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## **Original Article**

# The Impact of Heart Disease on the Characteristics of Pulmonary Tuberculosis: The Extent of Pulmonary Involvement, Evolution under Treatment & Treatment Outcome

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ARTICLEINFO	ABSTRACT
Article history:	Methods: We report a retrospective study analysing the characteristics of pulmonary tuberculosis in patients
Received: 26 August, 2020	with pulmonary tuberculosis with heart disease and in tuberculosis patients with no obvious history, treated
Accepted: 13 October, 2020	in the pulmonology department between 2017 and June 2020.
Published: 29 October, 2020	Results: Tuberculosis patients with heart disease present more extensive forms than patients without a
Keywords:	history (p <0.001), with more occurrence of treatment failure and sequelae (p = $0.01$ ), and more risk of death
Heart disease	compared to the control group without heart disease but without significant difference compared to the
tuberculosis	literature. While the two groups did not differ in terms of cure and negativation of bacteriological tests after
pulmonary	two months of treatment $(p > 0.05)$ .
	Conclusion: Heart disease has a significant impact on the history of pulmonary tuberculosis therefore they
	affect the quality of life of patients.

#### Introduction

At present, tuberculosis (TB) is the most widespread infectious disease in the world, it is a bacterial and contagious disease and a chronic granulomatous disease with a unique latent stage caused by the acid-fast bacillus (AFB) *Mycobacterium tuberculosis*. The lung is the most affected location. Globally, the incidence estimated by WHO at 10.4 million cases in 2016, is the second leading cause of death from infectious disease and was responsible for 1.674 million deaths in 2016 [1]. TB the ninth leading cause of death and for the past 5 years, the leading cause of death from a single infectious disease agent [1, 2]. The clinical and paraclinical presentations of tuberculosis vary according to the terrain, the antecedents and the immune status of the host, we report a retrospective study allowing to analyse the peculiarities of pulmonary tuberculosis in patients with heart disease in comparison with patients with no history.

#### Methods

### I Patients

These are male and female patients aged over 14, treated in the pulmonology service of the military hospital of Rabat and Guelmim and who represented new cases of pulmonary tuberculosis, uncomplicated and without multiple involvement (in this study, only one location was retained, it is the pulmonary location only), with and without heart disease whatever its form (valve disease, arrhythmia, arterial hypertension, etc.). In fact, the target patients of the study were divided into 2 populations, pulmonary tuberculosis patients with no history and pulmonary tuberculosis patients with heart disease. Patients are excluded from the study if they had unstable or untreated heart disease within 4 weeks of the screening visit, if they had another associated chronic pathology, or if they had a relapse of the tuberculosis or a resistant form, the lost to follow-up are also excluded.

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#### II Study Design

This is a retrospective study, analysing, in patients with pulmonary tuberculosis with heart disease and in tuberculosis patients with no obvious history treated in the pulmonology department between 2017 and June 2020, the characteristics of pulmonary tuberculosis in time of diagnosis, during treatment and after the end of the total expected duration of this anti-bacillary treatment. The diagnosis is based either on bacteriological confirmation or on a set of clinical biological and radiological arguments in the absence of bacteriological evidence in favor. After the screening visit, patients are hospitalized in the department for at least a week to perform a clinical and laboratory examination, the purpose of which is to assess the general condition and to initiate anti-bacillary treatment. After this run-in period, the patients benefited from a monthly medical follow-up, a bacteriological followup in the 2<sup>nd</sup>, 4<sup>th</sup> and 6<sup>th</sup> month of treatment, with a radiological control at the end of treatment in order to compare with the radiological image at the time of diagnosis and discover possible pulmonary sequelae.

#### III Assessment

Thanks to the diagnostic means and the medical and paramedical followup of the patients, it was possible to determine the particularities of pulmonary tuberculosis in the two populations. The evolution is said to be unfavorable if during the follow-up visits the patients do not show clinical improvement and/or the tests for *Mycobacterium tuberculosis* in the sputum remain positive on direct examination or in culture. For this study, treatment outcomes distinguished between cure, sequelae, treatment failure, and death.

#### **IV Statistical Methods**

This is a study seeking to demonstrate the impact of heart disease on the presentation of pulmonary tuberculosis at the time of screening (extensive pulmonary tuberculosis [involvement of more than two lobes] or not), on the course of the disease (favorable or not) and the results of

Table 1: Basic cha	aracteristics of the	patients.
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the treatment. The basic characteristics of the patients in each group were collected:

i. Mean age, mean weight and mean body mass index (BMI) ± standard deviation (SD).

ii. The sex as a percentage (%) of the size of each group.

