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Glucose-potassium ratio and pulmonary capillary wedge pressure as complementary prognostic markers in ischemic heart failure with preserved ejection fraction

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Heart failure with preserved ejection fraction (HFpEF) is a complex syndrome characterized by multi-organ involvement, systemic inflammation, and metabolic dysregulation. Pulmonary capillary wedge pressure (PCWP) reflects hemodynamic congestion, while the glucose-potassium ratio (GPR) has emerged as a non-invasive marker of renal tubular dysfunction and metabolic stress. The prognostic value of GPR, alone and in combination with PCWP, remains underexplored in patients with ischemic HFpEF.

Aim. To investigate the independent and complementary prognostic significance of the glucose-potassium ratio (GPR) and pulmonary capillary wedge pressure (PCWP) in predicting 5-year adverse outcomes in patients with ischemic HFpEF.

Materials and methods. Eighty-eight patients with ischemic HFpEF (NYHA functional class II–IV, stage II A–B; 41 men, 47 women; 59 with sinus rhythm and 29 with atrial fibrillation) were prospectively followed for 5 years. Baseline PCWP was estimated non-invasively using transthoracic echocardiography according to ESC/ASE recommendations, with the formula: PCW P (mmHg) = 1.24 × (E / e') + 1.9, where E is the early mitral inflow velocity and e' is the early diastolic mitral annular velocity. GPR was calculated from serum glucose and potassium. Receiver operating characteristic (ROC) analysis identified optimal cut-offs (GPR >1.18, PCWP >14.16 mmHg). Univariate and multivariate logistic regression models assessed the association with the composite endpoint of heart failure hospitalization or cardiovascular death/

Results. During follow-up, 9 patients (10.2 %) reached the composite endpoint. In univariate analysis, GPR >1.18 and PCWP >14.16 mmHg predicted adverse events (OR 11.15, p = 0.0048; OR 8.52, p = 0.0044, respectively). Serum glucose and potassium levels considered separately were not associated with outcomes. In multivariate analysis, both GPR (OR 9.79, p = 0.039) and PCWP (OR 7.51, p = 0.019) remained independent predictors. The combined model demonstrated high discriminative ability (AUC 0.837, p = 0.0007), indicating complementary but non-overlapping prognostic information.

Conclusions. In ischemic HFpEF, GPR and PCWP are robust, independent predictors of long-term adverse outcomes. GPR serves as a practical non-invasive surrogate of hemodynamic stress, offering prognostic insight comparable to invasive measurement. Their combined assessment may enhance risk stratification and guide personalized management strategies.

Ключові слова: ХСНзбФВ ЛШ, глюкозо-калійове відношення, тиск заклинювання легеневих капілярів, кардіоренальний синдром.

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Глюкозо-калієве відношення та тиск заклинювання в легеневих капілярах як додаткові прогностичні маркери при ішемічній серцевій недостатності зі збереженою фракцією викиду

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Серцева недостатність зі збереженою фракцією викиду лівого шлуночка (ХСНзбФВ ЛШ) – складний синдром, що характеризується мультиорганним ураженням, системним запаленням і метаболічною дисрегуляцією. Тиск заклинювання легеневих капілярів (ТЗЛК) характеризує гемодинамічну застійну перевантаженість, а глюкозо-калієве відношення (ГКВ) останнім часом визначають як неінвазивний маркер тубулярного та метаболічного стресу нирок. Прогностичне значення ГКВ і самостійно, і в поєднанні з ТЗЛК залишається недостатньо вивченим у пацієнтів із ХСНзбФВ ЛШ ішемічного ґенезу.

Мета роботи – дослідити незалежну та взаємодоповнювальну прогностичну значущість ГКВ і ТЗЛК у прогнозуванні п'ятирічних несприятливих наслідків у пацієнтів з ішемічною серцевою недостатністю зі збереженою фракцією викиду лівого шлуночка.

