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REVIEW ARTICLE

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Scoping review of post-TB pulmonary vascular disease: Proceedings from the 2nd International Post-Tuberculosis Symposium

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Abstract

Tuberculosis (TB) may cause significant long-term cardiorespiratory complications, of which pulmonary vascular disease is most under-recognized. TB is rarely listed as a cause of pulmonary hypertension (PH) in most PH guidelines, yet PH may develop at various stages in the time course of TB, from active infection through to the post-TB period. Predisposing risk factors for the development of PH are likely multifactorial, involving active TB disease and post-TB lung disease (PTLD), host-related and environment-related factors. Moreover, post-TB PH should likely be classified in Group 3 PH, with the pathogenesis similarly complex and multi-factorial as other Group 3 PH causes. Identifying risk factors that predispose to post-TB PH may aid in developing risk stratification criteria for early identification and referral for confirmatory diagnostic tests. Given that universal screening for PH in TB survivors may be impractical and unfeasible, a targeted screening approach for high-risk individuals would be sensible. In this scoping review of post-TB PH, resulting from the proceedings of the 2nd International Post-Tuberculosis Symposium, we aim to describe the epidemiology, risk factors, and pathophysiology

of post-TB PH. We emphasize diagnosing PH with an alternative set of diagnostic guidelines in resource-constrained settings where right heart catheterization may not be feasible. Research to describe the burden and distribution of post-TB PH should be prioritized as there is a current gap in knowledge regarding the prevalence and incidence of post-TB PH among persons with TB.

KEYWORDS
chronic lung disease, post-tuberculosis lung disease, pulmonary hypertension

INTRODUCTION

Over the last 5 years, 40 million people were treated for tuberculosis (TB), which remains one of the leading causes of death worldwide and contributes significantly to the global burden of disease.[1] In 2021, there were an estimated 10.6 million incident cases of TB, with approximately 1.6 million deaths directly ascribed to TB.[1] TB disproportionately affects countries with lower socioeconomic circumstances, with more than 90% of incident cases occurring in low- and middle-income countries (LMICs).[1,2] Recent advancements in the diagnosis and treatment of TB have led to approximately 86% of TB patients being treated.[1] Although this figure is somewhat reassuring initially, it is now appreciated that increased morbidity and mortality may occur long after the microbiological cure of the disease.[3] In 2020, there were an estimated 155 million TB survivors worldwide, of which most live in LMICs,[4] where constrained health resources may limit adequate care of the vulnerable post-TB population.[3,5] Post-TB consequences have been estimated to account for 47% (almost half) of the total burden of disability-adjusted life years (DALYs) attributed to TB, resulting in a significant economic burden to society.[3,6,7] In addition, the economically active sectors of the population appear disporportinately affected, making the cost of TB, both to individuals and society profound.[4,6]

TB may cause significant long-term cardiorespiratory complications, and pulmonary vascular disease in the form of pulmonary hypertension (PH) is likely an under-recognized TB complication, that is contributing to the increased morbidity and mortality in TB survivors.[8,9] PH may develop at various stages in the time course of TB, from active infection (active TB PH) through to the post-TB period (post-TB PH). PH defined as a mean pulmonary arterial pressure (mPAP) greater than 20 mmHg, measured with right heart catheterization (RHC), is estimated to affect approximately 1% of the global population.[10,11]

Even mild PH is associated with increased mortality and globally there is a drive toward earlier diagnosis and treatment of PH.[12–14] Given that the classic clinical signs of PH (right ventricular hypertrophy, loud P2, features of right heart failure) appear late in the disease process and RHC is often unavailable in under-resourced hospitals in LMICs, other imaging and clinical criteria are used as surrogate diagnostic tools for identifying PH, resulting in post-TB PH being under-appreciated in the global literature.[15]

This scoping review of post-tuberculous pulmonary vascular disease, resulting from the proceedings of the 2nd International Post-Tuberculosis Symposium, aims to describe the epidemiology, risk factors, pathophysiology, screening, and diagnostic strategies, outcomes, and research opportunities in the context of post-TB PH.

EPIDEMIOLOGY OF POST-TB PH

TB may influence the risk of PH at various stages in the time course of TB, ranging from the acute-active infection through to the post-TB period. The development of PH during active pulmonary TB (active TB PH) has long been reported in the early TB studies,[16,17] and the current reported prevalence ranges from 8% to 27%.[18–22] Active TB PH may portend a poor prognosis, but in some cases, may resolve during TB treatment and consecutive lung parenchymal recovery, invoking a potentially reversible acute pathogenesis.[18,19,23]

Once the initial episode of TB has been treated and symptoms of TB have resolved, post-TB PH may be detected approximately 5–11 years thereafter.[24–28] However, this period vary significantly, with some studies detecting signs of PH within 1 year post-TB and others reporting a mean duration of 32 years.[25,29] This discordance can be attributed to different subtypes or pathogenic pathways of post-TB PH; with one that evolves from active pulmonary TB and then either resolves or persists, while others are purely related to a post-TB phenomena, develop years after the initial episode of TB. In both scenarios, however, post-TB PH appears to develop earlier in the course of the disease than PH due to other chronic respiratory diseases (e.g., COPD).[24] Thus, it is important for researchers to discriminate between active TB

PH (i.e., developing during acute TB disease) and post-TB PH (i.e., developing after treatment completion and resolution of TB symptoms).

In a large retrospective cohort study of inpatients with acute TB, 9.7% (74/777) had PH based on echocardiography.[19] In high TB prevalence areas, PH was found in 46%–89% of symptomatic patients with post-TB lung disease (PTLD), many of whom had cor pulmonale.[25,30] In a cross-sectional study among non-healthcare seeking outpatients with prior TB, probable PH prevalence was 16% based on screening echocardiography.[27] In these patients, no other known risk factors for PH were present, and active TB was excluded, indicating a purely post-infectious phenomenon.[25,27]

Regardless, previous TB is rarely listed as a predisposing factor for PH, in the WHO or ESC/ERS guidelines.[10] This may be partly explained by both the under-diagnosis of PH in LMICs and that most PH literature arises from high-income countries, with low TB burdens.[5,31] Data from the Pan-African Pulmonary Hypertension Cohort (PAPUCO) study demonstrated that previous TB was identified in 20% proportion of African patients with PH, and TB was the most common risk factor linked with PH independent of HIV coinfection.[15] Similarly, in studies from India, TB appears to be important in the etiology of PH, where approximately 12%–15% of patients with PH had previous or current TB.[32,33] A recent meta-analysis of the prevalence of PH post-TB found that the literature is limited. This study found that the prevalence of PH post-TB is high, particularly in those with chronic respiratory failure (67.0%, 95% CI 50.8–81.4) or who are symptomatic or hospitalized (42.4%, 95% CI 31.3–54.0), and lower in non-healthcare-seeking outpatients (6.3%, 95% CI 2.3–11.8). Active TB PH was further estimated to affect approximately 10% of the TB population.[34]

RISK FACTORS FOR THE DEVELOPMENT OF POST-TB PH

It is important to identify the risk factors for developing post-TB PH for several reasons. First, awareness of the risk factors for post-TB PH may aid early identification and referral for confirmatory diagnostic tests, thereby allowing for a streamline of scarce screening interventions. Second, risk factor identification may provide clues about the pathogenesis of post-TB PH, with a view to preventative and early intervention measures. Several factors contribute to the development of post-TB PH, but robust data is still lacking, and further work needs to be done in this area. These risk factors, although multifactorial, can be considered in three categories: TB- and PTLD-related; host-related and environment-related factors (Table 1).

TB-related and PTLD-related factors

TB-related factors

Multiple previous episodes of pulmonary TB is a risk factor for the development of post-TB PH.[27] Progressive and accumulative pulmonary decline have been documented with each sequential episode of pulmonary TB and it is plausible that the impact of multiple TB episodes on the pulmonary vasculature is additive if not exponential.[35] A community-based cross-sectional study among 100 non-healthcare-seeking subjects found the odds for developing post-TB PH increased 2.13-fold (95% CI 1.17–3.88; $p = 0.013$) for each additional episode of TB.[27] Although a useful association, it should also be noted that up to half of those with post-TB PH reported only one episode of previous TB.[27,30]

TABLE 1 Factors related to the development of post-TB pulmonary hypertension.

TB related and PTLD related	Host related	Environment related
TB related	Age 40–60 years	Smoking
Number of episodes	Male sex	Biomass exposure
Interrupted/incomplete treatment	HIV infection	Occupational exposure
Drug-resistant TB	CTD	Socioeconomic circumstances
VTE event during active TB	Diabetes mellitus	Illicit drugs
Post-TB lung disease (PTLD)		Medication
Parenchymal damage		
Pulmonary functional abnormalities		

Abbreviations: CTD, connective tissue disease; HIV, human immunodeficiency virus; TB, tuberculosis; VTE, venous thromboembolic.

