

LETTER OF REPLY (September 24th, 2021)

Dear Editor and reviewers,

Thank you for your comments and suggestions. We truly appreciate the encouragement. We agree with majority of the suggestions commented and made the changes in the main text and we listed below. There are some information that could not be added because it was not included in our database.

Comments	Answer	
Introduction		
You could add very briefly in the introduction the sensitivity and specificity of TST in solid organ transplant population.	Unfortunately, the sensitivity and specificity for the TST in this population is not well defined due to the absence of a gold standard test for LTBI diagnosis. Other studies in liver transplant recipients found TST positivity rate ranging from 24% to 38%. This topic is discussed in “ <i>Discussion</i> ” section.	Information added to “ <i>Introduction</i> ” and the findings of other studies are mentioned in the “ <i>Discussion</i> ” section.
Methods		
You should describe a little more the characteristics of your hospital. Does it receive patients from areas of different prevalence of TB ? Or is it homogeneous?	The hospital is a high-complexity teaching hospital providing medical care for patients from all regions of Minas Gerais state. Tuberculosis prevalence in our state is homogeneous without marked difference among different cities. Our transplant program provides transplantation of hearts, livers and kidneys, and during the period of study >80% of the livers transplanted in the state were done at the facility.	Information added to “ <i>Population study</i> ” in “ <i>Materials and Methods</i> ” section.
You should mention with more details the characteristics of the	There is a TB screening program since the beginning of transplant	Information added to “ <i>Population study</i> ” in “ <i>Materials and Methods</i> ”

LTBI detection program in your hospital. You should clearly state when the implementation started, what the implementation consists of, does it include an infectious diseases consultation? Why did it take too long to be well implemented?	activities, back in 1994, but it was restructured in 2009/2010, when institutional protocols were reviewed. Screening includes epidemiological, clinical, radiological and TST data. So far we do not have interferon-gamma release assays available, except in research protocols.	section.
Also, you mention that INH 6 months is the standard of care since 2010, you should clearly state in the methods if there was no treatment indication for LTBI prior to 2010, and the reason.	Actually, there was always the recommendation to use INH for patients with high risk of ILTB reactivation, but after 2010 an effort was made to standardize the approach, when a TB protocol was fully implemented.	Information added to “ <i>Treatment regimen for LTBI</i> ” in “Materials and Methods” section.
Also, if TST implementation was low and no treatment was available prior to 2010, should you only include patients from 2010? What is the benefit of including patients from 2005 to 2010, if you are not including them in the TST prevalence data nor in the analysis for LTBI treatment?	<p>Only patients who underwent the TST were included in the analysis. The aim was to assess the positivity of the test and clinical and laboratory variables that could be related.</p> <p>Although the test took place less frequently in the period (2005-2010), data were collected for those who performed it.</p> <p>This study was also carried out to assess adherence to the protocol and reinforce guidelines for diagnosis and therapeutic management.</p>	
And why not include patients after 2012,	This study was structured to assess the	

when you finally managed to get a TST performance of >90% ?	response of the service and to improve patient care and management of TB. After the goal was achieved, there was no continuity. Currently, the implementation of the interferon-gamma release assays is awaited for update.	
Results		
Why was TST performed in less than 50% of the study population? Was it purely due to lack of implementation or also due to shortage periods?	Especially because it was difficult to implement the test in the pre-transplant exams. In some periods there was a lack of TST, as well as implementation failure. Among the objectives of the study was the improvement of screening. There was an increasing percentage of adherence to the protocol, however the final mean was low.	
A way to see if there is no bias of selection would be to compare the general characteristics of the patients tested and the patients not tested, so you can say they are similar or not.	Unfortunately, these data were not collected for patients who did not undergo TST.	
Is there a risk of zoonotic TB in your hospital area? If so, do you have information on epidemiological risk factors for Bovis MTB?	MTB bovis disease is not a relevant problem in the population attended by our service. In the pre-transplant interview, epidemiological data on exposure to tuberculosis and also to other fungal and protozoan diseases (eg Chagas disease and Toxoplasmosis) are questioned. It is noteworthy that the patients are mostly	

	inhabitants of small towns but usually not from a rural environment. This is not objective of our study.	
Post transplant tuberculosis: Were there any cases of TB in the group that did not receive a TST? That would be important to clarify and comment on.	There is no compilation of this data, but this analysis would be interesting in a future study.	
Discussion		
Considering international guidelines recommend shorter treatments for LTBI, would it be an option to consider them in you patients' population? To tackle the issue of treatment abandonment. You should comment on that.	Certainly, shorter treatments would be desirable and possibly easier to manage for these patients.	Inserted in " <i>Discussion</i> " section
Considering the importance of LTBI detection, are there any recommendations to improve TST application? From 2012 until now, are you still confronted with problems of TST?	Although there has been substantial improvement in adherence to the testing protocol for candidates with TST after 2010, we have experienced issues with TST availability. To improve LTBI diagnosis, besides TST, the group has relied on epidemiological, clinical and radiological screening. IGRA is not available yet.	Inserted in " <i>Conclusion</i> " section
You should add in your discussion a paragraph on limitations of your study. Are there potential confounders? Is there a potential bias considering the population not tested? Are your results	This study presents several limitations that are inherent to retrospective studies and also related to patient enrollment occurring over a long period of time with the possible consequences of	Inserted in " <i>Discussion</i> " and " <i>Conclusion</i> " section

representative? For who?	<p>different protocols and no standardized management across the years.</p> <p>Another point is the fact we are evaluating a disease with a relatively low incidence - 15.8 per 100,000 habitants per year in our population. Even though liver transplantation increases the incidence of TB, we would still need a much larger number of patients to be observed to assess the impact of screening and treatment strategies.</p> <p>Despite the limitations, this study presents some important information regarding the approach and management of LTBI in liver transplant candidates and recipients in a middle income country.</p>	
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If you have any other issues, let us know so we can answer it as soon as possible.

Sincerely,

The authors