Матеріали і методи. У проспективне дослідження залучено 88 пацієнтів з ішемічною ХСНзбФВ ЛШ (II–IV ФК за NYHA, II А–Б стадія): 41 чоловіка та 47 жінок; 59 осіб із синусовим ритмом, 29 – із фібриляцією передсердь. Тривалість спостереження – 5 років. Базальний ТЗЛК оцінювали неінвазивно за допомогою трансторакальної ехокардіографії за рекомендаціями ESC/ASE з використанням формули: ТЗЛК (мм рт. ст.) = 1,24 × (E / e') + 1,9, де E – швидкість раннього діастолічного трансмітрального потоку, e' – швидкість раннього діастолічного руху кільця мітрального клапана. ГКВ обчислювали як відношення рівня глюкози сироватки до рівня калію. За допомогою ROC-аналізу визначали оптимальні порогові значення (ГКВ >1,18; ТЗЛК >14,16 мм рт. ст.). Зв'язок із комбінованою кінцевою точкою (госпіталізація з приводу серцевої недостатності або серцево-судинна смерть) оцінювали за допомогою уніваріантної та мультиваріантної логістичної регресії.

Результати. Протягом періоду спостереження комбінованої кінцевої точки досягли 9 (10,2 %) пацієнтів. В унівaріантному аналізі ГКВ >1,18 та ТЗЛК >14,16 мм рт. ст. достовірно прогнозували несприятливі події (ВШ 11,15; p = 0,0048 та ВШ 8,52; p = 0,0044 відповідно), а рівні глюкози та калію окремо прогностичного значення не мали. У мультиваріантному аналізі ГКВ (ВШ 9,79; p = 0,039) та ТЗЛК (ВШ 7,51; p = 0,019) залишалися незалежними предикторами. Комбінована модель характеризувалася високою прогностичною точністю (AUC 0,837; p = 0,0007), підтверджуючи незалежну та комплементарну прогностичну цінність маркерів.

Висновки. У пацієнтів з ішемічною ХСНзбФВ ЛШ глюкозо-калієве відношення та ТЗЛК – надійні незалежні предиктори віддалених несприятливих подій. ГКВ можна використовувати як практичний неінвазивний маркер гемодинамічного стресу з прогностичною цінністю, що зіставна з інвазивним оцінюванням. Їх комбіноване застосування покращує стратифікацію ризику та підтримує персоналізований підхід до ведення пацієнтів.

Heart failure with preserved ejection fraction (HFpEF) remains one of the most challenging conditions in contemporary cardiology, characterized by high burden of morbidity and a complex, multi-organ pathophysiological profile [1,2]. Unlike heart failure with reduced ejection fraction, the progression of HFpEF is driven not only by myocardial stiffness but also by systemic inflammation, metabolic dysregulation, and early involvement of extracardiac organs [3,4]. Recent consensus documents, including the 2025 HFA/ESC position papers, emphasize that venous congestion and its impact on end-organ function – particularly within the cardiorenal axis – are critical determinants of disease progression and adverse clinical outcomes [5,6].

The central pathophysiological hallmark of HFpEF is the elevation of left ventricular filling pressures, which is hemodynamically represented by the pulmonary capillary wedge pressure (PCWP). While PCWP is the gold standard for diagnosing hemodynamic congestion in cardiology, its significance extends far into nephrological practice [7,8]. Recent studies have demonstrated that estimated PCWP serves as a reliable marker for assessing fluid overload and determining "dry weight" in patients with renal dysfunction, underscoring its role as a universal indicator of systemic congestion [9].

In the context of the cardiorenal syndrome, elevated PCWP leads to retrograde venous congestion, which increases renal venous outflow pressure and impairs the transrenal pressure gradient. This hemodynamic stress is particularly detrimental to the renal tubulointerstitium – a metabolic powerhouse highly sensitive to hypoxia [10,11]. Chronic congestion-induced tubular injury disrupts the reabsorption of essential electrolytes and metabolites, contributing to progressive renal dysfunction and adverse prognosis [12,13]. However, despite its importance, the routine use of invasive PCWP measurement for longitudinal risk stratification is limited by procedural complexity and associated risks [14,15].

These limitations have stimulated interest in identifying non-invasive biochemical markers capable of reflecting the renal metabolic response to hemodynamic stress. The glucose-potassium ratio (GPR) has recently emerged as a promising indicator of tubulointerstitial and metabolic dysfunction [10,12]. Integrating alterations in glucose metabolism, potassium handling, insulin resistance, and sympathetic nervous system activation, GPR may capture the systemic biological response to venous congestion more sensitively than either parameters considered individually [12,16]. While GPR has shown prognostic relevance in short-term follow-up, its relationship with invasive hemodynamic parameters remains insufficiently explored, particularly in patients with ischemic HFpEF – a high-risk subgroup with pronounced microvascular dysfunction and susceptibility to cardiorenal interactions [4,16].

