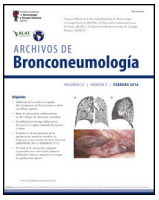
Archivos de Bronconeumología xxx (xxxx) xxx–xxx

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE
Bronconeumología

www.archbronconeumol.org



Editorial

Post-TB Lung Disease: Where are we to Respond to This Priority?

More than 10 million people are diagnosed with tuberculosis (TB) worldwide each year. In 2023, TB returned to being the world's leading infectious disease killer, surpassing coronavirus disease 2019 (COVID-19).[1] Patients surviving TB face considerable ongoing morbidities such as neurological impairments, cardiac disorders, psychosocial challenges, reduced health-related quality of life,[2,3] and one third of patients have post-TB lung disease (PTLD). PTLD includes persistent symptoms, spirometric abnormalities, bronchiectasis, colonization and infection with *Aspergillus fumigatus* and non-tuberculous mycobacteria, and pulmonary hypertension.[4–9] Furthermore, patients with PTLD have a mortality rate 3 to 6 times higher than the general population.[10,11]

Despite the alarming numbers, PTLD is not considered a topic of interest in most national and international TB guidelines. Many countries with high TB prevalence do not have a plan for PTLD and they do not even know the actual burden of disease. Furthermore, the vast majority of scientific contributions on PTLD are focused on etiopathogenesis, epidemiology and diagnosis and do not consider the need for pulmonary rehabilitation. For several decades national TB control programs considered their work completed when the patients have achieved treatment success. This is only in part true, as an important proportion of these patients cannot return to work, are limited in their daily activities and have hampered Quality of Life.[12,13]

In 2021, the first consensus-based set of Clinical Standards for PTLD was published.[12] This document influenced the development of the Brazilian Thoracic Association (Sociedade Brasileira de Pneumologia e Tisiologia – SBPT) recommendations for the management of PTLD,[13] which included pulmonary rehabilitation as a pillar, making Brazil the first country to produce guidelines on this subject. This example was followed by the Latin America Thoracic Association (Asociación Latinoamericana de Tórax – ALAT) which developed recommendations for PTLD in 2024.[14] Concurrently, the World Health Organization (WHO) published a policy brief on TB-associated disability, reinforcing the need for PTLD to be addressed by national TB control programs.[15] WHO has then convened an expert committee which is presently working at the development of a policy guidance document on this subject.

There are several other barriers to overcome in order to adequately address this priority. The diagnosis of PTLD is not always made after completion of TB treatment and, when it is made, it is often not done properly. Many healthcare facilities only have spirometry available for the diagnosis of PTLD, which is not sufficient for a comprehensive assessment of PTLD; plethysmography and diffusion capacity are usually available only at tertiary care level. In addition, in many settings, chest tomography is not available, especially at primary care level. Furthermore, after completing TB treatment, many patients lose their linkage to the healthcare system and do not have the opportunity for PTLD evaluation and diagnosis. Without long-term follow-up, they do not have access to treatment and rehabilitation if necessary.[15] Interestingly, when WHO revised its outcome definitions, the concept of 'sustained treatment success' was introduced, referring to patients who remain relapse-free after 12 months of follow-up. As it was considered not feasible to introduce programmatic follow-up of all patients for one year, WHO suggested to use this outcome definition for patients followed-up over time for research purposes. The patients with PTLD undergoing pulmonary rehabilitation program (PRP), who are the most severely affected, represent an additional group entitled to be followed up for one year or even more.[12,13,15] Furthermore, in absence of a consistent approach to PTLD diagnosis, we presently lack reliable data which are necessary to plan for a quality management of this condition, including the identification of human and financial resources.

For patients diagnosed with PTLD, pharmacological treatment recommendations are limited.[12,13] Even recommended pharmacological treatments and pulmonary rehabilitation are often only available in the public health system for patients with other diseases, such as, for example, chronic obstructive pulmonary disease. Rehabilitation should be considered an essential health service for patients with PTLD.[15] In a recent systematic review and meta-analysis,[16] rehabilitation programs have demonstrated to be effective interventions for preventing PTLD. Additionally, patients with chronic hypoxemia must have access to long-term oxygen therapy. Moreover, PTLD should be considered a chronic respiratory disease, which may have infectious complications preventable by vaccines. Several vaccines, such as influenza, pneumococcal, and COVID-19, should be recommended and be available for patients with PTLD.[17,18]

Another gap in PTLD concerns research. Existing studies regarding epidemiology, diagnosis, pharmacological treatment and rehabilitation are limited and not robust.[19,20] This is particularly true for pulmonary rehabilitation. So far, no study had ever compared the long-term outcome of patients undergoing pulmonary rehabilitation versus those without this opportunity.

