Original Article

# Underutilization of potential donors for lung transplantation at a tertiary care center in North India

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## ABSTRACT

**Objective:** Lung transplantation is infrequently performed in India due to several constraints, and whether the poor lung transplantation rates in India are due to a lack of eligible lung donors is unclear. In this study, we explored the availability of donors for lung transplantation. **Materials and Methods:** This was a retrospective analysis of all brain-dead participants who underwent assessment of eligibility for lung donation between August 2015 and June 2018. All participants underwent a detailed clinical evaluation that included history, physical examination, arterial blood gas analysis, chest radiograph, and bronchoscopy. The final eligibility for lung donation was assessed using the existing "ideal" criteria and the less stringent "extended" criteria. **Results:** A total of 55 brain-dead participants (41 [74.5%] males) were assessed for eligibility for lung donation. The mean (standard deviation [SD]) age of the participants was 38.4 (17.2) years. The mean (SD) duration of prior invasive mechanical ventilation at the time of assessment was 4 (3.1) days, with a mean (SD) partial pressure of arterial oxygen: inspired oxygen fraction ratio ($PaO_2$:$FiO_2$) of 326.6 (153.5). The proportion of participants who were found suitable for lung donation was 16 (29.1%) and 35 (63.6%) on employing the ideal and the extended criteria, respectively. Inadequate oxygenation status, abnormal chest radiograph, and sepsis were the most common reasons for excluding participants using either criteria. Despite the availability of adequate lung donors, only one lung transplantation could be performed. **Conclusion:** Even with the most stringent criteria for lung assessment, nearly one-third of the brain-dead participants had lungs suitable for lung transplantation. Lack of eligible lung donors is not a reason for the poor lung transplantation rates in India.

**KEY WORDS:** Brain death, end-stage lung disease, lung allocation, lung donation, lung transplantation

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## INTRODUCTION

The outcome of individuals with end-stage lung diseases is dismal despite maximal medical therapy and supportive care.[1] Lung transplantation is the only definitive therapy available for such individuals. Worldwide, about 4000 lung transplantations are performed each year.[2] However, lung transplantation is not widely available in India with only a handful of centers performing it.[1,3] In addition, very few patients in India opt for lung transplantation, possibly due to factors such as poor availability, socioeconomic constraints, and the modest outcomes following transplantation.[1]

Worldwide, the demand for lungs is far greater than the supply and the waiting period could extend over several months.[4] The disparity between lung demand and availability could be because of several reasons. Unlike

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transplantation of other organs, including kidneys or liver where live donors are the predominant source of organs, in lung transplantation, brain-dead participants form the main donor pool.[5] Lung donation by healthy individuals is rarely performed due to concerns regarding donor morbidity.[6] In addition, organ retrieval rates for lungs from deceased donors is only 20%–30% as compared to other organs (85%–90%, 80%, and 32% for the kidney, liver, and heart, respectively).[7,8] This is likely due to lungs being subjected to several insults such as chest trauma, aspiration, pulmonary edema, ventilator-induced lung injury, and hospital-acquired pneumonia, which might preclude their utilization for transplantation.[9]

The deceased organ donor rate in India is <1 per million population (pmp) as compared to about 20–35 pmp in more developed countries.[10] In addition, the factors which might adversely affect harvestable lungs in brain-dead participants may be different in the developing world due to differences in the quality of available medical care and the incidence of infectious complications. The scarcity of brain-dead participants with lungs suitable for donation, coupled with the abysmal deceased organ donation rates in India could markedly limit the supply of lungs, and this could be an additional factor limiting lung transplantation in India. However, there is no published data on potential lung donors from India.

In this study, we evaluated the eligibility of brain-dead participants for lung donation at a tertiary care center in North India.

## MATERIALS AND METHODS

We performed a retrospective analysis of all brain-dead participants who underwent eligibility assessment for lung donation between August 2015 and June 2018. Due consent was obtained from the participant's family for the donation of lungs and other organs. All participants who were assessed for lung donation were included in this study regardless of whether lungs were eventually procured or not. The study protocol was approved by the Institute Ethics Committee. The requirement for informed consent was waived off due to the retrospective nature of the study and the use of anonymized patient data.

We collected the information regarding demography, etiology of brain death, history of smoking, prior history of chronic lung diseases, and cardiothoracic surgery. All participants were assessed for evidence of chest trauma and the requirement for intercostal tube drainage. Arterial blood gas analysis was performed with inspired oxygen fraction ($FiO_2$) of 1.0 and positive end-expiratory pressure of 5 cm $H_2O$, and the ratio of the arterial partial pressure of oxygen ($PaO_2$) to $FiO_2$ was calculated.