Therefore, the aim of this study was to evaluate the independent and combined prognostic significance of the GPR and non-invasively measured PCWP for predicting 5-year adverse outcomes in patients with ischemic HFpEF.

Aim

To evaluate the independent and combined prognostic value of the glucose-potassium ratio and non-invasively measured pulmonary capillary wedge pressure for predicting 5-year adverse outcomes in patients with ischemic heart failure with preserved ejection fraction.

Materials and methods

This prospective cohort study was conducted at the Department of Propaedeutics of Internal Medicine, Radiation Diagnostics and Radiation Therapy, Zaporizhzhia State Medical and Pharmaceutical University, based in the cardiology department "City Hospital No. 6," Zaporizhzhia, Ukraine, in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol was approved by the local Ethics Committee, and all participants provided written informed consent.

After signing informed consent, 88 patients with ischemic chronic heart failure (CHF), New York Heart Association (NYHA) functional class II–IV, stage II A–B, were enrolled. Of these, 41 (46.6 %) were male and 47 (53.4 %) female. According to heart rhythm, 59 patients (67 %) had sinus rhythm and 29 (33 %) had atrial fibrillation. The two groups were comparable in baseline characteristics: age (70.30 ± 10.16 years vs. 69.59 ± 8.45 years, p = 0.483), height (167.20 ± 10.21 cm vs. 170.24 ± 8.68 cm, p = 0.345), body weight (80.21 ± 17.66 kg vs. 86.93 ± 19.92 kg, p = 0.317), and body surface area (1.89 ± 0.23 m^2 vs. 1.97 ± 0.24 m^2, p = 0.153).

Inclusion criteria: age ≥18 years; clinical and objective evidence of CHF (NYHA II–IV); documented ischemic heart disease (history of MI, stable angina, or ECG / angiographic evidence of coronary artery disease); previous PCI or CABG; written informed consent.

Exclusion criteria: acute coronary syndrome or stroke within the previous 6 months; acute infection or decompensated diabetes mellitus; severe renal impairment glomerular filtration rate (GFR <30 mL/min/1.73 m^2); significant hepatic disease, malignancy, or psychiatric illness; patient refusal to participate.

Ischemic CHF was diagnosed according to the 2021 Recommendations for the Diagnosis and Treatment of Chronic Heart Failure by the Ukrainian Cardiology Association and the Ukrainian Association of Heart Failure Specialists. HFpEF diagnosis was confirmed according to the HFA-PEFF diagnostic algorithm [17,18]. Echocardiographic assessment was performed using an Esaote MyLab Eight system (Italy) in accordance with standard guidelines. Parameters measured included LV end-diastolic and end-systolic dimensions (LVEDD, LVESD), left ventricular ejection fraction (LVEF), relative wall thickness (RWT), LV myocardial mass index (LVMI, Penn convention), left atrial volume index (LAVI), early diastolic filling velocity (E), medial and lateral mitral annular early diastolic velocities (E'med, E'lat), and the E/e' ratio [19,20].

Baseline blood samples were collected for determination of serum glucose and potassium. The glucose-potassium ratio was calculated using the following formula: GPR = serum glucose (mmol/L) / serum potassium (mmol/L).

Baseline pulmonary capillary wedge pressure was estimated non-invasively using transthoracic echocardiography according to current ESC/ASE recommendations [9]. Early diastolic mitral inflow velocity (E, cm/s) and early diastolic mitral annular velocity (e', cm/s) were measured at the septal and lateral annulus. The mean E/e' ratio calculated and used to estimate PCWP using the formula: PCWP (mmHg) = 1.24 × (E / e') + 1.9.

Additional echocardiographic parameters, including LAVI and peak tricuspid regurgitation velocity (TRV), were assessed to improve the accuracy of PCWP estimation [21].

Data were analyzed using Statistica 13.0 (StatSoft Inc., USA), license No. JPZ804I382130ARCN10-J and MedCalc 10.2.0.0. Continuous variables were tested for normality using the Shapiro–Wilk test and presented as mean ± SD or median (Q25–Q75), as appropriate. Between-group comparisons were performed using T-tests or Mann–Whitney tests. Receiver operating characteristic (ROC) curve analysis was used to determine optimal cut-off values for GPR and PCWP. Univariate and multivariate logistic regression analyses were performed to estimate odds ratios (ORs) and 95 % confidence intervals (CIs) for adverse cardiovascular events over a 5-year follow-up. Statistical significance was set at $p < 0.05$.