- The categorical data are expressed in absolute numbers and as a percentage of the size of each group studied, they are:
- i. The extent of pulmonary involvement at diagnosis (percentage of extensive involvement in each group)
- The course of the disease (clinical examination and bacteriological control according to the set schedule)
- iii. Treatment results, with the calculation of the relative risk (RR) for the occurrence of death at a 95% confidence interval (CI), the sequelae of tuberculosis and treatment failure are also explored.

The expected degree of statistical significance is represented by the P-value, or 0.05.

#### Results

87 patients with new cases of pulmonary tuberculosis associated with heart disease were recorded during the study period, 7 patients were excluded because they presented another associated pathology. The size retained for the first group is thus 80 (n1) patients. We also chose 80 (n2) patients with no history and with pulmonary tuberculosis to form the second group, the same size as the first group to ensure more statistical relevance. The difference is significant between the two groups concerning the occurrence of extensive pulmonary tuberculosis (n1 = 55% vs n2 = 21.25%; p <0.001), the unfavorable evolution at the end of the 6<sup>th</sup> month and the occurrence of treatment failure ( n1 = 12.5% vs n2 = 7.5%; p = 0.01), the 1<sup>st</sup> group is most affected by the sequelae of tuberculosis in 47.5% of patients vs. 18.75% in the 2<sup>nd</sup> group (p = 0.01). In addition, patients with heart disease have 3 times the risk of death than the control group with no history (RR 3; 95% CI, 0.24-5.76) (Tables 1 & 2).

Characteristics:	Group 1 (with heart disease) n1=80	Group 2 (without heart disease) n2=80
Mean age (SD) (Ys)	53,88±(8,47)	35,62±(12,59)
Mean weight (SD) (Kg)	68,3±(8,95)	58,6±(7,40)
Mean BMI (SD) (Kg/m <sup>2</sup> )	19,8±(3,22)	19,7±(1,83)
Male n (%)	66 (82,5)	53 (66,25)

**Table 2:** Categorical characteristics of patients.

Characteristics:	Group 1 (with heart disease)	Group 2 (without heart disease)	RR (95%, CI)	p value
Extensive pulmonary tuberculosis n (%):	44 (55)	17 (21,25)		<0,001
Unfavorable evolution n (%):				
End of 2nd month	25 (31,25)	20 (25)		0,2
End of 4th month	18 (22,5)	11 (12,75)		
End of the 6th month	10 (12,5)	6 (7,5)		0,01
Results n (%):				
Healing	62 (77,5)	70 (87,5)		0,2
Failure	10 (12,5)	6 (7,5)		0,01
Sequelae	38 (47,5)	15 (18,75)		0,01
Death	6 (7,5)	2 (2,5)	3 [0,24-5,76]	0,2

#### Discussion

Our study made it possible to show that heart disease has a significant impact on the history of pulmonary tuberculosis, in fact tuberculosis patients with heart disease present more extensive forms than patients without a history (p <0.001), with more occurrence of treatment failure and sequelae (p = 0.01), and more risk of death compared to the control group without heart disease but without significant difference compared to the literature. While the two groups did not differ in terms of cure and negativation of bacteriological tests after two months of treatment (p> 0.05). At present, tuberculosis (TB) is the most widespread infectious disease in the world, it is a contagious disease whose physiopathology and immune response observed in infected subjects leads to two nosological entities: latent tuberculosis infection (LTBI) and tuberculosis disease (TBD). The transition from LTBI to TBD can be favored by several factors including stress, immune deficiency, toxic habits and chronic pathologies such as diabetes, psychiatric disorders and cardiovascular pathologies which are themselves influenced by the above factors and can contribute to endogenous reactivation of the disease [3].

