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ORIGINAL RESEARCH

Assessment of Effective Anti-TB Regimens and Adverse Outcomes Related Risk Factors in the Elderly and Senile-Aged TB Patients

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Objective: Compared to younger patients with tuberculosis (TB), elderly and senile-aged patients with TB had a higher incidence of adverse outcomes particularly in terms of lost to follow-up and deaths. Our study aimed to gain insight into the effectiveness of anti-tuberculosis (anti-TB) treatment in the elderly or senile-aged patients and identify the risk factors for adverse outcomes.

Methods: The case information was obtained from the "Tuberculosis Management Information System". From January 2011 to December 2021, this retrospective analysis was conducted in Lishui City, Zhejiang Province to observe and record the outcomes of elderly patients diagnosed with TB who agreed to receive anti-TB and(or) traditional Chinese medicine(TCM) treatment. We also employed a logistic regression model to analyze the risk factors for adverse outcomes.

Results: Among the 1191 elderly or senile-aged patients with TB who received the treatment, the success rate was 84.80% (1010/1191). Using logistic regression analysis, several risk factors for adverse outcomes (failure, death, loss to follow-up) were identified, including age ≥ 80 years (OR 2.186, 95% CI 1.517~3.152, $P<0.001$), lesion area ≥ 3 lung fields (OR 0.410, 95% CI 0.260~0.648, $P<0.001$), radiographic lesions failing to improve after 2 months of treatment (OR 2.048, 95% CI 1.302~3.223, $P=0.002$), sputum bacteriology failing to turn negative after 2 months of treatment (OR 2.213, 95% CI 1.227~3.990, $P=0.008$), lack of a standardized treatment plan (OR 2.095, 95% CI 1.398~3.139, $P<0.001$), and non-involvement of traditional Chinese medicine (OR 2.589, 95% CI 1.589~4.216, $P<0.001$).

Conclusion: The anti-TB treatment success rate in the elderly and senile-aged patients is suboptimal. Contributing factors include advanced age, extensive lesions, and low sputum negative conversion rate during the intensive treatment phase. The results will informative and could be useful for policy maker for to control of reemergence of TB in big cities.

Keywords: anti-tuberculosis treatment, lung, senile-aged patients, Tuberculosis, risk factors

Introduction

Tuberculosis (TB) is a chronic infectious disease that is primarily transmitted through the respiratory tract, and remains a significant global public health and social problem.[1] According to the World Health Organization (WHO) Global Tuberculosis Report 2022,[2] the estimated number of new TB cases in China in 2021 was 780,000 (down from 842,000 in 2020), with an estimated incidence rate of 55/100,000 (down from 59/100,000 in 2020). In 2021, it is estimated that there will be about 450,000 new cases of multidrug-resistant tuberculosis/rifampicin resistant tuberculosis (MDR/RR-TB) in the world, an increase of 3.1% over the 437,000 cases in 2020. It is estimated that 3.6% of new patients and 18% of retreated patients worldwide are MDR/RR-TB. The top three countries with the highest incidence of MDR/RR-TB are India (119,000, 26%), Russia (38,000, 8.5%), and Pakistan (36,000, 7.9%). The estimated incidence of MDR/RR-TB in China is 33,000 (7.3%), ranking fourth in the world. In 2021, approximately 191,000 patients worldwide died due to MDR/RR-TB.

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TB in senile-aged patients refers to the pulmonary TB suffered by the elderly aged 60 years or more.[3] This includes initially treated TB resulting from endogenous relapse and/or exogenous reinfection mechanisms, relapse of previous TB, as well as persistent retreated and chronic TB. Population aging is a prominent problem that many countries are facing today. As population ages, the proportion of senile-aged patients with TB is consistently increasing each year.[4] Most cases of TB in the elderly are linked to the reactivation of lesions that have remained dormant. The awakening of these lesions is attributable to changes in the immune system related to senescence.[5,6] We summarized the clinical characteristics of early stage TB in senile-aged patients as follows:[7] patients are typically elderly and frail with low immunity and multiple comorbidities, the lesions tend to spread more easily, the probability of sputum smear and culture positive pulmonary TB is higher compared to other populations. In addition, the adverse drug reaction rate is higher, drug-resistant TB is more likely to occur, and mortality rate from tuberculosis remains higher in elderly patients. As a result, the elderly are considered a high-risk group for TB.[8] The above unfavorable factors may lead to a low success rate of treatment for elderly and senile-aged patients with TB, but it has not been confirmed.

Due to the atypical clinical symptoms and imaging manifestations of elderly and senile-aged patients with TB, many complications and low positive rate of some laboratory tests, it has become a difficulty and challenge in tuberculosis control.

