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Comorbidity Patterns Associated with Renal Dysfunction Across COPD Severity Stages and Clinical Phenotypes

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is frequently accompanied by cardiovascular, metabolic, haematological and urinary system comorbidities. The presence of renal dysfunction may further modify the clinical profile and prognostic significance of these comorbid conditions.

Objective: To comparatively evaluate comorbidities associated with renal dysfunction in patients with COPD across different disease severity stages and clinical phenotypes.

Methods: A total of 609 patients with COPD were included in this retrospective study. Patients were analysed according to COPD severity (GOLD stages I–IV) and to the bronchitic, emphysematous and mixed clinical phenotypes. The estimated glomerular filtration rate (eGFR) was calculated with the 2021 CKD-EPI creatinine equation, and renal function was categorised as an eGFR ≤89 versus ≥90 mL/min/1.73 m². The prevalence of ischaemic heart disease, arterial hypertension, diabetes mellitus, anaemia, urinary tract infection and other comorbidities was

compared between patients with and without renal dysfunction using Pearson's chi-square test.

Results: Renal dysfunction was significantly associated with COPD severity ($\chi^2 = 18.79$; $p < 0.001$). In stage III COPD, anaemia (41.6% vs 22.5%, $p < 0.05$) and urinary tract infection (53.5% vs 22.5%, $p < 0.001$) were more frequent in patients with an eGFR ≤89 mL/min/1.73 m². In stage IV, ischaemic heart disease (83.6% vs 72.2%, $p < 0.01$) and anaemia (42.3% vs 25.2%, $p < 0.01$) were significantly more prevalent. The bronchitic phenotype showed the greatest number of significant comorbidity associations, whereas in the emphysematous phenotype only ischaemic heart disease differed significantly.

Conclusion: Reduced renal filtration function in COPD is associated with distinct comorbidity patterns depending on disease severity and clinical phenotype. The strongest associations were observed in advanced COPD and in the bronchitic phenotype, supporting integrated assessment of renal function and major comorbidities in these patients.

Keywords: chronic obstructive pulmonary disease; renal dysfunction; comorbidity; ischaemic heart disease; urinary tract infection; clinical phenotype.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous chronic respiratory disorder characterised by persistent airflow limitation; however, its clinical burden extends well beyond the bronchopulmonary system. Cardiovascular, metabolic, haematological, renal and other systemic comorbidities are highly prevalent among patients with COPD and may substantially influence disease course and prognosis [1]. A systematic review published in 2022 demonstrated a high prevalence of arterial hypertension, coronary artery disease, diabetes mellitus and several other comorbid conditions among patients with COPD [1].

Recent evidence suggests that the relationship between COPD and comorbid conditions is complex and multifactorial. A 2025 systematic review and meta-analysis of Mendelian randomisation studies identified associations between COPD and gastro-oesophageal reflux disease, depression, obesity, heart failure, hypertension, rheumatoid arthritis, osteoarthritis, anaemia and several other systemic conditions [2]. These findings support the concept that COPD should be considered not only as a localised pulmonary disorder but also as a disease associated with substantial multisystem comorbidity.

Renal dysfunction is increasingly recognised as an important systemic comorbidity in COPD. A systematic review and meta-analysis published in 2024 demonstrated that patients with COPD had a significantly increased risk of chronic kidney disease compared with controls, with a pooled odds ratio of 1.54 (95% CI 1.28–1.84). Chronic kidney disease was also associated with increased short- and long-term mortality among patients with COPD [3].

Renal function impairment in COPD is likely to be multifactorial and may involve chronic hypoxaemia, systemic inflammation, oxidative stress, endothelial dysfunction, neurohumoral activation and alterations in renal haemodynamics. A multicentre observational study evaluating renal function over time in patients with COPD demonstrated progressive deterioration of renal function and identified metabolic and cardiovascular factors associated with renal function worsening [4].

The interaction between the lungs and the kidneys is bidirectional and pathophysiologically complex. Renal dysfunction may influence fluid and electrolyte balance, acid–base homeostasis, vascular tone and inflammatory pathways, whereas hypoxia, systemic inflammation, oxidative stress and haemodynamic disturbances associated with chronic lung disease may adversely affect renal perfusion and function. Gembillo et al. characterised this lung–kidney interaction as a complex network of multiple interconnected mechanisms [5].

Cardiovascular diseases represent one of the most clinically important groups of comorbidities in COPD. COPD and ischaemic heart disease share several common risk factors and pathophysiological pathways, including cigarette smoking, chronic systemic inflammation, oxidative stress, endothelial dysfunction and hypoxaemia. A systematic review and meta-analysis by Chen et al. demonstrated an increased burden of cardiovascular comorbidity among patients with COPD [6]. When impaired renal function is also present, additional haemodynamic and metabolic abnormalities may further increase the clinical relevance of cardiorenal interactions.