Regular monitoring of the patient is necessary in order to evaluate the effectiveness of the treatment and to detect any possible adverse effects, Monitoring the effectiveness of the treatment is based on: clinical examination (monitoring of temperature, weight and functional symptoms); chest X-ray, indeed it is recommended to perform a chest Xray at the end of treatment; and bacteriological examinations, the bacteriological negativation of the sputum is generally obtained during the first 2 months of treatment, Several studies report a proportion greater than 20% of initially bacilliferous patients, keeping direct positive microscopic examinations after two months of treatment [4]. In a Portuguese series, at two months of treatment, 25% of patients had direct positive examinations and 27% a positive culture [5]. Although some radiographic signs of post-primary tuberculosis may be common to those of primary tuberculosis, an upper lobe predominance, an absence of lymphadenopathy and a tendency to excavation are more readily found [6].

Reactive tuberculosis usually occurs in secondary foci in the apical and posterior segments of the upper lobes, less frequently in the apical segments of the lower lobes. Bilateral upper lobe localization is noted in 32 to 64% of cases, with an asymmetric appearance in most cases [7]. Multilobar involvement is common, progression to complete lobe or pulmonary involvement with destruction may be encountered. The sequelae of primary infection are often visualized. Indeed, radiological manifestations of pulmonary tuberculosis may vary depending on host factors, particularly history of tuberculosis, age and immune status of the subject [6]. Regression without radiological sequelae is observed in two thirds of cases. In a third of cases, the scar persists, sometimes calcified: this is the Ghon complex. The association of hilar ganglia and a calcified parenchymal scar is called the Ranke complex [8].

TB related indicators were established by the United Nations (UN) 2000 to 2015 Millennium Development Goals (MDGs) with the aim of reversing the TB incidence. The Stop TB Partnership developed 2 additional targets including reducing TB prevalence and mortality by 50% by 2015 compared with 1990, the WHO developed a set of milestones and targets for 2025 and 2035 The proportion of people who die from TB must be reduced from 17% in 2015 to 10% by 2020 and

6.5% in 2025 [2]. Drug-susceptible TB is treated with a 6-month regimen that includes isoniazid, rifampicin, ethambutol, and pyrazinamide for the first 2 months followed by isoniazid and rifampicin in the subsequent 4 months [9, 10].

Treatment outcomes reported to the WHO have demonstrated success rates of 80% to 86% since 2000 [2]. Reasons of treatment failure are still unknown and the death rate due to TB is increasing. After going through the treatment there are several outcomes that a patient may fall into. Those outcomes include completed, cured, died, failure, lost to follow up, still on treatment and relapse. If the therapy went successful, then the patient is tagged as cured of TB disease and died in case of the patient's death during or after the treatment. Treatment failure cases are increasing in the world due to many reasons such as irregularity is one of the main causes of treatment failure like the presence of pulmonary excavation, the absence of supervised treatment delivery (directly observed therapy [DOT]), and resistance to rifampicin [11]. The difficulty in controlling the disease comes from the high prevalence of latent tuberculosis cases, susceptible to reactivation. The groups most at risk are migrants, disadvantaged socioeconomic backgrounds and patients with chronic diseases [12]. Pulmonary tuberculosis, the most common form of the disease, is a significant but underestimated cause of chronic lung disease associated with significant global morbidity and mortality [13].

Tuberculosis rarely requires admission to intensive care. The latest studies report that only 5 to 6% of patients hospitalized for active tuberculosis require intensive care, but the mortality of patients admitted to intensive care for respiratory failure attributed to tuberculosis is high with mortality varying from 17% to 85% in the literature [14]. A prospective cohort study among adults treated for pulmonary tuberculosis in Vietnam found that patients with tuberculosis had a markedly elevated risk of death, particularly in the post-treatment period. In total, 9% of patients died within 2-3 years of treatment initiation; 3.1% during treatment and 5.8% after discharge. The standardized mortality ratio compared with population controls, in a setting with a low prevalence of HIV infection, was 4.0 (95% CI 3.7-4.2) [15]. A systematic review of 6922 deaths in 40781 tuberculosis cases and community controls calculated a pooled standardized mortality ratio of 2.91 (95% CI 2.21-3.84), which increased to 3.76 (3.04-4.66) when restricted to tuberculosis cases with confirmed treatment completion or cure [16]. Study heterogeneity was pronounced, and few confounding factors could be considered. However, the direction of the effect and effect estimates were similar when stratified by tuberculosis type, sex, age, and country-income category.