Poor adherence to TB drugs has been associated with an increased risk for the development of PH (OR 3.94, $p = 0.03$) and select studies have shown that 24%–43% of patients with post-TB PH did not complete the course of TB treatment.[24,26,30] Drug-resistant TB is often associated with treatment delays, recurrent therapy, and lengthy regimens with poor adherence and tends to cause more severe pulmonary destruction and functional impairment.[36] As a result of these combined factors, people with previous drug-resistant TB likely are at an increased risk for post-TB PH. However, data on the association between drug-resistant TB and post-TB PH is scarce, and a significant correlation has not yet been established well enough,[30] especially as many studies exclude patients with multidrug-resistant or extreme drug-resistant TB, and many patients may have deceased before developing PH, however, this will change with the new shortened all-oral treatment regimens for drug-resistant TB.[37]

PTLD-related factors

Cavitation, parenchymal destruction, and fibrotic changes have been found to be common among hospitalized patients with PTLD and PH.[26,30,38] In symptomatic post-TB PH patients, fibro cavitation has been reported as the most common radiological abnormality, present in 25%−50% of patients, and PTLD-associated fibrotic changes have been found to be more frequent in those with post-TB PH.[24,28,30] It should be noted that many patients (up to 40%) have a combination of different PTLD-related clinical patterns and these subjects appear to have a greater risk for post-TB PH.[30]

The increasing extent of the structural impairment caused by PTLD correlates with the risk for developing post-TB PH. Those with extensively damaged lungs (i.e., three or more affected lobes) are more at risk (OR 3.49; 95% CI 1.58−7.73, $p < 0.05$) for PH.[29,38] This is consistent with one of the proposed mechanisms for the development of post-TB PH, namely the destruction of the pulmonary bed and reduced cross-sectional area of the pulmonary vasculature are thought to result in increased pulmonary pressures.[24,39]

Although structural abnormalities likely contribute to the development of post-TB PH, the presence of pulmonary functional abnormalities may be equally important in predicting the onset of PH in PTLD. In hospitalized patients, the detection of any abnormality at spirometry resulted in a statistically significantly increased risk for post-TB PH.[30] Interestingly, however, in a study of outpatients with previous TB, a third of those with probable PH had normal spirometry and no correlation of lung functions with PH, possibly implying that the mechanism in post-TB PH may be more complicated than only the effects of lung destruction and pulmonary function impairment.[27] PTLD is heterogenous and in keeping with this, a variety of pulmonary functional abnormalities have been reported in post-TB PH as well.[33] In a retrospective cohort study comparing patients with COPD-related PH and post-TB PH, it was found that those with post-TB PH had lower forced vital capacity (FVC) than those with COPD PH, but less severe airflow limitation.[29] Restrictive and mixed patterns (obstructive pattern with reduced FVC) on spirometry have been reported as the predominant functional pattern in patients with post-TB PH in several studies.[27,30,40] When patients with PTLD and either small airway obstructive disease or diffuse parenchymal fibrosis were compared, it was found that those with the restrictive phenotype had higher pulmonary pressures.[30,33] It is also plausible that those with a combined functional impairment, due to mixed fibrosis and small airway disease in the context of PTLD, have a particularly heightened risk of post-TB PH, analogous to the clinical entity combined pulmonary fibrosis with emphysema (CPFE).[41]

Venous thromboembolic (VTE) events during the episode of TB

There is a known association between TB and thromboembolism,[42] and multiple mechanisms by which TB predisposes to VTE events are documented. In retrospective studies of patients with thromboembolism in TB-endemic countries, 12.5%−53% of VTE episodes are associated with TB.[43,44] Acute VTE predisposes to chronic thromboembolic PH (CTEPH) and a retrospective cohort of 134 patients diagnosed with CTEPH from Korea (a medium burden TB country) showed that 4.5% had a history of TB.[45] Both in situ pulmonary thrombosis during active TB, and documented VTE may increase the odds of developing post-TB PH, however, more evidence is needed to support this association. There is no published data on the etiology and incidence of pulmonary embolism where PTLD is the sole risk factor.[46]

Host-related factors

Despite a wide variation in the age of patients presenting with post-TB PH, the most affected and at-risk age category is 40−60 years old.[21,28,30,38] Post-TB PH affects people at a younger age compared to other respiratory (Group 3) causes of PH such as COPD.[29,47] This may indicate a more rapid and aggressive pathophysiology in patients with post-TB PH compared to the more steady decline seen in patients with COPD.[29] Males are a higher risk for post-TB PH, which is in keeping with the male predominant TB infection rates (60% of survivors being

male), however, among patients with PTLD, males are up to 2.55 times more likely to develop PH ($p = 0.03$).[24,26,30] This correlation is likely complex and multifactorial as males are more likely to have other pulmonary risk factors (such as smoking and occupational exposure) and have poorer adherence to TB treatment.[1,32]

Given that approximately 7% of those diagnosed with TB are people living with HIV (PLWH) on a global scale, it is important to consider this comorbidity, in post-TB PH.[1] Additionally, HIV is an acknowledged etiology of pulmonary arterial hypertension (PAH, Group 1) and may be etiological in up to 30% of PAH in high-burden HIV settings.[31,48] This confounding factor can make it difficult to distinguish PAH-HIV from post-TB PH, with some studies on the latter condition even excluding PLWH.[49] However, PAPUCO study findings suggest that HIV, in the presence of PTLD, should be considered comorbid and not causative of the PH.[15] A plausible explanation for this finding is that HIV-associated TB tends to be associated with less lung destruction and appears protective against extensive PTLD.[50]

Patients with other specific comorbidities may be at a higher risk for the development of post-TB PH. The presence of comorbid autoimmune connective tissue diseases (CTD), such as systemic sclerosis and systemic lupus erythematosus, may increase the risk of post-TB PH.[51,52] For example PH develops in approximately 20% of patients with systemic sclerosis and patients with systemic sclerosis are more likely to develop TB (IRR 2.81; 95% CI 1.36−5.37; $p = 0.004$).[53,54] Previous TB may increase the likelihood of PH in these patients; however, the significance of this contribution is largely unknown and likely to be only a small proportion of overall post-TB PH cases.[54] Theoretically, the associated vasculitis and endarteritis obliterans that may develop due to TB heighten the risk for the development of PH in these patients. In addition, TB has been associated with certain autoimmune vascular diseases such as Takayasu's Arteritis. In a retrospective study of 1105 patients with Takayasu's Arteritis, 10% had previous TB, and pulmonary artery involvement with PH was more frequent in Takayasu's Arteritis associated with TB.[55] Further, there is a well-established link between diabetes and TB, and diabetes is often uncontrolled in patients with TB. The confounding effect of diabetes on post-TB PH is yet to be explored, but these patients have a significant cardiovascular disease risk and are at risk for more severe TB, which both may contribute to a theoretically higher risk of post-TB PH.[56]

Environment-related factors

Environmental risk factors like biomass and occupational exposure of tobacco may contribute to the risk of PH progression in patients with PTLD and is context specific. Smoking is a significant risk factor for the development post-TB PH and in one study all subjects with probable post-TB PH were either current smokers or had a smoking history (OR 3.67; 95% CI 0.77−17.46).[27] Additionally, biomass exposure has been reported in up to 23.3% of patients with post-TB PH,[25] and there is a strong association between occupational dust exposure and an increase in the risk for PTLD.[50] In a retrospective review over a 28-year period of the causes of death in patients with pneumoconiosis, decompensated cor pulmonale was most frequently observed in patients with a combination of TB and silicosis.[57]

The compounded effect of poor socioeconomic circumstances on PH is yet to be determined. Inadequate food security with poor nutritional status and poor access to adequate healthcare, together with the increased risk of multiple environmental exposures and risk of recurrent TB, all add to a greater risk of the development of PH in this vulnerable post-TB population.[30,58] Lastly, numerous medications (including traditional or herbal medications) and illicit drugs (such as methamphetamines) may increase the risk for post-TB PH either directly (by independently being associated with elevated pulmonary pressures) or indirectly, such as predisposing individuals to recurrent pulmonary TB.[10,59]

PATHOGENESIS AND PATHOBIOLOGY OF POST-TB PH

Multiple mechanisms are likely involved in the pathogenesis of post-TB PH, which can be described in broad terms as vascular bed involvement, thrombosis, arteriopathy, compressive disease, and coexistent left heart disease (Figure 1).

Loss of pulmonary vascular bed due to parenchymal fibrosis/destruction/obliterative bronchiolitis

Several proinflammatory and pro-fibrotic mediators, cytokines, and cell types are involved in the development of PTLD, including fibroblasts, myofibroblasts, transforming growth factor (TGF-β), TNF, extracellular matrix (ECM) proteins, IL-1β, IL-4, IL-13, IL-10, and MMP-1, 8, 9.[60–62] PTLD is heterogenous and may include cavitation, fibrosis, bronchiectasis, small-airways disease, airway stenosis, fibrosing mediastinitis (FM), and fibrothorax.[62] Features of fibrosis have been found in 70%−93% of patients with previous TB on CT imaging.[63,64] Furthermore, obliterative bronchiolitis has been found to develop post-TB, and this can

