Proceedings of the 14th International Scientific and Practical Conference «Global and Regional Aspects of Sustainable Development»

(September 16-18, 2026). Copenhagen, Denmark

No 309

MEDICINE AND PHARMACY

Clinical and Laboratory Features of Renal Dysfunction in Chronic Obstructive Pulmonary Disease Comorbid with Ischemic Heart Disease

Nurullayev Bakhtiyor Azimbayevich[1], Turakulov Rustam Ismatullaevich[2]

[1]Assistant; Department of Internal Medicine in Family Medicine; *Tashkent State Medical University, Uzbekistan*

[2]Professor at the National Medical Center, Doctor of Medical Sciences; *Tashkent State Medical University, Uzbekistan*

Background. Chronic obstructive pulmonary disease (COPD) is characterized not only by progressive airflow obstruction but also by systemic inflammation, hypoxemia, endothelial dysfunction, and multiorgan damage. When ischemic heart disease (IHD) coexists with COPD, hypoxia, hemodynamic stress, and microcirculatory disorders reinforce one another, creating conditions for an early decline in renal function. Recent meta-analyses have also demonstrated a significant association between COPD and chronic kidney disease and have shown that renal impairment worsens the prognosis of COPD [1]. Therefore, detecting subclinical renal dysfunction using cystatin C and estimated glomerular filtration rate (eGFR), even in patients whose creatinine remains within the reference range, is of considerable clinical relevance [2].

Objective. To comparatively assess renal functional status and markers of endothelial dysfunction and systemic inflammation across COPD stages II-IV in patients with and without concomitant IHD.

Materials and methods. This comparative clinical study included 135 patients with stage II-IV COPD. The main group comprised 90 patients with COPD and IHD (30 at each stage); the comparison group included 45 patients with COPD without IHD (stage II, n=10; stage III, n=13; stage IV, n=22). Clinical symptoms, pulmonary function, and arterial blood gases were assessed. Serum cystatin C and creatinine were

measured, and eGFR was calculated. Endothelial dysfunction, systemic inflammation, and cardiac stress were evaluated using E-selectin, tumor necrosis factor-alpha (TNF-alpha), and N-terminal pro-B-type natriuretic peptide (NT-proBNP), respectively. Quantitative variables are presented as M±m. Pearson's chi-square test and comparative between-group methods were used; $p<0.05$ was considered statistically significant.

Results. Clinical analysis showed that dyspnea and cough became more frequent as COPD severity increased, while the presence of IHD further intensified symptom severity, particularly at stage IV. At stage IV, dyspnea during fast walking was observed in 60.0% of patients in the COPD+IHD group versus 31.8% in the group without IHD (chi-square=15.781; $p<0.001$). Dyspnea after walking 100 meters occurred in 80.0% and 36.0% of patients, respectively (chi-square=39.737; $p<0.001$). Cough was also more common in the comorbid group at stage IV: 90.0% versus 59.0% (chi-square=25.293; $p<0.001$). These findings indicate that concomitant IHD aggravates functional limitations in COPD.

Renal biomarker analysis revealed the most pronounced differences in cystatin C and eGFR. At COPD stage II, cystatin C was 1.39±0.02 mg/L in the COPD+IHD group and 1.20±0.03 mg/L without IHD ($p<0.001$). At stage III, the values were 1.72±0.04 and 1.54±0.04 mg/L ($p<0.01$); at stage IV, they increased to 2.00±0.04 and 1.90±0.03 mg/L, respectively ($p>0.05$). Within the comorbid group, differences among all stages were highly significant ($p<0.001$). The progressive rise in cystatin C reflects a stage-dependent reduction in renal functional reserve. Its weaker dependence on muscle mass than creatinine further enhances its clinical value [3].

At stage II, serum creatinine was 98.3±2.2 micromol/L in the comorbid group and 83.5±2.2 micromol/L in the comparison group, with a statistically significant difference ($p<0.001$). At stage III, the corresponding values were 97.7±1.9 and 91.3±3.6 micromol/L, whereas at stage IV they were 115.0±1.92 and 109.4±4.2 micromol/L; the between-group differences at the latter two stages were not significant ($p>0.05$). These findings confirm the limited sensitivity of creatinine to early functional changes.

eGFR declined inversely to the increase in cystatin C. At stage II, eGFR was 70.1±1.5 mL/min/1.73 m² in the COPD+IHD group and 81.8±1.7 mL/min/1.73 m² in the group without IHD ($p<0.001$). At stage III, the respective values were 61.4±1.2

and 67.1±1.8 mL/min/1.73 m² ($p<0.05$). At stage IV, eGFR decreased to 44.6±1.2 and 46.6±1.4 mL/min/1.73 m², respectively ($p>0.05$). The progressive decline in eGFR across all stages was statistically significant ($p<0.001$). The effect of comorbidity was most evident at stages II and III; at stage IV, the difference diminished because marked renal dysfunction had developed in both groups.

E-selectin, a marker of endothelial dysfunction, was 64.5±1.6 ng/mL in the comorbid group and 50.0±2.2 ng/mL in the group without IHD at stage II; at stage III, the corresponding values were 74.0±2.1 and 62.4±1.7 ng/mL ($p<0.001$ for both comparisons). At stage IV, E-selectin increased to 86.0±1.7 and 81.5±3.9 ng/mL, respectively, although the between-group difference was not significant ($p>0.05$). The increase across disease stages was significant in all comparisons ($p<0.001$), indicating progressive endothelial injury in parallel with increasing COPD severity.

At stage II, the systemic inflammatory marker TNF-alpha was 16.7±1.4 ng/mL in the COPD+IHD group and 10.8±1.3 ng/mL in the group without IHD ($p<0.01$). At stage III, the corresponding values were 24.6±2.1 and 15.2±1.9 ng/mL ($p<0.001$), and at stage IV they were 32.5±2.2 and 20.2±1.7 ng/mL ($p<0.001$). The stage-dependent increase in this marker demonstrates intensification of inflammatory activity with COPD progression and in the presence of concomitant IHD. Previous studies have likewise linked declining renal function in COPD to systemic inflammation and endothelial dysfunction [4].

NT-proBNP most clearly reflected the effect of comorbidity. At stage II, its concentration was 365.4±13.9 pg/mL in the COPD+IHD group versus 116.7±19.1 pg/mL in the group without IHD. At stage III, the corresponding values were 487.4±23.8 and 170.7±23.7 pg/mL, and at stage IV they were 601.9±21.4 and 232.5±10.6 pg/mL ($p<0.001$ for all comparisons). These data indicate persistently greater cardiac stress and cardiorenal interaction in patients with IHD across all stages of COPD severity.

Taken together, intensification of hypoxemia, systemic inflammation, and endothelial dysfunction in COPD with IHD adversely affects renal perfusion and filtration. The rise in cystatin C and decline in eGFR as early as stage II indicate subclinical renal dysfunction before a marked creatinine change. Thus, renal risk assessment in COPD+IHD should include cystatin C and eGFR rather than serum creatinine alone.

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Conclusions. 1. In patients with COPD comorbid with IHD, clinical symptoms, systemic inflammation, endothelial dysfunction, and cardiac stress are more pronounced than in patients with COPD without IHD. 2. The stage-dependent rise in cystatin C from 1.39±0.02 to 2.00±0.04 mg/L and decline in eGFR from 70.1±1.5 to 44.6±1.2 mL/min/1.73 m² demonstrate progressive renal dysfunction in comorbid patients. 3. Cystatin C is a more sensitive marker than creatinine during the early stages of COPD+IHD; its combined use with eGFR enables earlier detection of subclinical renal impairment.

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