Recently, a prospective multicentre study,[21] which included a complete functional evaluation before and after PRP, demonstrated the benefits from PRP in patients with PTLD, including improvements in lung function and in exercise capacity. This study is the first and largest study evaluating patients with PTLD who under-

https://doi.org/10.1016/j.arbres.2025.03.001

Please cite this article as: D.R. Silva, E. Pontali, Y. Kherabi et al., Post-TB Lung Disease: Where are we to Respond to This Priority? Archivos de Bronconeumología, https://doi.org/10.1016/j.arbres.2025.03.001

went PR, and comparing them with a cohort of non-rehabilitated patients. Future studies, especially clinical trials evaluating new treatment regimens, should evaluate not only microbiological cure but also prevention and rehabilitation of PTLD.[22]

Finally, funding for diagnosis, management, and research on PTLD remains limited, particular in this new era signed by the withdrawal of the majority of the USA funds previously allocated to fight TB. Even rehabilitation, which already has consistent evidence of benefit in patients with PTLD,[16,21] is often not linked to TB in most TB high-burden settings, and consequently does not receive adequate attention and funding from governments.[15] A barrier to more research focused on PTLD is the perception that this cannot be done in resource-limited settings, that it is technically demanding and therefore not feasible in high TB burden countries. The leadership of Brazil and ALAT testify that this is not true. For example, a TB REACH project in Bangladesh managed by the Damien Foundation is ongoing to evaluate the feasibility and impact of implementing PRP at the programmatic level in rural areas and with large numbers.

In the Global Plan to End TB 2023–2030,[23] attention was drawn to the need to provide care to PTLD. In the same way, the Global Fund recently issued a note to national TB programs encouraging them to consider PTLD as a priority intervention.[24]

In conclusion, PTLD should be considered a priority by national TB control programs and guidelines should be updated to include recommendations on the diagnosis and management of PTLD, which includes pulmonary rehabilitation.[25] A more comprehensive diagnosis, treatment and prevention of PTLD will have, as a positive 'side effect', the improved management of all chronic respiratory conditions in thousands of patients around the world.

Artificial Intelligence Involvement

None of the material has been partially or totally produced with the help of any artificial intelligence software or tool.

Funding of the Research

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript.

Acknowledgements

The article is part of the scientific activities of the Global Tuberculosis Network (GTN), hosted by the World Association for Infectious Diseases and Immunological Disorders (WAiDID). This work was partially supported for Istituti Clinici Scientifici Maugeri, by the "Ricerca Corrente", funding scheme of the Italian Ministry of Health.