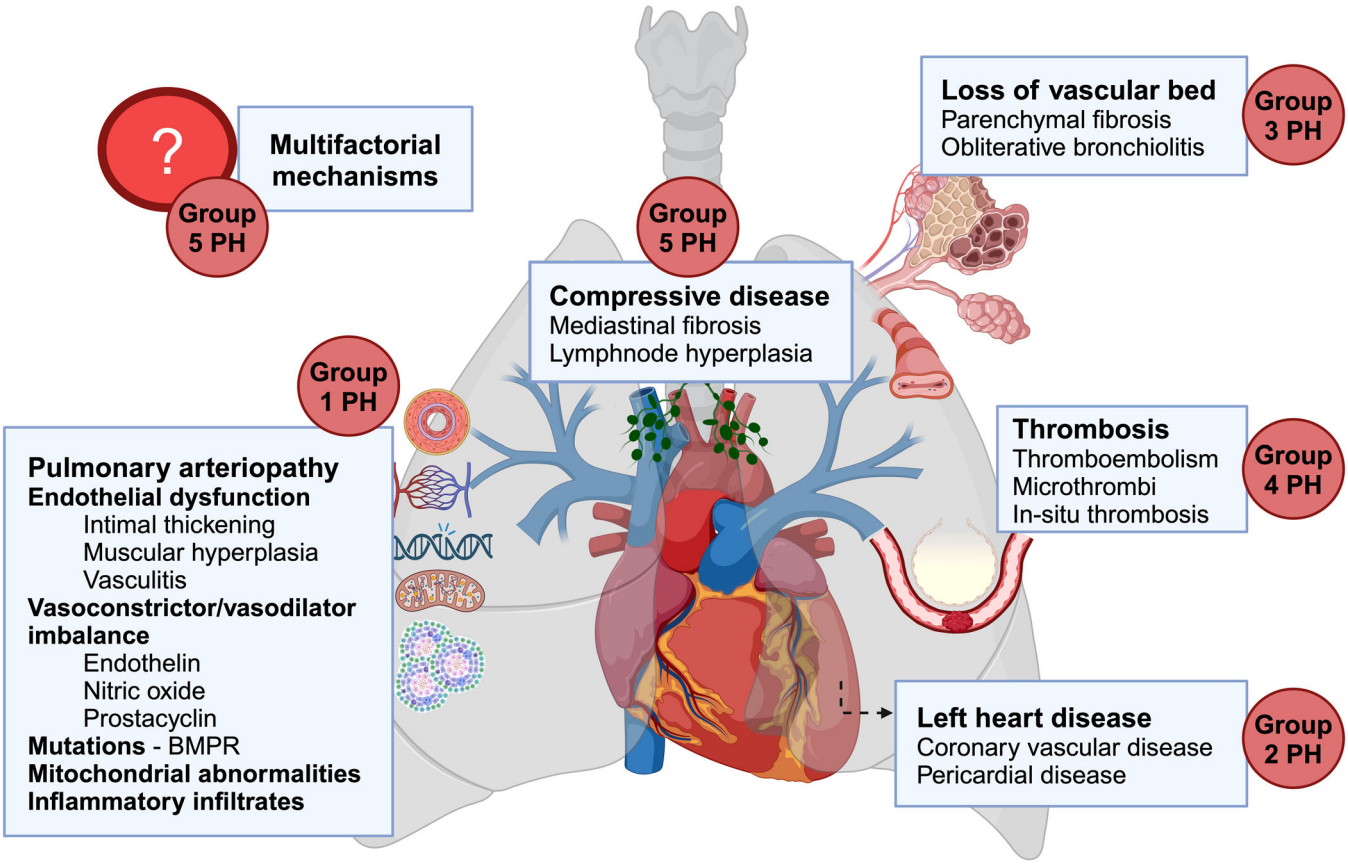

FIGURE 1 Proposed mechanisms of post-TB pulmonary hypertension. PH, pulmonary hypertension; TB, tuberculosis.

lead to PH due to chronic hypoxia-induced pulmonary vasoconstriction in addition to vaso-destruction and vaso-obliteration.[65] Most data of PH complicating fibrotic lung disease emanates from idiopathic pulmonary fibrosis (IPF) literature where—interestingly—there seems to be a limited correlation between the PH severity, lung function impairment, and high-resolution CT fibrosis scores, which implies more than fibrosis alone, (with corresponding loss pulmonary vascular bed) is involved mechanistically.[66] In post-TB PH vascular changes in areas of preserved architecture may similarly contribute to the development of increased pulmonary vascular resistance, as in other chronic lung diseases [67,68]

Thromboembolism/microthrombi/ in situ thrombosis

The risk of TB and thromboembolic disease can be risk stratified into two phases of the illness. The initial phase is during the active phase of treatment and the second phase is as a complication of PTLD.[43] The pathogenesis in patients with active TB is multifactorial, affecting all three aspects of Virchow's triad induced by the proinflammatory state associated with active TB. These include enlargement of lymph nodes which can lead to compression of venous system and stasis coupled with active TB favouring bed rest, limiting peripheral muscles contractions needed for venous return from the lower limbs.[69] A hypercoagulable state induced by elevated plasma fibrinogen with impaired fibrinolysis coupled with a decrease in antithrombin III and reactive thrombocytosis with increased platelet aggregation contributes to the pro-thrombotic state.[70–72] Furthermore, chronic inflammation linked to the presence of *Mycobacterium tuberculosis* organism, and the use of rifampicin as a TB drug promote direct endothelial inflammation.[73] This procoagulant state promotes in situ pulmonary thrombosis as well as pulmonary embolism from deep venous thrombosis.[72]

Pulmonary arteriopathy

Pulmonary arteriopathy is a hallmark of constrictive (medial and intimal remodeling) or multifocal complex (plexiform and dilatative lesions) lesions that obstruct the pulmonary arterial lumen.[74] This is underpinned by the excessive proliferation of pulmonary artery smooth muscle cells and their

resistance to apoptosis.[75] This process is linked with the activation of a proliferative pathway that includes TGF-β and bone morphogenetic protein (BMP),[76] reduced expression of potassium channels,[77] and Smad1/5/8.[78] Furthermore, normal regulation of the metabolic state of key cells in the pulmonary vessel is impaired and results in mitochondrial dysfunction, which contributes to PH in experimental models and patients.[79] In concert, these factors lead to increased vasoconstriction, increased apoptosis, and excessive proliferation of pulmonary artery endothelial cells.

The result of these pathophysiological processes, is pulmonary arteriopathy comprising medial hypertrophy, intimal thickening and eccentric intimal fibrosis.[80] The latter is triggered by BMPR-2 and vascular endothelial growth factor, which leads to endothelial-to-mesenchymal transition, where mesenchymal cells self-transform into fibroblasts that are responsible for the formation of fibrotic tissue/fibrosis.[81] PTLD associates with cavitation that may progress to debilitating fibrosis,[82] while pulmonary fibrosis also predisposes to the pathogenesis of PH, but it is not known to what extent the TB-fibrotic process results in arteriopathy in the pulmonary vascular bed.[83]

Mediastinal fibrosis/compressive disease

FM, also known as sclerosing mediastinitis, is an insidious and rare condition, with aggressive fibrosis of the mediastinum resulting in extrinsic compression of the mediastinal bronchovascular structures or viscera with a variable natural history.[84,85] The postulated mechanism is that infection with a microorganism in the respiratory tract results in leakage of antigens from the lymph nodes into the mediastinal space causing a hypersensitivity reaction, followed by an intense, uncontrolled fibrotic response.[86,87] The development of fibrotic infiltrates which obliterate fat planes have the potential to encase and compress mediastinal vascular structures resulting in PH as a severe complication, although rare.[85,87,88] Most commonly the causal organism is said to be *Histoplasma capsulatum* with TB also been described in some cases.[86,89] The prevalence of TB fibrosing mediastinitis (TB-FM) is unknown; however, in China, most cases of FM are due to TB.[85,87] The pathogenesis of *M. tuberculosis* related FM has not been reported, it is speculated to be similar to that of histoplasmosis as a trigger to FM.[85] PH complicating MF has been placed under Group 5 according to the World Health Organization PH classification.[88,90] PH secondary to FM is clinically classified into three types, type 1 referring to FM causing stenosis of the pulmonary arteries, type 2 referring to causing stenosis of the pulmonary vein, and type 3 resulting in stenosis of pulmonary artery, vein, and bronchus.[85]

Left heart disease

It has been found that survivors of TB have an increased risk of coronary vascular disease.[91–96] TB may affect cardiovascular disease risk by increasing systemic inflammation, immune activation, hypercoagulability, and dyslipidemia, promoting atherogenesis.[96–98] It may also have direct effects on the myocardium and pericardium.[99] It is unknown to what degree this "post-capillary" PH contributes to post-TB PH.

SCREENING, DIAGNOSIS, & CATEGORIZATION

The rationale for screening for PH post-TB is not only of scientific interest but also has important clinical implications due to the impact on quality of life, exercise limitation, and outcomes of mortality. In the absence of proven therapy, an argument can be made that screening for post-TB PH will not be of benefit to the patient and will consume already scarce resources in most high-burden TB settings. However, as with other lung disease-associated PH, screening and earlier diagnosis will have an impact on research into the understanding of the disease and the development of treatment strategies. Due to the overlap of symptoms of PH with the PTLD, the diagnosis of PH can be significantly delayed. Furthermore, clinical signs, such as jugular venous distension, pedal edema, and tricuspid murmur regurgitation only appear late in PH and thus have poor sensitivity.[100]

There is no single modality that accurately predicts PH and a combination of tests in addition to clinical suspicion should be used to decide which patients to screen for PH and then to proceed to confirmation with RHC. Because of limited access in LMICs, RHC for post-TB PH should be reserved for patients in whom it will affect management, including lung transplantation, initiation of vasoactive therapy, and for research purposes. The sensitivity and specificity of different screening modalities in patients with PTLD is unknown and optimal thresholds for screening in PTLD is also unknown, with further research needed to determine the most appropriate context-specific screening algorithms. Unfortunately, there may be important limitations to some of these modalities in the setting of PTLD (Table 2).

Available screening modalities

Electrocardiography ECG

Many of the features of PH on ECG may be obscured due to the concealment of the atrial and ventricular electrical forces

TABLE 2 Sensitivity and specificity of different modalities in detecting pulmonary hypertension.

