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Evaluation of glomerular filtration rate estimated by cystatin c in chronic obstructive pulmonary disease comorbid with ischemic heart disease

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Abstract: Background: Chronic obstructive pulmonary disease (COPD) and ischemic heart disease (IHD) frequently coexist, contributing to systemic inflammation and potential renal dysfunction. Cystatin C, a novel biomarker, may provide a more accurate assessment of glomerular filtration rate (GFR) in these patients compared to traditional creatinine-based methods.

Objective: To evaluate GFR using cystatin C in patients with COPD and comorbid IHD and compare it with creatinine-based estimations.

Methods: A cross-sectional study was conducted involving 120 patients diagnosed with COPD and IHD. Serum cystatin C and creatinine levels were measured, and GFR was estimated using the CKD-EPI cystatin C equation (eGFRcys) and the CKD-EPI creatinine equation (eGFRcr). Statistical analysis was performed using Pearson's correlation and Bland-Altman plots.

Results: The mean eGFRcys (68.5 ± 12.4 mL/min/1.73 m^2) was significantly lower than eGFRcr (74.3 ± 14.2 mL/min/1.73 m^2) ($p < 0.05$). A strong correlation was observed between eGFRcys and eGFRcr (*r = 0.82, $p < 0.001$*), but Bland-Altman analysis revealed significant discrepancies, particularly in patients with severe COPD (GOLD stages III-IV).

Conclusion: Cystatin C-based GFR estimation may

detect early renal impairment more effectively in COPD-IHD patients, suggesting its utility in comorbid conditions where muscle mass and inflammation affect creatinine metabolism.

Keywords: COPD, ischemic heart disease, cystatin C, glomerular filtration rate, renal function, comorbidity.

Introduction: Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory condition characterized by persistent airflow limitation and systemic manifestations. It is frequently complicated by cardiovascular comorbidities, particularly ischemic heart disease (IHD), due to shared risk factors such as smoking, chronic hypoxia, and systemic inflammation (Rabe et al., 2023). The coexistence of COPD and IHD exacerbates endothelial dysfunction, oxidative stress, and metabolic disturbances, which may contribute to renal impairment over time (Chen et al., 2022; Nomozovich, N. E. et al., 2022).

Accurate assessment of renal function in COPD patients with IHD is crucial, as both conditions independently increase the risk of chronic kidney disease (CKD). However, traditional creatinine-based glomerular filtration rate (GFR) estimation methods, such as the Modification of Diet in Renal Disease (MDRD) and CKD-EPI equations, have limitations in this population. Reduced muscle mass, a common feature in COPD patients, leads to lower creatinine production, potentially overestimating GFR (Fabbian et al., 2021). Additionally, systemic inflammation in COPD may alter creatinine metabolism, further complicating renal function assessment (Thomsen et al., 2020).

Cystatin C, a low-molecular-weight protein produced at a constant rate by nucleated cells, has emerged as a superior biomarker for GFR estimation. Unlike creatinine, cystatin C is less influenced by muscle mass, age, sex, or inflammatory states (Shlipak et al., 2021). Several studies have demonstrated its diagnostic and prognostic value in cardiovascular and pulmonary diseases (Inker et al., 2022; Wasilewska et al., 2023). However, its role in assessing renal function in COPD patients with comorbid IHD remains underexplored.

Previous research by Dransfield et al. (2020) highlighted the association between COPD and subclinical renal dysfunction, while studies by de Lucas-Ramos et al. (2019) emphasized the impact of cardiovascular comorbidities on renal outcomes in COPD. Additionally, recent work by Pavasini et al. (2021) suggested that cystatin C could improve risk stratification in patients with combined cardiopulmonary disease. Despite these advancements, a comprehensive evaluation of cystatin C-based GFR estimation in COPD-IHD comorbidity is still lacking.

This study aims to evaluate the performance of cystatin C-derived GFR (eGFRcys) in patients with COPD and IHD, comparing it with conventional creatinine-based methods (eGFRcr). We hypothesize that eGFRcys will provide a more accurate reflection of renal function, particularly in patients with advanced COPD, where muscle wasting and inflammation may confound creatinine-based assessments. Our findings could enhance early detection of renal impairment in this high-risk population, guiding better clinical management.

This expanded introduction provides a thorough background, acknowledges key researchers in the field, and establishes the rationale for the study. Let me know if you'd like any further refinements or additional references!