Anaemia is another clinically important systemic comorbidity in COPD. Its development may involve chronic inflammation, disturbances in iron metabolism and other systemic mechanisms, while impaired renal function may additionally affect erythropoietin-related pathways. Kunitomo et al. demonstrated that persistent or developing anaemia in patients with COPD was associated with an unfavourable disease trajectory [7]. In addition, anaemia has been associated with increased long-term mortality among patients hospitalised for COPD exacerbations [8].

Thus, renal dysfunction in COPD may be considered not only as an isolated comorbid condition but also as part of a broader

systemic process interconnected with cardiovascular, metabolic, haematological and other diseases. These relationships may vary according to disease severity and clinical characteristics. However, data simultaneously comparing comorbidities between COPD patients with renal dysfunction and those with preserved renal function across both disease severity stages and bronchitic, emphysematous and mixed clinical phenotypes remain limited.

The aim of this study was to compare the prevalence of comorbidities in patients with COPD with renal dysfunction (eGFR ≤89 mL/min/1.73 m²) and with preserved renal function (eGFR ≥90 mL/min/1.73 m²) according to disease severity and clinical phenotype.

2. Materials and Methods

2.1 Study design and participants

The study used a retrospective design and included the medical records of 609 patients with chronic obstructive pulmonary disease (COPD) of varying severity. The patients' medical records were reviewed retrospectively, and clinical, functional and laboratory data as well as information on comorbid conditions were analysed. The study is reported in accordance with the STROBE statement for observational studies.

2.2 Assessment of COPD severity and clinical phenotype

The diagnosis of COPD and the assessment of disease severity were based on the recommendations of the Global Initiative for Chronic Obstructive Lung Disease (GOLD, 2024). According to the severity of bronchial airflow limitation, the patients were divided into four groups: stage I, mild — 23 patients (3.8%); stage II, moderate — 117 patients (19.2%); stage III, severe — 141 patients (23.2%); and stage IV, very severe — 328 patients (53.9%).

According to clinical phenotype, the patients were classified as having a bronchitic, emphysematous or mixed phenotype. Overall, 272 patients had the bronchitic phenotype, 125 the emphysematous phenotype and 212 the mixed phenotype.

2.3 Assessment of renal function

To assess renal functional status, serum creatinine concentration was determined. On the basis of serum creatinine concentration, age and sex, the creatinine-based estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD-EPI equation and expressed in mL/min/1.73 m².

In accordance with the study objective, the patients were divided into two main groups according to renal function. The first main group comprised 383 patients (62.9%) with COPD accompanied by renal dysfunction and an eGFR ≤89 mL/min/1.73 m², whereas the second, comparative group consisted of 226 patients (37.1%) with COPD without renal dysfunction and an eGFR ≥90 mL/min/1.73 m². In the first main group there were 200 men (52.2 ± 2.6%) and 183 women (47.8 ± 2.6%); in the second group there were 167 men (73.9 ± 2.9%) and 59 women (26.1 ± 2.9%).

2.4 Assessment of comorbid conditions

Comorbid conditions were assessed on the basis of the patients' medical records, medical history, clinical examination findings and available laboratory and instrumental investigation results. The analysis included ischaemic heart disease, arterial hypertension, diabetes mellitus, anaemia, gastrointestinal diseases, liver diseases, urinary tract infection, neurological disorders, bronchial asthma, pneumonia and bronchiectasis, joint diseases and thyroid disorders. The prevalence of these conditions was evaluated according to COPD severity stage and clinical phenotype.

To determine the characteristics of the relationship between renal dysfunction, comorbid conditions and COPD severity, the prevalence of comorbidities was compared separately within each COPD severity stage between patients with an eGFR ≤89 mL/min/1.73 m² and those with an eGFR ≥90 mL/min/1.73 m². The same analytical approach was applied within the bronchitic, emphysematous and mixed clinical phenotypes.

