Original Article

Heart Failure With Preserved Left Ventricular Ejection Fraction in Chronic Kidney Disease

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ABSTRACT

Background: Chronic kidney disease (CKD) can lead to left ventricular (LV) systolic and diastolic dysfunction. Cardiovascular disease is a primary cause of mortality in this patient population. This study aimed to use the H2FPEF score to identify patients with CKD who have a high probability of heart failure with preserved ejection fraction (HFpEF).

Methods: We included 100 patients with CKD stages III through V and dyspnea suggestive of heart failure with an ejection fraction greater than 50%. All patients were evaluated for demographic data, CKD, and cardiovascular disease risk factors. Comprehensive echocardiography was performed, and LV global longitudinal strain (GLS) was assessed in patients in sinus rhythm. The H2FPEF score was calculated to predict the probability of HFpEF, with scores interpreted as follows: less than 2, unlikely; 2 to 5, intermediate; and 6 or greater, high.

Results: The probability of HFpEF was high in 29% of patients, intermediate in 66%, and low in 5%. Patients with a high probability of HFpEF had significantly worse LV GLS (–14.08 ± 1.084 vs –15.07 ± 1.24%; $P = 0.01$) and lower hemoglobin levels (9.71 ± 0.66 vs 10.7 ± 1.33 g/dL; $P < 0.001$). The H2FPEF score correlated positively with LV GLS ($r = 0.406$; $P < 0.001$). A hemoglobin level of 9.7 g/dL or less predicted a high H2FPEF score with an overall accuracy of 72.6%.

Conclusions: Using the simple, noninvasive H2FPEF score, we found that nearly one-third of patients with CKD had a high probability of HFpEF. LV systolic function declined as the H2FPEF score increased. Hemoglobin level was an independent predictor of a high probability of HFpEF. ***(Iranian Heart Journal 2025; 26(4): 34-45)***

KEYWORDS: Cardio-renal syndrome; Heart failure; Left ventricular diastolic dysfunction; Renal anemia; Systolic dysfunction.

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Cardiovascular disease (CVD) is a pivotal cause of mortality in patients with chronic kidney disease (CKD).[1–3] These conditions share common risk factors, such as hypertension and diabetes mellitus.[4] They also contribute to each other in cardio-renal syndrome.[5] CKD can lead to systolic and diastolic ventricular dysfunction; nonetheless, the left ventricular (LV) ejection fraction is often preserved.[6] Confirmation of heart failure with preserved ejection fraction (HFpEF) typically requires invasive measurement of LV diastolic pressure.[7] As an alternative, validated noninvasive scores, such as the H2FPEF and the Heart Failure Association–Preserved Ejection Fraction (HFA-PEFF) scores, can identify a high probability of HFpEF.[8, 9] Unlike the more complex HFA-PEFF score, which includes numerous cardiac functional and structural parameters, the H2FPEF score relies primarily on clinical parameters and does not incorporate direct measures of LV systolic function.[8, 9]

In this study, we aimed to identify patients with CKD who have a high probability of HFpEF using the H2FPEF score and to relate this score to LV global longitudinal strain (GLS) as a measure of LV systolic function.

METHODS

We conducted an observational, prospective study at Ain Shams University Hospitals from January to December 2023. The study included 100 patients with CKD stages III through V and dyspnea suggestive of HF, corresponding to New York Heart Association (NYHA) functional class II through IV, with a preserved ejection fraction greater than 50% as measured by the modified Simpson method on echocardiography. The diagnosis of CKD was based on the glomerular filtration rate calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.[10] Exclusion criteria were cardiogenic shock, pulmonary edema, history of myocardial infarction, significant primary valvular disease (defined as more than moderate aortic or mitral regurgitation or stenosis), and suboptimal transthoracic image quality. Patients with permanent atrial fibrillation were excluded from the LV GLS analysis. The research ethics committee of Ain Shams University approved the study (FMASU MD 195/2021), which adhered to the principles of the Declaration of Helsinki, as revised in 2008. All participants provided written informed consent. A clinical trial number was not applicable.