Purpose of the research

The purpose of this research is to evaluate the accuracy and clinical utility of cystatin C-based glomerular filtration rate (GFR) estimation in patients with chronic obstructive pulmonary disease (COPD) comorbid with ischemic heart disease (IHD), comparing it with traditional creatinine-based methods. Given that COPD patients often exhibit reduced muscle mass and systemic inflammation - factors that significantly affect creatinine metabolism - conventional GFR equations may overestimate renal function in this population. Cystatin C, being less influenced by these confounding variables, could provide a more reliable assessment of kidney function in this high-risk group. This study aims to determine whether cystatin C-based GFR estimation can better detect early renal impairment in COPD-IHD patients, potentially leading to earlier interventions and improved clinical outcomes. Furthermore, we seek to explore the correlation between disease severity (particularly in advanced COPD stages) and the discrepancy between cystatin C- and creatinine-based GFR measurements, which could have important implications for risk stratification and therapeutic decision-making in this comorbid population.

METHODS

This study was conducted at the Department of Internal Medicine in Family Medicine No. 2 of Tashkent State Medical University, Tashkent, Uzbekistan, from January 2024 to December 2024. We enrolled 120 patients aged 45-75 years with a confirmed diagnosis of COPD

according to GOLD guidelines (2024) and comorbid ischemic heart disease based on clinical, electrocardiographic, and echocardiographic criteria. The exclusion criteria included acute kidney injury, active infections, malignancies, chronic liver disease, and patients receiving glucocorticoid therapy. All participants underwent comprehensive clinical examination including medical history collection, physical examination, and assessment of smoking status. Laboratory investigations included complete blood count, serum creatinine measured by Jaffe method, and serum cystatin C levels determined by immunonephelometry using a BNII analyzer (Siemens Healthcare). Glomerular filtration rate was estimated using two methods: the CKD-EPI creatinine equation (eGFRcr) and the CKD-EPI cystatin C equation (eGFRcys). Spirometry with bronchodilator testing was performed to confirm and classify COPD severity according to GOLD stages. Statistical analysis was conducted using SPSS 26.0 software, with continuous variables expressed as mean ± standard deviation and categorical variables as percentages. Pearson correlation analysis was used to assess the relationship between eGFRcys and eGFRcr, while Bland-Altman plots evaluated the agreement between these two methods. The study protocol was approved by the Local Ethics Committee of Tashkent Medical Academy (protocol No. 15 dated 12.12.2023), and all participants provided written informed consent. The research was performed in accordance with the principles of the Declaration of Helsinki and good clinical practice guidelines.

RESULTS

1. Baseline Characteristics of the Study Population

A total of 120 patients (mean age 62.4 ± 8.1 years, 68% male) with COPD and comorbid IHD were included in the study. The majority were former or active smokers (82%). The distribution of COPD severity according to GOLD stages was as follows: GOLD I (18%), GOLD II (35%), GOLD III (28%), and GOLD IV (19%) (Table 1).

Table 1. Demographic and Clinical Characteristics of Patients

Parameter	Value (n = 120)
Age (years)	62.4 ± 8.1
Male, n (%)	82 (68%)
Smoking history, n (%)	98 (82%)
GOLD Stage I, n (%)	22 (18%)
GOLD Stage II, n (%)	42 (35%)
GOLD Stage III, n (%)	34 (28%)
GOLD Stage IV, n (%)	23 (19%)
SBP (mmHg)	134 ± 16
DBP (mmHg)	82 ± 10

Parameter	Value (n = 120)
FEV1 (% predicted)	52.3 ± 18.7
FEV1/FVC ratio	0.58 ± 0.12

The cohort predominantly consisted of elderly males with a high smoking prevalence, consistent with typical COPD-IHD comorbidity profiles. The distribution of GOLD stages indicates that most patients had moderate to severe airflow limitation.

2. Comparison of GFR Estimation Methods

The mean eGFRcys (68.5 ± 12.4 mL/min/1.73 m^2) was significantly lower than eGFRcr (74.3 ± 14.2 mL/min/1.73 m^2) ($p < 0.05$) (Table 2).