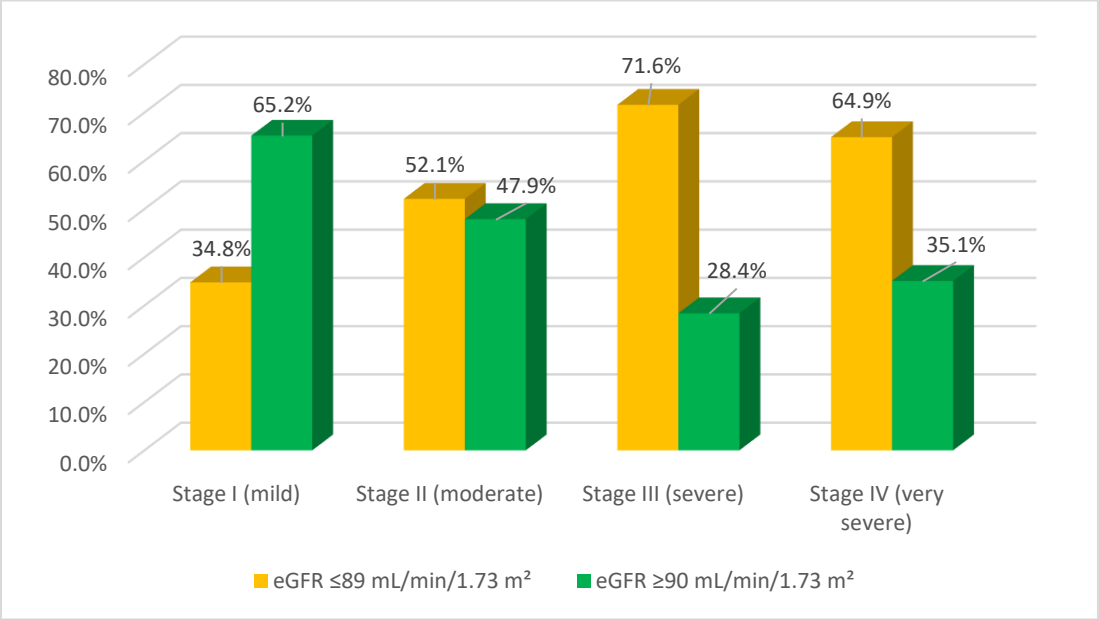
2.5 Statistical analysis

Categorical variables are presented as absolute numbers and percentages, n (%). The standard error of the proportion was calculated for relative values. Differences between categorical variables were assessed using Pearson's chi-square (χ^2) test, and Fisher's exact test was used when expected cell frequencies were small. A p value < 0.05 was considered statistically significant.

3. Results

3.1 Renal dysfunction and COPD severity

A statistically significant association was identified between COPD severity and the presence of renal dysfunction ($\chi^2 = 18.79$; df = 3; $p < 0.001$). The proportion of patients with an eGFR ≤89 mL/min/1.73 m² was 34.8% in stage I, 52.1% in stage II, 71.6% in stage III and 64.9% in stage IV COPD. These findings demonstrate an overall tendency towards a higher prevalence of reduced renal filtration function with increasing COPD severity (Figure 1).



3.2 Comorbidities according to COPD severity stage

The prevalence of comorbid conditions across the different COPD severity stages is presented in Table 1. Ischaemic heart disease (IHD) was identified in 65.2% of patients with stage I COPD, 60.7% with stage II, 68.8% with stage III and 79.6% with stage IV disease, with a highly statistically significant difference across severity stages ($\chi^2 = 18.124$; $p < 0.001$). Diabetes mellitus was observed in 0.0%, 11.1%, 17.7% and 8.2% of patients, respectively, and the between-group difference was statistically significant ($\chi^2 = 12.188$; $p < 0.01$). The prevalence of anaemia was 0.0% in stage I, 10.3% in stage II, 9.9% in stage III and 16.2% in stage IV COPD ($\chi^2 = 8.299$; $p < 0.05$).

Urinary tract infection (UTI) was observed in 43.5% of patients with stage I COPD, 36.8% with stage II, 51.1% with stage III and 32.3% with stage IV disease, with the highest prevalence recorded in stage III severe COPD ($\chi^2 = 15.090$; $p < 0.01$). Neurological disorders were present in 30.4%, 12.8%, 34.0% and 24.1% of patients across stages I–IV, respectively ($\chi^2 = 16.052$; $p < 0.01$). Joint disorders were observed in 30.4% of patients with stage I COPD, 7.7% with stage II, 16.3% with stage III and 10.1% with stage IV disease ($\chi^2 = 13.260$; $p < 0.01$). No statistically significant differences across COPD severity stages were found for arterial hypertension, gastrointestinal diseases, liver diseases or thyroid disorders ($p > 0.05$).

