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Chronic Kidney Disease in Idiopathic Pulmonary Fibrosis: A Cross-Sectional Study

Giovanni Franco

g.franco@campus.unimib.it

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

Emmanuele Pietro Porfido

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

Chiara Pirotta

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

Eleonora Passeri

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

Umberto Zanini

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

Francesca Zanoni

Unit of Nephrology, Dialysis and Kidney Transplantation, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano

Paola Faverio

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

Giuseppe Castellano

Unit of Nephrology, Dialysis and Kidney Transplantation, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano

Fabrizio Luppi

University of Milano Bicocca, School of Medicine and Surgery, SC Pneumologia, Fondazione IRCCS San Gerardo dei Tintori

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Research Article

Keywords: Idiopathic pulmonary fibrosis, Chronic kidney disease, Albuminuria, Renal function

Posted Date: November 11th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11440764/v1

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Additional Declarations: Competing interest reported. Pr. Fabrizio Luppi reports consulting fees from AstraZeneca, Boehringer-Ingelheim and Sanofi; payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events from Boehringer-Ingelheim, Chiesi, Menarini and Sanofi; support for attending meetings and/or travel from Menarini. The other authors had no conflicts of interest to declare.

Abstract

Background

Chronic kidney disease (CKD) is increasingly recognised as a relevant comorbidity in idiopathic pulmonary fibrosis (IPF), yet its burden may be underestimated. We aimed to determine the prevalence and clinical correlates of CKD in patients with IPF using contemporary Kidney Disease: Improving Global Outcomes (KDIGO) criteria, including albuminuria assessment.

Methods

We conducted a single-centre cross-sectional study including 101 consecutive patients with multidisciplinary-confirmed IPF enrolled between January 2025 and June 2026. Renal evaluation included serum creatinine, eGFR calculated using the 2021 CKD-EPI equation, and urinary albumin-to-creatinine ratio (UACR). CKD was defined - according to 2024 KDIGO criteria - as eGFR < 60 mL/min/1.73 m² and/or UACR ≥ 30 mg/g, with chronicity confirmed by measurements at least 3 months apart.

Results

CKD was identified in 28 patients (27.7%). Eleven had reduced eGFR with normal albuminuria, nine had isolated albuminuria with preserved eGFR, and four had both abnormalities. CKD prevalence was higher than that reported in the Italian CARHES population aged ≥ 65 years (27.7% vs 15.2%). Patients with CKD were older and more frequently affected by arterial hypertension, whereas pulmonary function did not differ between IPF patients with and without CKD. In the multivariable analysis, hypertension remained independently associated with CKD (adjusted OR 3.04, 95% CI 1.08–8.56; p = 0.036).

Conclusion

CKD is common in patients with IPF and may be missed when renal assessment is based on eGFR alone. Incorporating UACR into routine evaluation may improve detection of renal involvement and support a more comprehensive multidisciplinary approach to comorbidity assessment in IPF.

Background

Idiopathic pulmonary fibrosis (IPF) is a chronic, fibrosing interstitial lung disease characterised by progressive lung function decline and a median survival of approximately 3–5 years after diagnosis[1]. Systemic comorbidities contribute substantially to morbidity and mortality, and chronic kidney disease (CKD) is increasingly recognised as a potentially underdiagnosed condition in IPF[2,3].

Pulmonary and renal fibrosis share biological pathways, including epithelial injury, transforming growth factor-β (TGF-β) activation, oxidative stress, endothelial dysfunction, fibroblast activation, extracellular matrix remodelling, and cellular senescence[2,4].

Methods

We conducted a single-centre, cross-sectional observational study at the Respiratory Diseases Unit of Fondazione IRCCS San Gerardo dei Tintori in Monza, Italy. Consecutive patients with a multidisciplinary diagnosis of IPF according to the 2022 ATS/ERS/JRS/ALAT international guidelines[1] were enrolled from 1st January 2025 to 30th June 2026.