Results

During a 5-year follow-up period, 9 patients (10.2 %) reached the composite primary endpoint of heart failure hospitalization or cardiovascular death.

The diagnosis of HFpEF in all enrolled patients was confirmed using a structured, multiparametric approach, primarily based on the HFA-PEFF diagnostic algorithm [17]. Each patient underwent scoring of major and minor criteria, resulting in a total score of 5 points, which is consistent with the threshold for HFpEF and reflects structural, functional, and hemodynamic abnormalities characteristic of this syndrome.

In addition to the HFA-PEFF score, further supported by complementary diagnostic algorithms and criteria recommended in current guidelines. Echocardiographic assessment of diastolic function performed according to ASE/EACVI recommendations, included evaluation of E/E' ratio, LAVI, and pulmonary artery systolic pressure (PASP). These parameters confirmed impaired diastolic relaxation and elevated filling pressures consistent with HFpEF. Moreover, a systematic exclusion of alternative causes of heart failure symptoms, including significant valvular disease, pulmonary hypertension from non-cardiac causes, and primary cardiomyopathies, was conducted to ensure diagnostic specificity.

Together, these multiple layers of assessment – structural, functional, and hemodynamic – provided robust confirmation of HFpEF, complementing the HFA-PEFF score. This multiparametric validation increases confidence in the accuracy of the study cohort and strengthens the interpretation of subsequent prognostic analyses.

Baseline demographic and clinical characteristics did not differ significantly between patients with and without adverse events *(Table 1)*.

Baseline echocardiographic and hemodynamic parameters, as presented in *Table 1,* showed that left atrial diameter (LAd) was significantly larger in patients with atrial fibrillation, reflecting atrial remodeling associated with arrhythmia. Early diastolic velocities (E' med and E' lat) were higher in this group, suggesting altered diastolic relaxation and reduced myocardial compliance. Other parameters, including LV dimensions, ejection fraction, pulmonary pressures, and metabolic indices, were comparable across rhythm subgroups, indicating similar baseline cardiac function.

To determine the optimal cut-off value of the glucose-potassium ratio for predicting adverse outcomes in this population of patients, ROC analysis was performed.

According to the ROC analysis, the optimal cut-off value of the GPR for predicting the composite endpoint was ≥1.1697, with a sensitivity of 88.9 % and a specificity of 60.8 %. Area under the curve 0.758; standard error 0.101; 95 % CI 0.655–0.843; z statistic 2.671; $p = 0.0076$ *(Fig. 1)*.

Clinically, GPR reflects the combined effects of glucose metabolism and potassium homeostasis, which may capture subtle metabolic and tubulointerstitial stresses that predispose patients to adverse outcomes. Elevated GPR likely represents enhanced myocardial vulnerability to metabolic perturbations, which is not apparent when evaluating glucose or potassium individually.

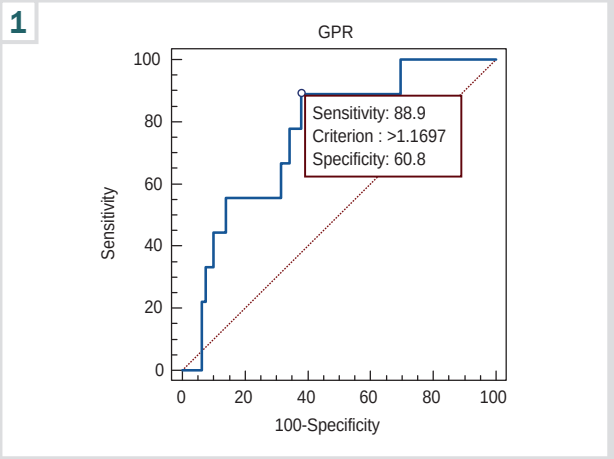
Similarly, ROC curve analysis identified an optimal cut-off value of >14.16 mmHg for pulmonary capillary wedge pressure, demonstrated sensitivity 77.78 %, specificity 74.68 %. Area under the curve 0.714; standard error 0.0966; 95 % CI 0.608–0.806; $p = 0.0076$.

