Enhancing Diagnostic Precision: Characterizing Subgroup Variability within WHO Group 3 Pulmonary Hypertension Using ICD-10 Code I27.23 and Manual EHR Review

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Background

Pulmonary hypertension (PH) is a progressive condition characterized by elevated pulmonary artery pressures and is associated with significant morbidity and mortality. It is classified into five WHO groups based on underlying causes, clinical presentation, and hemodynamic characteristics.[1] Group 3 PH encompasses patients with PH due to lung diseases and/or hypoxia, including chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD), which are among the most prevalent subtypes of PH.[2] Despite its clinical importance, use of the specific Group 3 ICD-10 I27.23 code "Pulmonary hypertension due to lung diseases and hypoxia" is significantly underutilized, with most patients still being coded as either ICD-10 I27.20 "PH, unspecified" or ICD-10 I27.2 "Other secondary PH" (Table 1). It is estimated that Group 3 PH represents between 30-48% of all PH,[3] but in a large U.S. claims database analysis of 1.8 million patients coded for PH, only 3.2% of all PH patients are coded with I27.23.

Table 1. Attribution of PH subgroups based on ICD-10 codes from patients coded for PH

WHO Group	Code Description	ICD10 Code	Percent
Non-Specific	Pulmonary hypertension, unspecified	I27.20	72.3%
Non-Specific	Other secondary pulmonary hypertension	I27.2	23.1%
Group 1	Idiopathic pulmonary arterial hypertension	I27.0	17.9%
Group 1	Secondary pulmonary arterial hypertension	I27.21	8.3%
Group 2	Pulmonary hypertension due to left heart disease	I27.22	4.0%
Group 3	Pulmonary hypertension due to lung diseases and hypoxia	I27.23	3.2%
Group 4	Chronic thromboembolic pulmonary hypertension	I27.24	0.7%
Group 5	Pulmonary hypertension with unclear multifactorial mechanisms	I27.29	8.1%

Inovalon US claims database, 198 million covered lives 2016-2024

The ICD-10 code I27.23, introduced in 2017, was designed to provide greater granularity in the classification of PH. However, it still lacks the specificity required to make it distinguishable among the subgroups within Group 3 PH. Accurate classification of PH is critical for advancing epidemiologic research, yet the limitations of ICD coding as a research tool remain evident. The disconnect between the clinical classification of PH and the ICD framework hampers efforts to accurately assess disease prevalence, healthcare utilization, management costs, and mortality. This misalignment significantly restricts the reliability of inferences derived from database analyses that rely solely on these codes.

Aims

1. Quantify the utilization of the ICD-10 code I27.23 relative to other PH-related ICD codes.
2. Identify overlapping ICD codes among patients assigned the I27.23 designation.
3. Examine comorbid conditions frequently observed in Group 3 PH, distinguishing those not directly contributing to PH.
4. Determine the distribution of PH subtypes—including PH-ILD, CTD-ILD (connective tissue disease-ILD), PH-COPD, PH-OSA (PH caused by obstructive sleep apnea), and PH-CPFE (PH caused by combined pulmonary fibrosis and emphysema)—within the I27.23 cohort.
5. Analyze hemodynamic and pulmonary function parameters across subgroups and assess their statistical significance.
6. Report patterns of medication usage, focusing on treatments for non-transplanted PH-ILD, CTD-ILD, and CPFE

Methods

Study Design: This was a retrospective observational study utilizing data from a multisite electronic health records (EHR) database. The study aimed to identify and characterize patients ICD-10 coded as having WHO Group 3 pulmonary hypertension (I27.23) via manual chart review of clinical notes and structured data by two independent reviewers, with a focus on the subgroup disease entities.

Data Sources and Patient Selection: De-identified patient-level data were extracted from the Loopback Platform, a comprehensive EHR-based real-world database in the United States. The dataset includes notes, demographic details, and ICD-10 codes. To be included in the analysis, a patient's record must have at least two instances of ICD-10 code I27.23 (PH due to lung disease and/or hypoxia) recorded at least 30 days apart, with at least one code coming after June 2023. Eligible patients were randomly selected from 8 hospital sites (14-15 patients/site), and clinical records from January 2015 through February 2024 were considered. Cases were classified into 5 categories based on the PH diagnosis entered in the manual notes: PH-COPD, PH-ILD, PH-CPFE, PH-OSA, & CTD-ILD. Review of CT scan images were not available for classification purposes.