Diagnosis is difficult as symptoms of active TB are nonspecific and less pronounced in the elderly. Comorbidities, which are more common in older patients, may mask the symptoms of TB. For example, those with chronic coughing due to COPD may have a delayed presentation or diagnosis. However, conversely, they may also have closer healthcare contact.[9]

Acid-fast bacilli (AFB) staining is still the most widely used rapid diagnostic method for tuberculosis. The sensitivity of microscopic examination of acid-fast bacilli (AFB) in sputum specimens is 50% or less. The WHO recommends mycobacterial culture, which exhibits high sensitivity for detecting M. tuberculosis as the diagnostic gold standard. Unfortunately, due to the slow growth of M. tuberculosis, mycobacterial culture cannot meet the clinical needs of the diagnosis and treatment of TB. Rapid molecular biology techniques complement traditional cultures, allowing rapid diagnosis and study of genotypic bacterial resistance particularly to rifampicin with the GeneXpert MTB/RIF assay. Early diagnosis and analysis of drug resistance are crucial for effective patient management and prevention of the spread of MDR-TB.

GeneXpert MTB/RIF is a method that uses real-time fluorescence quantitative nucleic acid amplification technology to detect the presence of Mycobacterium tuberculosis infection and whether the bacterium is resistant to rifampicin. It can quickly diagnose within 2 hours. Current research shows that[10] The real-time fluorescence quantitative nucleic acid amplification detection technology for Mycobacterium tuberculosis/rifampicin resistance (GeneXpert MTB/RIF) has a sensitivity of 98% to 100% for sputum smear positive specimens, 57% to 83% for sputum smear negative specimens, and a specificity of 65% to 97%. Research report[11] Among elderly suspected pulmonary tuberculosis patients, the sensitivity of sputum GeneXpert MTB/RIF was 45.45%, significantly higher than sputum smear (22.73%). Sputum GeneXpert MTB/RIF can help clinical detection of pulmonary tuberculosis patients from the perspective of etiology faster, improving the diagnostic rate.

Furthermore, with extended families being common in China, young parents often go out to work, leaving their children to be taken care of by the grandparents, in which case senile-aged patients with TB are a potential source of infection for TB in children.

Traditional Chinese medicine (TCM) has been used for the treatment of TB for thousands of years, and modern medical research has also confirmed that TCM could play a role in improving patients' clinical symptoms, regulating host immune function, and preventing adverse drug reactions by assisting in the treatment of pulmonary tuberculosis through syndrome differentiation and comprehensive treatment of TCM. It could effectively compensate for the shortcomings of Western medicine chemotherapy schemes, increase the cure rate, and reduce the mortality rate. In China, TCM assisted treatment is an indispensable part of promoting the development of TB prevention and control. Therefore, this study also analyzed the impact of participation in TCM treatment on the outcome of elderly TB treatment.

From January 2011 to December 2021, a retrospective analysis was conducted in Lishui City, Zhejiang Province to observe and record the outcomes of elderly patients diagnosed with TB who agreed to receive anti-TB and(or) traditional Chinese medicine(TCM) treatment. We also employed a logistic regression model to analyze the factors that may have influenced the outcome. The aim of this study was to examine the efficacy of anti-TB and(or) traditional Chinese medicine(TCM) treatment administered over a period of 11 years to elderly or senile aged patients with TB in Lishui, Zhejiang Province, China and determine its associated influencing factors, to provide objective reference for policy makers.

Participants and Methods

Study Participants

The case information for this study was obtained from the "Tuberculosis Management Information System", a subsystem of the "China Information System for Disease Control and Prevention". In this study, we collected data from senile-aged patients with TB diagnosed in designated hospitals for TB in Lishui between January 2011 and December 2021. Diagnosis and treatment flow of TB patients was showed in Figure 1. Patients who met the following inclusion criteria were included: ① Diagnosed of rifampicin-sensitive TB or TB of unknown drug resistance, including clinical diagnosis cases and confirmed cases; ② Aged 60 years and above; ③ possessing a registered residence or temporary residence permit to reside in Lishui; ④ with complete treatment results information. Patients who stopped treatment due to "change in diagnosis" or "changed treatment to rifampicin-resistant treatment" were excluded. Case screening in this study was showed in Figure 2.

Study Methods

The study participants were treated with first-line anti-TB drugs. Sputum smear test for acid-fast bacilli (AFB) and/or mycobacteria culture and identification were performed at the end of Month 2, Month 5, and the end of treatment course. Patients who had a positive AFB result at the end of Month 2 were required to undergo an additional sputum smear test and/or mycobacteria culture and identification at the end of Month 3. Chest X-ray or chest computed tomography (CT) scans were performed at the end of Month 2 and the course of treatment course. Blood routine, liver function, and kidney function were tested once a month, and clinical symptoms and adverse reactions were recorded until the end of the study period.

The treatment outcomes were evaluated using the evaluation criteria for rifampicin-sensitive patients with TB in the *Technical Specifications for Tuberculosis Prevention and Control in China (2020 Edition)*. The outcomes were classified as cured, treatment completion, treatment failure, death, and lost to follow-up. In this study, cured and treatment completion were defined as treatment success, while treatment failure, death, and lost to follow-up were classified as adverse outcomes. The factors that influenced treatment outcomes in senile-aged patients with TB were analyzed.

Related Definitions

Cured

Patients with positive etiological results who completed the full course of treatment, and their smear or culture results at the end of the final month of treatment and the last test results were negative.