Clinical Data

History-taking focused on risk factors for cardiovascular disease (CVD), including age, sex, smoking status, diabetes mellitus, hypertension (noting the number of antihypertensive drugs), dyslipidemia, and family history of premature CVD. We also assessed the history of previous CVD (myocardial infarction, coronary intervention, and cerebrovascular disease), history of paroxysmal atrial fibrillation, and risk factors for CKD. For patients with end-stage renal disease who were receiving dialysis, we obtained data on the duration and frequency of dialysis. The clinical examination focused on signs of HF. Weight and height were measured to calculate body mass index (BMI) and body surface area (BSA); heart rate and blood pressure were also recorded.

Laboratory Data

Blood samples were obtained to measure kidney function, electrolyte levels, complete blood count, and parathyroid hormone levels. CKD staging was based on the estimated glomerular filtration rate, calculated using the CKD-EPI formula, and followed the 2012 clinical practice guidelines established by the Kidney

Disease: Improving Global Outcomes (KDIGO) organization.[11]

ECG and Echocardiography

All patients underwent a 12-lead surface ECG to diagnose permanent AF. ECG-gated transthoracic echocardiography in the left lateral decubitus position was performed according to the American Society of Echocardiography guidelines, [12, 13] by an experienced echocardiographer using a Vivid S70N ultrasound machine (GE Healthcare, Norway). In patients on dialysis, echocardiography was performed immediately after dialysis to avoid the effect of volume load.

In the parasternal long-axis view using two-dimensional imaging, interventricular septum (IVS) and posterior wall (PW) diameters were measured at end-diastole, along with LV end-diastolic diameter, LV end-systolic diameter, and LV mass. From apical four- and two-chamber views, LV ejection fraction was measured using a modified Simpson's method, and left atrial (LA) volume index was calculated. Using pulsed-wave Doppler in the apical four-chamber view at the mitral valve inflow, the E/A ratio and deceleration time (DT) were obtained. Tissue Doppler imaging was used to measure lateral e′, septal e′, and average e′ to calculate E/e′.

Color Doppler and continuous-wave Doppler in the apical four-chamber view were used to identify a tricuspid regurgitation jet to calculate right ventricular systolic pressure. In the parasternal short-axis view at the level of the great vessels, color and continuous-wave Doppler were used to identify a pulmonary regurgitation jet to calculate pulmonary artery systolic pressure (PASP). From the subcostal window, the inferior vena cava diameter and collapsibility were evaluated.

Digital loops of the LV were obtained from apical two-, three-, and four-chamber views for LV GLS quantification using speckle-tracking echocardiography and the automated functional imaging software of GE Healthcare (EchoPAC). LV GLS greater than –16% was considered abnormal.[14]

The H2FPEF Score

The H2FPEF score comprises six variables: BMI greater than 30 kg/m² (2 points); two or more antihypertensive medications (1 point); AF (paroxysmal or persistent) (3 points); PASP greater than 35 mm Hg (1 point); age greater than 60 years (1 point); and E/e′ greater than 9 (1 point). Patients with an H2FPEF score less than 2 are unlikely to have HFpEF; those with a score of 2 to 5 have an intermediate probability of HFpEF; and those with a score of 6 or greater have a high probability of HFpEF.[8]

Statistical Analysis

Data were collected, coded, and entered into SPSS software, version 23 (IBM Corp.). Qualitative data are presented as numbers and percentages. Parametric quantitative data with a normal distribution are presented as mean and standard deviation (SD), and nonparametric quantitative data are presented as median and interquartile range (IQR). Comparisons between patients with a high H2FPEF score versus those with intermediate and low scores were performed using the χ^2 test or the Fisher exact test for qualitative data and the independent *t*-test or the Mann-Whitney *U* test for quantitative data. The Spearman rank correlation coefficient was used to evaluate the correlation between the H2FPEF score and LV GLS. Receiver operating characteristic (ROC) curve analysis was used to determine the hemoglobin cutoff value for predicting a high-probability H2FPEF score.

RESULTS

This study included 100 patients with CKD who were referred to the cardiology

outpatient clinic for dyspnea or from the nephrology department for cardiac evaluation. The baseline characteristics of the study group are presented in Table 1. Based on the calculated H2FPEF score, 5 patients (5%) had a low probability of heart failure with preserved ejection fraction (HFpEF), 66 patients (66%) had an intermediate probability, and 29 patients (29%) had a high probability. LV GLS was measured in 82 patients (82%) who did not have permanent atrial fibrillation. Of these, 54 patients (65.85%) had an LV GLS worse than –16%.

