using administrative ICD-10-CM diagnosis codes rather than direct clinical, echocardiographic, or invasive hemodynamic data, these diastolic and systolic heart-failure codes served as a proxy for the underlying clinical phenotype. The NIS does not report left ventricular ejection fraction, natriuretic peptide levels, or hemodynamic filling pressures; therefore, the codes used to define HFpEF cannot confirm a preserved ejection fraction or verify that patients met contemporary hemodynamic diagnostic criteria for HFpEF, and some misclassification relative to echocardiographically confirmed HFpEF is possible.

The primary outcome was the occurrence of VAs among patients with HFpEF. Secondary outcomes included: In-hospital mortality, Length of hospital stay (LOS), Total hospitalization charges, and discharge disposition.

Additionally, comparative analyses between HFpEF and HFrEF cohorts were performed to evaluate differences in VA prevalence and in-hospital mortality.

Baseline variables included demographic and clinical characteristics known to influence heart failure outcomes and arrhythmogenesis. Demographics included Age, Sex, and race/ethnicity. Clinical Comorbidities included: Hypertension, Diabetes mellitus, Obesity, Hypothyroidism, Chronic kidney disease, Chronic obstructive pulmonary disease, Cirrhosis, and Obstructive sleep apnea. Electrolyte Abnormalities included: Hyperkalemia and hypokalemia, Hypermagnesemia and hypomagnesemia, Hypercalcemia and hypocalcemia. Complete ICD-10-CM code

definitions for every comorbidity and electrolyte abnormality used to construct the study cohort are provided in Supplementary **Appendix** Table S1 to allow independent reproduction of the cohort definitions.

All analyses accounted for the complex survey design of the NIS using discharge-level weights, stratification, and clustering variables to generate nationally representative estimates. Categorical variables were expressed as weighted percentages and compared using the chi-square test, while continuous variables were expressed as survey-weighted means with standard errors and compared using the Student's t-test. To identify independent predictors of VAs in patients with HFpEF, we performed multivariable logistic regression analysis, adjusting for demographic variables, comorbidities, and electrolyte abnormalities. Results were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). A two-sided p-value < 0.05 was considered statistically significant. All analyses were performed using Stata version 17.0 (StataCorp, College Station, TX). Because the NIS captures diagnoses present at any point during a single hospitalization without timestamps for individual conditions, the database cannot establish whether electrolyte abnormalities, acute kidney injury, or VAs occurred before, during, or after the index admission; accordingly, these variables are best interpreted as factors concurrently present during the same hospitalization rather than as clinical predictors with an established temporal or causal relationship to ventricular arrhythmias.

3. Results

A total of 1,289,705 adult heart failure hospitalizations were identified from the NIS between 2016 and 2018. The mean age was 72.5 ± 13.1 years, and 52.1% were women. Most patients were White (71.0%), followed by Black (16.8%) and Hispanic (7.5%) individuals. HFpEF accounted for 66.1% of hospitalizations, whereas HFrEF accounted for 33.9%. Baseline characteristics are summarized in Table 1; Table 2 highlights the in-hospital outcomes; and Table 3 shows VAs and in-hospital outcomes by HF type.

Table 1. Baseline characteristics of hospitalizations with HFpEF and HFrEF.

Variable	Overall (N = 1,289,705)
Age, mean ± SD	72.5 ± 13.1
Female sex	52.1%
White race	71%
Black race	16.8%
Hispanic race	7.5%
Asian/Pacific Islander	1.9%
Hypertension	13.3%
Diabetes Mellitus	47.9%
Obesity	24.5%

Continued

Morbid obesity	11.6%
Hypothyroidism	18.8%
Chronic kidney disease	45.8%
Acute kidney injury	31.5%
Chronic obstructive pulmonary disease	37.3%
Obstructive sleep apnea	16.1%
Liver cirrhosis	2.2%
Alcohol use	3.1%

Table 2. In-hospital outcomes.

Outcome	Value
In-hospital mortality	3.9% (HFpEF-3.64%; HFrEF 4.46%, $p < 0.001$)
Length of stay, days	6.1 ± 6.9
Total hospitalization charges, USD	61,781 ± 100,943

Table 3. Ventricular arrhythmias and in-hospital outcomes by HF phenotype.