Modality	Sensitivity (%)	Specificity (%)	Comments on the use in lung disease
Clinical examination[100]	53	95	Poor sensitivity, clinical features of PH occur late in the disease
ECG[101,102]	6–48	79–100	Distorted anatomy in PTLD may lead to ECG features being obscured More readily available, noninvasive, inexpensive
Echocardiography[103–106]			Lower sensitivity in lung disease
RVSP	81–93	61–79	Difficult acoustic windows may impair measurements
RVOT-AT	84	84	
TRV_{max} > 2.9 m/s	83	91	
CT scan[100,107–109]			Fibrosis of the upper lobes in PTLD may give an impression of PAD dilatation
Enlarged PA/aorta ratio >0.9	65–74	81–83	
PAD > 29 mm	55–79	70–83	Unsure of the use in post-TB patients
Biomarkers			Accuracy in post-TB uncertain may be confounded by left heart disease
BNP/Pro-BNP[100,110]	76	61–80	
Physiology			
6MWD < 350m[100]	78	90	Little equipment needed, reproducible, noninvasive
HR recovery < 13 bpm[111]	52	74	
DLCO < 40%[100]	72	71	Diffusion studies not readily available, exact cut-off values specific to post-TB not known
Need for supplemental oxygen[100]	85	55	Advanced disease present

Abbreviations: BNP, brain natriuretic peptide; DLCO, diffusion capacity of the lungs for carbon monoxide; ECG, electrocardiogram; HR, heart rate; PA, pulmonary artery; PAD, pulmonary artery diameter; PH, pulmonary hypertension; PTLD, post-tuberculous lung disease; RVOT-AT, right ventricular outflow tract acceleration time; RVSP, right ventricular systolic pressure; TB, tuberculosis; TRV_{max}, maximal tricuspid regurgitant velocity; 6MWD, 6 min walking distance test.

by underlying structural lung disease or hyperinflation.[101] The low sensitivity of ECG makes it insufficient for screening without complementary tests, but it is simple, more readily available, noninvasive and inexpensive and, when used in addition to other tests may be useful.[101,102]

Transthoracic echocardiography (TTE)

The best screening tool for PH is TTE.[112] The maximal tricuspid regurgitation velocity (TRV_{max}) is used in most studies for the estimation of pulmonary artery systolic pressure (PASP), with current guidelines suggesting a cut-off value of 2.9 m/s.[113] With the recent lowering of cut-off values of mPAP for PH diagnosis at RHC, there may be adjustments of the cut-off used on TTE, but a recent study suggests that this will reduce the positive predictive value.[114] TTE has its limitations in the setting of patients with lung disease, with a lower sensitivity of 81% (95% CI 70%–88%) and specificity of 61% (95% CI 53%–69%) in PH diagnosis, compared to those without underlying lung disease.[104,115] In up to 40% of patients an adequate doppler signal for measuring tricuspid regurgitation cannot be obtained as lung structural lung disease may impair acoustic windows, and an estimation error of >15% is made.[116,117] Therefore, other parameters besides PASP have been suggested, including RV/LV basal diameter ratio >1.0, LV eccentricity index >1.1, RVOT AT <105 ms (pulmonary acceleration time) or notching, early diastolic PA regurgitation velocity >2.2 m/s, PA diameter of >25 mm, RA area >18 cm^3, IVC diameter of >21 mm and decreased IVC collapse, decreased fractional area change, and tricuspid annular plane excursion.[10,103,118] The best sensitivity from an indirect measurement is the RVOT-AT.[103] This is measurable in more than 90% of patients, with a meta-analysis showing a pooled sensitivity of 84% (95% CI, 75%–90%) and a pooled specificity of 84% (95% CI, 78%–89%).[105]

Radiology—CT

A large meta-analysis involving 2134 subjects, including 1268 subjects with PH from varying causes not only involving underlying lung disease, showed a sensitivity of

79% (95% CI 72%−84%); specificity, 83% (95% CI 75% −89%) for pulmonary artery diameter (PAD) and sensitivity, 74% (95% CI 66%−80%); specificity, 81% (95% CI 74%−86%) for PA/A ratio.[108] Another meta-analysis showed a sensitivity of 65% (95% CI 58%−72%) and specificity of 83% (95% CI 80%−88%) for PA/A > 1.[107] However, pulmonary artery dilatation can occur in the presence of pulmonary fibrosis in the absence of PH,[119,120] and in PTLD often there is significant fibrosis in the upper lobes, leading to a lower specificity of 65% using the PA/A ratio on CT in PTLD, as shown in a recent study.[121]

MRI

Cardiac MRI may be another noninvasive method to establish a PH diagnosis, although not widely accessible, especially in resource-poor settings. Measurement of the ventricular mass index as a feature of PH has a sensitivity and specificity of 84% (95% CI, 79%−87%) and 82% (95% CI, 73%−89%), respectively.[122]

Functional tests and biomarkers

A 6MWD test can be performed with little equipment, is reproducible and an important noninvasive measurement in risk stratification, outcome and treatment endpoints of PH.[100] Additionally, abnormal heart rate recovery at 1 min after the 6MWD test (less than 13 bpm) has a negative predictive value of 82% for PH.[111] The use of 6MWD, brain-natriuretic peptide (BNP)/NT-proBNP and WHO functional class correlate with risk of long-term health outcome and morbidity and in combination may be a good screening tool to use in deciding if further investigations are needed.[123] Diffusing capacity of the lungs for carbon monoxide (DLCO) can be impaired in up to 79% of patients with previous TB,[124] though values of less than 40% accurately predict PH in patients with other parenchymal lung disease.[125] There is currently no data on the use of cardiopulmonary exercise testing (CPET) parameters like VE/VCO_2 slope, oxygen pulse, breathing, and circulatory reserve in post-TB disease. One of the future directions may be additional measurements like gas-exchange derived pulmonary vascular capacitance during submaximal CPET in combination to PASP on echocardiogram and FVC/DLCO ratio used to predict PH.[126] Elevated NT-proBNP levels above 50 pg/mL have good accuracy to diagnose increased pulmonary pressures and decreased RV function in patients with ILD.[110] It is uncertain what the accuracy is in patients with PTLD and importantly, BNP/NT-proBNP can be confounded by coexistent left heart disease.

In the absence of better data, we propose a screening algorithm (Figure 2) for post-TB PH for resource-constrained settings taking risk factors into account, being aware that clinical signs and symptoms occur late in the course of the disease and is not specific, using other available testing modalities in conjunction in deciding which patients should undergo echocardiography to assess for the probability of PH. RHC should only be considered if the diagnosis is uncertain, where it will alter management, including lung transplantation, initiation of vasoactive therapy, and for research purposes.

Categorization of post-TB PH as Group 3 PH

As noted, and depending on precise pathophysiology, patients with post-TB-PH can be classified into any of the five WHO PH categories (Figure 1), although Group 4 PH needs to be excluded as treatment strategies may involve surgery. Technically, the pathogenesis of post-TB PH can be multifactorial and could be classified as Group 5 PH. However, we consider post-TB PH in Group 3, as the majority of post-TB PH cases are likely to have parenchymal involvement (chronic lung disease) as their main disease mechanism and similar to the other causes of Group-3 PH (e.g., IPF and COPD), the pathogenesis is complex and multifactorial.

OUTCOMES

Patients with previously treated pulmonary TB have an increase in all-cause mortality when compared to the general population and cardiovascular disease has been listed as the leading cause of death in people with previous TB.[7] Patients with extensive PTLD tend to have reduced quality of life, an elevated risk of recurrent TB, more frequent hospitalization, and an increased respiratory-related mortality.[127–129] The contribution of post-TB PH to morbidity and mortality in PTLD is currently unknown; however, it may predict worse outcomes.[5] Data inferred from studies looking at chronic lung diseases from other aetiologies suggest that the development of PH is associated with increased mortality.[130,131] The mean time to death in those with PH developing from other respiratory causes has been documented as only 4 years and even shorter lifespans are noted proportionally to the severity of the PH.[132] Compared to PH from other Group 3 aetiologies (e.g., COPD), those with post-TB PH have a markedly higher mortality rate (approximately threefold increase) compared to those with PH from other Group 3 aetiologies

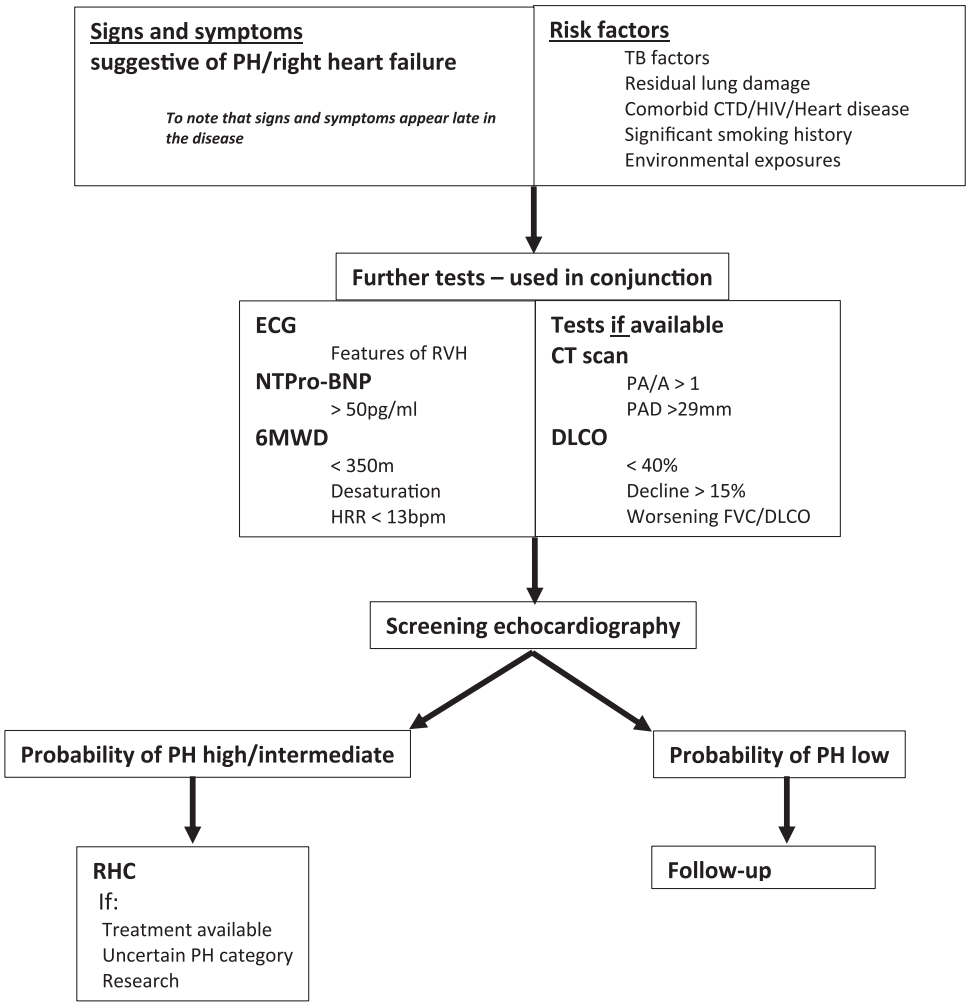

FIGURE 2 Proposed screening algorithm in a resource-constrained setting. A, aorta; DLCO, diffusion capacity of the lungs for carbon monoxide; ECG, electrocardiogram; FVC, forced vital capacity; HRR, heart rate recovery; NTpro-BNP, N-terminal pro-b-type natriuretic peptide; PA, pulmonary artery; PAD, pulmonary artery diameter; PH, pulmonary hypertension; RHC, right heart catheterization; RVH, right ventricular hypertrophy; TB, tuberculosis; 6MWD, 6 min walking distance test.

