

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-290>

Review Comments

Reviewer A

Congratulations the outcome and high percentage of donor utilization. A few questions come to mind:

Thank you very much for your suggestive comments and questions.

Comment 1: What was the ventilatory strategy used?

Reply 1: The ventilatory strategy is usually a lung-protective ventilation strategy, with a tidal volume of 6-8 ml/kg ideal body weight, plateau pressure less than 30 cm H₂O, end-expiratory positive pressure 8-10 cm H₂O, and FiO₂ as low as possible, in accordance with the "Manual for Patient Evaluation and Management with a View to Organ Donation and Intraoperative Management" developed by the Research Project for Transplantation Medical Infrastructure Development funded by the Ministry of Health, Labor and Welfare on March 31, 2022 (7).

Changes in the text: The above texts and reference have been added to section of **2-1. Tasks of lung medical consultants** (see Page 6, lines 98-104).

Comment 2: When was prone positioning utilized?

Reply 2: The timing of prone positioning depends on the donor's attending physicians' approach. Usually, it was initiated when the donor's attending physicians noticed atelectasis or pneumonia in the donor and continued until prior to donor organ harvesting.

Changes in the text: None.

Comment 3: What was the donor fluid management?

Reply 3: The donor fluid management was usually done to maintain a urine output of at least 0.5 to 1.0 ml/kg/hr, while taking care not to overfluidize the donor (7).

Changes in the text: The above texts and reference have been added to the section of **2-1. Tasks of lung medical consultants** (see Page 6, lines 104-106).

Comment 4: Did etiology of brain death/death have a relation to the eventual donor utilization?

Reply 4: Whether etiology of brain death/death has a relation to the donor lung utilization rates was not examined in the cited paper (5).

Changes in the text: None.

Comment 5: Was EVLP used?

Reply 5: No, EVLP was not used for the donor lungs in the cited paper (5).

Changes in the text: None.

Comment 6: Did you also use DCD donors?

Reply 6: No, we did not use DCD donors.

Changes in the text: None.

Comment 7: Did you do sputum/bronchial wash and culture and manage with antibiotics?

Reply 7: Yes, we did sputum/bronchial suctioning (not washing) and culture to manage with antibiotics.

Changes in the text: We added text “culture of the aspirates to manage with antibiotics” to the sentence “MC performs phlegm aspiration with a bronchoscope and present proposals for respiratory therapy, including postural drainage, mechanical ventilation, infection control, and circulatory management of donors” in the section of **2-1. Tasks of lung medical consultants** (see Page 5, lines 95-96).

Comment 8: Was lung compliance more important or the P/F ratio?

Reply 8: For donor lung evaluation, we usually focused more on the P/F ratio than on lung compliance.

Changes in the text: None.

Comment 9: And finally would it not be possible to do all the fine-tuning remotely or via smartphone rather than sending out physicians physically?

Reply 9: I fully agree with the reviewer's opinion. Ideally, in the future, it would be possible to do all the fine-tuning remotely or via smartphone rather than sending out physicians physically.

Changes in the text: We added the sentence “in the future, it would be possible to do all the fine-tuning remotely or via smartphone rather than sending out transplant surgeons physically” to the end of conclusion (see Page 10, lines 210-211).

Reviewer B

The review article entitled “Donor management and extremely high donor lung utilization rate in Japan” written by Hoshikawa et al. was reviewed. The importance of MC (medical consultant) participation was well described, which appeared to be a key factor of high donor lung utilization rate in Japan. Authors are to be congratulated for summarizing convincing data.

We deeply appreciate your thoughtful comments and helpful suggestions.

Comment 1: What are the donor lung utilization rates in USA and Europe? It would be helpful to include these data in the introduction or in the discussion.

Reply 1: We entirely agree with the reviewer's suggestion. the donor lung utilization rate from brain-dead donors per lung, when counting a single lung as 1 and bilateral lung as 2, was 51% (1176 lungs/2285 lungs) in 2022 in eight European countries (Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, Netherlands, and Slovenia) (10). And in the U.S., the lung utilization rate per donor was reported to be 17.6% (2443/13862donors) in 2021 (11). We added these data in the section “**2-3. Recent**

status of medical consultant system”.