Table 1. Prevalence of comorbid conditions according to COPD severity stage

Comorbidities	Stages of chronic obstructive pulmonary disease				χ^2	p
	Stage I, n = 23	Stage II, n = 117	Stage III, n = 141	Stage IV, n = 328		
Ischaemic heart disease (IHD), n (%)	15 (65.2)	71 (60.7)	97 (68.8)	261 (79.6)	18.124	<0.001

Arterial hypertension (AH), n (%)	15 (65.2)	62 (53.0)	87 (61.7)	199 (60.7)	2.839	>0.05
Diabetes mellitus (DM), n (%)	0 (0.0)	13 (11.1)	25 (17.7)	27 (8.2)	12.188	<0.01
Anaemia, n (%)	0 (0.0)	12 (10.3)	14 (9.9)	53 (16.2)	8.299	<0.05
Gastrointestinal diseases, n (%)	3 (13.0)	22 (18.8)	17 (12.1)	46 (14.0)	2.532	>0.05
Liver diseases, n (%)	4 (17.4)	19 (16.2)	34 (24.1)	78 (23.8)	3.491	>0.05
Urinary tract infection (UTI), n (%)	10 (43.5)	43 (36.8)	72 (51.1)	106 (32.3)	15.090	<0.01
Neurological disorders, n (%)	7 (30.4)	15 (12.8)	48 (34.0)	79 (24.1)	16.052	<0.01
Joint diseases, n (%)	7 (30.4)	9 (7.7)	23 (16.3)	33 (10.1)	13.260	<0.01
Thyroid disorders, n (%)	0 (0.0)	5 (4.3)	6 (4.3)	6 (1.8)	3.840	>0.05

3.3 Comorbidities according to renal filtration status within COPD severity stages

The prevalence of comorbid conditions was comparatively analysed among patients with different COPD severity stages according to renal filtration status, defined as an eGFR ≤89 mL/min/1.73 m² and an eGFR ≥90 mL/min/1.73 m² (Table 2). In patients with stage I mild COPD, no statistically significant between-group differences were observed in the prevalence of IHD, arterial hypertension, UTI, anaemia or other comorbid conditions ($p > 0.05$). Although anaemia was recorded in 37.5% of patients with an eGFR ≤89 mL/min/1.73 m² and in 6.7% of those with an eGFR ≥90 mL/min/1.73 m², and UTI was observed in 62.5% and 33.3%, respectively, these differences did not reach statistical significance, most probably because of the small group sizes.

Similarly, in patients with stage II moderate COPD, no statistically significant differences in the prevalence of comorbidities were identified between the eGFR groups. IHD was present in 62.3% of patients with an eGFR ≤89 mL/min/1.73 m² and in 58.9% of those with an eGFR ≥90 mL/min/1.73 m². The corresponding values for arterial hypertension were 47.5% and 58.9%, for anaemia 24.6% and 25.0%, and for UTI 31.1% and 37.5%, respectively (all $p > 0.05$).

In stage III severe COPD, more pronounced differences were observed for selected comorbidities. Anaemia was identified in 41.6% of patients with an eGFR ≤89 mL/min/1.73 m² compared with 22.5% of those with an eGFR ≥90 mL/min/1.73 m² ($\chi^2 = 4.520$; $p < 0.05$). UTI was also significantly more prevalent in the eGFR ≤89 mL/min/1.73 m² group, occurring in 53.5% of patients compared with 22.5% in the eGFR ≥90 mL/min/1.73 m² group ($\chi^2 = 11.115$; $p < 0.001$). No statistically significant differences were found between the groups for IHD, arterial hypertension, diabetes mellitus, liver diseases, neurological disorders or joint diseases ($p > 0.05$).

In stage IV very severe COPD, IHD was observed in 83.6% of patients with an eGFR ≤89 mL/min/1.73 m² compared with 72.2% of those with an eGFR ≥90 mL/min/1.73 m² ($\chi^2 = 5.965$; $p < 0.01$). Anaemia was also significantly more prevalent in the group with reduced renal filtration function, occurring in 42.3% compared with 25.2% ($\chi^2 = 9.376$; $p < 0.01$). No statistically significant differences were identified between the groups for arterial hypertension, diabetes mellitus, gastrointestinal diseases, liver diseases, UTI, neurological disorders, joint diseases or thyroid disorders ($p > 0.05$).

Thus, the most prominent differences in comorbidity patterns among patients with an eGFR ≤89 mL/min/1.73 m² were observed in stage III and stage IV COPD. These findings indicate that, in patients with more severe COPD, reduced renal filtration function is associated with a higher prevalence of selected cardiovascular, haematological and urinary infectious comorbidities.