Treatment Completion

Patients with negative etiological results, who completed the prescribed course of treatment and had negative sputum smear or culture results at the end of the treatment course or no sputum test was performed. Patients with positive etiological results, who completed the prescribed course of treatment and there was no sputum test result at the end of the course of treatment, however, the last sputum smear or culture result was negative.

Treatment Failure

The sputum smear or culture result at the end of the Month 5 of treatment or at the end of the course of treatment was positive.

Death

The patient died for any reason before or during the treatment.

Lost to Follow-Up

The treatment was not started, or treatment was interrupted for 2 consecutive months or more.

Bacteriological Negative Conversion

The results of two consecutive sputum smear or sputum culture tests were negative (at an interval of at least 30 days), and the date of negative conversion is the date of collection of sputum samples with the first negative result.

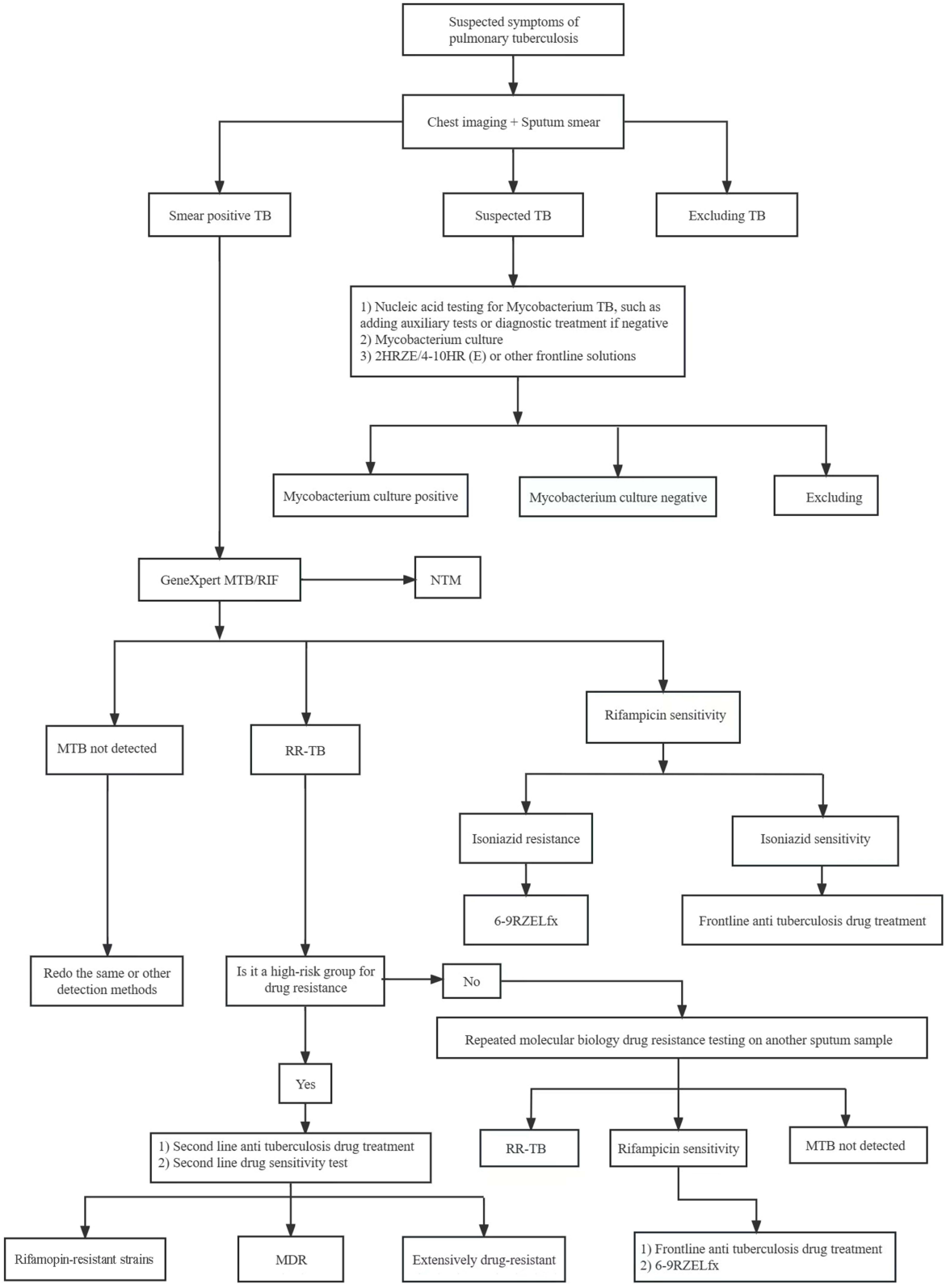

Figure 1 Diagnosis and Treatment Flow Chart of Pulmonary Tuberculosis Patients.