(e.g., COPD), potentially indicating a more aggressive phenotype.[133] In LMICs where resources are limited, late diagnoses and limited available treatment options may result in higher mortality rates for patients with PH.[12–14]

PH is associated with worsened morbidity in patients with PTLD. Patients with post-TB PH tend to have longer hospital stays and an increase in hospital readmissions than their counterparts without PH.[25,133] Additionally, in patients with PTLD, PH may increase the risk for acute exacerbation of respiratory symptoms as well as the frequency of exacerbations per year.[29] Moreover, the development of PH may worsen functional capacity and impede the quality of life in patients with PTLD.[134] In patients specifically with TB-associated obstructive pulmonary disease (small airway disease), PH was associated with poorer outcomes; however, the principle prognostic determinant was the severity of the ventilatory impairment and not the PH.[135]

The prognosis of post-TB PH may vary according to the degree of PH. Severe PH is associated with a very poor prognosis (mean survival approximately 10 months), and patients with PTLD and right ventricular failure predictably have a higher mortality.[133,136] However, mild PH may also contribute to reduced survival.[136] More data is needed on whether other discriminants such as age, 6MWD, and NT-proBNP can be used to predict survival in patients with post-TB PH and used for screening purposes.[137]

CONCLUSION AND FUTURE RESEARCH DIRECTIONS

As the world advances toward eliminating TB, it is important the be aware of the large number of global TB survivors still facing a significant burden of complications from TB.

Research regarding post-TB sequelae, particularly post-TB PH, should be prioritized. The burden of post-TB PH on communities is currently largely unknown but likely substantial. The prevalence needs to be accurately described by studying large numbers of patients with previously treated TB.

Emphasis should be placed on developing diagnostic algorithms for diagnosing PH in resource-constrained settings where RHC may not be available.[5] Given that universal screening for PH in TB survivors may be impractical and unfeasible, a targeted screening approach of high-risk individuals would be sensible. This requires research into better understanding the degree to which certain risk factors and cofactors contribute to the development of PH in patients with previous TB. Clinical scores, utilized with or without biomarkers, should be investigated and validated to identify those with previous TB who require follow-up and monitoring for the development of post-TB PH.

Furthermore, studies are needed to determine the duration from the incident episode of TB to the development of PH, as this may have important implications for long-term follow-up, screening, and treatment. Mortality data on post-TB PH is also needed, specifically considering whether PH predicts reduced survival and whether this correlates to the severity of the PH. Post-mortem studies may aid in understanding the pathophysiology and pathobiology of post-TB PH. Further research and understanding of the pathophysiology are needed to accurately categorize and describe post-TB PH and this may pave the way for the development of therapeutic modalities and interventions which could prevent the development or delay the progression of PH in patients with PTLD.

AUTHOR CONTRIBUTIONS

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The authors declare no conflict of interest.

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The authors have nothing to report.

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REFERENCES

1. World Health Organisation. Global tuberculosis report. 2022. https://www.who.int/publications/i/item/9789240061729
2. Ntoumi F, Nachega JB, Aklillu E, Chakaya J, Felker I, Amanullah F, Yeboah-Manu D, Castro KG, Zumla A. World Tuberculosis Day 2022: aligning COVID-19 and tuberculosis innovations to save lives and to end tuberculosis. Lancet Infect Dis. 2022;22:442–4.
3. Menzies NA, Quaife M, Allwood BW, Byrne AL, Coussens AK, Harries AD, Marx FM, Meghji J, Pedrazzoli D, Salomon JA, Sweeney S, van Kampen SC, Wallis RS, Houben RMGJ, Cohen T. Lifetime burden of disease due to incident tuberculosis: a global reappraisal including post-tuberculosis sequelae. Lancet Global Health. 2021;9:e1679–87.
4. Dodd PJ, Yuen CM, Jayasooriya SM, van der Zalm MM, Seddon JA. Quantifying the global number of tuberculosis survivors: a modelling study. Lancet Infect Dis. 2021;3099:1–9.
5. Walsh KF, Lui JK. Post-tuberculosis pulmonary hypertension: a case of global disparity in health care. Lancet Global Health. 2022;10:e476.
6. Quaife M, Houben RMGJ, Allwood B, Cohen T, Coussens AK, Harries AD, van Kampen S, Marx FM, Sweeney S, Wallis RS, Menzies NA. Post-tuberculosis mortality and morbidity: valuing the hidden epidemic. Lancet Respiratory Med. 2020;8:332–3.
7. Romanowski K, Baumann B, Basham CA, Ahmad Khan F, Fox GJ, Johnston JC. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. Lancet Infect Dis. 2019;19:1129–37.
8. Allwood BW, Maarman GJ, Kyriakakis CG, Doubell AF. Post-pulmonary tuberculosis complications in South Africa and a potential link with pulmonary hypertension: premise for clinical and scientific investigations. SAMJ. 2018;108:529.
9. Raine R. Screening for pulmonary hypertension secondary to pulmonary tuberculosis. African J Thoracic Critical Care Med. 2020;26:128.

10. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RM, Brida M, Carlsen J, Coats AJ, Escribano-Subias P, Ferrari P, Ferreira DS. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG). Eur Heart J. 2022;43(38):3618–731.
11. Hoeper MM, Humbert M, Souza R, Idrees M, Kawut SM, Sliwa-Hahnle K, Jing ZC, Gibbs JSR. A global view of pulmonary hypertension. Lancet Respiratory Med. 2016;4:306–22.
12. Dzudie A, Dzekem BS, Tchoumi CT, Aminde LN, Mocumbi AO, Abanda M, Thienemann F, Kengne AP, Sliwa K. Pulmonary hypertension as seen in a rural area in sub-Saharan Africa: high prevalence, late clinical presentation and a high short-term mortality rate during follow up. Cardiovasc J Afr. 2018;29:208–12.
13. Thienemann F, Katoto PDMC, Azibani F, Kodogo V, Mukasa SL, Sani MU, Karaye KM, Mbanze I, Mocumbi AO, Dzudie A, Sliwa K. Long-term follow-up of human immunodeficiency virus-associated pulmonary hypertension: clinical features and survival outcomes of the Pan Africa Pulmonary Hypertension Cohort (PAPUCO). Open Forum Infect Dis. 2022;9:ofac604.
14. Thienemann F, Blauwet L, Burton R, Tibazarwa K, Maarman G, Dzudie A, Mocumbi A, Sliwa K, Grp PA. Mortality of patients with HIV-associated pulmonary hypertension in a densely populated, peri-urban townshipin South Africa. In European Heart Journal. Vol. 35. Oxford University Press; 2014:73.
15. Thienemann F, Dzudie A, Mocumbi AO, Blauwet L, Sani MU, Karaye KM, Ogah OS, Mbanze I, Mbakwem A, Udo P, Tibazarwa K, Damasceno A, Keates AK, Stewart S, Sliwa K. The causes, treatment, and outcome of pulmonary hypertension in Africa: insights from the Pan African Pulmonary Hypertension Cohort (PAPUCO) Registry. Int J Cardiol. 2016;221:205–11.
16. Widimský J, Valach A, Dejdar R, Fejfar Z, Bergmann K, Vysloužil Z, Lukeš M. Cardiac failure in cor pulmonale due to pulmonary tuberculosis. Cardiology. 1959;35:154–70. https://doi.org/10.1159/000166499
17. Levinsky L. Tuberculosis and cardiopulmonary failure. Dis Chest. 1961;40:564–71. https://doi.org/10.1378/chest.40.5.564
18. Tiwari M, Gami SP. Pulmonary hypertension in pulmonary tuberculosis: a prognostic indicator. Eur Resp J. 2017; 50(Suppl 61):PA2432. https://doi.org/10.1183/1393003.congress-2017.pa2432
19. Marjani M, Baghaei P, Malekmohammad M, Tabarsi P, Sharif-Kashani B, Behzadnia N, Mansouri D, Masjedi MR, Velayati AA. Effect of pulmonary hypertension on outcome of pulmonary tuberculosis. Braz J Infect Dis. 2014;18:487–90.
20. Wen-Ting L, Chang-Wei W, De-Jian B, Wei S. Arterial partial pressure of oxygen and procalcitonin levels correlate with pulmonary artery systolic pressure in patients with active pulmonary tuberculosis. Int J Infect Dis. 2022;117:87–92. https://doi.org/10.1016/j.ijid.2022.01.060
21. Kotresh K, Raghavendra, Jaligidad K. Study of prevalence of cor pulmonale in patients with pulmonary tuberculosis with reference to ECG, echocardiographic changes and radiological extent of the disease. Int J Med Res. 2016;1:27–9.
22. Obaidy MWAI, Ficms F. Pulmonary hypertension in active pulmonary tuberculosis patients. Survival. 2018;55:57.
23. Saleh A, Mohammed AA, Raines P. An unexpected cause of right heart strain. BMJ Case Rep. 2013:bcr2013200216. https://doi.org/10.1136/bcr-2013-200216
24. Ahmed AEH, Ibrahim AS, Elshafie SM. Pulmonary hypertension in patients with treated pulmonary tuberculosis: analysis of 14 consecutive cases. Clin Med Insights: Circulatory, Resp Pulmonary Med. 2011;5:CCRPM.S6437.
25. Jafri S, Jawad N, Ahmed N, Saifullah N, Siddiqui IA. Post pulmonary tuberculosis: the right heart story. Biol Med. 2020;12:1–5.
26. Chordia R. Clinical profile of pulmonary artery hypertension in treated patients of pulmonary tuberculosis at a tertiary hospital. MedPulse Int J Med. 2021;20:23–6.
27. Louw E, Baines N, Maarman G, Osman M, Sigwadhi L, Irusen E, Koegelenberg C, Doubell A, Nathan S, Channick R, Allwood B. The prevalence of pulmonary hypertension after successful tuberculosis treatment in a community sample of adult patients. Pulm Circ. 2023;13(1):e12184. https://doi.org/10.1002/pul2.12184
28. Patel AK, Parekh AB, Adalja MH. Clinicoradiological and cardiac profile of pulmonary artery hypertension in treated patients of pulmonary tuberculosis in a tertiary center. Indian J Resp Care. 2020;9:62–7.
29. Jo YS, Park JH, Lee JK, Heo EY, Chung HS, Kim DK. Risk factors for pulmonary arterial hypertension in patients with tuberculosis-destroyed lungs and their clinical characteristics compared with patients with chronic obstructive pulmonary disease. Int J Chronic Obstruct Pulm Dis. 2017;12:2433–43.
30. Rajeev GS. Pulmonary hypertension in post tuberculosis pulmonary sequelae: attention needed. Chest. 2020;157:A406.
31. Maarman GJ, Shaw J, Allwood B. Pulmonary hypertension in majority countries: opportunities amidst challenges. Curr Opin Pulm Med. 2020;26:373–83. https://doi.org/10.1097/MCP.0000000000000702
32. Patel V, Khaped K, Solanki B, Patel A, Rathod H, Patel J. Profile of pulmonary hypertension patients profile of pulmonary hypertension patients coming to civil hospital, Ahmedabad. Int J Res Med. 2013;2:94–7.
33. Bhattacharyya P, Saha D, Bhattacherjee P, Das S, Bhattacharyya P, Dey R. Tuberculosis associated pulmonary hypertension: the revelation of a clinical observation. Lung India. 2016;33:135–9.
34. van Heerden JK, Louw EH, Thienemann F, Engel ME, Allwood BW. The prevalence of pulmonary hypertension in post-tuberculosis and active tuberculosis populations: a systematic review and meta-analysis. Eur Respir Rev. 2024;33:230154. https://doi.org/10.1183/16000617.0154-2023
35. Hnizdo E. Chronic pulmonary function impairment caused by initial and recurrent pulmonary tuberculosis following treatment. Thorax. 2000;55:32–8. https://doi.org/10.1136/thorax.55.1.32
36. Di Naso FC, Pereira JS, Schuh SJ, Unis G. Functional evaluation in patients with pulmonary tuberculosis sequelae.