A chest radiograph was performed in all participants. Airway secretions obtained by endotracheal suctioning were sent for Gram staining and bacterial culture. Participants also underwent flexible bronchoscopy to look for the presence of any endobronchial lesion or purulent secretions. Sepsis was defined using standard criteria.[11] Aspiration pneumonia was considered when opacities were noted in the dependent regions of the lung on a chest radiograph with or without the presence of gastric contents or enteral feed in the endotracheal aspirate.

Using ideal lung donor criteria, participants were considered to be ineligible for lung donation if any of the following conditions were met: age ≥55 years, preexisting chronic lung disease, history of prior cardiothoracic surgery, smoking history ≥20 pack-years, significant chest trauma, any opacities on chest radiograph, $PaO_2$:$FiO_2$ ratio ≤300, purulent secretions on bronchoscopy, organisms on gram stain of endotracheal aspirate, and evidence of sepsis or aspiration pneumonia.[12,13]

In addition, participants were also assessed with the less stringent extended lung donor criteria and were considered unsuitable for lung donation if any of the following conditions were met: age ≥70 years, preexisting chronic lung disease except asthma, smoking history ≥40 pack-years, and $PaO_2$:$FiO_2$ ratio ≤250.[14] Under the extended criteria, chest trauma, minor diffuse or moderate focal opacities on chest radiograph, purulent secretions on bronchoscopy, and minor sepsis or aspiration pneumonia were considered irrelevant if the $PaO_2$:$FiO_2$ ratio was good, stable, or improving. In addition, the history of prior cardiothoracic surgery or the presence of organisms on gram stain of endotracheal aspirate was not considered as contraindications for lung donation.

## RESULTS

During the study period, 55 brain-dead participants who had consented for organ donation were assessed for eligibility for donation of lungs [Table 1]. The majority of the participants (74.5% males) were young, with a mean (standard deviation [SD]) age of 38.4 (17.2) years. The mean (SD) height of the participants was 165.2 (13.5) cm and 10.9% were smokers. The most common etiology for brain death was head injury (89.1%). The mean (SD) duration of invasive mechanical ventilation at the time of assessment was 4 (3.1) days, with a mean (SD) $PaO_2$:$FiO_2$ ratio of 326.6 (153.5). The kidney (78.2%), cornea (50.9%), and liver (34.5%) were the most common organs that were finally harvested from the donors for transplantation. Only one lung transplantation (1.8%) could be performed at the center during the study period.

Overall, 16 and 35 participants were found to be fit for lung donation using the ideal and extended criteria, respectively [Table 2]. With the use of the ideal criteria, 39 (70.9%) of the participants were found to be unfit for lung donation. The most common reasons for ineligibility were $PaO_2$:$FiO_2$ ratio ≤300 ($n$ = 23, 41.8%), abnormal

**Table 1: Characteristics of potential donors screened for lung transplantation (*n*=55)**

| Characteristics | *n* (%) |
|---|---|
| Male gender | 41 (74.5) |
| Age (years), mean (SD) | 38.4 (17.2) |
| Height (cm), mean (SD) | 165.2 (13.5) |
| Smokers | 6 (10.9) |
| Days of invasive mechanical ventilation, mean (SD) | 4 (3.1) |
| $PaO_2$:$FiO_2$ ratio, mean (SD) | 326.6 (153.5) |
| Etiology of brain death | |
| Head injury | 49 (89.1) |
| Cerebrovascular accident | 5 (9.1) |
| Gunshot injury | 1 (1.8) |
| Blood group* | |
| A positive | 7 (14.3) |
| B positive | 28 (57.1) |
| AB positive | 8 (16.3) |
| O positive | 6 (12.2) |
| Organs harvested for transplantation | |
| Kidney | 43 (78.2) |
| Cornea | 28 (50.9) |
| Liver | 19 (34.5) |
| Pancreas | 5 (9.1) |
| Heart | 3 (5.5) |
| Lung | 1 (1.8) |

*Data available for only 49 participants. $FiO_2$: Fraction of inspired oxygen, $PaO_2$: Arterial partial pressure of oxygen, SD: Standard deviation