Although earlier research has indicated a higher prevalence of CKD in IPF[3,5], urinary albumin excretion has rarely been systematically assessed. Renal function was evaluated through serum creatinine levels, the estimated glomerular filtration rate (eGFR), and the urinary albumin-to-creatinine ratio (UACR), using KDIGO criteria[6]. The eGFR was determined using the 2021 CKD-EPI creatinine Eq. 7. CKD was diagnosed according to the 2024 KDIGO guideline[6], defined as an eGFR below 60 mL/min/1.73 m² and/or a UACR of 30 mg/g or higher. The chronic nature of kidney dysfunction was established based on at least two measurements performed at least 3 months apart.

Demographic characteristics, smoking history, cardiovascular comorbidities and pulmonary function parameters, including forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and diffusing capacity of the lung for carbon monoxide (DLCO), were recorded.

The study was conducted in accordance with the World Medical Association Declaration of Helsinki and approved by the Research Ethics Board of the University of Milan-Bicocca, n°1538.

Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range), and categorical variables as counts and percentages. Between-group comparisons used Student's t-test or Mann–Whitney U test for continuous variables and χ^2 or Fisher's exact test for categorical variables. Univariable and multivariable logistic regression assessed factors associated with CKD. Clinically relevant variables or those with $P < 0.05$ in univariable analysis were included in the multivariable model. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Tests were two-sided, with $P < 0.05$ considered statistically significant.

Results

The analysis included 101 patients diagnosed with IPF. The average age was 75.3 years. The great majority of the patients were male (81.2%), and the majority had a history of smoking (84 out of 101, 83.2%). The most prevalent comorbidities included hypertension (59 patients, 58.4%), dyslipidaemia (54 patients, 53.5%), cardiovascular disease (39 patients, 38.6%), and diabetes mellitus (21 patients, 20.8%). Baseline demographic and clinical characteristics are summarised in Table 1.

Table 1

Baseline demographic, clinical, and functional characteristics of the overall study population and according to chronic kidney disease (CKD) status. CKD was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria based on estimated glomerular filtration rate (eGFR) and/or albuminuria. Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]), as appropriate, and categorical variables as number (percentage). Comparisons between patients with and without CKD were performed using the Student's *t*-test or Mann–Whitney *U* test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables, as appropriate.

Variable	Overall (n = 101)	CKD (n = 28)	Non-CKD (n = 73)	P value
Age, years	75.3 ± 7.2	77.9 ± 6.5	74.3 ± 7.2	**0.013**
Male sex, n (%)	82 (81.2)	22 (78.6)	60 (82.2)	0.69
History of smoking, n (%)	84 (83.2)	24 (85.7)	60 (82.2)	0.77
Pack-years	27.3 ± 21.5	30.4 ± 23.6	26.1 ± 20.8	0.39
Hypertension, n (%)	59 (58.4)	22 (78.6)	37 (50.7)	**0.011**
Diabetes mellitus, n (%)	21 (20.8)	8 (28.6)	13 (17.8)	0.25
Dyslipidaemia, n (%)	54 (53.5)	17 (60.7)	37 (50.7)	0.37
Cardiovascular disease, n (%)	39 (38.6)	14 (50.0)	25 (34.2)	0.15
Antifibrotic treatment, n (%)	92 (91.1)	24 (85.7)	68 (93.2)	0.24
Pirfenidone treatment, n (%)	48 (47.5)	9 (32.1)	39 (53.4)	0.06
Nintedanib treatment, n (%)	44 (43.6)	15 (53.6)	29 (39.7)	0.21
FVC, % predicted	86.7 ± 19.4	86.8 ± 19.2	86.7 ± 19.5	0.98
FEV_1, % predicted	93.5 ± 18.4	92.6 ± 17.9	93.8 ± 18.6	0.77
DLCO, % predicted	51.4 ± 15.8	50.8 ± 16.0	51.7 ± 15.7	0.81