Table 2. Prevalence of comorbidities in patients with and without renal dysfunction across different COPD severity stages

Comorbidities	Stages of chronic obstructive pulmonary disease											
	Stage I, mild, n = 23		p	Stage II, moderate, n = 117		p	Stage III, severe, n = 141		p	Stage IV, very severe, n = 328		p
	eGFR ≤89, n = 8	eGFR ≥90, n = 15		eGFR ≤89, n = 61	eGFR ≥90, n = 56		eGFR ≤89, n = 101	eGFR ≥90, n = 40		eGFR ≤89, n = 213	eGFR ≥90, n = 115	
Ischaemic heart disease (IHD), n (%)	5 (62.5)	10 (66.7)	– >0.05	38 (62.3)	33 (58.9)	χ^2=0.139; >0.05	73 (72.3)	24 (60.0)	χ^2=2.012; >0.05	178 (83.6)	83 (72.2)	χ^2=5.965; <0.01
Arterial hypertension (AH), n (%)	6 (75.0)	9 (60.0)	– >0.05	29 (47.5)	33 (58.9)	χ^2=1.520; >0.05	65 (64.4)	22 (55.0)	χ^2=1.061; >0.05	131 (61.5)	68 (59.1)	χ^2=0.176; >0.05
Diabetes mellitus (DM), n (%)	0 (0.0)	0 (0.0)	–	7 (11.5)	6 (10.7)	χ^2=0.017; >0.05	19 (18.8)	6 (15.0)	χ^2=0.285; >0.05	20 (9.4)	7 (6.1)	χ^2=1.078; >0.05
Anaemia, n (%)	3 (37.5)	1 (6.7)	– >0.05	15 (24.6)	14 (25.0)	χ^2=0.003; >0.05	42 (41.6)	9 (22.5)	χ^2=4.520; <0.05	90 (42.3)	29 (25.2)	χ^2=9.376; <0.01
Gastrointestinal diseases, n (%)	1 (12.5)	2 (13.3)	– >0.05	9 (14.8)	13 (23.2)	χ^2=1.369; >0.05	16 (15.8)	1 (2.5)	– >0.05	29 (13.6)	17 (14.8)	χ^2=0.084; >0.05
Liver diseases, n (%)	2 (25.0)	2 (13.3)	– >0.05	13 (21.3)	6 (10.7)	χ^2=2.410; >0.05	26 (25.7)	8 (20.0)	χ^2=0.516; >0.05	52 (24.4)	26 (22.6)	χ^2=0.134; >0.05
Urinary tract infection (UTI), n (%)	5 (62.5)	5 (33.3)	– >0.05	19 (31.1)	21 (37.5)	χ^2=0.524; >0.05	54 (53.5)	9 (22.5)	χ^2=11.115; <0.001	71 (33.3)	34 (29.6)	χ^2=0.487; >0.05
Neurological disorders, n (%)	3 (37.5)	4 (26.7)	– >0.05	10 (16.4)	5 (8.9)	χ^2=1.456; >0.05	35 (34.7)	13 (32.5)	χ^2=0.059; >0.05	56 (26.3)	23 (20.0)	χ^2=1.616; >0.05
Joint diseases, n (%)	3 (37.5)	4 (26.7)	– >0.05	7 (11.5)	2 (3.6)	– >0.05	16 (15.8)	7 (17.5)	χ^2=0.058; >0.05	21 (9.9)	12 (10.4)	χ^2=0.027; >0.05
Thyroid disorders, n (%)	0 (0.0)	0 (0.0)	–	4 (6.6)	1 (1.8)	– >0.05	3 (3.0)	3 (7.5)	– >0.05	4 (1.9)	2 (1.7)	– >0.05

eGFR is expressed in mL/min/1.73 m². "–" indicates that Fisher's exact test was applied because of small expected cell frequencies.

3.4 Comorbidities according to renal filtration status within clinical phenotypes

The prevalence of comorbid conditions was comparatively analysed among patients with different clinical phenotypes of COPD according to renal filtration status (Table 3). In the bronchitic phenotype, several comorbid conditions were significantly more prevalent among patients with reduced renal filtration function than among those with an eGFR ≥90 mL/min/1.73 m². IHD was identified in 84.1% of patients with an eGFR ≤89 mL/min/1.73 m² compared with 69.4% of those with an eGFR ≥90 mL/min/1.73 m² (χ^2 = 8.286; p < 0.01). The prevalence of arterial hypertension was 70.7% and 58.3%, respectively (χ^2 = 4.449; p < 0.05). Anaemia was also significantly more common among patients with reduced renal filtration function, occurring in 37.2% versus 21.3% of patients (χ^2 = 7.711; p < 0.01). Liver diseases were observed in 23.8% versus 13.9% of patients (χ^2 = 4.004; p < 0.05), while UTI was recorded in 42.1% versus 28.7%, respectively (χ^2 = 5.007; p <

0.05). No statistically significant between-group differences were found for diabetes mellitus, gastrointestinal diseases, neurological disorders, joint diseases or thyroid disorders ($p > 0.05$).