Variable	HFpEF	HFrEF	p-value
Any ventricular arrhythmia	1.89%	6.48%	<0.001
In-hospital mortality	3.64%	4.46%	<0.001

Overall, VAs occurred in 3.44% of all heart failure hospitalizations. However, the prevalence differed markedly according to heart failure phenotype, occurring significantly less frequently in patients with HFpEF than in those with HFrEF (1.89% vs. 6.48%, $p < 0.001$). Ventricular tachycardia was the predominant arrhythmia subtype (3.23%), whereas ventricular fibrillation (0.35%) and ventricular flutter (<0.01%) were uncommon. Overall in-hospital mortality was 3.9% and was significantly lower among patients with HFpEF than HFrEF (3.64% vs. 4.46%, $p < 0.001$). The mean hospital length of stay was 6.1 ± 6.9 days, with mean hospitalization charges of $61,781.

On multivariable logistic regression (Table 4), male sex emerged as the strongest demographic predictor of VAs (aOR 1.71, 95% CI 1.66 - 1.77; $p < 0.001$). Increasing age and Black race were also independently associated with higher odds of VAs. Among comorbid conditions, diabetes mellitus (OR ~1.16, $p < 0.001$), obesity (OR ~1.06, $p = 0.002$), hypothyroidism (OR ~1.17, $p < 0.001$), acute kidney injury (OR ~1.12, $p < 0.001$), chronic kidney disease (OR ~1.03, $p = 0.042$), chronic obstructive pulmonary disease (OR ~1.19, $p < 0.001$), and alcohol use (OR ~1.12, $p = 0.012$) were independently associated with higher odds of VAs. Hypertension was not significantly associated with VAs ($p = 0.41$). Figure 1 provides a forest plot representation of independent predictors of VAs in HFpEF.

Table 4. Multivariable logistic regression for predictors of ventricular arrhythmias.

Variable	Adjusted Odds ratio	95% CI	p-value
Demographics			
Male sex	1.71	1.66 - 1.77	<0.001
Age 40 - 64 vs 18 - 39 years	1.44	1.21 - 1.72	<0.001
Age ≥ 65 vs 18 - 39 years	1.78	1.50 - 2.12	<0.001
Black race vs White	1.19	1.14 - 1.24	<0.001
Cardiometabolic Comorbidities			
Hypertension	1.02	0.97 - 1.08	0.41
Diabetes Mellitus	1.16	1.12 - 1.20	<0.001
Obesity	1.06	1.02 - 1.11	0.002
Hypothyroidism	1.17	1.12 - 1.22	<0.001
Renal/systemic factors			
Acute kidney injury	1.12	1.08 - 1.16	<0.001
Chronic kidney disease	1.04	1.00 - 1.08	0.043
Chronic obstructive pulmonary disease	1.19	1.15 - 1.23	<0.001
Liver cirrhosis	1.2	1.07 - 1.33	0.001
Alcohol use	1.13	1.03 - 1.24	0.012
Obstructive sleep apnea	1.06	1.01 - 1.11	0.010
Electrolyte abnormalities			
Hypokalemia	1.17	1.12 - 1.23	<0.001
Hyperkalemia	1.01	0.96 - 1.06	0.77
Hypocalcemia	1.16	1.04 - 1.3	0.007
Hypomagnesemia	1.37	1.29 - 1.46	<0.001

Among electrolyte abnormalities, hypomagnesemia demonstrated the strongest association with VAs (aOR 1.37, 95% CI 1.29 - 1.46; $p < 0.001$), followed by hypokalemia and hypocalcemia. Hyperkalemia was not independently associated with VAs. Overall, although VA were substantially less common in HFpEF than in HFrEF, their occurrence in HFpEF was consistently associated with distinct demographic, cardiometabolic, renal, and electrolyte risk factors, suggesting a multifactorial arrhythmogenic substrate in this population.