Changes in the text: We added the above sentences in the section “**2-3. Recent status of medical consultant system**” (see Pages 9-10, lines 189-193) and cited two new references [10] and [11].

Comment 2: In line 142, “has been charge of” should be “has been in charge of”.

Reply 2: Thank you for pointing out the mistake.

Changes in the text: We corrected it (see Page 9, line 178).

Comment 3: Precise information of bronchoscopic findings provided by MC is very helpful. It should be mentioned.

Reply 3: Thank you for your suggestion. I completely agree with you.

Changes in the text: We added the sentence “precise information of bronchoscopic findings provided by the MC is extremely useful in helping the lung transplant team decides whether to accept a donor lung” to the section “**2-1. Tasks of lung medical consultants**” (see Page 5, lines 93-94).

Reviewer C

I had a great pleasure in reviewing this study introducing and verifying the ongoing effort of Japanese transplant community to maintain the high lung utilization rate. Different nations and regions have different social, geographical and logistic challenges to build up an efficient and effective organ allocation policy. Japan's unique approach that has come out of the needs and hurdles can provide some insights to other international communities. I have several comments to strengthen the paper as below. Thank you so much for your thoughtful comments and helpful suggestions.

Comment 1: It is obvious that a thorough donor management by transplant professionals is effective in successful organ recovery, but my question is how long it should need before procurement to reap the benefit. The authors should add a description about the length of the actual donor management available in their cohort.

Reply 1: Information on the exact period of time during which donor management was available is not presented in reference 5. Lung MC intervention is usually performed in the evening or night of the day the first brain death examination is made; the second brain death examination is usually made the following morning, after which the procedure to confirm the recipient's will for transplantation is initiated. Since a minimum interval of 24 hours is planned between the confirmation of the recipient's willingness to undergo transplantation and the recovery operation, donor lung management is possible at least one and a half days after the lung MC intervention, and actually a little more than two days after the lung MC intervention since most recovery operations are performed before dawn.

Changes in the text: The above texts have been added to the section **2-1. Tasks of lung medical consultants** (see Page 6, lines 111-119).

Comment 2: The authors mentioned the MC was composed of nationwide lung

transplant surgeons, but I wonder if the quality donor management does not necessarily have to be conducted by surgeon. What kind of actual skills and experience do the authors consider is necessary for the MC? The authors should discuss the minimal qualification for the MC through their experience.

Reply 2: Thank you for your valuable question. As described in the section **2-1. Tasks of lung medical consultants**, the lung MCs tasks include assessment of donor lungs, communicating the donor lung condition to the lung transplantation teams, and management of the donor lungs. Therefore, the lung MCs must have a good grasp of donor lung indication criteria for transplantation based on knowledge and experience, and must be able to accurately evaluate donor lungs by tools including imaging findings and bronchoscopy. They must also have a good understanding of the characteristics of brain-dead donors and be able to recommend to the donor's attending physician measures to maintain or improve the condition of the donor lungs. During the study period of the reference 5, there were no lung transplant physicians, who have recently been active in Japan, and only lung transplant surgeons possessed the knowledge and skills described above.

Changes in the text: We added the sentences “In light of the above, the lung MCs must have a good grasp of donor lung indication criteria for transplantation based on knowledge and experience, and must be able to accurately evaluate donor lungs by tools including imaging findings and bronchoscopy. They must also have a good understanding of the characteristics of brain-dead donors and be able to recommend to the donor's attending physician measures to maintain or improve the condition of the donor lungs.” to the end of the section 2-1. (see Pages 6-7, lines 120-125)

Comment 3: Despite an achievement of excellent organ utilization, the organ management system consulting transplant surgeons seems significantly demanding for transplant centers. The effort might be implementable when the number of donations is small. However, I am afraid that it would be unsustainable if the donation increases. I would like to have authors' comments for the possible policies for future potential increase in organ donation in Japan.