Revista Portuguesa de Pneumologia (English Edition). 2011;17:216–21. https://doi.org/10.1016/j.rppnen.2011.06.005
37. Vanino E, Granozzi B, Akkerman OW, Munoz-Torrico M, Palmieri F, Seaworth B, Tiberi S, Tadolini M. Update of drug-resistant tuberculosis treatment guidelines: a turning point. Int J Infect Dis. 2023;130 Suppl:S12–5.
38. Kapoor SC. Cor pulmonale in pulmonary tuberculosis: a preliminary report of 66 patients. Indian J Tuberc. 1959;6: 51–64.
39. Verma A. Tuberculosis and pulmonary hypertension: commentary. Lung India. 2016;33:232. https://doi.org/10.4103/0970-2113.177455
40. Tegegne KT, Zenebe A, Assefa AA, Bifato B, Tegegne ET, Tessema MK. Iron with folic acid supplemenation and birth weight in Ethiopia: systemic review and meta-analysis. Medico Research Chronicles. 2021;8:136–48.
41. Cottin V, Selman M, Inoue Y, Wong AW, Corte TJ, Flaherty KR, Han MK, Jacob J, Johannson KA, Kitaichi M, Lee JS, Agusti A, Antoniou KM, Bianchi P, Caro F, Florenzano M, Galvin L, Iwasawa T, Martinez FJ, Morgan RL, Myers JL, Nicholson AG, Occhipinti M, Poletti V, Salisbury ML, Sin DD, Sverzellati N, Tonia T, Valenzuela C, Ryerson CJ, Wells AU. Syndrome of combined pulmonary fibrosis and emphysema: an official ATS/ERS/JRS/ALAT research statement. Am J Respir Crit Care Med. 2022;206:e7–e41.
42. Danwang C, Bigna JJ, Awana AP, Nzalie RNT, Robert A. Global epidemiology of venous thromboembolism in people with active tuberculosis: a systematic review and meta-analysis. J Thromb Thrombolysis. 2021;51:502–12.
43. Marjani M, Tabarsi P, Baghaei P, Shamaei M, Gorgi Biani P, Mansouri D, Masjedi MR, Velayati AA. Incidence of thromboembolism in hospitalized patients with tuberculosis and associated risk factors. Archiv Clinical Infec Dis. 2012;7(2). https://doi.org/10.5812/archcid.13950
44. Moodley P, Martinson NA, Joyimbana W, Otwombe KN, Abraham P, Motlhaoleng K, Naidoo VA, Variava E. Venous thromboembolic disease in adults admitted to hospital in a setting with a high burden of HIV and TB. African J Thoracic Critical Care Med. 2021;27:99. https://doi.org/10.7196/AJTCCM.2021.v27i3.155
45. Park SY, Lee SM, Shin JW, Choi BW, Kim H, Lee JS, Lee SD, Park SS, Moon HS, Park YB. Epidemiology of chronic thromboembolic pulmonary hypertension in Korea: results from the Korean registry. Korean J Intern Med. 2016;31:305–12. https://doi.org/10.3904/kjim.2014.122
46. Zahn DW, Peirce CT. Venous thrombosis and pulmonary embolism in tuberculosis. Am J Med. 1948;5:716–28.
47. Samaria JK, Kumar H, Yadav P. Cardiac involvement in chronic obstructive pulmonary disease (COPD) secondary to post-TB bronchiectasis v/s non-post TB bronchiectasis. 2012. https://doi.org/10.1164/ajrccm-conference.2012.185.1_meetingabstracts.a4524
48. Stewart S, Mocumbi AO, Carrington MJ, Pretorius S, Burton R, Sliwa K. A not-so-rare form of heart failure in urban black Africans: pathways to right heart failure in the Heart of Soweto Study cohort. Eur J Heart Fail. 2011;13: 1070–7.
49. Miri A, Kalla I, Seedat F. Occult pulmonary arterial hypertension in patients with previous pulmonary tuberculosis. African J Thoracic Critical Care Med. 2020;26:133. https://doi.org/10.7196/AJTCCM.2020.v26i4.110
50. Allwood BW, Byrne A, Meghji J, Rachow A, van der Zalm MM, Schoch OD. Post-tuberculosis lung disease: clinical review of an under-recognised global challenge. Respiration. 2021;100:751–63. https://doi.org/10.1159/000512531
51. Fei Y, Shi X, Gan F, Li X, Zhang W, Li M, Hou Y, Zhang X, Zhao Y, Zeng X, Zhang F. Death causes and pathogens analysis of systemic lupus erythematosus during the past 26 years. Clin Rheumatol. 2014;33:57–63.
52. de Rezende RPV, Gismondi RA, Maleh HC, de Miranda Coelho EM, Vieira CS, Rosa MLG, Mocarzel LO. Distinct mortality profile in systemic sclerosis: a death certificate study in Rio de Janeiro, Brazil (2006–2015) using a multiple causes of death analysis. Clin Rheumatol. 2019;38: 189–94.
53. Erzer JN, Jaeger VK, Tikly M, Walker UA. Systemic sclerosis in sub-saharan Africa: a systematic review. Pan African Medical Journal. 2020;37:1–18.
54. Ou SM, Fan WC, Cho KT, Yeh CM, Su VYF, Hung MH, Chang YS, Lee YJ, Chen YT, Chao PW, Yang WC, Chen TJ, Wang WS, Tsao HM, Chen LF, Lee FY, Liu CJ. Systemic sclerosis and the risk of tuberculosis. J Rheumatol. 2014;41: 1662–9.
55. Zhang Y, Fan P, Luo F, Zhang HM, Song L, Ma WJ, Wu HY, Cai J, Wang LP, Zhou XL. Tuberculosis in Takayasu arteritis: a retrospective study in 1105 Chinese patients. J Geriatric Cardiol: JGC. 2019;16:648–55.
56. Ugarte-Gil C, Alisjahbana B, Ronacher K, Riza AL, Koesoemadinata RC, Malherbe ST, Cioboata R, Llontop JC, Kleynhans L, Lopez S, Santoso P, Marius C, Villaizan K, Ruslami R, Walzl G, Panduru NM, Dockrell HM, Hill PC, Mc Allister S, Pearson F, Moore D, Critchley JA, van Crevel R. Diabetes mellitus among pulmonary tuberculosis patients from 4 tuberculosis-endemic countries: the TANDEM study. Clin Infect Dis. 2020;70:780–8.
57. Bunatova K, Kohout J, Sefrna F. Cause of death in patients with pneumoconiosis. Pr Lek. 2001;53:158–63.
58. Bloomfield GS, Lagat DK, Akwanalo OC, Carter EJ, Lugogo N, Vedanthan R, Velazquez EJ, Kimaiyo S, Sherman CB. Conditions that predispose to pulmonary hypertension and right heart failure in persons exposed to household air pollution in LMIC. Global Heart. 2012;7:249–59.
59. Vercellino A, Giorgis GE, Galietti F, Ardizzi A, Barberis S, Gays E. [Problems of pulmonary pathology in drug addicts]. Minerva Med. 1983;74:635–9.
60. Stek C, Allwood B, Walker NF, Wilkinson RJ, Lynen L, Meintjes G. The immune mechanisms of lung parenchymal damage in tuberculosis and the role of host-directed therapy. Front Microbiol. 2018;9:1–16.
61. Shanmugasundaram K, Talwar A, Madan K, Bade G. Pulmonary functions and inflammatory biomarkers in post-pulmonary tuberculosis sequelae. Tuberc Respir Dis. 2022;85: 175–84.
62. Singh S, Allwood BW, Chiyaka TL, Kleyhans L, Naidoo CC, Moodley S, Theron G, Segal LN. Immunologic and imaging signatures in post tuberculosis lung disease. Tuberculosis. 2022;136:102244.