4. Discussion

In this nationwide analysis of hospitalized patients with HFpEF, VAs occurred in approximately 3.4% of hospitalizations and were independently associated with a distinct profile of demographic, cardiometabolic, renal, and electrolyte risk factors. Although VAs were substantially less frequent than in HFrEF, their occurrence identifies a clinically important subgroup with potentially increased risk of

adverse outcomes. Male sex, Black race, diabetes mellitus, obesity, hypothyroidism, chronic kidney disease, acute kidney injury, chronic obstructive pulmonary disease, alcohol use, liver cirrhosis, and electrolyte abnormalities independently predicted VAs, highlighting the multifactorial nature of arrhythmogenesis in HFpEF.

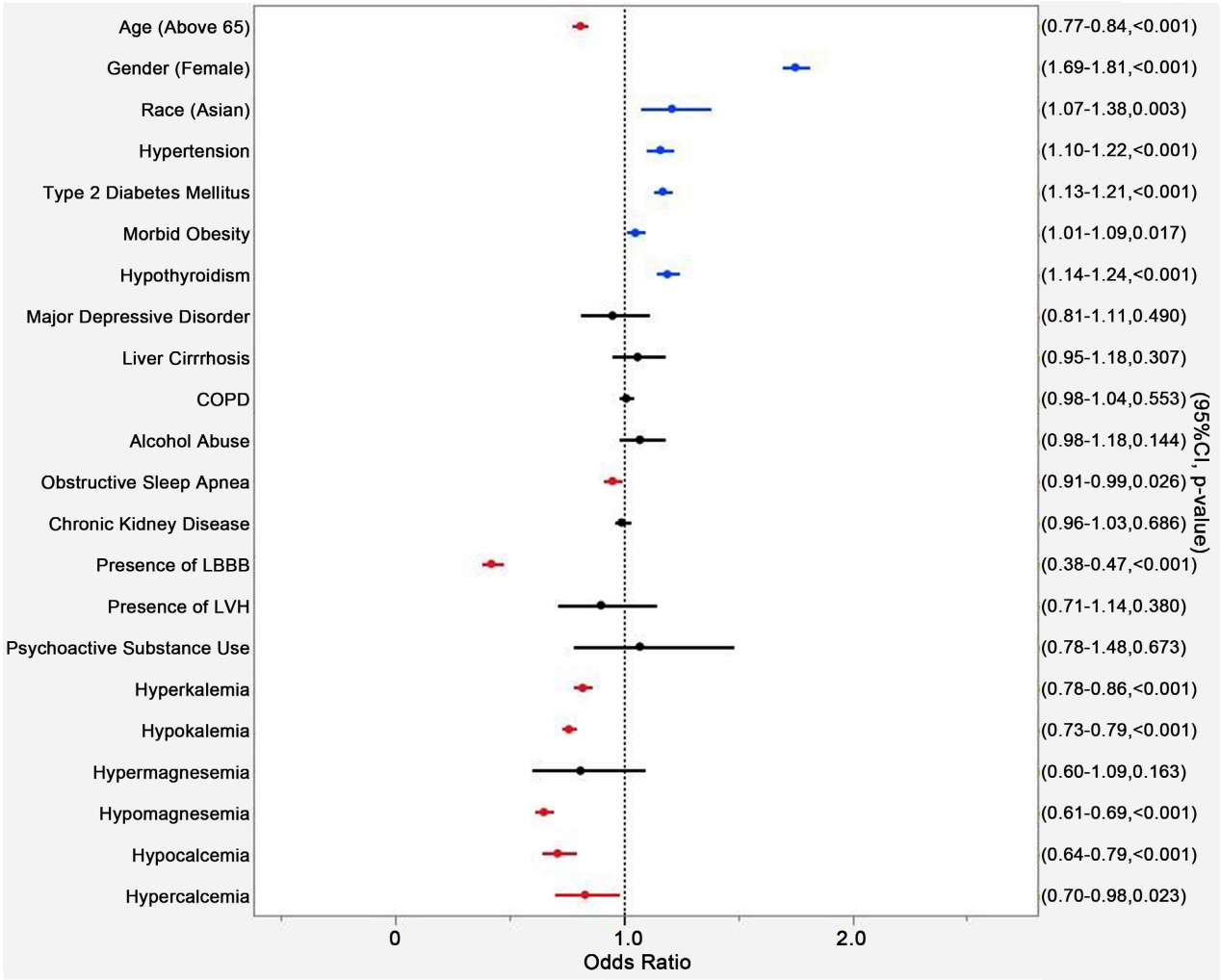

Figure 1. Forest plot of independent predictors of ventricular arrhythmias in HFpEF.