Reply 3: As noted in the **2-3. Recent status of medical consultant system** and conclusion sections, we are now beginning to consider ways to gradually delegate these MC tasks to donor hospitals skilled in brain-dead donor management and multi-organ donation. As Reviewer B pointed out, precise information on bronchoscopic findings provided by MCs is extremely helpful in the decision to accept or reject a donor lung. We have just released a form for the observations and description of bronchoscopic findings that can be done without a lung transplant surgeons or physicians.

Changes in the text: Following sentence “one of the most important future topics of discussion is the transfer of lung MC services to experienced procurement hospitals” in the **2-3. Recent status of medical consultant system** section, the following texts were added; “As mentioned earlier in this review, precise information on bronchoscopic findings provided by MCs is extremely helpful in the decision to accept or reject a donor lung. We have just released a form for the observations and description of bronchoscopic findings that can be done without a lung transplant surgeons or physicians.” (see Page

10, lines 198-201)

Reviewer D

This is an interesting article reviewing lung transplant donor management and utilization in Japan, an East Asian country where the cultural background sets some barriers for obtaining donor organs. The utilization rate is thus extremely important in this setting to maximize available donor lungs.

Thank you so much for your thoughtful comments and helpful suggestions.

Comment 1: The lung utilization rate was reported to be extremely high in this review, ranging from ~60% in early years to ~75% currently, compared with the ~25% utilization rate in the US. The first question I have is how exactly was utilization rate calculated? Was it the number of lung donors that had at least one lung transplant/number of donors that at least had one organ procured for transplant?

Reply 1: Thank you very much for your helpful questions. Per-donor lung utilization rate was calculated by dividing the total number of transplanted lungs by the number of donors, counting as 1 whether single or bilateral lungs donated by a single donor were transplanted. Meanwhile, per-lung value was calculated by dividing the total number of transplanted lungs by the number of donors x2, counting 1 if only single lung was transplanted and 2 if bilateral lungs were transplanted.

Changes in the text: The above texts have been added to the section **2-2. Efficacy of lung medical consultant system** (see Page 7, lines 136-141).

Comment 2: I'm also wondering if the authors have data regarding how many of the procured donors were considered extended criteria donors per ISHLT criteria.

Reply 2: Thank you for your important question. Variance from at least 1 standard donor criterion out of 10 ISHLT criteria (6) occurred in 65.5% and 69.4% of lung transplants performed in phases I and II respectively, before the intervention by the lung medical consultants started, whereas its frequency has become much higher (90.0%) in phase III, since the emergence of the lung MCs ($p=0.0004$) (5). We have shown by multivariate analysis of donor factors adjusted with recipient factors that the presence of 4 or more of the variances from the standard donor lung criteria constituted a significant risk factor for graft survival after lung transplantation among 173 brain-dead lung transplant cases in Japan from March 2000 to June 2013 (8). In reference 5, the proportion of lung transplants with 4 or more of the extended criteria was much higher in phase III (20.0%), after the beginning of the lung MC system, than in phases I (6.9%) and II (4.8%).

Changes in the text: The above texts and a new reference 8 have been added to the section **2-2. Efficacy of lung medical consultant system** (see Page 8, lines 154-166).

Comment 3: Has ex-vivo lung perfusion been employed in Japan?

Reply 3: Only three extended criteria donor lungs were transplanted after ex-vivo lung perfusion at Kyoto University (2 of them) and Okayama University (1 of them). Otherwise, ex-vivo lung perfusion has not been employed in Japan.

Changes in the text: [None](#).

Comment 4: Primary graft dysfunction rate was also reported and it appeared to be very low in this review. What was the definition of PGD in this particular study? Was it based on P/F ratio at 72 hours, and what cutoff (what grade of PGD) was used?