References

1. World Health Organization. Global Tuberculosis Report 2024 [accessed 28 Feb 2025]. Available from: https://iris.who.int/bitstream/handle/10665/379339/9789240101531-eng.pdf?sequence=1.
2. Zawedde J, Abelman R, Musisi E, Nyabigambo A, Sanyu I, Kaswabuli S, et al. Lung function and health-related quality of life among adult patients following pulmonary TB treatment. Int J Tuberc Lung Dis. 2024;28(9):419–26.
3. Nightingale R, Carlin F, Meghji J, McMullen K, Evans D, van der Zalm MM, et al. Post-TB health and wellbeing. Int J Tuberc Lung Dis. 2023;27(4):248–83.
4. McDonald AK, Nakkonde D, Kaggwa P, Zalwango S, Joseph A, Buregyeya E, et al. Prevalence of TB-related symptoms and self-reported disability among adult TB survivors. IJTLD Open. 2024;1(12):540–6.
5. Thomson H, Baines N, Huisamen T, Koegelenberg CFN, Irusen EM, Mapahla L, et al. A new understanding of clinical patterns in post-TB lung disease. Int J Tuberc Lung Dis. 2024;28(3):115–21.
6. Hoole AS, Ilyas A, Munawar S, Cant M, Hameed R, Gill S, et al. Post-TB bronchiectasis: clinical characteristics and microbiology. Int J Tuberc Lung Dis. 2024;28(8):405–6.
7. Pontali E, Silva DR, Marx FM, Caminero JA, Centis R, D'Ambrosio L, et al. Breathing back better! A state of the art on the benefits of functional evaluation and rehabilitation of post-tuberculosis and post-COVID lungs. Arch Bronconeumol. 2022;58(11):754–63.
8. Menzies NA, Quaife M, Allwood BW, Byrne AL, Coussens AK, Harries AD, et al. Lifetime burden of disease due to incident tuberculosis: a global reappraisal including post-tuberculosis sequelae. Lancet Glob Heal. 2021;9(12):e1679–87.
9. Martinez-Garcia MA, Guan WJ, de-La-Rosa D, Athanazio R, Oscullo G, Shi MX, et al. Post-TB bronchiectasis: from pathogenesis to rehabilitation. Int J Tuberc Lung Dis. 2023;27(3):175–81.
10. Miller TL, Wilson FA, Pang JW, Beavers S, Hoger S, Sharnprapai S, et al. Mortality hazard and survival after tuberculosis treatment. Am J Public Health. 2015;105(5):930–7.
11. 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(10):1129–37.
12. Migliori GB, Marx FM, Ambrosino N, Zampogna E, Schaaf HS, van der Zalm MM, et al. Clinical standards for the assessment, management and rehabilitation of post-TB lung disease. Int J Tuberc Lung Dis. 2021;25(10):797–813.
13. Rossato Silva D, Paula Santos A, Visca D, Bombarda S, Maria Pretti Dalcolmo M, Galvão T, et al. Brazilian Thoracic Association recommendations for the management of post-tuberculosis lung disease. J Bras Pneumol. 2024;49, e20230269.
14. Janete Inwentarz S, Migliori GB, Lagrutta L, Bornengo F, Falco JL, De Sosa Márquez Y, et al. Recomendaciones para el manejo de la Enfermedad Pulmonar Post Tuberculosis. Respirar. 2024;16(3):271–88.
15. World Health Organization. Policy brief on tuberculosis-associated disability. 2023 [accessed 28 Feb 2025]. Available from: https://www.who.int/publications/i/item/9789240077799.
16. Alene KA, Hertzog L, Gilmour B, Clements ACA, Murray MB. Interventions to prevent post-tuberculosis sequelae: a systematic review and meta-analysis. EClinicalMedicine. 2024;70:102511.
17. Silva DR, Santos AP, Visca D, Bombarda S, Dalcolmo MMP, Galvão T, et al. The potential for vaccines to aid the treatment of post-TB lung disease. Int J Tuberc Lung Dis. 2024;28(2):111–2.
18. Nasiri MJ. Vaccination role in post-tuberculosis lung disease management: a review of the evidence. Pulmonology. 2025;31(1):2416801.
19. Ando M, Mori A, Esaki H, Shiraki T, Uemura H, Okazawa M, et al. The effect of pulmonary rehabilitation in patients with post-tuberculosis lung disorder. Chest. 2003;123(6):1988–95.
20. Visca D, Zampogna E, Sotgiu G, D'Ambrosio RCL, Saderi L, Pegoraro V, et al. Pulmonary rehabilitation is effective in patients with tuberculosis pulmonary sequelae. Eur Respir J. 2019;53(3):1802184.
21. Silva DR, Mello FCQ, Galvão T, Dalcolmo MP, Santos APV, Torres DFM, et al. Pulmonary rehabilitation in patients with post-tuberculosis lung disease: a prospective multicentre study. Arch Bronconeumol. 2025, https://doi.org/10.1016/j.arbres.2025.02.007
22. du Cros P, Greig J, Alffenaar JWC, Cross GB, Cousins C, Berry C, et al. Standards for clinical trials for treating TB. Int J Tuberc Lung Dis. 2023;27(12):885–98.
23. Stop TB Partnership. Global plan to end TB 2023–2030; 2022 [accessed 28 Feb 2025]. Available from: https://www.stoptb.org/what-we-do/advocate-endtb/global-plan-end-tb/global-plan-end-tb-2023-2030.
24. The Global Fund. Information Note – Tuberculosis Allocation Period 2023–2025; 2022. Available from: https://resources.theglobalfund.org/media/14324/cr_tuberculosis_infonote_en.pdf. Accessed 28 February 2025.
25. Silva DR, Inwentarz S. Guidelines for the diagnosis and management of post-TB lung disease: a call to action. IJTLD Open. 2024;1(13):101.

Denise Rossato Silva [a], Emanuele Pontali [b], Yousra Kherabi [c,d], Lia D'Ambrosio [e], Rosella Centis [f], Giovanni Battista Migliori [f,*]

[a] *Faculdade de Medicina, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil*
[b] *Department of Infectious Diseases, Galliera Hospital, Genoa, Italy*
[c] *Infectious and Tropical Diseases Department, Bichat-Claude Bernard Hospital, Assistance Publique-Hôpitaux de Paris, Université Paris Cité, Paris, France*
[d] *Université Paris Cité, Inserm, IAME, Paris, France*
[e] *Public Health Consulting Group, Lugano, Switzerland*
[f] *Servizio di Epidemiologia Clinica delle Malattie Respiratorie, Istituti Clinici Scientifici Maugeri IRCCS, Tradate, Italy*

*Corresponding author.
E-mail address: giovannibattista.migliori@icsmaugeri.it (G.B. Migliori).