Table 1. Baseline characteristics of the study patients

Variables	N (%) / Mean ± SD / Median (IQR)
Demographics	
Sex (male)	58 (58%)
Age (y)	43.2 ± 15.77
Age > 60 years	13 (13%)
BMI (kg/m^2)	22.51 ± 5.13
BMI > 30 kg/m^2	12 (12%)
BSA (m^2)	1.66 ± 0.27
NYHA Functional Class	
Class I/II	61 (61%)
Class III/IV	39 (39%)
Risk Factors	
Smoking	21 (21%)
HTN	95 (95%)
≥2 HTN drugs	90 (90%)
DM	28 (28%)
Permanent or paroxysmal AF	30 (30%)
Paroxysmal AF	12 (12%)
CKD	
CKD Stage	
III	43 (43%)
IV	5 (5%)
V	52 (52%)
Dialysis	52 (52%)
Duration of dialysis (y)	8 (5-15)
Laboratory Tests	
Creatinine (mg/dL)	2.9 (1.9-4.6)
Urea (mg/dL)	29 (22-37)
GFR (mL/min)	25 (13-35)
Hemoglobin (g/dL)	10.41 ± 1.26
Echocardiography	
IVSd (mm)	12.18 ± 1.66
PWd (mm)	12.53 ± 1.37
LVEDD (mm)	48.7 ± 4.54
LVESD (mm)	29.94 ± 4.15
EF by modified Simpson's method %	53.14 ± 1.75
LV mass index (g/m^2)	147.28 ± 35.07
E/e'	13.44 ± 2.6
E/e' >9	93 (93%)
PASP (mm Hg)	41.21 ± 9.09
PASP > 35 mm Hg	81 (81%)
LV GLS %	-14.92 ± 1.26
Impaired LV GLS worse than −16%	54 (65.85 %)
H2FPEF score	
Low probability (<2 points)	5 (5%)
Intermediate probability HFpEF (2–5 points)	66 (66%)
High probability HFpEF (≥6 points)	29 (29%)

AF: atrial fibrillation; BMI: body mass index; BSA: body surface area; CKD: chronic kidney disease; DM: diabetes mellitus; EDD: end diastolic diameter; EF: ejection fraction; ESD: end systolic diameter; GFR: glomerular filtration rate; GLS: global longitudinal strain; HTN: hypertension; IQR: interquartile range; IVSd: interventricular septal diameter; LV: left ventricle; NYHA: New York Heart Association; PASP: pulmonary artery systolic pressure; PWd: posterior wall diameter; RV: right ventricle; SD: standard deviation

A comparison of clinical, laboratory, and echocardiographic variables between patients with low/intermediate and high H2FPEF scores is shown in Table 2. Regarding demographic and clinical variables, patients with a high H2FPEF score had a significantly higher prevalence of hypertension (100% vs. 82.75%; $P <$ 0.001), a lower prevalence of diabetes mellitus (14.3% vs. 35.2%; $P = 0.01$), and a higher prevalence of atrial fibrillation (100% vs. 1.4%; $P < 0.001$). Among patients with end-stage renal disease who were receiving dialysis, the duration of dialysis was longer in those with a high H2FPEF score (median, 8 [IQR, 8–24.5] years vs. 5 [IQR, 3–8] years; $P <$ 0.001). In the comparison of laboratory data, patients with a high H2FPEF score had significantly lower hemoglobin levels (9.71 ± 0.66 vs. 10.7 ± 1.33 g/dL; $P <$ 0.001), higher urea levels (median, 37 [IQR, 22-–0] mg/dL vs. 25 [IQR, 22–30] mg/dL; $P < 0.001$), and higher potassium levels (4.66 ± 0.52 vs. 4.13 ± 0.56

mEq/L; $P < 0.001$). Conversely, there were no statistically significant differences in creatinine levels, estimated glomerular filtration rate, or CKD stage between the groups.

