Peer Review File
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Review Comments

Reviewer A:

Shiraishi et al. presented a history of lung transplant in Japan and their single center experience.

The unique situation of transplant history in Japan is interesting, but the text needs profound revision. It looks literal translation into English from Japanese article of transplant history. Professional proofreading with native English speaker is strongly recommended.
Moreover, there is a lack of detail in many aspects. The recipients in Japan might be relatively stable since they need to wait for more than years after listing. The marginal donors might be utilized due to the significant donor shortage. Authors need to provide more information for both recipients and donors if the author wants to show how unique the lung transplant in Japan is: recipient urgency, donor quality (acceptance of marginal donor). Rate of single lung vs double lung. Actual ischemic time and distance (? correlation since they use public transplantation). Any difference in selection criteria/recipient population for brain death vs living donor. Data comparison vs other countries.
It will be helpful to show even the data in the table from single center. However, it would be preferrable to use national data to compare Japan with other countries, such as US. The list of reference should not be such short if they investigated thoroughly the uniqueness of lung transplant in Japan in multiple aspects.

For Reviewer A:

Comment 1:

Professional proofreading with native English speaker is strongly recommended.

Reply 1:

As suggested, we have now had a professional medical editor whose native language is English proofread the revised manuscript.

Comment 2:

Authors need to provide more information for both recipients and donors if the author wants to show how unique the lung transplant in Japan is: recipient urgency, donor quality (acceptance of marginal donor). Rate of single lung vs double lung. Actual ischemic time and distance (? correlation since they use public transplantation). Any difference in selection criteria/recipient population for brain death vs living donor. Data comparison vs other countries.

Reply 2:

1) The donor lung allocation policy in Japan is described in page 12, line3-7 (red text). Lung grafts are strictly allocated in sequential order of registration. Adjusting priority based on the prognostic prediction or severity of the disease, as is seen in other programs in the US or Europe, is not practiced in Japan.
2) Unfortunately, it is impossible to comment on the donor quality (brain-dead donor) based on the data currently available.
3) More details concerning the Japanese lung transplant system have been added, focusing on living donor transplants, recipient selection criteria, primary diseases, and transplant procedures including comparisons of some data versus the US or Europe. Please see the new text in "3) General result of lung transplantation in Japan" section from page 13, line 4 to page 15, line 7 (red text).

Comment 3

It will be helpful to show even the data in the table from single center. However, it would be preferrable to use national data to compare Japan with other countries, such as US. The list of reference should not be such short if they investigated thoroughly the uniqueness of lung transplant in Japan in multiple aspects.

Reply3:

I have now presented our institutional data in Table 1 (new), including information on the transplant procedure, ischemic time, organ transport method, and outcome (long-term survival).

Changes in the text

Please see Table 1 (new).

Reviewer B:

Can you give more details on the Wada heart transplant. Were there ethical concerns? Why did Japanese society have this reaction and not in other countries?
What are the other causes for delay? Is there other cultural resistance to transplant?
Why was there deep-seated opposition that brain death is human death? How did the transplant professionals dispel the public distrust?
What do you mean by severe social pressure and historical turmoil? High expectations? Continuing skepticism regarding the brain dead donor?
The introduction is too long. Shorten it and lengthen the main body.
Where did the long history of negative public opinion come from? The Wada heart transplant? Anything else?
If you could put the Revised Transplant Act into figure 1 or comments that would be helpful to show its relevance.
"Initial transplant results of those four institutes satisfied international standards" - like what? 1-year survival?
What are the downsides to such a strict oversight process? It seems to promote quality but may limit quantity.
Allocation is based on registration date still? The LAS score in the US prioritizes how

sick someone is and their diagnosis. Not perfect, but sicker patients get transplanted more quickly than someone who is listed very early. Is there any other way to get sick patients transplanted quickly?
Why did the number of lung transplant increase after 2015?
There is a high waitlist mortality. Are there efforts to prioritize sicker patients?
Can you comment on average ischemia times with the commercial transport. Are both air and train used? I found this is very interesting.

For Reviewer B:

Comment 1

Can you give more details on the Wada heart transplant. Were there ethical concerns? Why did Japanese society have this reaction and not in other countries?

Reply 1:

While I believe that the Wada transplant has been adequately described in the "The history of the development of the Japanese Lung Transplant System" section (page 6), I have added new text at page 6, line 9-10 (red text) to facilitate readers' understanding.

Comment 2

What are the other causes for delay? Is there other cultural resistance to transplant? Why was there deep-seated opposition that brain death is human death? How did the transplant professionals dispel the public distrust?