In the emphysematous phenotype, a statistically significant difference was observed only for IHD, which was present in 73.6% of patients with renal dysfunction compared with 52.6% of those without renal dysfunction ($\chi^2 = 5.257$; $p < 0.05$). Although anaemia was more prevalent in patients with renal dysfunction than in those with preserved renal function (34.5% vs 23.7%), the difference did not reach statistical significance ($\chi^2 = 1.437$; $p > 0.05$). No statistically significant differences were observed between the groups for the remaining comorbid conditions ($p > 0.05$).

In the mixed clinical phenotype, no statistically significant differences were observed in the prevalence of any of the investigated comorbid conditions between patients with an eGFR ≤89 mL/min/1.73 m² and those with an eGFR ≥90 mL/min/1.73 m² (all $p > 0.05$). The prevalence of IHD was 69.7% and 68.8%, respectively; arterial hypertension was observed in 56.1% and 61.3%, anaemia in 28.8% and 26.2% and UTI in 37.1% and 30.0% of patients, respectively.

Thus, among the different clinical phenotypes, the comorbidity pattern associated with reduced renal filtration function was most pronounced in the bronchitic phenotype. These findings indicate that the comorbidity profile associated with renal dysfunction is not uniform across COPD clinical phenotypes.

Table 3. Prevalence of comorbidities in patients with and without renal dysfunction across different clinical phenotypes of COPD

Comorbidities	Clinical phenotypes of chronic obstructive pulmonary disease								
	Bronchitic phenotype, n = 272		p	Emphysematous phenotype, n = 125		p	Mixed phenotype, n = 212		p
	eGFR ≤89, n = 164	eGFR ≥90, n = 108		eGFR ≤89, n = 87	eGFR ≥90, n = 38		eGFR ≤89, n = 132	eGFR ≥90, n = 80	
Ischaemic heart disease (IHD), n (%)	138 (84.1)	75 (69.4)	χ^2=8.286; <0.01	64 (73.6)	20 (52.6)	χ^2=5.257; <0.05	92 (69.7)	55 (68.8)	χ^2=0.021; >0.05
Arterial hypertension (AH), n (%)	116 (70.7)	63 (58.3)	χ^2=4.449; <0.05	41 (47.1)	20 (52.6)	χ^2=0.321; >0.05	74 (56.1)	49 (61.3)	χ^2=0.551; >0.05
Diabetes mellitus (DM), n (%)	25 (15.2)	9 (8.3)	χ^2=2.843; >0.05	5 (5.7)	3 (7.9)	– >0.05	16 (12.1)	7 (8.8)	>0.05
Anaemia, n (%)	61 (37.2)	23 (21.3)	χ^2=7.711; <0.01	30 (34.5)	9 (23.7)	χ^2=1.437; >0.05	38 (28.8)	21 (26.2)	χ^2=0.160; >0.05
Gastrointestinal diseases, n (%)	22 (13.4)	13 (12.0)	χ^2=0.110; >0.05	13 (14.9)	6 (15.8)	χ^2=0.015; >0.05	20 (15.2)	14 (17.5)	χ^2=0.204; >0.05
Liver diseases, n (%)	39 (23.8)	15 (13.9)	χ^2=4.004; <0.05	18 (20.7)	6 (15.8)	χ^2=0.409; >0.05	36 (27.3)	21 (26.2)	χ^2=0.027; >0.05
Urinary tract infection (UTI), n (%)	69 (42.1)	31 (28.7)	χ^2=5.007; <0.05	31 (35.6)	14 (36.8)	χ^2=0.017; >0.05	49 (37.1)	24 (30.0)	χ^2=1.119; >0.05
Neurological disorders, n (%)	47 (28.7)	23 (21.3)	χ^2=1.847; >0.05	17 (19.5)	5 (13.2)	χ^2=0.743; >0.05	40 (30.3)	17 (21.2)	χ^2=2.077; >0.05

Joint diseases, n (%)	20 (12.2)	13 (12.0)	χ^2=0.002; >0.05	8 (9.2)	3 (7.9)	– >0.05	19 (14.4)	9 (11.2)	χ^2=0.430; >0.05
Thyroid disorders, n (%)	6 (3.7)	2 (1.9)	χ^2=0.484; >0.05	4 (4.6)	2 (5.3)	– >0.05	1 (0.8)	2 (2.5)	– >0.05

eGFR is expressed in mL/min/1.73 m². "–" indicates that Fisher's exact test was applied because of small expected cell frequencies.