In the comparison of echocardiographic data, patients with a high H2FPEF score had a significantly higher E/e′ ratio (14.51 ± 1.88 vs. 13 ± 2.7; $P = 0.007$) and worse LV GLS (–14.08 ± 1.084% vs. –15.07 ± 1.24%; $P = 0.01$). An abnormal LV GLS (≥–16%) was significantly more prevalent in patients with a high H2FPEF score (100% vs. 60%; $P = 0.006$). A statistically significant positive correlation was found between the H2FPEF score and LV GLS ($r = 0.406$; $P < 0.001$) (Figure 1). Multivariate analysis (Table 3) identified hemoglobin level ($P < 0.001$), atrial fibrillation ($P < 0.001$), PASP ($P < 0.001$), and BMI ($P = 0.03$) as independent predictors of a high H2FPEF score. ROC characteristic curve analysis showed that a hemoglobin level of 9.7 g/dL or lower could predict a high H2FPEF score with a sensitivity of 72.41%, a specificity of 71.83%, a positive predictive value of 51.2%, a negative predictive value of 86.4%, and an overall accuracy of 72.6% (Figure 2).

Table 2. Comparison between low/intermediate H2FPEF scores and high H2FPEF scores

Variables	Low/Intermediate H2FPEF scores (<6 points) (No. = 71)	High H2FPEF Scores (≥6 points) (No. = 29)	*P*
Demographics			
Sex (male)	41 (57.7%)	17 (58.6%)	0.93
Age (y)	43.01 ± 15.22	43.65 ± 17.32	0.85
BMI (kg/m^2)	21.99 ± 3.82	23.77 ± 7.36	0.12
BMI > 30 kg/m^2	4 (5.63%)	8 (27.5%)	**0.002***
BSA (m^2)	1.66 ± 0.2	1.64 ± 0.4	0.73
NYHA Functional Class			
Class II	54 (76%)	17(24%)	0.08
Class III	17(58.6%)	12(41.4%)	
Risk Factors			
Smoking	15 (21.1%)	6 (20.7%)	0.96
HTN	71 (100%)	24 (82.75%)	**<0.001**
≥2 antihypertensive drugs	66 (92.9%)	29 (100%)	0.14
DM	25 (35.2%)	3 (14.3%)	**0.01***
Permanent or paroxysmal AF	1 (1.4%)	29 (100%)	**<0.001***
CKD			
CKD Stage			
III- IV	34 (47.88%)	14 (48.28%)	0.97
V	37 (52.12%)	15 (51.72%)	
Dialysis	37 (52.11%)	15 (51.72%)	0.97
Duration of dialysis (y)	5 (3-8)	8 (8-24.5)	**<0.001***
Laboratory Tests			
Creatinine (mg/dL)	2.8 (1.9-4.6)	3.7 (1.8-5.4)	0.92
Urea (mg/dL)	25 (22-30)	37 (22-40)	**0.004***
GFR (mL/min)	25 (13-35)	19 (13-29)	0.12
Hemoglobin (g/dL)	10.7 ± 1.33	9.71± 0.66	**<0.001***
Platelets	218.56 ± 66.26	198.55 ± 34.47	0.12
Total leucocytic count	6.43 ± 2.62	6.14 ± 1.7	0.58
Na (mEq/L)	133.76 ± 4.9	132.41 ± 3.5	0.18
K (mEq/L)	4.13 ± 0.56	4.66 ± 0.52	**<0.001***
Ca (mg/dL)	8.08 ± 0.95	7.95 ± 0.85	0.51
Mg (mg/dL)	1.97 ± 0.45	1.99 ± 0.42	0.84