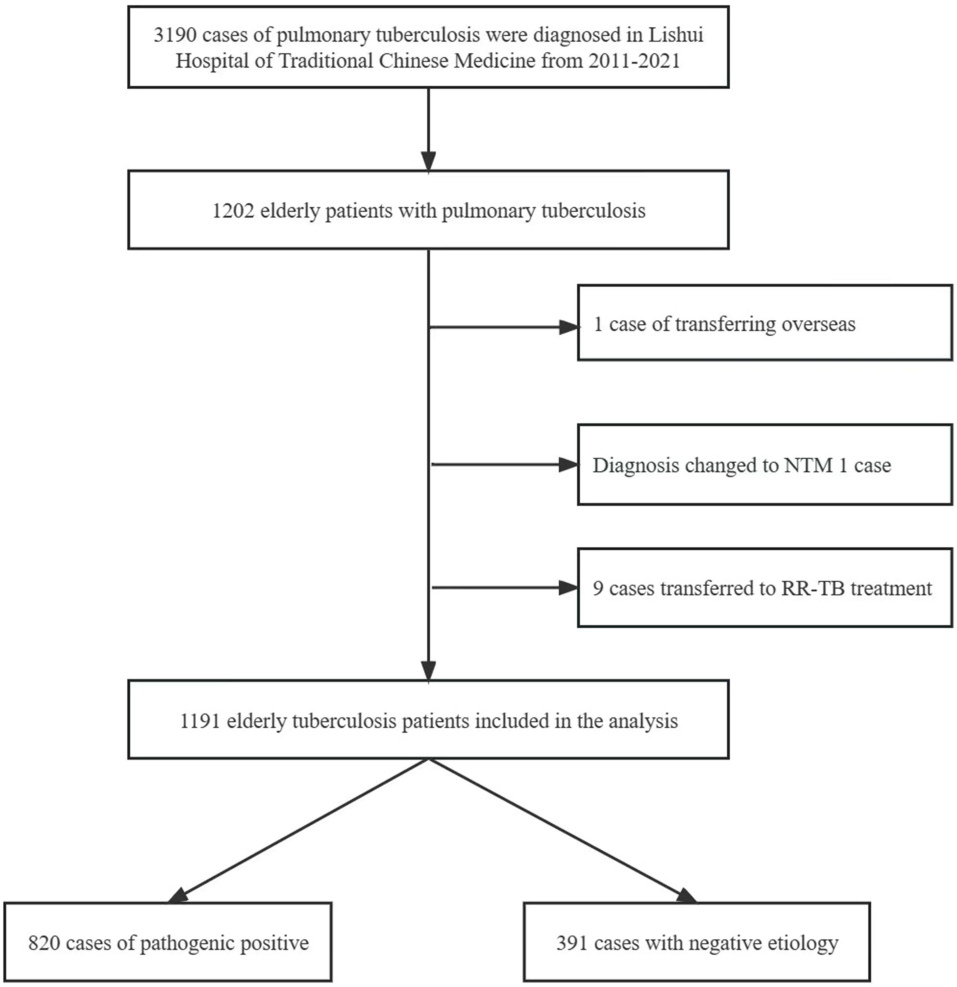

Figure 2 Flow Chart of Case Screening in this Study.

Delayed Treatment

The time interval from the onset of symptoms to the first visit of the patient exceeded 2 weeks.[12]

Involvement of Traditional Chinese Medicine (TCM)

During anti-TB treatment, if anti-TB mixture was orally administered and/or external acupoint was applied according to the syndrome differentiation for 2 or more months, it was recorded as TCM involvement. Otherwise, it was recorded as non-involvement of TCM.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics 23.0 software. To analyze the influencing factors of the treatment outcome of the senile-aged patients with TB, the single-factor analysis was performed using chi-squared test. To control the effects of confounding factors including age, lesion range, radiographic lesion improved after 2 months of treatment, sputum bacteriological result turned negative after 2 months of treatment, use of standardized treatment plan, use of FDC, and involvement of TCM on the outcome of interest, the multi-factor analysis was performed using the binary logistic regression model. The difference was statistically significant when $P < 0.05$.

Results

General Information of the Participants

A total of 1191 senile-aged patients with TB were included, consisting of 911 males (911/1191, 76.49%) and 280 females (280/1191, 23.51%). 951 cases had a local registered residence (951/1191, 79.85%), and 240 cases had a non-local registered residence (240/1191, 20.15%). There were 1063 initially treated cases (1063/1191, 89.25%) and 128 retreated cases (128/1191, 10.75%); 800 patients were etiologically positive (800/1191, 67.17%) while 391 patients were etiologically negative (391/1191, 32.83%). Moreover, 913 patients experienced delayed treatment (913/1191, 76.66%); 631 patients received standardized treatment plan (631/1191, 52.98%); 211 patients were treated with fixed dose combination (FDC) anti-TB drugs (211/1191, 17.72%). TCM was administered for ≥ 2 months to 1021 patients (1021/1191, 85.73%). Of the 389 patients who underwent isoniazid drug sensitivity results, 359 (359/389, 92.29%) were isoniazid-sensitive while 30 (30/389, 7.71%) were isoniazid-resistant.