PCWP is a direct measure of left ventricular filling pressure and hemodynamic congestion, which are central in the pathophysiology of HFpEF. Patients exceeding this threshold are more prone to volume overload, pulmonary congestion, and symptomatic deterioration, explaining the observed association with hospitalization and cardiovascular death.

No significant difference in discriminative performance between GPR and PCWP was observed (ΔAUC = 0.0436; $p = 0.744$), suggesting complementary roles in risk stratification The lack of a significant difference in AUC between GPR and PCWP (ΔAUC = 0.0436; $p = 0.744$) suggests

Table 1. Structural-geometric and functional parameters of the heart in patients with ischemic CHF with preserved left ventricular ejection fraction

Parameter, measurement units	HFpEF, n = 88	HFpEF with sinus rhythm, n = 59	HFpEF with atrial fibrillation, n = 29	p
Age, years	69.46 ± 9.33	69.32 ± 10.31	69.59 ± 8.45	0.968
Height, cm	168.44 ± 9.90	166.57 ± 10.86	170.24 ± 8.68	0.167
Weight, kg	85.32 ± 18.78	83.64 ± 17.73	86.93 ± 19.92	0.539
Body mass index, kg/m^2	25.20 ± 4.72	24.99 ± 4.39	25.40 ± 5.08	0.774
Body surface area, m^2	1.95 ± 0.23	1.92 ± 0.23	1.98 ± 0.24	0.296
LAd, cm	5.05 ± 0.69	4.81 ± 0.67	5.29 ± 0.64	0.015
LVEDD, cm	5.30 ± 0.74	5.47 ± 0.84	5.12 ± 0.60	0.129
LVESD, cm	3.38 ± 0.67	3.47 ± 0.78	3.30 ± 0.54	0.566
LVEF, %	65.26 ± 7.82	66.46 ± 7.64	64.10 ± 7.95	0.257
RWT, cm	0.42 ± 0.15	0.43 ± 0.18	0.42 ± 0.13	0.962
LVMI, g/m^2	126.49 ± 40.71	129.86 ± 48.03	123.24 ± 32.67	0.743
PASP, mmHg	47.19 ± 11.39	44.18 ± 11.92	49.66 ± 10.50	0.145
E/e' med, c. u.	8.78 ± 5.41	8.11 ± 3.87	9.44 ± 6.57	0.534
E' med, cm/s	9.12 ± 3.41	7.61 ± 2.04	10.59 ± 3.84	0.001
E' lat, cm/s	11.79 ± 4.09	10.04 ± 3.44	13.41 ± 4.03	0.001
LAVI, ml/m^2	47.23 ± 17.23	43.40 ± 6.96	50.42 ± 22.98	0.855
PCWP, mmHg	12.36 ± 5.97	11.95 ± 4,80	12,78 ± 7.15	0.898
Systolic blood pressure	149.61 ± 12.06	149.61 ± 13.75	149.62 ± 10.43	0.774
Potassium, mmol/l	4.37 ± 0.31	4,36 ± 0,35	4,38 ±0,27	0.930
Sodium, mmol/l	143.77 ± 3.22	143,24 ± 2,95	144,28 ± 3,42	0.254
Blood glucose, mmol/l	5.08 ± 1.04	5,24 ± 1,20	4,92 ± 0,86	0.434
GPR	1.17 ± 0.25	1,21 ± 0,29	1,13 ± 0,20	0.350



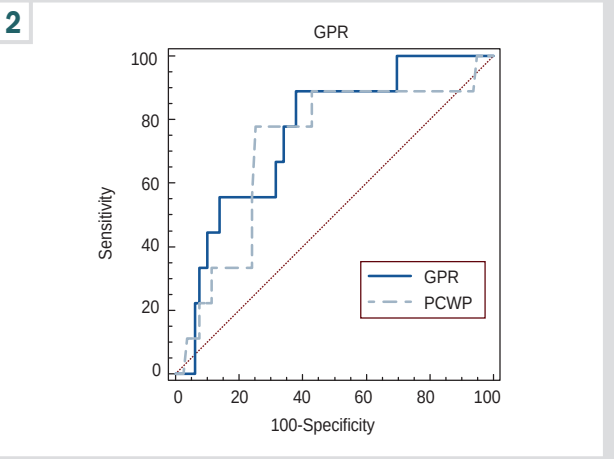


Fig. 1. Cut-off point for the glucose-potassium ratio ≥1.1697, sensitivity 88.9 %, specificity 60.8 %; p = 0.0076.