PO4 (mg/dL)	4.99 ± 1.33	5.16 ± 0.96	0.54
Parathyroid hormone (pg/mL)	425 (379.5-615)	350 (320-768)	0.44
Echocardiography			
IVSd (mm)	11.98 ± 1.54	12.65 ± 1.85	0.06
PWd (mm)	12.32 ± 1.21	13.03 ± 1.59	**0.02***
LVEDD (mm)	49 ± 3.69	47.96 ± 6.18	0.3
LVESD (mm)	30.32 ± 3.42	29 ± 5.5	0.15
EF by modified Simpson's method %	53.15 ± 1.83	53.1 ± 1.56	0.89
LV mass index (g/m^2)	147.76 ± 34.3	146.09 ± 37.47	0.83
E/A	1.66 ± 0.76	1.81 ± 0.71	0.36
DT (ms)	187.64 ± 55.55	165.48 ± 39.75	0.05
Lateral E' (cm/s)	8.28 ± 1.84	7.07 ± 1.16	**0.001***
Septal E' (cm/s)	6.74 ± 1.64	5.65 ± 0.97	**0.001***
E/e'	13 ± 2.7	14.51 ± 1.88	**0.007***
E/e' >9	64 (90.1%)	29 (100%)	0.08
LV S' (cm/s)	8.1 ± 1.57	8.29 ± 1.66	0.58
LA volume index (mL/m^2)	44.48 ± 6.31	46.86 ± 10.67	0.17
TR velocity (m/s)	2.9 ± 0.52	3.07 ± 0.16	0.09
RVSP (mm Hg)	43.78 ± 13.27	47.47 ± 5.02	0.15
PASP (mm Hg)	40.14 ± 10.27	43.82 ± 4.26	0.06
PASP ≥ 35 mm Hg	52 (73.23%)	29 (100%)	**0.002***
LV GLS %	-15.07 ± 1.24	-14.08 ± 1.084	**0.01***
Impaired LV GLS worse than −16%	42/ 70 (60%)	12/12 (100%)	**0.006***

AF: atrial fibrillation; BMI: body mass index; BSA: body surface area; CKD: chronic kidney disease; DM: diabetes mellitus; DT: deceleration time; EDD: end diastolic diameter; EF: ejection fraction; ESD: end systolic diameter; GFR: glomerular filtration rate; GLS: global longitudinal strain; HTN: hypertension; IVSd: interventricular septal diameter; LA: left atrium; LV: left ventricle; NYHA: New York Heart Association; PASP: pulmonary artery systolic pressure; PWd: posterior wall diameter; RV: right ventricle; RVSP: right ventricular systolic pressure; TR: tricuspid regurgitation

Table 3. Independent predictors of high H2FPEF scores

	Unstandardized Coefficients		Standardized Coefficients	*t*	*P*
	B	Standard Error	β		
GLS	-0.001	0.05	-0.001	-0.01	0.99
BMI	0.03	0.01	0.111	2.21	0.03*
AF	2.75	0.19	0.7	14.53	<0.001*
PASP	0.05	0.01	0.36	4.81	<0.001*
Hemoglobin	-0.22	0.05	-0.2	-3.81	<0.001*
E/e'	-0.05	0.03	-0.1	-1.56	0.12
a. Dependent Variable: the H2FPEF score					

AF: atrial fibrillation; BMI: body mass index; GLS: global longitudinal strain; PASP: pulmonary artery systolic pressure

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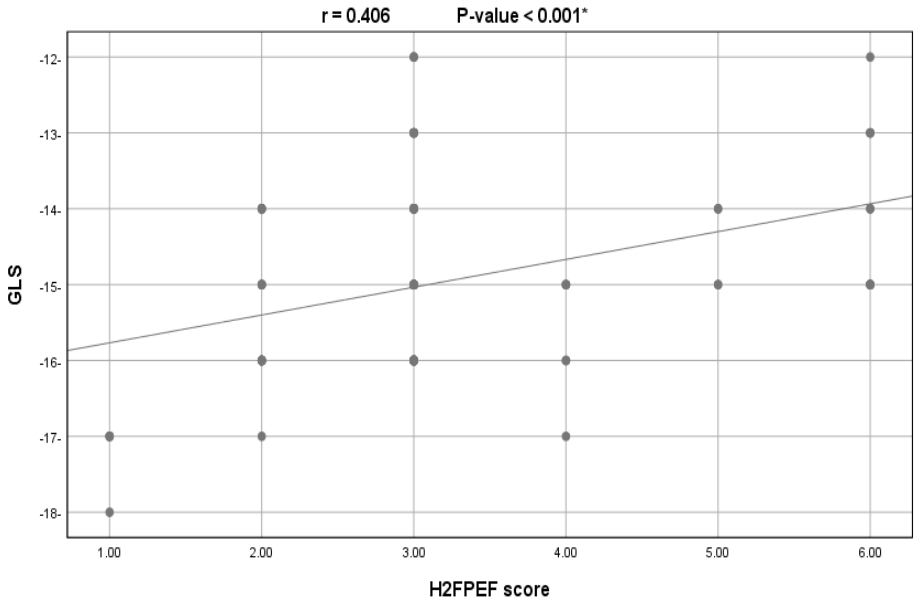

Figure 1. The image depicts the correlation between the H2FPEF score and LV GLS.