Treatment Outcome

The treatment success rate of 1191 senile-aged patients with TB was 84.80% (1010/1191), of which 601 cases were cured, accounting for 50.46%; 409 cases completed the course of treatment, accounting for 34.34%; 11 cases failed the treatment, accounting for 0.92%; 94 cases were lost to follow-up, accounting for 7.89%; and 76 cases died, accounting for 6.38%. During the COVID-19, the mortality rate of elderly TB patients in 2020 and 2021 was 10.11% and 11.35%, respectively. The missed follow-up rate of elderly TB patients in 2021 was 16.76% (See Table 1).

Analysis of Influencing Factors of Treatment Outcome in Senile-Aged Patients with TB

Single-Factor Analysis

Among the 1191 senile-aged patients with TB, 1010 cases were successfully treated, accounting for 84.80%; 181 cases had adverse outcomes, accounting for 15.19%. Factors such as age ≥ 80 years, lesion area ≥ 3 lung fields, radiographic lesion improvement after 2 months of treatment, sputum bacteriological result turning negative after 2 months of treatment, use of standardized treatment plan, use of FDC, and involvement of TCM were statistically correlated to the treatment outcome of senile-aged patients with TB ($P < 0.05$). However, factors such as gender, registered residence, occupation, initial treatment/retreatment, positive or negative etiological result, diabetes, delayed treatment, isoniazid resistance, and occur anti-tuberculosis drugs induced hepatotoxicity (ADIH) were not statistically correlated to the treatment outcome of senile-aged patients with TB ($P > 0.05$) (See Table 2).

Table 1 Treatment Outcomes of 1191 Senile-Aged Patients with TB from 2011 to 2021

Year	Total Number	Cured		Treatment Completion		Treatment Failure		Lost to Follow-Up		Death	
		n	%	n	%	n	%	n	%	n	%
2011	90	32	35.56	46	51.11	0	0	8	8.89	4	0.44
2012	87	35	40.23	30	34.48	0	0	17	19.54	5	0.57
2013	68	36	52.94	29	45.65	1	1.47	2	2.91	0	0
2014	72	37	51.39	32	44.44	2	2.78	1	1.39	0	0
2015	75	38	50.67	35	46.67	0	0	2	2.67	0	0
2016	86	42	48.84	36	41.86	0	0	5	5.81	3	3.49
2017	96	50	52.08	31	32.29	1	1.04	5	5.21	9	9.38
2018	102	58	56.86	29	28.43	1	0.98	7	6.86	7	6.86
2019	152	89	58.55	42	27.63	2	1.32	10	6.58	9	5.92
2020	178	113	63.48	39	21.91	2	1.12	6	3.37	18	10.11
2021	185	71	38.38	60	32.43	2	1.08	31	16.76	21	11.35
Total	1191	601	50.46	409	34.34	11	0.92	94	7.89	76	6.38

Table 2 Single-Factor Analysis of Influencing Factors of Treatment Outcome for TB in Senile-Aged Patients

Item	Treatment Success (n=1010)		Adverse Outcome (n=181)		χ^2-value	*P*-value
	Number	Proportion (%)	Number	Proportion (%)		
Gender					0.751	0.386
Male	768	84.30	143	15.70		
Female	242	86.43	38	13.57		
Age (year)					36.615	<0.001*
≥ 80	200	73.26	73	26.74		
< 80	810	88.24	108	11.76		
Registered residence					0.094	0.759
Non-local	202	84.17	38	15.83		
Local	808	84.96	143	15.04		
Occupation					0.413	0.520
Non-farmers	154	83.24	31	16.76		
Farmers	856	85.09	150	14.91		
Initial treatment/ retreatment					0.855	0.355
Retreatment	105	82.03	23	17.97		
Initial treatment	905	85.14	158	14.86		
Diagnosis					0.868	0.351
Etiologically positive	673	84.13	127	15.88		
Etiologically negative	337	86.19	54	13.81		
Diabetes					2.734	0.098
Yes	89	79.46	23	20.54		
No	921	85.36	158	14.64		
Lesion range ≥ 3 lung fields					8.692	0.003*
No	310	89.60	36	10.40		
Yes	700	82.84	145	17.16		
Radiographic lesion improved after 2 months of treatment					13.979	<0.001*
Yes	915	86.16	147	13.84		
No	95	73.64	34	26.36		
Sputum bacteriological result turned negative after 2 months of treatment					6.041	0.014*
Yes	957	85.45	163	14.55		
No	53	74.65	18	25.35		
Delayed treatment					0.276	0.600
Yes	777	85.10	136	14.90		
No	233	83.81	45	16.19		
Use of standardized treatment plan					31.845	<0.001*
Yes	570	90.33	61	9.67		
No	440	78.57	120	21.43		
Use of FDC					5.473	0.019*
Yes	190	90.05	21	9.95		
No	820	83.67	160	16.33		
Isoniazid resistance					0.452	0.798
Yes	25	83.33	5	16.67		
No	301	83.84	58	16.16		
Unspecified	684	85.29	118	14.71		
Involvement of TCM					5.501	0.019*
Yes	876	85.80	145	14.20		
No	134	78.82	36	21.18		

(*Continued*)

Table 2 (Continued).

Item	Treatment Success (n=1010)		Adverse Outcome (n=181)		χ^2-value	*P*-value
	Number	Proportion (%)	Number	Proportion (%)		
Occur ADIH					0.818	0.366
Yes	126	82.35	27	17.65		
No	884	85.16	154	14.84		

Note: *P<0.05 has a statistic significance.