Cardiovascular disease was the most common cause of death among those in whom this could be assessed, and mechanisms linking the tuberculosis and cardiovascular disease epidemics have been considered [17]. The presence of extensive residual lung lesions may be a predictor of permanent disability following tissue destruction, and susceptibility to opportunistic infections, leading to reduced quality of life [18]. In addition, the extent of disease is one of the risk factors involved in TB mortality rates [19]. The histopathological findings resulting from tuberculosis include the formation of caseous granuloma, tissue liquefaction and formation of pulmonary cavities [18]. From these changes, residual lesions remain in many patients, resulting in pulmonary sequelae. Delays in the diagnosis of TB lead to the increase in lung damage and more frequent co-morbidities and impairment of quality of life [20].

#### Conclusion

the repercussions of heart disease on the quality of life of tuberculosis patients is obvious; this requires therapeutic reinforcement on the cardiac level from the start of tuberculosis treatment, the interest of screening in this category of patients.

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#### **Conflicts of Interest**

None.

#### REFERENCES

- 1. World Health Organization (2017) Global tuberculosis report 2017.
- Floyd K, Glaziou P, Zumla A, Raviglione M (2018) The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. *Lancet Respir Med* 6: 299-314. [Crossref]
- Maitre T, Robert J, Veziris N (2018) Introduction-Epidemiology of latent and active tuberculosis. *Rev Mal Respir* 35: 859-861. [Crossref]
- Ben Amar J, Dhahri B, Aouina H, Azzabi S, Baccar MA et al. (2015) Traitement de la tuberculose. *Rev Pneumol Clin* 71: 122-129. [Crossref]
- Caetano Mota P, Carvalho A, Valente I, Braga R, Duarte R (2012) Predictors of delayed sputum smear and culture conversion among a Portuguese population with pulmonary tuberculosis. *Rev Port Pneumol* 18: 72-79. [Crossref]
- Goo JM, Im JG (2002) CT of tuberculosis and nontuberculous mycobacterial infections. *Radiol Clin North Am* 40: 73-87. [Crossref]
- McAdams HP, Erasmus J, Winter JA (1995) Manifestations radiologiques de la tuberculose pulmonaire. *Radiol Clin North Am* 33: 655-678.

- Fockyee C, Beigelman C, Daou S, Soussan M, Brauner M et al. (2013) Imagerie de la tuberculose pulmonaire. *Radiol Image Med Cardiovasc Thorac Cervic* 31: 1-21.
- World Health Organization (2018) Early detection of tuberculosis: an overview of approaches, guidelines and tools. *Geneva (Switzerland)*.
- World Health Organization (2015) Implementing tuberculosis diagnostics: policy framework. *Geneva (Switzerland)*.
- Muhammad A, Azhar M, Usman M (2020) A machine learning-based framework for Predicting Treatment Failure in tuberculosis: A case study of six countries. *Tuberculosis* 123: 101944. [Crossref]
- Horsburgh CR, Rubin EJ (2011) Clinical practice. Latent tuberculosis infection in the United States. N Engl J Med 364: 1441-1448. [Crossref]
- Byrne AL, Marais BJ, Mitnick CD, Lecca L, Marks GB (2015) Risk factors for and origins of COPD. *Lancet* 385: 1723-1724. [Crossref]
- Erbes R, Oettel K, Raffenberg M, Mauch H, Schmidt Ioanas M et al. (2006) Caractéristiques et évolution des patients atteints de tuberculose pulmonaire active nécessitant des soins intensifs. *Eur Respir J* 27: 1223-1228.1
- Fox GJ, Nguyen VN, Dinh NS, Nghiem LPH, Le TNA et al. (2019) Post-treatment mortality among patients with tuberculosis: a prospective cohort study of 10 964 patients in Vietnam. *Clin Infect Dis* 68: 1359-1366. [Crossref]
- Romanowski K, Baumann B, Basham CA, Khan FA, Fox GJ et al. (2019) Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 19: 1129-1137. [Crossref]
- Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M (2009) Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med* 68: 2240-2246. [Crossref]
- Pasipanodya JG, Miller TL, Vecino M, Manguia G, Garmon R et al. (2007) Pulmonary impairment after tuberculosis. *Chest* 131: 1817-1824. [Crossref]
- Kim HY, Song KS, Goo JM, Lee JS, Lee KS et al. (2001) Thoracic sequelae and complications of tuberculosis. *Radiographics* 21: 839-858. [Crossref]
- Lee JH, Chang JH (2003) Lung function in patients with chronic airflow obstruction due to tuberculous destroyed lung. *Respir Med* 97: 1237-1242. [Crossref]