Fig. 2. Discriminative performance between GPR and PCWP.

that these parameters provide complementary prognostic information, reflecting distinct pathological axes: metabolic stress versus hemodynamic burden *(Fig. 2)*.

In univariate logistic regression analysis, GPR >1.18 was associated with a markedly increased risk of the composite endpoint (OR 11.15; 95 % CI 1.33–93.50; p = 0.0048). Serum glucose and potassium, when analyzed as individual continuous variables, were not significantly associated with outcomes. This underscores the clinical relevance of integrated metabolic assessment in HFpEF, where isolated parameters may fail to reveal underlying risk.

Similarly, PCWP >14.16 mmHg emerged as a significant univariate predictor (OR 8.52; 95 % CI 1.65–44.14; p = 0.0044). This confirms the importance of hemodynamic congestion as a driver of clinical deterioration. Elevated PCWP represents a direct measure of left ventricular filling pressures and correlating with exercise intolerance, pulmonary congestion, and increased hospitalization risk.

In the multivariate model including both parameters, GPR (OR 9.79; 95 % CI 1.12–85.68; p = 0.039) and PCWP (OR 7.51; 95 % CI 1.38–40.96; p = 0.019) remained independent predictors, emphasizing the additive value of combining metabolic and hemodynamic assessments *(Table 2)*.

Finally, a combined model PCWP and GPR achieved the highest prognostic discrimination (AUC 0.837, p = 0.0007), supporting the concept that coupling hemodynamic congestion with metabolic tubulointerstitial stress provides a more comprehensive assessment of risk in

Table 2. Multivariate prediction model of adverse cardiovascular events during the five year of follow-up for glucose-potassium ratio and PCWP

Variable	Odds Ratio	95 % CI	p
GPR	9.7888	1.1183 – 85.6830	0.0393
PCWP	7.5091	1.3767 – 40.958	0.01984

ischemic HFpEF. These findings highlight the potential utility of early identification of high-risk patients to guide targeted therapeutic interventions.

Discussion

The present study demonstrates that in patients with ischemic HFpEF, the glucose-potassium ratio and pulmonary capillary wedge pressure serve as robust, independent, and complementary predictors of long-term adverse outcomes. During a 5-year follow-up, 9 patients (10.2 %) reached the composite primary endpoint of heart failure hospitalization or cardiovascular death. Baseline demographic and clinical characteristics did not differ significantly between patients with and without adverse events, underscoring the limitations of conventional clinical parameters for risk stratification. While PCWP remains the established gold standard for assessing hemodynamic congestion [3], our findings highlight GPR as a practical biochemical surrogate that reflects the renal metabolic response to elevated filling pressures [10].

PCWP elevation represents the mechanical component of venous congestion, a central pathophysiological driver in HFpEF. Persistent elevation of left ventricular filling pressures leads to retrograde venous congestion, thereby increasing renal venous pressure and impairing oxygen delivery to the renal medulla [11]. This contributes to tubular hypoxia, tubulointerstitial injury, and progressive cardiorenal dysfunction. In our cohort, PCWP >14.16 mmHg was significantly associated with adverse outcomes (OR 8.52; 95 % CI 1.65–44.14; p = 0.0044), confirming that hemodynamic overload is a key predictor of long-term risk. These results corroborate prior findings in nephrology, where surrogate estimates of PCWP reflects systemic congestion and guides fluid management in dialysis patients [9].

GPR integrates changes in glucose metabolism and potassium handling, serving as a sensitive marker of renal tubular stress. In our study, GPR >1.18 predicted a markedly increased risk of the composite endpoint (OR 11.15; 95 % CI 1.33–93.50; p = 0.0048), whereas glucose and potassium analyzed individually were not significant. This supports a dual-hit model: mechanical stress, represented by PCWP, triggers metabolic and tubular dysfunction, which is then mirrored by an elevated GPR. In multivariate analysis including both parameters, GPR (OR 9.79; 95 % CI 1.12–85.68; p = 0.039) and PCWP (OR 7.51; 95 % CI 1.38–40.96; p = 0.019) remained independent predictors, emphasizing their additive and complementary prognostic value.