4. Discussion

In the present study, a reduction in renal filtration function among patients with COPD was associated with different comorbid conditions depending on disease severity and clinical phenotype. The most relevant findings were a higher prevalence of anaemia and UTI in patients with stage III severe COPD, and of IHD and anaemia in patients with stage IV very severe COPD, among those with an eGFR ≤89 mL/min/1.73 m². Analysis according to clinical phenotype showed that the greatest number of statistically significant between-group differences was observed in the bronchitic phenotype.

Our findings are consistent with contemporary evidence indicating an association between COPD and renal dysfunction. In a 2024 systematic review and meta-analysis, Liu et al. demonstrated that COPD was significantly associated with chronic kidney disease (CKD), with a higher pooled likelihood of CKD among patients with COPD, and emphasised that impaired renal function may adversely affect the prognosis of COPD [3]. Similarly, a multicentre observational study by Pelaia et al. documented progressive deterioration of renal function over time in patients with COPD [4].

The pathophysiological basis of this relationship may involve several shared mechanisms. In COPD, chronic hypoxaemia, systemic inflammation, oxidative stress and endothelial dysfunction may adversely affect renal microcirculation and renal perfusion. Conversely, impaired renal function may further compromise pulmonary and cardiovascular status through disturbances in fluid and electrolyte balance, acid–base homeostasis and cardiovascular haemodynamics. Gembillo et al. described this lung–kidney interaction as a bidirectional and potentially mutually reinforcing pathological process [5].

In our study, among patients with stage III severe COPD, anaemia was present in 41.6% of patients with an eGFR ≤89 mL/min/1.73 m² compared with 22.5% of those with an eGFR ≥90 mL/min/1.73 m² (χ^2 = 4.520; $p < 0.05$). In stage IV very severe COPD, the corresponding prevalence rates were 42.3% and 25.2%, respectively, with an even stronger statistical difference (χ^2 = 9.376; $p < 0.01$). These findings indicate that anaemia becomes clinically more relevant when advanced COPD coexists with reduced renal filtration function.

Anaemia is an important comorbid condition in COPD. In a systematic review including 59 studies, Alisamir et al. reported that anaemia in COPD was associated with exacerbations, prolonged hospitalisation, poorer quality of life and increased long-term mortality [9]. Garcia-Pachon and Padilla-Navas also reported in 2024 that anaemia was an important prognostic marker of long-term mortality among patients hospitalised for COPD exacerbation [8].

The higher prevalence of anaemia observed in our patients with stage III–IV COPD and reduced eGFR is pathophysiologically plausible. Chronic systemic inflammation in COPD may impair iron metabolism and erythropoiesis, whereas deterioration of renal function may additionally contribute through insufficient erythropoietin production. At the same time, anaemia reduces the oxygen-carrying capacity of the blood and may aggravate pre-existing hypoxaemia in COPD [7,9]. Thus, a mutually reinforcing functional interaction between COPD, renal dysfunction and anaemia may occur in these patients. Nevertheless, the present findings demonstrate an association and do not establish a causal relationship, because of the retrospective design of the study.

Another important finding was that, in stage III severe COPD, UTI was present in 53.5% of patients with an eGFR ≤89 mL/min/1.73 m² compared with 22.5% of those with an eGFR ≥90 mL/min/1.73 m² (χ^2 = 11.115; $p < 0.001$), which represented one of the strongest statistical associations identified in the study. Increased susceptibility to infection in patients with reduced renal function may be related to impaired immune responses, coexisting metabolic disorders, older age and repeated healthcare interventions. Conversely, recurrent or complicated UTIs may adversely affect the renal parenchyma and potentially contribute to further deterioration of renal function [11]. Reviews addressing CKD and urinary tract infections have emphasised that UTIs may occur more frequently and follow a more complicated course in patients with impaired renal function [11]. However, in our study a statistically significant difference in UTI prevalence was observed only in stage III COPD, and this association should therefore not be generalised uniformly across all COPD severity stages.

In stage IV very severe COPD, IHD was documented in 83.6% of patients with an eGFR ≤89 mL/min/1.73 m² compared with 72.2% of those with an eGFR ≥90 mL/min/1.73 m² ($\chi^2 = 5.965$; $p < 0.01$). The high burden of cardiovascular comorbidity in COPD has been well documented: Dos Santos et al. identified arterial hypertension and coronary artery disease among the most prevalent comorbid conditions in patients with COPD [1], and the meta-analysis by Chen et al. demonstrated an increased risk of various cardiovascular comorbidities in this population [6]. The higher coexistence of IHD and reduced renal function in stage IV COPD may be explained by shared pathophysiological mechanisms: chronic hypoxaemia, activation of the sympathetic nervous system and the renin–angiotensin–aldosterone system, endothelial dysfunction and systemic inflammation may contribute both to coronary atherosclerosis and to impaired renal perfusion [5,6]. From this perspective, our findings suggest that particular attention should be paid to cardiorenal comorbidity in patients with very severe COPD.