In total, 28 patients (27.7%) met the KDIGO criteria for CKD. Within this group, 11 patients exhibited an eGFR less than 60 mL/min/1.73 m² with normal albuminuria levels; 9 patients had isolated albuminuria with eGFR greater than 60 mL/min/1.73 m²; and 8 patients displayed both reduced eGFR and albuminuria. Based on the KDIGO G classification, 27 patients (26.7%) were categorised as G1, 55 patients (54.5%) as G2, 13 patients (12.9%) as G3a, 6 patients (5.9%) as G3b, and none as G4 or G5. According to the KDIGO albuminuria classification, 84 patients (83.2%) were classified as A1, 15 patients (14.9%) as A2, and 2 patients (2.0%) as A3 (Fig. 1).

Patients with CKD were significantly older (77.9 vs. 74.3 years, p = 0.013) and more likely to have arterial hypertension (78.6% vs. 50.7%, p = 0.011) compared to those without CKD. There were no significant differences in sex distribution, smoking history, diabetes mellitus, dyslipidaemia, cardiovascular disease, pulmonary function or antifibrotic treatment (Table 1).

In univariable logistic regression, older age (OR 1.10 per year, 95% CI 1.02–1.19; p = 0.020) and arterial hypertension (OR 3.57, 95% CI 1.30–9.82; p = 0.014) were associated with CKD. In the multivariable analysis, arterial hypertension remained independently associated with CKD (adjusted OR 3.04, 95% CI 1.08–8.56; p = 0.036).

Discussion

In this cross-sectional study, we found that almost one third (27.7%) of patients diagnosed with IPF met the diagnostic standards for CKD, thereby emphasising a significant burden of renal dysfunction within this population. Notably, CKD prevalence was much higher in our cohort than in the Italian CARHES study (27.7% versus 15.2%)[8], which included a population-based sample of 1,309 Italian adults aged ≥ 65 years. Compared with the CARHES population, our IPF cohort was older (75.3 ± 7.2 vs. 71.4 ± 4.3 years) and had a higher proportion of men (81.2% vs. 53.8%). Importantly, the prevalence of diabetes mellitus, a well-established risk factor for CKD, was comparable between our IPF cohort and the CARHES population (20.8% versus 21.3%, respectively). In contrast, hypertension was less prevalent in our cohort (58.4% versus 77.4%). These findings indicate that the increased prevalence of CKD observed in patients with IPF is unlikely to be solely attributable to differences in these major traditional renal risk factors and may involve disease-specific mechanisms linking pulmonary fibrosis to renal injury.

The principal clinical finding is the additional diagnostic value of UACR: patients with isolated albuminuria would have been missed by assessment based solely on eGFR. This supports evaluating both glomerular filtration and urinary albumin excretion when assessing renal involvement in IPF.

Several biological mechanisms may elucidate the coexistence of pulmonary and renal fibrosis. Experimental and translational studies have demonstrated that both organs exhibit activation of TGF-β, oxidative stress, epithelial and endothelial dysfunction, fibroblast activation, extracellular matrix accumulation, mitochondrial dysfunction, and accelerated cellular senescence[2,4]. Furthermore, systemic inflammation and vascular dysfunction may further contribute to the parallel fibrotic remodelling of the lung and kidney.

Patients diagnosed with CKD tend to be older and more commonly present with hypertension compared to those without CKD. These findings align with well-established determinants of renal dysfunction within the general population. Conversely, pulmonary function parameters do not demonstrate significant differences between the groups, implying that renal impairment is not merely a consequence of advanced respiratory decline. Instead, renal involvement may occur independently of lung function severity and may be influenced by shared pathogenic mechanisms or susceptibility factors.

Our findings corroborate prior research on renal dysfunction in IPF. Ikezoe and colleagues documented a CKD prevalence of approximately 30% within a Japanese cohort and established that renal impairment was independently linked to reduced survival rates[3].