LV GLS: left ventricular global longitudinal strain

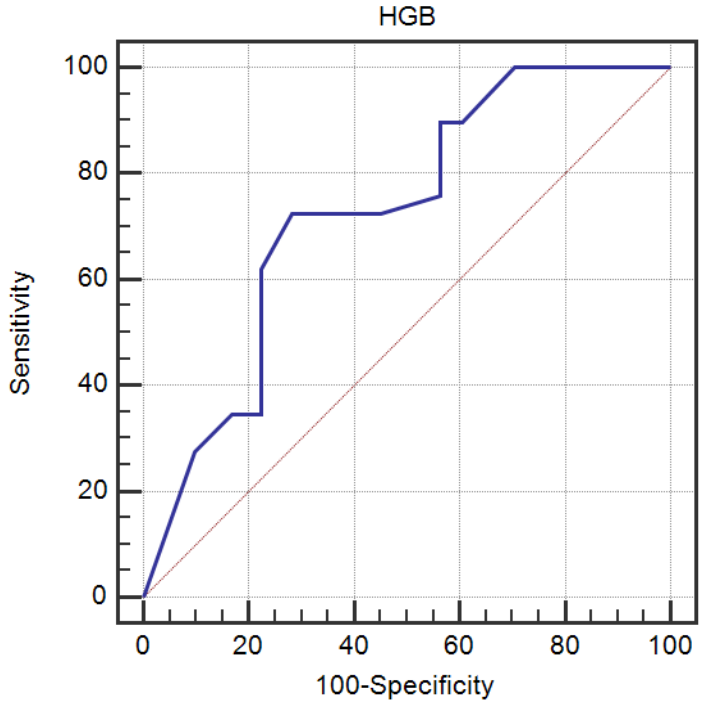

Figure 2. The image presents the cutoff value of the hemoglobin level for predicting a high H2FPEF score.

DISCUSSION

The main findings of this study were that nearly one-third of patients with CKD and preserved EF with symptoms suggestive of HFpEF had a high probability of HFpEF (H2FPEF score ≥6), whereas two-thirds had abnormal LV GLS (≥–16%). There was a positive correlation between the H2FPEF

score and LV GLS, indicating a decline in LV systolic function with increasing H2FPEF score. Hemoglobin level was an independent predictor of a high probability of HFpEF, with a cutoff value of 9.7 g/dL and an overall accuracy of 72.6%.

The H2FPEF score

The H2FPEF score is a validated tool in the noninvasive identification of HFpEF.[8] Compared with the HFA-PEFF score,[9] it is simpler and does not rely on measuring brain natriuretic peptide (BNP), which may be deranged in patients with CKD due to reduced renal clearance.[15] Still, it does not include LV GLS, which reflects LV systolic function.

In this study, only 5% of patients with CKD had a low probability of HFpEF with an H2FPEF score <2, as most patients had PASP ≥35 mm Hg, E/e′ >9, and were receiving at least 2 antihypertensive drugs, giving them at least 3 points on the H2FPEF score and categorizing them as having at least an intermediate probability of HFpEF. The presence of AF added 3 points, so 29 of 30 patients with AF (29% of the study group) scored at least 6 points on the H2FPEF score (high probability of HFpEF). This finding suggests that AF in patients with CKD may be considered a marker for HFpEF. This observation confirms the strong association between AF and HFpEF.[16]

The remaining 66 patients (66%) had an intermediate probability of HFpEF with an H2FPEF score of 2 to 5. This group requires further hemodynamic evaluation to diagnose or exclude HFpEF.[8]

There is an interplay between HFpEF and CKD under the umbrella of cardiorenal syndrome, as they share common risk factors such as hypertension and diabetes mellitus, in addition to common pathophysiological mechanisms such as increased central venous pressure, renin-angiotensin-aldosterone system activation, microvascular disease, myocardial fibrosis, LV geometric alteration, and systemic inflammation. This combination substantially increases the morbidity and mortality of these patients.[5, 17, 18]

In patients with a high probability of HFpEF, hemoglobin levels were significantly lower, and hemoglobin was an independent predictor of high probability of HFpEF, with a cutoff value of 9.7 g/dL. Anemia is common in CKD due to iron deficiency and defective erythropoiesis, which may aggravate HF.[19] Tissue hypoxia from impaired oxygen-carrying capacity could explain this association with anemia.[20] Although the results of stimulating erythropoiesis in CKD have not been encouraging,[21] detection and treatment of iron deficiency remain crucial in CKD and HF.[22, 23] A meta-analysis including 28,735 patients with HFpEF, of whom 47% were anemic, concluded that anemia has an adverse prognostic effect on HFpEF.[24] This study underscores the importance of further research to evaluate whether treating anemia can reduce LV filling pressures.