Analysis according to clinical phenotype revealed the most characteristic findings in the bronchitic phenotype, in which patients with an eGFR ≤89 mL/min/1.73 m² had a significantly higher prevalence of IHD (84.1% vs 69.4%; $p < 0.01$), arterial hypertension (70.7% vs 58.3%; $p < 0.05$), anaemia (37.2% vs 21.3%; $p < 0.01$), liver disease (23.8% vs 13.9%; $p < 0.05$) and UTI (42.1% vs 28.7%; $p < 0.05$). Differences in multimorbidity patterns according to COPD phenotype have also been reported previously: Figueira-Gonçalves et al. showed that the structure of multimorbidity networks in COPD varies according to clinical characteristics, including the presence of chronic bronchitis, and that the strength and pattern of relationships between comorbid conditions are not uniform across different phenotypic presentations of COPD [10].

In the bronchitic phenotype, persistent bronchial inflammation, chronic sputum production and recurrent infectious exacerbations may contribute to a greater systemic inflammatory burden. Systemic inflammation, in turn, is associated with endothelial dysfunction, atherosclerotic processes and impaired vascular reactivity [1,5,6]. In this context, the higher prevalence of IHD and arterial hypertension among bronchitic patients with reduced eGFR is biologically plausible. However, the observed association with liver disease should be interpreted cautiously, because the present study did not stratify patients according to the type or severity of liver disease or to associated metabolic factors.

In the emphysematous phenotype, the only statistically significant difference was observed for IHD (73.6% vs 52.6%; $\chi^2 = 5.257$; $p < 0.05$), an association that may also be related to impaired pulmonary gas exchange and to the adverse cardiovascular effects of chronic hypoxaemia [5,6]. The absence of statistically significant differences for the other comorbidities in this phenotype may indicate a distinct comorbidity pattern; current literature increasingly recognises COPD as a heterogeneous disease with diverse clinical and systemic manifestations rather than as a single uniform clinical entity [1,10].

In the mixed phenotype, no statistically significant differences in the prevalence of the investigated comorbidities were observed between the eGFR groups. This finding should not be interpreted as evidence that renal dysfunction has no relationship with comorbidity in the mixed phenotype. Rather, the mixed phenotype may represent a clinically heterogeneous population in which several mechanisms coexist, potentially diluting the statistical effect of individual comorbid conditions. Further phenotype-oriented studies are therefore warranted.

Overall, our findings indicate that comorbidity in COPD should be evaluated not only according to the presence of the pulmonary disease itself, but also in relation to COPD severity, clinical phenotype and renal filtration function. Systematic reviews have likewise demonstrated a high prevalence of hypertension, coronary artery disease, diabetes mellitus and other comorbid conditions in COPD and have shown that these conditions may adversely affect clinical outcomes [1,2].

4.1 Limitations

Several limitations should be considered when interpreting the present findings. First, because of the retrospective design, the observed associations cannot establish causality. Second, potential confounding factors — including age, sex, smoking history, diabetes mellitus, arterial hypertension, medication use and other clinical characteristics — may simultaneously influence both renal function and comorbidity patterns. Third, a single creatinine measurement was used to estimate the glomerular filtration rate, so that transient reductions in eGFR cannot be distinguished from established chronic kidney disease. Future studies should evaluate these associations using multivariable regression models and, where possible, prospective designs.

5. Conclusion

Reduced renal filtration function in patients with COPD was associated with distinct comorbidity patterns depending on disease severity and clinical phenotype. In patients with an eGFR ≤89 mL/min/1.73 m², anaemia and urinary tract infection were significantly more frequent in stage III COPD, whereas ischaemic heart disease and anaemia were more prevalent in stage IV disease. Among the clinical phenotypes, the most pronounced comorbidity profile was observed in the bronchitic phenotype,

which showed significant associations with ischaemic heart disease, arterial hypertension, anaemia, liver disease and urinary tract infection; in the emphysematous phenotype the principal significant difference was limited to ischaemic heart disease. These findings support the need for integrated assessment of renal function and clinically relevant comorbidities in patients with COPD, particularly in advanced disease stages and in those with the bronchitic phenotype.

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