Notes and References

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For more information about Pulmovant and the Phase 2 'Phocus' study in Group 3 PH-ILD, visit pulmovant.com and phocusstudy.com.

References: 1. M. Humbert et al, *Eur Respir J.* 2022:2200879. 2. Wijeratne et al, *Circ Cardiovasc Qual Outcomes*. 2018;11(2):e003973. 3. Hoeper et al, *Lancet Respir Med*. 2016;4(4). 4. E. de Belen et al, *J Am Heart Assoc.* 2023;12(2)

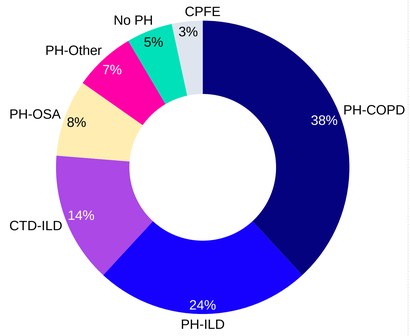
Disclosures: This work is supported by Pulmovant and Roivant. RG, SA, TR, JS, SP, and BV are current employees of Roivant and hold Roivant stock; AD is a current employee of Pulmovant and holds Pulmovant and Roivant stock; CS is a current employee of Pulmovant and holds Pulmovant stock; JS is a former employee of Regeneron and holds Regeneron stock; SP holds Abbvie stock; RS is on the steering committee of Pulmovant, Liquidia, and Gossamer Bio. RS is a speaker and clinical trial investigator for Merck and United Therapeutics. RS is a consultant for Merck, Liquidia, & Gossamer Bio.

Results

Among the 118 patients coded with ICD-10 I27.23, 104 patients did have Group 3 PH by manual chart review of clinical notes. The analysis revealed significant heterogeneity between underlying disease entities (ILD, COPD, and OSA).

PH-COPD was the most common subgroup, representing 38% of cases (Figure 1). The ILDs represented by PH-ILD and CTD-ILD also totaled 38% combined. 6 patients did not have evidence of PH based on RHC or Echocardiogram. There were 8 additional non-Group 3 cases dominated by Group 2 PH and Group 1 PH due to medications or other toxic etiologies.

Figure 1. Subtypes coded with ICD-10 I27.23 (n-118)



Hemodynamic and pulmonary function test results show a statistically significant lower mPAP and FVC (predicted) in the ILD group compared to the COPD group

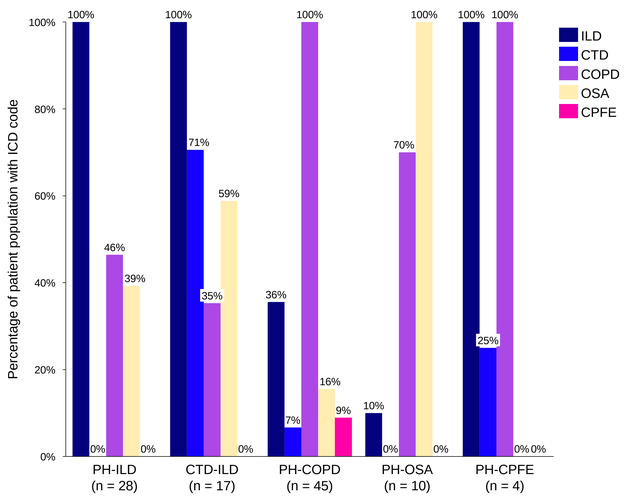
Table 2. Mean values of diagnostic tests (n=90). t-test compares ILD vs PH-COPD