Gutierrez *et al.* demonstrated a high prevalence of non-sustained ventricular tachycardia (NSVT) in HFpEF and showed an associated increase in mortality risk [24]. Similarly, Cho *et al.* reported increased ventricular tachycardia burden and QTc prolongation among HFpEF patients [25]. VIP-HF study demonstrated frequent NSVT episodes during follow-up [26]. Unlike prior studies that primarily evaluated ambulatory NSVT or sudden cardiac death in relatively small cohorts, our nationally representative analysis demonstrates that hospitalized patients with HFpEF exhibit distinct demographic, metabolic, renal, and electrolyte predictors of ventricular arrhythmias in real-world clinical practice.

A major finding of our study is the strong association between VAs and cardi-

ometabolic comorbidities, including diabetes mellitus, obesity, and hypothyroidism. These associations are biologically plausible. Diabetes mellitus promotes myocardial fibrosis, autonomic dysfunction, oxidative stress, and ion-channel remodeling, all of which increase ventricular electrical instability. Obesity contributes to systemic inflammation, epicardial adipose tissue expansion, and adverse ventricular remodeling, whereas hypothyroidism may prolong ventricular repolarization and increase susceptibility to VAs through alterations in ion-channel function. Collectively, these metabolic abnormalities likely amplify the arrhythmogenic substrate already present in HFpEF. Additional associations were observed with COPD, alcohol use, acute kidney injury, and chronic kidney disease, suggesting that systemic illness and metabolic stress may further contribute to arrhythmogenesis in HFpEF. Ito *et al.* reviewed the risk factors for fatal VA events, including SCD (composite event) in 2423 HFpEF patients from the CHART -2 study, where the mean age was around 69 years, and 35% females, and decline in EF and NSVT were found to be independent risk factors in multivariate analysis [27]. Lavu *et al.* found that PVCs and NSVT during the first 48 hours of admission did not predict long-term mortality. [28] In another study, Ito *et al.* found a new onset of anemia associated with increased risk of VAs and SCD in HFpEF. [29]

We also observed important demographic associations. Male sex was independently associated with increased arrhythmic risk, consistent with prior VA literature. Black race was also independently associated with higher odds of VAs. The NIS does not capture genetic data, socioeconomic status, granular measures of healthcare access, or detailed indices of clinical severity, and this administrative dataset therefore cannot adequately evaluate these factors as explanations for the observed association. We caution against attributing this finding to genetic susceptibility; more plausible contributors include unmeasured differences in comorbidity burden or disease severity, socioeconomic factors, and disparities in access to cardiovascular care, and residual confounding cannot be excluded. This finding warrants further investigation using data sources capable of directly assessing these social and clinical determinants.

Electrolyte abnormalities, particularly hypokalemia, hypomagnesemia, and hypocalcemia, were significantly associated with VAs. These findings are biologically plausible given the established role of electrolyte disturbances in promoting triggered activity, delayed afterdepolarizations, and ventricular electrical instability. Hypomagnesemia demonstrated the strongest electrolyte association with VAs. Magnesium plays a critical role in myocardial membrane stability, potassium homeostasis, and suppression of triggered activity. Deficiency promotes early and delayed afterdepolarizations, facilitating ventricular tachyarrhythmias. Similarly, hypokalemia and hypocalcemia contribute to delayed repolarization and increased ventricular electrical heterogeneity, providing biologically plausible mechanisms for the observed associations.