Table 3 Multi-Factor Logistic Regression Analysis Results of Influencing Factors of Treatment Outcome for TB in Senile-Aged Patients

Variable	Reference Group	*β*	*S.E.*	Wald	*P*	*OR*	95% CI
Age (year)							
≥80	<80	0.782	0.187	17.574	<0.001*	2.186	1.517–3.152
Lesion range ≥ 3 lung fields							
Yes	No	−0.891	0.233	14.651	<0.001*	0.410	0.260–0.648
Radiographic lesion improved after 2 months of treatment							
No	Yes	0.717	0.231	9.610	0.002*	2.048	1.302–3.223
Sputum bacteriological result turned negative after 2 months of treatment							
No	Yes	0.794	0.301	6.972	0.008*	2.213	1.227–3.990
Use of standardized treatment plan							
No	Yes	0.740	0.206	12.855	<0.001*	2.095	1.398–3.139
Use of FDC							
No	Yes	−0.043	0.290	0.022	0.883	0.958	0.543–1.690
Involvement of TCM							
No	Yes	0.951	0.249	14.597	<0.001*	2.589	1.589–4.216

Notes:*P<0.05 has a statistic significance; *β*: the "partial regression coefficient"; S.E.: the standard error of partial regression coefficient *β*; Wald: the Wald statistic used to test whether the population partial regression coefficient β has statistical significance with 0; OR: odds ratio, dominance ratio or ratio ratio which is the inverse natural logarithm of partial regression coefficient, ie exp (*β*).

Multi-Factor Logistic Regression Analysis

Multi-factor logistic regression analysis was performed to investigate the treatment outcome of senile-aged patients with TB, as the dependent variable (0 = treatment success, 1 = adverse outcome). The independent variables included age ≥ 80 years, the lesion area ≥ 3 lung fields, the improvement of radiographic lesions after two months of treatment, the negative conversion of sputum bacteriology after two months of treatment, the use of standardized treatment plan, the use of FDC, and the involvement of TCM. The results showed that age ≥ 80 years, lesion area ≥ 3 lung fields, no improvement of radiographic lesions after two months of treatment, no negative conversion of sputum bacteriology after two months of treatment, lack of standardized treatment plan, and absence of TCM involvement were identified as risk factors for the adverse treatment outcomes of senile-aged patients with TB (See Table 3).

Discussion

China ranks third among 30 countries with a high burden of TB, with the estimated cases (780,000) lower than Indonesia (969,000) and India (2,950,000).[2] With the aging population and increasing life expectancy, TB has become more prevalent among the elderly. WHO estimates that the proportion of the Chinese population aged 60 or above is expected to increase from 12.4% (168 million) in 2010 to 28.0% (402 million) in 2040.[13] According to the Fifth National Survey on Tuberculosis Prevalence in China in 2010,[14] the prevalence of TB increases with age, and reached the peak of 866/

100,000 in the age group of 75–79. The global treatment success rate of patients newly diagnosed with TB is 85%.[12] In this study, we screened 1191 senile-aged patients with TB who had complete treatment results information between 2011 and 2021. We summarized their treatment outcomes and analyzed the related factors causing adverse outcomes. The results of our study revealed that the treatment success rate of 1191 senile-aged patients with TB was 84.80% (1010/1191), which was higher than that reported in Zhejiang Province between 2015 and 2020 (71.19%).[15] Among them, 601 cases were cured, accounting for 50.46%; 409 cases completed the course of treatment, accounting for 34.34%; 11 cases failed treatment, accounting for 0.92%; 94 cases were lost to follow-up, accounting for 7.89%; and 76 cases died, accounting for 6.38%. Compared to younger patients with TB, senile-aged patients with TB had a higher incidence of adverse outcomes particularly in terms of lost to follow-up and deaths. In this study, the rate of lost to follow-up and mortality rate of senile-aged patients with TB in Lishui, Zhejiang Province were 7.89% and 6.38%, respectively, while the rates reported in India were 14.7% and 9.3%, respectively.[16] The reason for the adverse outcome may be the higher prevalence of complications and advanced/severe diseases in the elderly.[17,18] Therefore, it is important to provide more assistance and care for elderly patients to reduce the occurrence of adverse outcomes. Furthermore, we found that the treatment success rate of the elderly decreased, highlighting the need for more effective treatment strategies for this vulnerable population. In this study, the treatment success rate of senile-aged patients with TB aged 80 years and above was only 73.26% (200/273), indicating that advanced age is a risk factor for adverse outcomes of senile-aged patients with TB. Several studies have confirmed that patients above 85 years old have a higher risk of treatment failure.[19,20] It can be concluded that elderly patients with TB (≥ 80 years), are a target group of great concern, and these patients need to be closely monitored. The national TB program should consider actively screening cases among the elderly population and incorporating them into the prevention strategy.