Measure	Unit	ILD (n=45)		PH-COPD (n=45)	ILD vs PH-COPD	
		PH-ILD (n=28)	CTD-ILD (n=17)		T_statistic	P_value
mPAP	mmHg	33.2 (24)	35.1 (13)	43.2 (20)	-2.38	0.02
PCWP	mmHg	12.5 (19)	10.4 (9)	15.1 (11)	-0.96	0.35
PVR	Woods Units	5.6 (21)	4.9 (11)	4.5 (10)	1.20	0.24
FVC	% Predicted	54.1 (21)	55.1 (15)	68.8 (18)	-2.21	0.03
LVEF	%	58.5 (21)	61 (16)	57 (31)	0.65	0.52
6-min walk	meters	234 (16)	299 (13)	212 (8)	0.40	0.69

Differences in clinical measurements between the ILD (includes PH-ILD and CTD-ILD) and the COPD (includes PH-COPD) groups were assessed using independent two-sample t-tests. Each procedure was analyzed separately, assuming unequal variances, with statistical significance set at p<0.05. Analyses were performed using R software.

Patients with confirmed PH sub-group often show additional structured ICD codes in their chart for a different sub-group, indicating co-morbidities or coding that does not align with the clinical notes.

Figure 2. Concomitant ICD codes in PH patients by sub-group.

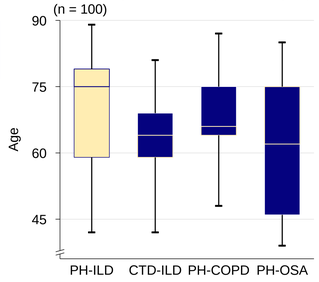


Age and sex distributions indicate PH-ILD patients may be older, with CTD-ILD patients predominantly female

Table 3. Sex distribution by main subgroups (n = 100)

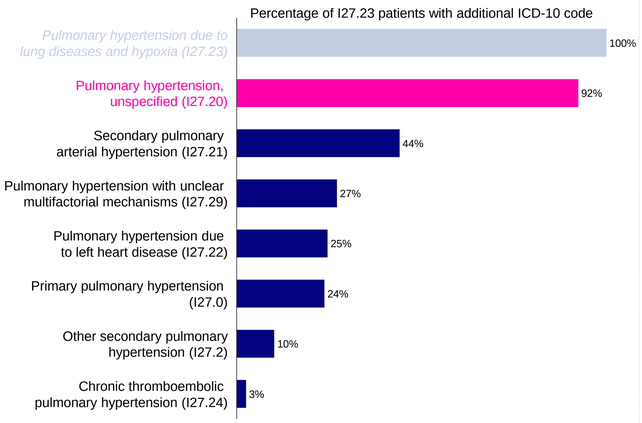
PH sub-group	# Patients	% female
PH-ILD	28	53.6%+-
CTD-ILD	17	94.1%
PH-COPD	45	51.1%
PH-OSA	10	60.0%

Figure 3. Age distribution by main subgroups (n = 100)



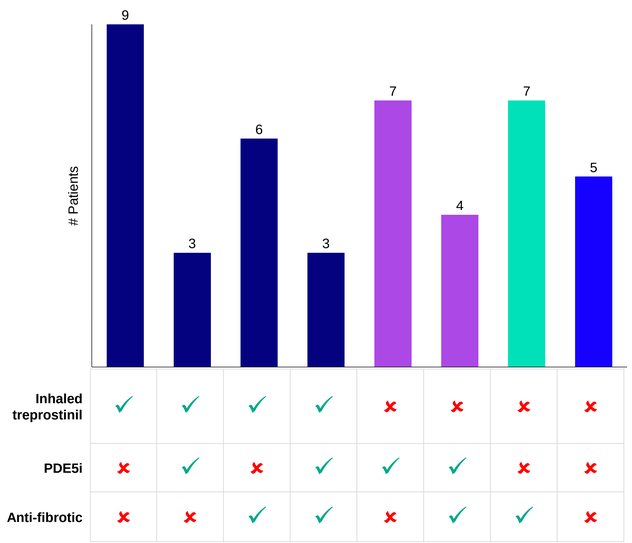
Co-existing general coding for "Pulmonary Hypertension, unspecified" was nearly universal, used in 92% of the original cohort of 118 patients with I27.23 designation.