Reply 2

After the Wada heart transplant, many intellectuals, politicians, religious leaders, and even medical specialists banded together in opposition to organ transplantation. Their reasons varied, but many were illogical and emotional. Japanese transplant practitioners promoting organ transplant medicine tried to dispel the populace's misconceptions, but their efforts were futile for a long time.

During this period, Japanese organ transplant specialists presented the brilliant achievements of organ transplant medicine in western countries and made effort to steadily dispel the fog surrounding organ transplantation for the public. I believe these aspects have been described sufficiently in the text.

Changes in the text

No additional change for this comment

Comment 3

What do you mean by severe social pressure and historical turmoil? High expectations? Continuing skepticism regarding the brain-dead donor?

Reply 3

Japanese transplant surgeons and physicians started their organ transplantation efforts in the face of strong social resistance from society. Therefore, they felt an atmosphere where failure was not allowed, so expectations were naturally quite high. Such an atmosphere manifested due to the historical turmoil after the aforementioned Wada

heart transplant incident. Skepticism concerning brain-dead donation is still present in part but is not nearly as strong as before.

Changes in the text

I changed the sentence in page 7, line 14-16 "Japanese organ transplant practitioners, including lung transplantation surgeons, developed their new transplant system in the face of severe social pressure and high expectations.."

Comment 4

The introduction is too long. Shorten it and lengthen the main body.

Reply 4:

The paragraph regarding Wada heart transplant in the Introduction section has now been moved to the beginning of the main body to shorten the Introduction and lengthen the main body.

Comment 5

Where did the long history of negative public opinion come from? The Wada heart transplant? Anything else?

Reply 5:

We believe that the general negative public opinion basically developed due to Dr. Wada's heart transplantation in 1967, which brought to light the question of whether brain death is human death, which therefore sparked national debate.

Comment 6

If you could put the Revised Transplant Act into figure 1 or comments that would be helpful to show its relevance.

Reply 6:

I appreciate your suggestion. I put the mark of "Revised Transplant Act" into figure 1.

Comment 7

"Initial transplant results of those four institutes satisfied international standards" - like what? 1-year survival?

Reply 7:

The first Japanese national lung transplant registry (2008) indicated that the survival of 87 post-transplant patients was 81% at 1 year, 77% at 2 years, 74% at 3 years, and 71% at 5 years, which was, we believe, remarkable for the first series of lung transplant.

Comment 8

What are the downsides to such a strict oversight process? It seems to promote quality but may limit quantity.

Reply 8:

While I agree with the reviewers' opinion here, fortunately, this rigorous scrutiny did not limit performing lung transplants. Indeed, the utility ratio of the lungs of brain-dead donors in Japan is over 60%, which is much higher than that reported in the US (approximately 20%), indicating that Japanese lung transplant surgeon do not hesitate

to perform BDDLT, even accepting marginal donor lungs.

Comment 9

Allocation is based on registration date still? The LAS score in the US prioritizes how sick someone is and their diagnosis. Not perfect, but sicker patients get transplanted more quickly than someone who is listed very early. Is there any other way to get sick patients transplanted quickly?

Reply 9:

Modification of donor allocation, such as LAS, has also been considered in Japan. However, the biggest problem in Japanese organ transplantation is the tragically small number of donors. We therefore suspected that if we introduced an allocation system based on patient severity, only highest-risk patients would receive donor lungs, which might result in overall poorer outcomes and would not reduce the rate of waiting list death.

Comment 10

Why did the number of lung transplant increase after 2015?

Reply 10:

The 1997 Japanese Organ Transplant Law was revised in 2010. The main points of the revision were follows: 1) even if an individual's intention is unclear, donation of their organs is possible with the family's consent; 2) written consent to organ donation is not necessary, so donation from individuals under 15 years old is possible, but only with the family's consent. Following these revisions of the law in 2010, the number of organ donations after brain death dramatically increased due to an increase in the number of donations in which organs were donated by family agreement.

Changes in the text

The new sentence is added in page 9, line 18 to page 10 line 1 (red text)

Comment 11

There is a high waitlist mortality. Are there efforts to prioritize sicker patients?

Reply11:

We have no specific counter-measures for saving the sickest patients other than to increase the number of donations by further educating the public or increasing the utility of lung donors by performing single lung transplant or accepting marginal donors. I have now added the text below to page 14 on this matter.

Changes in the text

Regarding the transplant procedure for BDDLT, single (unilateral) lung transplantation has been chosen more often than bilateral lung transplantation in Japan to maximize the number of transplantation by sharing the scarce donor. Actually 231(51.7%) lung transplants were performed as single lung transplantation among total 447 BDDLT as of the end of 2018 (12). Page 15, line 3-7

Comment 12

Can you comment on average ischemia times with the commercial transport. Are

both air and train used? I found this is very interesting.