63. Meghji J, Simpson H, Squire SB, Mortimer K. A systematic review of the prevalence and pattern of imaging defined post-TB lung disease. PLoS One. 2016;11:e0161176.
64. Deshpande SS, Joshi AR, Shah A. Aftermath of pulmonary tuberculosis: computed tomography assessment. Pol J Radiol. 2020;85:137–47.
65. Suhas H, Utpat K, Desai U, Joshi J. The clinico-radiological profile of obliterative bronchiolitis in a tertiary care center. Lung India. 2019;36:313–8.
66. Nathan SD, Barbera JA, Gaine SP, Harari S, Martinez FJ, Olschewski H, Olsson KM, Peacock AJ, Pepke-Zaba J, Provencher S, Weissmann N, Seeger W. Pulmonary hypertension in chronic lung disease and hypoxia. Eur Respir J. 2019;53:1801914. https://doi.org/10.1183/13993003.01914-2018
67. Colombat M, Mal H, Groussard O, Capron F, Thabut G, Jebrak G, Brugière O, Dauriat G, Castier Y, Lesèche G, Fournier M. Pulmonary vascular lesions in end-stage idiopathic pulmonary fibrosis: histopathologic study on lung explant specimens and correlations with pulmonary hemodynamics. Hum Pathol. 2007;38:60–5.
68. Judge EP, Fabre A, Adamali HI, Egan JJ. Acute exacerbations and pulmonary hypertension in advanced idiopathic pulmonary fibrosis. Eur Respir J. 2012;40:93–100.
69. Dentan C, Epaulard O, Seynaeve D, Genty C, Bosson JL. Active tuberculosis and venous thromboembolism: association according to international classification of diseases, ninth revision hospital discharge diagnosis codes. Clin Infect Dis. 2014;58:495–501.
70. Robson SC, White NW, Aronson I, Woollgar R, Goodman H, Jacobs P. Acute-phase response and the hypercoagulable state in pulmonary tuberculosis. Br J Haematol. 1996;93:943–9.
71. Turken O, Kunter E, Sezer M, Solmazgul E, Cerrahoglu K, Bozkanat E, Ozturk A, Ilvan A. Hemostatic changes in active pulmonary tuberculosis. The Int J Tuberculosis Lung Dis. 2002;6:927–32.
72. Ben Amar J, Dahri B, Aouina H, Bouacha H. Maladie veineuse thromboembolique au cours de la tuberculose. Rev Pneumol Clin. 2015;71:327–34.
73. Lang IM, Mackman N, Kriett JM, Moser KM, Schleef RR. Prothrombotic activation of pulmonary arterial endothelial cells in a patient with tuberculosis. Hum Pathol. 1996;27:423–7.
74. Zabka TS, Campbell FE, Wilson DW. Pulmonary arteriopathy and idiopathic pulmonary arterial hypertension in six dogs. Vet Pathol. 2006;43:510–22. https://doi.org/10.1354/vp.43-4-510
75. Maarman GJ. Natural antioxidants as potential therapy, and a promising role for melatonin against pulmonary hypertension. Adv Exp Med Biol. 2017;967:161–78. doi:10.1007/978-3-319-63245-2_10
76. Morrell NW. Pulmonary hypertension due to BMPR2 mutation: a new paradigm for tissue remodeling? Proc Am Thorac Soc. 2006;3:680–6.
77. Burg ED, Remillard CV, Yuan JXJ. Potassium channels in the regulation of pulmonary artery smooth muscle cell proliferation and apoptosis: pharmacotherapeutic implications. Br J Pharmacol. 2008;153:S99–S111.
78. Wei H, Zhang D, Liu L, Xia W, Li F. Rho signaling pathway enhances proliferation of PASMCs by suppressing nuclear translocation of Smad1 in PAH. Exp Ther Med. 2019;17:71–8.
79. Chan SY, Rubin LJ. Metabolic dysfunction in pulmonary hypertension: from basic science to clinical practice. Eur Respir Rev. 2017;26:170094.
80. Dickinson MG, Bartelds B, Borgdorff MAJ, Berger RMF. The role of disturbed blood flow in the development of pulmonary arterial hypertension: lessons from preclinical animal models. American J Physiol-Lung Cell Mol Physiol. 2013;305:L1–L14.
81. Ruffenach G, Hong J, Vaillancourt M, Medzikovic L, Eghbali M. Pulmonary hypertension secondary to pulmonary fibrosis: clinical data, histopathology and molecular insights. Respir Res. 2020;21:303.
82. Khan R, Malik NI, Razaque A. Imaging of pulmonary post-tuberculosis sequelae. Pak J Med Sci. 2020;36:75.
83. Arcasoy SM, Christie JD, Ferrari VA, Sutton MSJ, Zisman DA, Blumenthal NP, Pochettino A, Kotloff RM. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. Am J Respir Crit Care Med. 2003;167:735–40.
84. Lin J, Jimenez CA. Acute mediastinitis, mediastinal granuloma, and chronic fibrosing mediastinitis: a review. Semin Diagn Pathol. 2022;39:113–9.
85. Wang A, Su H, Duan Y, Jiang K, Li Y, Deng M, Long X, Wang H, Zhang M, Zhang Y, Cao Y. Pulmonary hypertension caused by fibrosing mediastinitis. JACC: Asia. 2022;2:218–34.
86. Mathisen DJ, Grillo HC. Clinical manifestation of mediastinal fibrosis and histoplasmosis. Ann Thorac Surg. 1992;54:1053–8.
87. Wu Z, Jarvis H, Howard LS, Wright C, Kon OM. Post-tuberculous fibrosing mediastinitis: a review of the literature. BMJ Open Respir Res. 2017;4:e000174.
88. Fijołek J, Wiatr E, Błasińska-Przerwa K, Roszkowski-Śliż K. Fibrosing mediastinitis as an untypical complication of tuberculosis. Pol Arch Med Wewn. 2009;119:752–5.
89. Akman C, Kantarci F, Cetinkaya S. Imaging in mediastinitis: a systematic review based on aetiology. Clin Radiol. 2004;59:573–85.
90. Seferian A, Steriade A, Jaïs X, Planché O, Savale L, Parent F, Amar D, Jovan R, Fadel E, Sitbon O, Simonneau G, Humbert M, Montani D. Pulmonary hypertension complicating fibrosing mediastinitis. Medicine. 2015;94:e1800.
91. Chung W-S, Lin C-L, Hung C-T, Chu YH, Sung FC, Kao CH, Yeh JJ. Tuberculosis increases the subsequent risk of acute coronary syndrome: a nationwide population-based cohort study. Int J Tuberc Lung Dis. 2014;18:79–83.
92. Lee HR, Yoo JE, Choi H, Han K, Jung JH, Park J, Lee H, Shin DW. Tuberculosis and risk of ischemic stroke: a nationwide cohort study. Stroke. 2022;53:3401–9.
93. Wang S-H, Chien W-C, Chung C-H, Lin FH, Peng CK, Chian CF, Shen CH. Tuberculosis increases the risk of peripheral arterial disease: a nationwide population-based study. Respirology. 2017;22:1670–6.
94. Huaman MA, Kryscio RJ, Fichtenbaum CJ, Henson D, Salt E, Sterling TR, Garvy BA. Tuberculosis and risk of acute myocardial infarction: a propensity score-matched analysis. Epidemiol Infect. 2017;145:1363–7.