LV GLS

In this study, 65.85% of patients with CKD evaluated for LV GLS had abnormal values (≥–16%), reflecting subtle LV systolic dysfunction despite preserved EF. Impaired LV GLS is associated with a worse prognosis, with increased morbidity and mortality.[25, 26] LV GLS was significantly lower in patients with a high probability of HFpEF, and there was a positive correlation between H2FPEF score and LV GLS. Despite this correlation, LV GLS could not independently predict a high probability of HFpEF. The presence of impaired LV GLS (≥–16%) in two-thirds of patients (including those with high and intermediate probabilities of HFpEF) may explain this finding, suggesting that LV GLS declines

before progression of HFpEF.[27] This also indicates the contribution of LV systolic function to LV diastolic function, as LA compliance in the reservoir phase partially depends on the downward motion of the mitral annuli during systole.[28] Our results are consistent with those of DeVore et al.,[29] who studied patients with preserved EF enrolled in the RELAX trial and concluded that LV GLS was impaired (median –14.6) in patients with HFpEF.

Future perspectives and clinical importance

This study highlighted the prevalence of the CKD phenotype of HFpEF in patients with CKD. Patients with a high probability of HFpEF can be readily identified using the H2FPEF score, particularly in the presence of AF. This score should be applied to all patients with CKD, as HFpEF is associated with morbidity and mortality. Evaluation of LV GLS should complement the H2FPEF score, as impaired LV GLS is common in these patients. This practice is especially valuable given the growing evidence of the beneficial effects of SGLT-2 inhibitors in HFpEF and CKD.[30]

Because worsening LV GLS correlated with H2FPEF score, it will be important to study the prognostic value of the H2FPEF score in patients with CKD. In addition, further research should assess the relationship between LV GLS and HFpEF in patients with an intermediate probability of HFpEF. Moreover, the association between LV filling pressures and correction of anemia in CKD warrants further evaluation.

Study Limitations

A salient limitation of the present study was that LV GLS could not be measured in patients with permanent AF. This limitation could potentially be addressed by evaluating 3D LV strain in this group. In addition, patients with an intermediate probability of HFpEF were not further evaluated.

CONCLUSIONS

The H2FPEF score is a simple tool for identifying patients with CKD who have a high probability of HFpEF. Nearly all patients with AF had a high H2FPEF score (≥6). An increasing H2FPEF score was associated with a greater decline in LV systolic function due to worsening LV GLS. Hemoglobin levels ≤9.7 g/dL may also identify patients with CKD who have a high probability of HFpEF.

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Conflict of Interest: None reported.

Ethics Approval and Consent to Participate: All data were treated confidentially and were available only to the principal investigator. The ethics committee of the Faculty of Medicine, Ain Shams University, Cairo, Egypt (FWA 000017585; FMASU MD 195/2021), approved the study protocol. Participation in the study was strictly voluntary. Written informed consent was obtained from all participants after they were provided with detailed information about the study objectives and procedures

Consent for Publication: All authors reviewed and approved the final manuscript and agreed with the presented results and conclusions. All patients provided consent for publication.

Availability of Data and Materials: The dataset supporting the conclusions of this article is included within the article.

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Conceptualization and Methodology: I. B., W. E., and M. S. H. jointly conceived the

study idea and developed the research tools. They also provided ongoing oversight and revisions during patient recruitment and tool refinement.

Data Collection and Analysis: T. S., M. S. H., and I. B. were responsible for collecting, analyzing, and interpreting the research data.

Manuscript Writing and Interpretation: T. S., S. E. H. E., W. E., M. S. H., and I. B. collaborated on defining the study methodology, interpreting the results, and drafting the manuscript.

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