Reply 4: [Thank you for your question about primary graft dysfunction \(PGD\) in reference 5. However, the paper reported on graft death rate due to PGD, but not PGD rate itself.](#)

Changes in the text: [None](#).

Comment 5: Is the procuring team always the transplanting team in Japan? Additionally, how often does a procuring/transplant team from the examining Medical Consultant's same institution come to retrieve and transplant the organ? I imagine that the utilization rate would be higher if the same team is responsible for the initial donor management as well as the final acceptance and transplantation.

Reply 5: [Yes, the procuring team is dispatched from the transplanting team in most cases in Japan. Exact data on how often the procurement/transplant team from the same medical institution as the Medical Consultant comes to retrieve and transplant the lung is not disclosed in reference 5. Such occurrences are rare, but they do happen. And as you pointed out, we have the impression that in those cases, even fairly marginal donor lungs are used in some cases.](#)

Changes in the text: [None](#).

Comment 6: Can the authors provide some data regarding the median ischemic time and the median donor hospital to transplant hospital distance?

Reply 6: [Data regarding the median ischemic time and the median distance from the donor hospital to the transplant hospital are not available in reference 5. The Japan Organ Transplant Network reported total ischemic time of 158 cadaveric bilateral lung transplants and 174 single lung transplants performed in Japan from 2000 to 2016 in the Organ Donation and Transplantation Databook 2017 \(\[https://www.jotnw.or.jp/files/page/datas/databook/doc/11_lungtx.pdf\]\(https://www.jotnw.or.jp/files/page/datas/databook/doc/11_lungtx.pdf\)\). According to the report, the average total ischemic time was 9 hours and 52 minutes for bilateral lung transplants and 7 hours and 3 minutes for single lung transplants. On the other hand, the ISHLT Registry Report 2017 \(Focus Theme: Allograft ischemic time\) showed median ischemic time was 5.5 hours for 10,883 bilateral lung transplants and 4.2 hours for 4,370 single lung transplants during January 2009 through June 2015. Therefore, allograft ischemic time tended to be longer in Japan than in the international registry data.](#)

Changes in the text: [None](#).

Comment 7: Overall, the donor management and utilization in Japan is a very important topic to review and is definitely worth a good article; however, the current manuscript may need to add more details to provide the readers with a comprehensive overview of the Japanese donor management system. This will provide some

guidance to other East Asian countries that are struggling with the lack of donor organs.

Reply 7: Thank you so much for your insightful suggestion. We completely agree with you. We would like to excerpt some recommendations for respiratory and circulatory management of brain-dead donors from the "Manual for Patient Evaluation and Management with a View to Organ Donation and Intraoperative Management" developed by the Research Project for Transplantation Medical Infrastructure Development funded by the Ministry of Health, Labor and Welfare on March 31, 2022.

Changes in the text: The words “**and donor management**” were added to the section name of **2-1. Tasks of lung medical consultants**, and the following texts were also added to that section; “The ventilatory strategy is usually a lung-protective ventilation strategy, with a tidal volume of 6-8 ml/kg ideal body weight, plateau pressure less than 30 cm H₂O, end-expiratory positive pressure 8-10 cm H₂O, and FiO₂ as low as possible, in accordance with the "Manual for Patient Evaluation and Management with a View to Organ Donation and Intraoperative Management" developed by the Research Project for Transplantation Medical Infrastructure Development funded by the Ministry of Health, Labor and Welfare on March 31, 2022 (7). The donor fluid management is usually done to maintain a urine output of at least 0.5 to 1.0 ml/kg/hr, while taking care not to overfluidize the donor (7). Because hypopituitarism can occur in brain-dead patients, replacement antidiuretic hormone is administered to maintain blood pressure (7). In addition, frequent repositioning and expectoration of sputum should be performed to prevent atelectasis. Because the cough reflex disappears in brain-dead patients, periodic bronchoscopic deep suctioning of sputum is also important (7). Frequent oral care should also be remembered for the purpose of preventing ventilator-associated pneumonia.” (lines 98-111)