It is worth mentioning that the COVID-19 has been raging all over the world since the end of 2019. The long duration of its pandemic has caused an unprecedented setback in the global tuberculosis prevention and treatment, reversing the progress made in recent years in improving basic tuberculosis diagnosis and treatment services, reducing the burden of tuberculosis. Firstly, compared with 2019, the number of newly diagnosed tuberculosis patients registered and reported in 2020 decreased from 7.1 million to 5.8 million, a decrease of 18%, the first decline in the past five years, and the number of registered and reported dropped back to the level in 2012. Although this study did not make statistics on whether the incidence rate of elderly TB patients was affected by the COVID-19, during the COVID-19, the mortality rate of elderly TB patients in 2020 and 2021 was 10.11% and 11.35% respectively, and the miss follow-up rate of elderly TB patients in 2021 was 16.76%. This indicates that the COVID-19 may increase the rate of lost visits and mortality of elderly TB patients.

Several studies have confirmed that the lost to follow-up of patients with TB is significantly correlated with occupation, smoking, alcohol use, marital status, and socioeconomic status;[21] age, registered residence, occupation, sputum smear results, and types of treatment are risk factors for treatment failure.[22] Furthermore factors such as advanced age, male, non-local registered residence, retreatment, non-standard treatment, delayed treatment, and smoking have been found to be associated with a high probability of treatment failure.[23,24] Similarly, age, gender, registered residence, sputum smear results, and types of treatment are risk factors for death in patients with TB.[23] Specifically, male gender, the elderly, HIV-positive patients, etiology-positive patients, and retreated patients are at a higher risk of death during anti-TB treatment.[25] The results of this study showed that there was no significant statistical association between treatment outcomes of senile-aged patients with TB and various factors such as gender, registered residence, occupation, initial treatment/retreatment, etiology-positive status, diabetes mellitus, delayed treatment, and isoniazid resistance. However, certain risk factors were identified including age ≥ 80, lesion area ≥ 3 lung fields, radiographic lesions failing to improve after 2 months of treatment, sputum bacteriology failing to turn negative after 2 months of treatment, no standard treatment being used, and no TCM being involved. These risk factors were found to be associated with adverse outcomes, including treatment failure, death, lost to follow-up, among senile-aged patients with TB.

Among patients with TB, there are radiologically differences between young and old patients. Young patients with TB tend to have more cavities, compared to the old.[9,26] On the other hand, the results of a cross-sectional study revealed that patients aged over 60 years tend to have bilateral multiregional involvement. Additionally, while infiltration is the most common radiological finding at any age, it tends to be more prevalent in the old compared to the young.[27] Monitoring the gradual absorption and improvement of radiographic lesions is an important indicator of successful TB treatment. The

results of our study indicated certain risk factors for adverse outcomes among senile-aged patients with TB, including lesion area ≥ 3 lung fields, and radiographic lesions failing to improve after 2 months of treatment. Therefore, early diagnosis and timely treatment, combined with careful monitoring of radiographic lesions after 2 months of treatment, are crucial for successful treatment.

Mycobacteria-containing sputum culture and examination provide an objective means to evaluate the content and infectivity of bacteria in patients with TB, and can also be used to assess the therapeutic effect. Specifically, sputum smear conversion after 2 months of treatment (at the end of the intensive phase) is an early indicator of successful treatment of TB.[28] Despite having better compliance with drug therapy, the elderly patients showed a lower sputum conversion rate at the end of 2 months of treatment when compared to younger patients.[29–31] The results of some studies suggest that the high incidence of adverse drug reactions, drug interactions, and complications may lead to dose reduction and malabsorption of anti-TB drugs.[32] Other studies attribute the low sputum negative conversion rate at the end of the intensive phase to the delayed sputum conversion and excretion caused by high bacterial loads.[33] The results of the study showed that failure of the sputum bacteriology to turn negative after 2 months of treatment was a risk factor for poor treatment outcomes of senile-aged patients with TB. Therefore, early negative conversion of sputum bacteriology is a key factor in successful treatment of senile-aged patients with TB.

Since the 1980s, the 2HRZE/4HR short-course chemotherapy regimen has been widely adopted in China and has achieved a cure rate of over 90% among initially treated TB patients, with large amounts of data proving its feasibility and efficiency.[34] According to the study, the standard treatment regimen had a significantly higher success rate of 90.33% (570/631) among senile-aged patients with TB, compared with the non-standard treatment regimen group (440/560, 78.57%). Adopting the standard treatment regimen can increase the treatment success rate among senile-aged patients with TB.

Anti-tuberculosis drugs induced liver injury (ADIH) is the most common and influential adverse reaction in clinical practice. The consequence may be a decrease in patient treatment compliance. Some patients may experience non-standard treatment, interruption or even cessation of treatment, ultimately affecting treatment effectiveness to varying degrees. This could lead to treatment failure, disease recurrence, or the production of drug-resistant Mycobacterium tuberculosis. Multiple studies have suggested that age is a risk factor for the occurrence of ATDILI, which may be related to organ aging, decreased physiological function, impact on drug pharmacokinetics in the elderly, and the frequent comorbidities of multiple diseases and other medications in the elderly.[35,36] The mechanism may be related to the reduction of liver regeneration function in the elderly, the reduction of mitochondrial DNA replication, the impact on the quality and quantity, the more likely occurrence of mitochondrial dysfunction, the general decline of immune function, the increase in the secretion of proinflammatory factors, as well as the damage of the intestinal barrier in the elderly, the increase of intestinal permeability, and the proliferation of proinflammatory factors into the blood. The results of this study showed that the incidence of anti-tuberculosis drug induced liver damage in elderly TB patients was 12.85% (153/1191), but its occurrence was not statistically correlated with the treatment outcomes of elderly TB patients. Avoiding liver damage caused by anti-tuberculosis drugs during the treatment process can help improve patient compliance and treatment success rate.