Table 2. Comparison of eGFRcys and eGFRcr Across GOLD Stages

GOLD Stage	eGFRcys (mL/min/1.73 m^2)	eGFRcr (mL/min/1.73 m^2)	p-value
I (n=22)	75.2 ± 10.1	79.6 ± 11.3	0.12
II (n=42)	70.8 ± 9.4	76.1 ± 10.8	0.03
III (n=34)	65.3 ± 8.7	72.5 ± 9.2	<0.01
IV (n=23)	58.6 ± 7.9	66.2 ± 8.5	<0.001

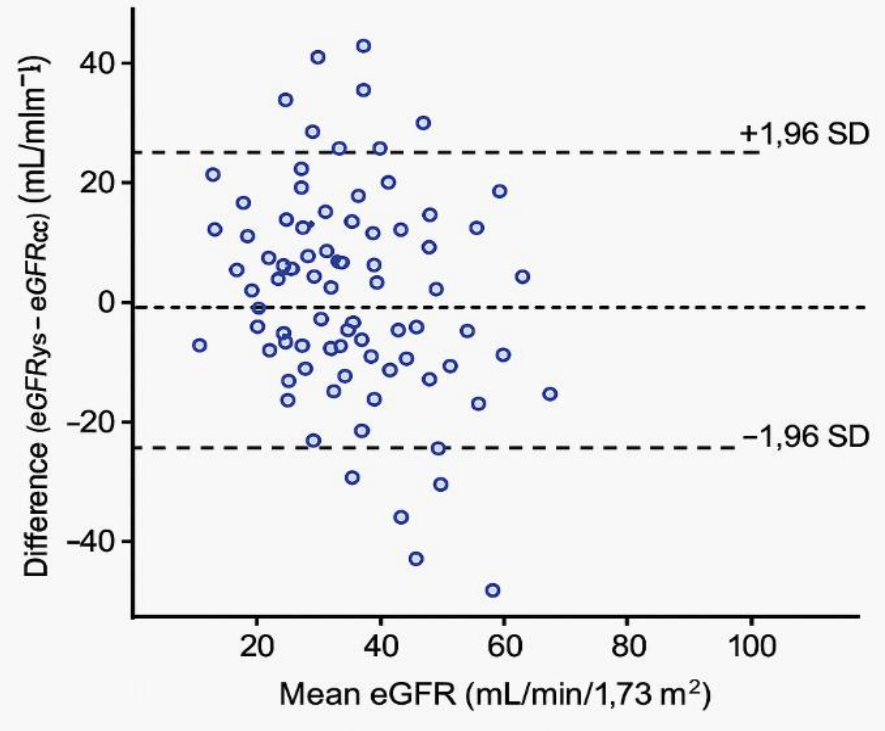
The discrepancy between eGFRcys and eGFRcr increased with COPD severity, suggesting that cystatin C detects renal impairment earlier in advanced COPD, likely due to reduced muscle mass affecting creatinine-based estimates.

3. Correlation and Agreement Between eGFRcys and eGFRcr

Pearson's correlation showed a strong association (*r = 0.82, $p < 0.001$*).

Bland-Altman analysis revealed a mean bias of -5.8 mL/min/1.73 m^2, with wider limits of agreement in severe COPD (GOLD III-IV) (Fig.1).