The combined assessment of GPR and PCWP demonstrated high prognostic accuracy (AUC 0.837; 95 % CI 0.743–0.907; p = 0.0007), indicating that these markers provide complementary, non-redundant information. GPR alone showed diagnostic performance comparable to invasive PCWP (AUC 0.758 vs. 0.714; ΔAUC = 0.0436; p = 0.744), supporting its utility as a non-invasive risk stratification tool in settings where right heart catheterization is not feasible [5,6]. The lack of statistical potentiation between GPR and PCWP suggests that they reflect partially overlapping yet pathophysiologically distinct aspects of the cardiorenal continuum.

Ischemic HFpEF is characterized by microvascular dysfunction, systemic inflammation, and metabolic derangements [2]. Insulin resistance, sympathetic overactivity, and subclinical tubular injury may amplify the adverse effects of venous congestion. GPR likely captures both renal stress and systemic metabolic alterations, linking hemodynamic overload with neurohumoral and metabolic dysregulation [4].

Identification of patients with a “dual-high” profile (GPR >1.18 and PCWP >14.16 mmHg) enables early recognition of an ultra-high-risk subgroup, who may benefit from intensive decongestion and early initiation of guideline-directed therapies, including SGLT2 inhibitors and mineralocorticoid receptor antagonists [3]. Incorporating GPR into longitudinal monitoring, alongside emerging tubular injury biomarkers such as NGAL and KIM-1, could further enhance risk stratification and enable personalized therapy adjustments [8,11]. Future studies should also explore integrating wearable-based hemodynamic monitoring with biochemical markers to refine individualized patient management and track response to therapy.

The study demonstrates that in ischemic HFpEF, a combined assessment of PCWP and GPR provides mechanistic and prognostic insight, linking hemodynamic congestion, renal tubular stress, and metabolic dysregulation. GPR emerges as a reliable, non-invasive surrogate of cardiorenal stress, complementing traditional hemodynamic measures holding potential to guide personalized risk stratification and therapeutic decision-making.

Conclusions

1. In patients with ischemic HFpEF, both the GPR and PCWP are robust, independent predictors of long-term adverse outcomes, including heart failure hospitalization and cardiovascular death. In univariate logistic regression analysis, GPR >1.18 was associated with a markedly increased risk of the composite endpoint (OR 11.15; 95 % CI 1.33–93.50; p = 0.0048), while PCWP >14.16 mmHg was similarly predictive (OR 8.52; 95 % CI 1.65–44.14; p = 0.0044).

2. The comparable prognostic performance of GPR and non-invasive estimated PCWP highlights the potential of GPR as a practical, non-invasive biochemical marker reflecting renal metabolic responses to hemodynamic congestion. While no direct synergistic interaction between the two parameters was observed, a combined model demonstrated the highest prognostic discrimination (AUC 0.837; p = 0.0007), indicating that integrating a hemodynamic measure with a metabolic marker of tub-

ulointerstitial stress provides a more comprehensive risk assessment in ischemic HFpEF. In multivariate analysis, both GPR (OR 9.79; 95 % CI 1.12–85.68; p = 0.039) and PCWP (OR 7.51; 95 % CI 1.38–40.96; p = 0.019) remained independent predictors, underscoring their complementary and non-redundant prognostic value.

3. These findings support a multidimensional approach to risk stratification that bridges mechanical congestion and metabolic tubular stress, enabling earlier identification of high-risk patients and informing personalized management strategies, including targeted decongestive therapy and guideline-directed pharmacologic interventions.

Prospects for further research. Future studies should focus on exploring the interactions between the glucose-potassium ratio, pulmonary capillary wedge pressure, and serum sodium levels in patients with HFpEF. Particular attention should be given to how combined metabolic and hemodynamic alterations influence disease progression and clinical outcomes. A better understanding of their interplay may contribute to improved risk stratification and support more individualized management strategies for high-risk HFpEF patients.

Ethical approval

The research program was reviewed and approved by the Bioethics Commission of Zaporizhzhia State Medical and Pharmaceutical University (Protocol No. 12 dated October 23, 2025) The article complies with all applicable requirements for research involving human participants, as established by international regulations and the current legislation of Ukraine. All participants provided written informed consent.

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