95. Lee HR, Yoo JE, Choi H, Han K, Lim YH, Lee H, Shin DW. Tuberculosis and the risk of ischemic heart disease: a nationwide cohort study. Clin Infect Dis. 2022;76:1576–84. https://doi.org/10.1093/cid/ciac946
96. Salindri AD, Wang J-Y, Lin H-H, Magee MJ. Post-tuberculosis incidence of diabetes, myocardial infarction, and stroke: retrospective cohort analysis of patients formerly treated for tuberculosis in Taiwan, 2002-2013. Int J Infect Dis. 2019;84:127–30.
97. Huaman MA, Henson D, Ticona E, Sterling TR, Garvy BA. Tuberculosis and cardiovascular disease: linking the epidemics. Trop Dis Travel Med Vaccines. 2015;1:10. https://doi.org/10.1186/s40794-015-0014-5
98. Magee MJ, Salindri AD, Gujral UP, Auld SC, Bao J, Haw JS, Lin HH, Kornfeld H. Convergence of non-communicable diseases and tuberculosis: a two-way street? Int J Tuberc Lung Dis. 2018;22:1258–68.
99. Lim K, Yang JH, Miranda WR, Chang SA, Jeong DS, Nishimura RA, Schaff H, Soo WM, Greason KL, Oh JK. Clinical significance of pulmonary hypertension in patients with constrictive pericarditis. Heart. 2021;107:1651–6.
100. Parikh R, Konstantinidis I, O'Sullivan DM, Farber HW. Pulmonary hypertension in patients with interstitial lung disease: a tool for early detection. Pulm Circ. 2022;12:1–11.
101. Al-Naamani K, Hijal T, Nguyen V, Andrew S, Nguyen T, Huynh T. Predictive values of the electrocardiogram in diagnosing pulmonary hypertension. Int J Cardiol. 2008;127:214–8.
102. Balieva I, Dzudie A, Thienemann F, Mocumbi AO, Karaye K, Sani MU, Ogah OS, Voors AA, Kengne AP, Sliwa K. Prevalence and predictive value of electrocardiographic abnormalities in pulmonary hypertension: evidence from the Pan-African Pulmonary Hypertension Cohort (PAPUCO) study. Cardiovasc J Afr. 2017;28:370–6.
103. D'Alto M, Di Maio M, Romeo E, Argiento P, Blasi E, Di Vilio A, Rea G, D'Andrea A, Golino P, Naeije R. Echocardiographic probability of pulmonary hypertension: a validation study. Eur Respir J. 2022;60:2102548. https://doi.org/10.1183/13993003.02548-2021
104. Ni JR, Yan PJ, Liu SD, Hu Y, Yang KH, Song B, Lei JQ. Diagnostic accuracy of transthoracic echocardiography for pulmonary hypertension: a systematic review and meta-analysis. BMJ Open. 2019;9:e033084. https://doi.org/10.1136/bmjopen-2019-033084
105. Wang YC, Huang CH, Tu YK. Pulmonary hypertension and pulmonary artery acceleration time: a systematic review and meta-analysis. J Am Soc Echocardiogr. 2018;31:201–10.e3.
106. Greiner S, Jud A, Aurich M, Hess A, Hilbel T, Hardt S, Katus HA, Mereles D. Reliability of noninvasive assessment of systolic pulmonary artery pressure by Doppler echocardiography compared to right heart catheterization: analysis in a large patient population. J Am Heart Assoc. 2014;3:1–8.
107. Chen R, Liao H, Deng Z, He Z, Zheng Z, Lu J, Jiang M, Wu X, Guo W, Huang Z, Chen H, Hong C, Zhong N. Efficacy of computed tomography in diagnosing pulmonary hypertension: a systematic review and meta-analysis. Front Cardiovasc Med. 2022;9:1–10.
108. Shen Y, Wan C, Tian P, Wu Y, Li X, Yang T, An J, Wang T, Chen L, Wen F. CT-base pulmonary artery measurementin the detection of pulmonary hypertension. Medicine. 2014;93:e256.
109. Nowroozpoor A, Hshemian SM, Malekmohammad M, Marjani M, Tabarsi P, Jamaati H, Khoundabi B, Moniri A. Usefulness of pulmonary artery diameter in diagnosing pulmonary hypertension in patients admitted to tuberculosis intensive care unit. Int J Mycobacteriol. 2016;5(Suppl 1):S56.
110. Ruocco G, Cekorja B, Rottoli P, Refini RM, Pellegrini M, Di Tommaso C, Del Castillo G, Franci B, Nuti R, Palazzuoli A. Role of BNP and echo measurement for pulmonary hypertension recognition in patients with interstitial lung disease: an algorithm application model. Respir Med. 2015;109:406–15.
111. Swigris JJ, Olson AL, Shlobin OA, Ahmad S, Brown KK, Nathan SD. Heart rate recovery after six-minute walk test predicts pulmonary hypertension in patients with idiopathic pulmonary fibrosis. Respirology. 2011;16:439–45.
112. Behr J, Nathan SD. Pulmonary hypertension in interstitial lung disease: screening, diagnosis and treatment. Curr Opin Pulm Med. 2021;27:396–404.
113. van de Veerdonk MC, Vonk-Noordegraaf A, Vachiery JL. Unbowed, unbent, unbroken: predicting pulmonary hypertension using echocardiography. Eur Respir J. 2022;60:2200481.
114. Gall H, Yogeswaran A, Fuge J, Sommer N, Grimminger F, Seeger W, Olsson KM, Hoeper MM, Richter MJ, Tello K, Ghofrani HA. Validity of echocardiographic tricuspid regurgitation gradient to screen for new definition of pulmonary hypertension. EClinicalMedicine. 2021;34:100822.
115. D'Alto M, Bossone E, Opotowsky AR, Ghio S, Rudski LG, Naeije R. Strengths and weaknesses of echocardiography for the diagnosis of pulmonary hypertension. Int J Cardiol. 2018;263:177–83.
116. Mutlak D, Aronson D, Lessick J, Reisner SA, Dabbah S, Agmon Y. Functional tricuspid regurgitation in patients with pulmonary hypertension. Chest. 2009;135:115–21.
117. Soliman D, Bolliger D, Skarvan K, Kaufmann BA, Lurati Buse G, Seeberger MD. Intra-operative assessment of pulmonary artery pressure by transoesophageal echocardiography. Anaesthesia. 2015;70:264–71.
118. Nowak J, Hudzik B, Jastrzębski D, Niedziela JT, Rozentryt P, Wojarski J, Ochman M, Karolak W, Żegleń S, Gierlotka M, Gąsior M. Pulmonary hypertension in advanced lung diseases: echocardiography as an important part of patient evaluation for lung transplantation. Clin Resp J. 2018;12:930–8.
119. Devaraj A, Wells AU, Meister MG, Corte TJ, Wort SJ, Hansell DM. Detection of pulmonary hypertension with multidetector CT and echocardiography alone and in combination. Radiology. 2010;254:609–16.
120. Devaraj A, Hansell DM. Computed tomography signs of pulmonary hypertension: old and new observations. Clin Radiol. 2009;64:751–60.
121. Almubarek M, Louw EH, Griffith-Richards S, et al. The performance of CT chest for the detection of pulmonary hypertension in patients with post-tuberculous lung disease. Afr J Thorac Crit Care Med. In press.
122. Wang N, Hu X, Liu C, Ali B, Guo X, Liu M, Peng X, Yang Y. A systematic review of the diagnostic accuracy of

cardiovascular magnetic resonance for pulmonary hypertension. Can J Cardiol. 2014;30:455–63.
123. Wronski SL, Mordin M, Kelley K, Anguiano RH, Classi P, Shen E, Manaker S. The role of noninvasive endpoints in predicting long-term outcomes in pulmonary arterial hypertension. Lung. 2020;198:65–86.
124. Allwood BW, Maasdorp E, Kim GJ, Cooper CB, Goldin J, van Zyl-Smit RN, Bateman ED, Dawson R. Transition from restrictive to obstructive lung function impairment during treatment and follow-up of active tuberculosis. Int J COPD. 2020;15:1039–47. https://doi.org/10.2147/COPD.S219731
125. Zou RH, Wallace WD, Nouraie SM, Chan SY, Risbano MG. Lower DLco% identifies exercise pulmonary hypertension in patients with parenchymal lung disease referred for dyspnea. Pulm Circ. 2020;10:1–11.
126. Joseph P, Savarimuthu S, Zhao J, Yan X, Oakland HT, Cullinan M, Heerdt PM, Singh I. Non-invasive determinants of pulmonary hypertension in interstitial lung disease. Pulm Circ. 2023;13(1):e12197. doi:10.1002/pul2.12197
127. Ryu YJ, Lee JH, Chun EM, Chang JH, Shim SS. Clinical outcomes and prognostic factors in patients with tuberculous destroyed lung. Int J Tuberculosis and Lung Dis. 2011;15:246–50.
128. Marx FM, Floyd S, Ayles H, Godfrey-Faussett P, Beyers N, Cohen T. High burden of prevalent tuberculosis among previously treated people in Southern Africa suggests potential for targeted control interventions. Eur Respir J. 2016;48:1227–30.
129. Pasipanodya JG, McNabb SJ, Hilsenrath P, Bae S, Lykens K, Vecino E, Munguia G, Miller TL, Drewyer G, Weis SE. Pulmonary impairment after tuberculosis and its contribution to TB burden. BMC Public Health. 2010;10:259. https://doi.org/10.1186/1471-2458-10-259
130. Corte TJ, Wort SJ, Gatzoulis MA, Macdonald P, Hansell DM, Wells AU. Pulmonary vascular resistance predicts early mortality in patients with diffuse fibrotic lung disease and suspected pulmonary hypertension. Thorax. 2009;64:883–8.
131. Öcal S, Portakal O, Öcal A, Demir AU, Topeli A, Çöplü L. Factors associated with pulmonary hypertension and long-term survival in bronchiectasis subjects. Respir Med. 2016;119:109–14.
132. Strange G, Playford D, Stewart S, Deague JA, Nelson H, Kent A, Gabbay E. Pulmonary hypertension: prevalence and mortality in the Armadale echocardiography cohort. Heart. 2012;98:1805–11.
133. Park SY, Lee CY, Kim C, Jang SH, Park YB, Park S, Hwang YI, Lee MG, Jung KS, Kim DG. One-year prognosis and the role of brain natriuretic peptide levels in patients with chronic cor pulmonale. J Korean Med Sci. 2015;30:442–9.
134. Septiyanti D, Sari AP, Aniwidyaningsih W, Antariksa BSB. The prevalence of pulmonary hypertension in destroyed lung due to post pulmonary tuberculosis and its relation to exercise capacity. J Respirologi Indones. 2018;38(4):227–31. https://doi.org/10.36497/jri.v38i4.24
135. Sasaki Y, Yamagishi F, Suzuki K, Kuriyama T. [Survival and pulmonary hemodynamics in patients with sequelae of pulmonary tuberculosis who received antituberculosis chemotherapy and home oxygen therapy]. Nihon Kokyuki Gakkai zasshi=J Japanese Respiratory Soc. 1998;36:934–8.
136. Vyslouzil Z, Polák J, Widimský J, Suková M. Pathogenesis of pulmonary hypertension in tuberculosis. Czech Med. 1980;3:123–31.
137. Vizza CD, Hoeper MM, Huscher D, Pittrow D, Benjamin N, Olsson KM, Ghofrani HA, Held M, Klose H, Lange T, Rosenkranz S, Dumitrescu D, Badagliacca R, Claussen M, Halank M, Vonk-Noordegraaf A, Skowasch D, Ewert R, Gibbs JSR, Delcroix M, Skride A, Coghlan G, Ulrich S, Opitz C, Kaemmerer H, Distler O, Grünig E. Pulmonary hypertension in patients with COPD. Chest. 2021;160:678–89.

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