Reply12:

Information regarding ischemic time is described in Table 1

Change in the text

Please see Table-1

Reviewer C:

Those reviews seem to be comments for the manuscript from Osaka University Group

Reviewer D:

This review paper is well described. I totally agree with the authors' idea that the Japanese transplant program can maintain better posttransplant outcomes because of the strict certification system to become a lung transplant center, a rigorous central monitoring system for posttransplant outcomes, and a third-party review system for the patient registration for the Japan Organ Transplantation Network. I have just one minor comment as follows.

For Reviewer D:

Comment

The authors can update the total number of lung transplants performed in Japan, according to the registry report in 2022.

Reply:

I appreciate the suggestion. Data from the "National registry of Japanese lung transplantation 2023" on the home page of the Japanese Society of Lung and Heart-Lung Transplantation have been added to the reference list.

For Reviewer E:

Comment 1

This reviewer also recommends that the authors employ an English editor to assist with preparation of the manuscript. A Microsoft Word document is attached with a list of recommendations (this reviewer is not a formal editor) and the list is not exhaustive. However, there are numerous grammatical and syntax errors including missing or incorrect use of articles (e.g. "a" and "the"), misuse of singular or plural forms of nouns, incorrect use of prepositions, and incorrect use of adverbs. There are also many sentences with awkward or confusing phrasing, and punctuation is sometimes incorrect. For example, using a semicolon (;) as opposed to a colon (:), is a common error. Dashes are used inappropriately instead of commas in at least once instance.

Reply 1

As suggested, we have now had a professional medical editor whose native language is English proofread the revised manuscript.

Comment 2

Finally, this reviewer highly recommends that the authors provide a review of the major contributions of Japanese lung transplant programs to the surgical literature. While a major focus of the review is on the increased use of brain dead donors for lung transplant, the use of living donors for lung transplant is a major contribution to lung transplant. A paragraph summarizing this and highlighting some of the relevant literature to this topic would be of interest, and any other techniques or advances in lung transplant that have been reported in the literature by Japanese lung transplant programs would be worth noting.

Reply 2:

As suggested, I have added some text regarding the difference between Japan and other countries, including with regard to transplant indication and procedures, and discussed the development of LDLT in Japan in the section "4) General results of lung transplantation in Japan"

Changes in the text

Please see pages 12-15, text in 4) General results of lung transplantation in Japan (red text)

Comment 3

I also suspect, although I do not know, that there has been some collaboration between Japanese lung transplant programs and other older and more established, high-volume lung transplant programs in Europe in the US. If there is historical knowledge or description of these collaborations which may have involved visiting surgeons, fellowship training, or programatic and case-based consultation, this would bear mentioning.

Reply 3:

Indeed, many Japanese surgeons who wished to pioneer lung transplantation in Japan trained in US or European institutes over the past four decades, which was extremely important for the development of the Japanese lung transplant system. However, these collaborations are undocumented, so I would like to avoid mentioning them here. However, we Japanese surgeons greatly appreciate the kind help offered by advanced institutes overseas to aid in the development of the Japanese lung transplant program.

<u>For Reviewer F:</u>

Comment 1

The Title should mention the word history rather than biography. For example: The Japanese Lung Transplantation History: A unique pathway to establishing the program and its initial success

Reply 1:

I appreciate the reviewer's suggestion and have revised the title to, "The history of Japanese lung transplantation: The unique pathway to establishing the program and its initial success."

Comment 2

Examples of editing suggestions are mentioned below (this is not a complete listing of all correctable/editable text elements):

Reply 2

As suggested, we have now had a professional medical editor whose native language is English proofread the revised manuscript.

Reviewer G:

Comments

The paper is well wretten and summarizes past and current unique status of Japanease lung transplant programs including Fukuoka University program. Authors are to be congratulated.

Reply

Thank you.

Reviewer H:

I appreciate this excellent comprehensive review on the history of lung transplantation in Japan. This would be a quite valuable record for future lung-transplant physicians and surgeons in Japan. Here is a very minor comment.

Comment

P3 second paragraph: "The number of brain-dead organ donations was extremely limited in the beginning. Thus, more than 60% of all lung transplants were performed as living-donor transplants."

Please specify in which period of time more than 60% of lung transplants were living as was described in P11.

Reply

This was during the first 9 years (1998-2006). I have now clarified the period in the text. Page 12