Treatment of TB by TCM is characterized by holism and treatment based on syndrome differentiation, emphasizing reinforcing healthy qi and improving body resistance, while playing its anti-TB effects with western medicine to reduce the toxic side effects of chemical drugs. In recent years, the material bases for the pharmaceutical effects of many Chinese herbal compound prescriptions for TB treatment have been specified using modern experimental methods, promoting the modernization of Chinese herbal compound prescriptions, and several novel Chinese patent medicine preparations against TB have been approved by the State Food and Drug Administration (SFDA). Combining Chinese patent medicine preparations with western medicine during initial treatment or retreatment of TB or multi-drug resistant TB can effectively enhance patient immunity, alleviate clinical symptoms, and promote negative conversion of sputum bacteria, absorption of lesions, and closure of cavity, so as to improve the efficacy.[37] In this study, the anti-TB mixture (essential drugs include: Stemonae Radix, Folium Mahonia Bealei, Codonopsis Radix, Astragali Radix, Bletillae Rhizoma, Fritillariae Thunbergii Bulbus, Humuli Scandentis Herba, Radix Adenophorae Strictae, and so on) may down-regulate the VEGF expression in peripheral blood of patients with multi-drug resistant TB to inhibit angiogenesis, and up-regulate the Th17 level and down-regulate the Treg level in these patients to improve the Th17/Treg balance, thus playing its anti-TB effect, providing a basis for the research of the immune mechanism of multi-drug-resistant TB treatment by TCM anti-TB mixtures.[38,39] The most

important finding of this study is that with TCM anti-TB mixtures, the treatment success rate of senile-aged patients with TB increased to 85.78%, improving the outcome and greatly reducing the gap with WHO's target value of 90%. We believe that thanks to the "effect-enhancing and toxicity-reducing" effect of TCM, TCM + standard regimen treatment for senile-aged patients with TB can make senile-aged patients with TB more compliant and improve the success rate of treatment in countries with high TB burdens. The use of TCM is an inevitable trend for future treatment of senile-aged patients with TB.

The battle against TB has been a long-standing battle for humanity. Managing senile-aged patients with TB, which is a common infection, requires a multidisciplinary approach. However, that treating senile-aged patients with TB with western medicine alone using a TB containment strategy may not be sufficient to increase the success rate of TB treatment in countries with a high TB burden. It is therefore crucial to strengthen management and raise awareness of the disease among patients. In addition, medical staff and researchers must continue to explore new short-course regimens that involve fewer types of drugs, complemented by comprehensive treatment with TCM, while also developing and verifying anti-TB drugs in a timely manner. The results of our study indicate that advanced age, wide lesion areas, and a low negative conversion rate of sputum during the intensive phase are the main factors contributing to poor therapeutic effects. These factors can help clinicians intervene with senile-aged patients with TB in a graded manner, predict outcomes,[40] and include TCM treatment in a timely manner. Standard regimens combined with TCM is the key to increasing the success rate of anti-TB treatment for senile-aged patients, and can serve as a reference and guide for controlling the TB epidemic in Lishui City, Zhejiang Province, and achieving the goal of eradicating TB by 2030.

This study has some limitations. Firstly, this study only included some cases in the "Tuberculosis Management Information System", a subsystem of the "China Disease Prevention and Control Information System". Although the sample size is sufficient, it still cannot comprehensively display the treatment outcome of all elderly pulmonary tuberculosis and the risk factors for poor prognosis, In particular, the elderly patients affected by the COVID-19 in 2020–2021 who died of other diseases before being diagnosed with "tuberculosis" were not included in the study. In addition, this study analyzed the factors most likely to affect the treatment outcome of elderly pulmonary tuberculosis, but there are still many factors that have not been included in the study. For example, due to the high rate of adverse drug reactions, drug-resistant tuberculosis is more likely to occur in the elderly and elderly patients, which is not taken into account in this study.

Conclusion

The anti-TB treatment success rate in the elderly and senile-aged patients in Lishui City, Zhejiang Province is suboptimal. Contributing factors include advanced age, extensive lesions, and low sputum negative conversion rate during the intensive treatment phase. However, combining a standardized treatment plan with traditional Chinese medicine has been shown to improve the treatment success rate of anti-TB treatment in senile-aged patients. The results will informative and could be useful for policy maker for to control of reemergence of TB in big cities.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the Lishui Hospital of Traditional Chinese Medicine.

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Disclosure

The authors declare that they have no competing interests.

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