Figure 4. Co-existing coding for other PH ICD-10 classifications from original cohort



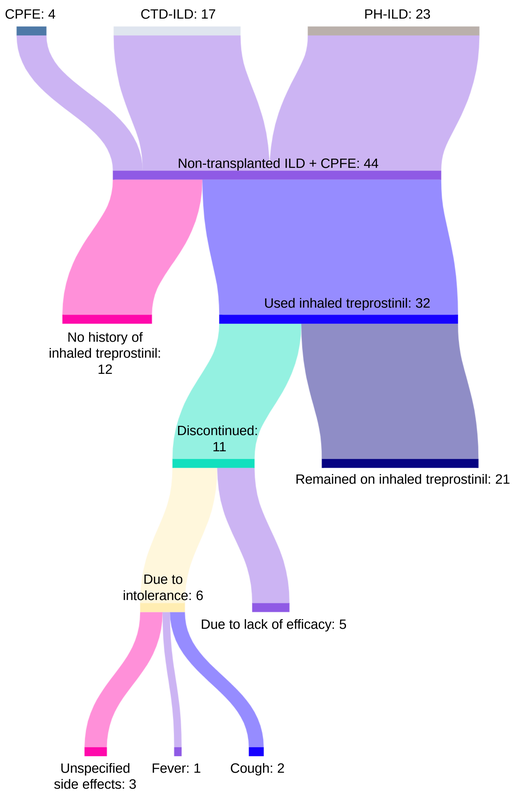
In non-transplanted Group 3 PH patients, a wide variety of directed therapy combinations were used for disease management as of their most recent note available. Inhaled treprostinil, approved by the FDA for the treatment of PAH and PH-ILD, had the highest use, with 21/44 patients, or 47.7%. Anti-fibrotic medications followed, with 20/44, or 45.5%. PDE5i, which is approved for use in PAH but not Group 3 PH, was used in 17/44, or 38.6%, of patients.

Figure 5. Use of directed therapy in non-transplanted ILD (i.e., PH-ILD, CTD-ILD) and CPFE patients (n=44)



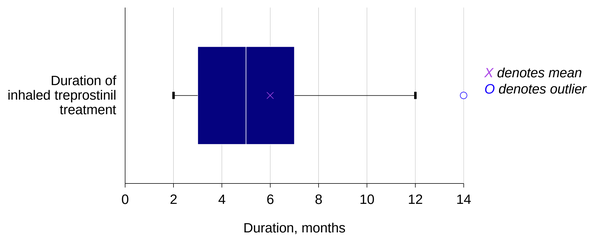
Of the 44 non-transplanted ILD (PH-ILD, CTD-ILD) and CPFE patients, 32 were reported to have been treated with inhaled treprostinil. 11 of those 32 had an explicit discontinuation of inhaled treprostinil in their record through January 2024.

Figure 6. Use and discontinuation of inhaled treprostinil in non-transplanted ILD (i.e.., PH-ILD, CTD-ILD) and CPFE patients (n=44)



For the 11 discontinuing patients, treatment with inhaled treprostinil lasted around an average of 6 months prior to discontinuation.

Figure 7. Duration of inhaled treprostinil use in patients who discontinued use.



Conclusions

- Despite its introduction with ICD-10 to improve granularity, the code I27.23 remains underutilized. The sustained usage of more general codes such as unspecified or other secondary PH, even in the face of more specific options like ICD-10 I27.23, underscores the difficulty of diagnosing and developing evidence-based treatment algorithms for such a heterogenous disease as PH with multiple groups.
- Even for those patients coded to Group 3, I27.23, there is still a large heterogeneity, encompassing diverse underlying disease processes such as ILD, COPD, CPFE and OSA. These findings today demonstrate notable differences in clinical characteristics, hemodynamic parameters, and medication use across I27.23, underscoring the potential for misdiagnosis associated with specific subgroups of PH. These variations emphasize the need for improved diagnostic precision and coding practices to enhance patient identification, supporting epidemiological studies that can facilitate appropriate treatment strategies.
- To address these challenges, future efforts should focus on refining ICD coding methodologies, incorporating advanced analytics to capture disease severity and etiology, and aligning coding systems with the clinical complexities of Group 3 PH. Such advancements are essential for optimizing a wide range of real-world data applications.