Similarly, AKI was associated with increased arrhythmic risk, likely reflecting the contribution of acute physiologic stress and metabolic derangements to ar-

rhythmogenesis. In contrast, the lack of association observed with hypertension and hyperkalemia may reflect residual confounding, treatment effects, or limitations inherent to administrative coding datasets. Consistent with the adjusted regression analysis, OSA was independently, though modestly, associated with higher odds of VAs in HFpEF (aOR 1.06, 95% CI 1.01 - 1.11). This modest association may reflect intermittent hypoxia, sympathetic activation, and autonomic dysfunction associated with untreated or undertreated sleep-disordered breathing, although residual confounding by comorbidity burden cannot be excluded. Further studies are needed to clarify the relationship between OSA and arrhythmogenesis in HFpEF.

The increasing prevalence of HFpEF highlights the importance of improved arrhythmic risk stratification in this population. Unlike HFrEF, current guideline-directed recommendations for implantable cardioverter-defibrillator therapy are largely based on reduced ejection fraction thresholds. Identification of these readily available clinical risk factors may facilitate earlier telemetry, ambulatory rhythm monitoring, timely electrophysiology referral, and optimization of modifiable metabolic and electrolyte abnormalities. As disease-modifying therapies for HFpEF continue to evolve, improved recognition of patients at increased arrhythmic risk may become increasingly important for individualized management strategies.

Our study has several strengths, including the use of a large nationally representative cohort and the evaluation of multiple demographic and clinical variables associated with VAs in HFpEF. However, several limitations should be acknowledged. The study relies on administrative ICD-10 coding and is therefore subject to coding inaccuracies and potential misclassification. The NIS lacks detailed clinical information, including medication use, imaging findings, arrhythmia burden, ventricular tachycardia morphology, and outpatient follow-up data. Temporal relationships and causality cannot be established, and residual confounding remains possible despite multivariable adjustment. In particular, because the NIS does not provide timestamps for individual diagnoses within a hospitalization, we cannot determine whether electrolyte abnormalities, acute kidney injury, or ventricular arrhythmias occurred before, during, or after the index event; these variables should therefore be interpreted as concurrent associations identified during the same hospitalization rather than as clinical predictors with demonstrated temporal precedence. Additionally, the NIS does not distinguish sustained from non-sustained ventricular arrhythmias and lacks information regarding antiarrhythmic therapy, implantable cardioverter-defibrillator use, catheter ablation, or sudden cardiac death occurring after discharge.

5. Conclusion

In conclusion, ventricular arrhythmias, although less common in HFpEF than in HFrEF, are associated with a distinct constellation of demographic, cardiometabolic, renal, and electrolyte risk factors. Recognition of these readily identifiable

predictors may improve risk stratification, rhythm surveillance, and early electrophysiology evaluation in hospitalized patients with HFpEF. Prospective studies are warranted to validate these findings and determine whether targeted modification of these risk factors reduces ventricular arrhythmia burden and improves clinical outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Supplementary Appendix

Table S1. ICD-10-CM code definitions used for cohort, comorbidity, and electrolyte-abnormality ascertainment.

Variable	ICD-10-CM code(s)
Hypertension	I10, I11.0, I11.9, I12.0, I12.9, I13.0, I13.10, I13.11, I13.2, I15.0 - I15.9
Diabetes mellitus	E08.xx-E13.xx (all subcodes)
Obesity	E66.0, E66.1, E66.2, E66.8, E66.9
Morbid obesity	E66.01, E66.2
Hypothyroidism	E00.x-E03.x
Chronic kidney disease	N18.1, N18.2, N18.3, N18.4, N18.5, N18.6, N18.9
Acute kidney injury	N17.0, N17.1, N17.2, N17.8, N17.9
Chronic obstructive pulmonary disease	J44.0, J44.1, J44.9
Liver cirrhosis	K70.30, K70.31, K74.5, K74.60, K74.69
Alcohol use	F10.10, F10.20, F10.90 (and associated subcodes)
Obstructive sleep apnea	G47.33
Hyperkalemia	E87.5
Hypokalemia	E87.6
Hypermagnesemia	E83.41
Hypomagnesemia	E83.42
Hypercalcemia	E83.52
Hypocalcemia	E83.51