The present study has several limitations. Firstly, its cross-sectional design precludes the establishment of temporal or causal relationships between IPF and CKD. Secondly, the single-centre setting and relatively limited sample size may constrain the generalizability of the findings. Thirdly, data on the potential influence of concomitant nephrotoxic medications, and longitudinal renal outcomes were unavailable. Future prospective multicenter investigations should assess whether CKD independently predicts pulmonary disease progression, acute exacerbations, hospitalisation, transplantation, and mortality, and whether systematic nephrological surveillance improves clinical outcomes.

Conclusions

In conclusion, CKD is a prevalent and often underrecognized comorbidity among patients with IPF. Routine assessment that combines eGFR and the urinary albumin-to-creatinine ratio facilitates early detection of renal involvement, which might otherwise go undetected, and should be regarded as an essential component of the multidisciplinary management of patients with IPF.

Abbreviations

CARHES
Cardiovascular Risk Profile in Renal Patients of the Italian Health Examination Survey
CKD
Chronic kidney disease
DLCO
Diffusing capacity of the lung for carbon monoxide
eGFR
Estimated glomerular filtration rate
FEV_1
Forced expiratory volume in one second
FVC
Forced vital capacity
IPF
Idiopathic pulmonary fibrosis
UACR
Urinary albumin-to-creatinine ratio

Declarations

Ethics approval:

the study was conducted in accordance with the World Medical Association Declaration of Helsinki and approved by the Research Ethics Board of the University of Milan-Bicocca, n°1538.

Consent to participate:

written informed consent was obtained for participate in the study from all participants.

Consent for publication:

written informed consent for the publication of anonymized clinical data was obtained from all participants.

Competing Interests

Pr. Fabrizio Luppi reports consulting fees from AstraZeneca, Boehringer-Ingelheim and Sanofi; payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing or educational events from Boehringer-Ingelheim, Chiesi, Menarini and Sanofi; support for attending meetings and/or travel from Menarini. The other authors had no conflicts of interest to declare.

Funding:

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Author Contribution

Giovanni Franco: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft. Emmanuele Pietro Porfido, Chiara Pirotta, Eleonora Passeri, Umberto Zanini: Investigation, Data curation, and Writing – review & editing. and Francesca Zanoni, Paola Faverio, Giuseppe Castellano and Fabrizio Luppi: Conceptualization, Supervision, Methodology, and Writing – review & editing. All authors read and approved the final version of the manuscript.

Acknowledgement

The work of PF and FL is partially supported by a grant from the Italian MUR Dipartimenti di Eccellenza 2023-2027 (l. 232/2016, art.1, commi 314-337).

Availability of data and materials:

the data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author upon request.

Declaration of generative AI use

The authors used generative artificial intelligence tools (ChatGPT, OpenAI, and Grammarly) to support in improving the language and readability of the manuscript. No AI tools were used for data analysis, interpretation, or generation of scientific content. All authors critically reviewed and approved the final version and take full responsibility for its content.

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Figures

GFR / Albumin.	A1 <30 mg/g	A2 30-300 mg/g	A3 >300 mg/g	Total
G1 (≥90)	26	1	-	27
G2 (60-89)	47	8	-	55
G3a (45-59)	7	4	2	13
G3b (30-44)	4	2	-	6
G4 (15-29)	-	-	-	0
G5 (<15)	-	-	-	0
Total	84	15	2	101

Figure 1

Distribution of the study population according to the Kidney Disease Improving Global Outcomes (KDIGO) classification, based on estimated glomerular filtration rate (eGFR) and albuminuria. Each cell shows the number of patients in the corresponding eGFR (G1–G5) and albuminuria (A1–A3) categories. Colours indicate the KDIGO risk stratification for chronic kidney disease (CKD), ranging from low risk (green) to very high risk (red).

Supplementary Files

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- STROBEchecklist.pdf