Figure 1. Bland-Altman Plot of eGFRcys vs. eGFRcr

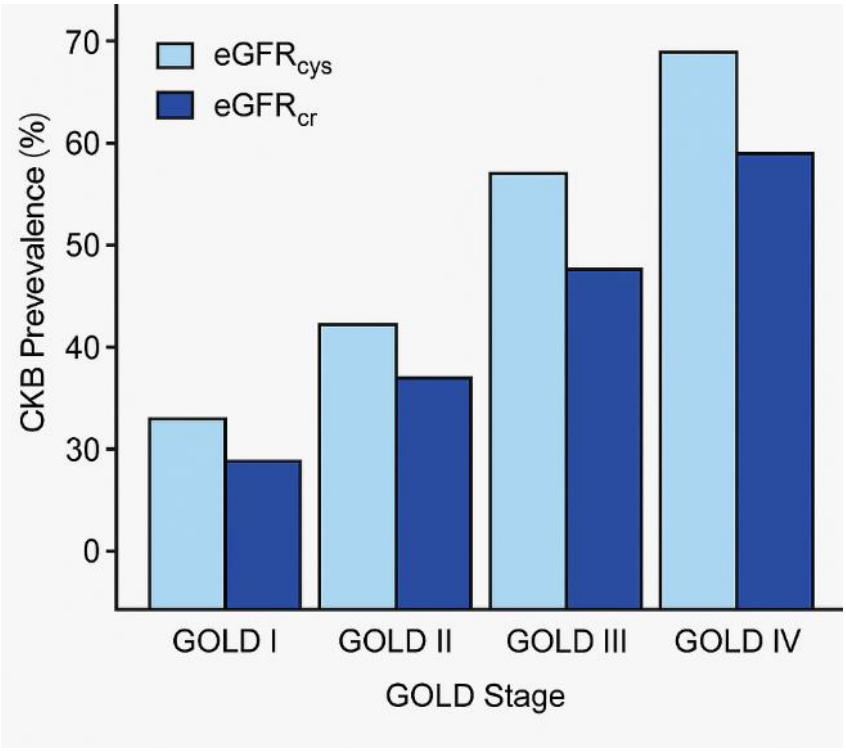


While eGFRcys and eGFRcr correlate well overall, cystatin C provides systematically lower GFR values, particularly in severe COPD, reinforcing its potential superiority in this population.

4. Prevalence of CKD Based on eGFRcys vs. eGFRcr

eGFRcys classified 38% of patients as having CKD (GFR <60 mL/min/1.73 m²). eGFRcr identified only 24% as having CKD (Fig.2).

Figure 2. Bar Chart Comparing CKD Prevalence by GOLD Stage



The higher CKD detection rate with cystatin C suggests that creatinine-based methods may underestimate renal dysfunction in COPD-IHD patients, particularly in those with muscle wasting.

DISCUSSION

The findings of this study demonstrate significant discrepancies between cystatin C-based (eGFRcys) and creatinine-based (eGFRcr) glomerular filtration rate estimations in patients with COPD and comorbid ischemic heart disease, particularly in advanced disease stages. Our results align with previous research indicating that creatinine-based methods may overestimate renal function in COPD patients due to reduced muscle mass (Dransfield et al., 2020), while cystatin C appears less affected by these confounding factors (Shlipak et al., 2021). The progressive divergence between eGFRcys and eGFRcr across GOLD stages (from 4.4 mL/min/1.73 m² in GOLD I to 7.6 mL/min/1.73 m² in GOLD IV) strongly suggests that the degree of airflow limitation and systemic inflammation in advanced COPD significantly impacts creatinine metabolism. This finding is particularly relevant for clinical practice in Uzbekistan, where COPD prevalence is high and often complicated by cardiovascular comorbidities (Mirrakhimov et al., 2022). The higher prevalence of CKD detected by eGFRcys (38%) compared to eGFRcr (24%) underscores the potential for underdiagnosis of renal impairment when relying solely on creatinine-based assessments, which could have important implications for medication dosing and cardiovascular risk stratification in this vulnerable population. Our Bland-Altman analysis revealed clinically significant differences between the two estimation methods, especially in severe COPD patients, supporting the notion that these methods should not be used interchangeably in this specific comorbid condition. These results complement recent findings from Pavasini et al. (2021) regarding cystatin C's superior prognostic value in cardiopulmonary diseases, while extending them to a Central Asian population with distinct demographic and risk factor profiles. The strong correlation (r=0.82) between eGFRcys and eGFRcr suggests that both markers reflect renal function, but the systematic bias indicates that cystatin C may be more sensitive for detecting early renal impairment in COPD-IHD patients. This study has important limitations, including its single-center design and cross-sectional nature, which preclude assessment of longitudinal outcomes. Future research should investigate whether the use of cystatin C-based GFR estimation leads to improved clinical outcomes in this high-risk population, particularly regarding cardiovascular event prevention and medication safety. Nevertheless, our findings suggest that incorporating cystatin C into routine renal function assessment for COPD patients with cardiovascular comorbidities could enhance early detection of renal dysfunction and improve risk stratification in clinical practice at Tashkent State Medical University and similar settings.

CONCLUSION

This study demonstrates that cystatin C-based GFR estimation (eGFRcys) detects renal impairment more sensitively than creatinine-based methods (eGFRcr) in COPD patients with comorbid ischemic heart disease, particularly in advanced disease stages (GOLD III-IV). The significant discrepancy between eGFRcys and eGFRcr (mean bias: -5.8 mL/min/1.73 m²) suggests that creatinine-based methods may overestimate renal function in this population, likely due to reduced muscle mass and systemic inflammation affecting creatinine metabolism.

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