**Table 2: Individuals unfit for lung donation (*n*=55)**

| Characteristic | *n* (%) |
|---|---|
| Excluded by ideal criteria* | 39 (70.9) |
| Age ≥55 years | 13 (23.6) |
| Smoking history ≥20 pack years | 1 (1.8) |
| Prior chronic lung disease | 0 |
| Prior cardiothoracic surgery | 0 |
| Chest trauma | 4 (7.3) |
| Aspiration | 2 (3.6) |
| Evidence of sepsis | 14 (25.5) |
| Abnormal chest radiograph (any parenchymal opacity) | 15 (27.3) |
| $PaO_2$:$FiO_2$ ratio ≤300 | 23 (41.8) |
| Purulent secretions on bronchoscopy | 1 (1.8) |
| Positive Gram stain on tracheal aspirate | 4 (7.3) |
| Excluded by extended criteria* | 20 (36.4) |
| Age ≥70 years | 0 |
| Smoking history ≥40 pack years | 1 (1.8) |
| Prior chronic lung disease | 0 |
| Clinically significant chest trauma† | 2 (3.6) |
| Clinically significant aspiration† | 0 |
| Evidence of clinically significant sepsis† | 8 (14.5) |
| Significantly abnormal chest radiograph (minor diffuse or moderate focal opacities)† | 8 (14.5) |
| $PaO_2$:$FiO_2$ ratio ≤250 | 20 (36.4) |
| Clinically significant purulent secretions on bronchoscopy† | 0 |

*Each individual may have met more than one exclusion criterion, †Along with the lack of a good, stable, or improving $PaO_2$:$FiO_2$ ratio. $FiO_2$: Fraction of inspired oxygen, $PaO_2$: Arterial partial pressure of oxygen

chest radiograph ($n$ = 15, 27.3%), and clinical evidence of sepsis ($n$ = 14, 25.5%).

Although four participants had clinical evidence of chest trauma, only two participants had coexistent low $PaO_2$:$FiO_2$ ratio (≤300). While clinical evidence of sepsis was noted in 14 (25.5%) participants, only 8 (14.5%) participants had poor $PaO_2$:$FiO_2$ ratio (≤300). The chest radiograph was abnormal in 15 (27.3%) participants, but only in 8 (14.5%) participants, it was associated with a poor $PaO_2$:$FiO_2$ ratio (≤300). Purulent secretions on bronchoscopy or positive Gram stain on endotracheal aspirate were noted in five participants (9.1%). In four of these participants, endotracheal aspiration showed growth of a bacterial pathogen (*Staphylococcus aureus* [$n$ = 2] and *Acinetobacter baumanii* [$n$ = 2]). Aspiration pneumonia was diagnosed in two participants. However, the $PaO_2$:$FiO_2$ ratio was >300 in both participants, and hence, it was not considered clinically significant. When the less stringent extended criteria as described above were applied, only 20 (36.4%) participants were found to be unfit for lung donation. The most common reasons precluding lung donation using the extended criteria were $PaO_2$:$FiO_2$ ratio ≤250 ($n$ = 20, 36.4%), clinically significant abnormality in chest radiograph ($n$ = 8, 14.5%), and clinically significant sepsis ($n$ = 8, 14.5%).

## DISCUSSION

The results of this study indicate that nearly one-third of the brain-dead donors at our center could be potential lung donors even with the most stringent assessment criteria. This is similar to the data from centers worldwide.[7,8,15] The most common reasons for excluding an individual from lung donation were unfavorable oxygenation status, abnormal chest radiograph, or clinical evidence of sepsis.

Criteria for selecting ideal lung donors have been published.[12,13] However, these criteria are extremely stringent and are not evidence-based. Participants who have positive Gram stain on tracheal aspirate or any opacity on chest radiograph were excluded by these criteria. When these strict criteria for assessment were followed, the lung retrieval rates from deceased donors were only 5%–10% in the early nineties.[15]

The annual number of lung transplantations worldwide has more than quadrupled since then.[2,15] As the demand for lungs has outgrown the supply of lungs, the waiting list for lung transplantation has increased and the mortality while waiting for lung transplantation can be as high as 42.5% at some centers.[4,16] To overcome this issue, several lung transplant centers have utilized lungs from participants with less than optimal characteristics for lung transplantation (referred to as "extended donors").[17] In fact, lungs from these extended donors now account for more than one-third to half of the lung transplantations performed at many centers.[18-21] Several investigators have also described comparable clinical outcomes with these criteria although some have advised caution.[18-21] The increase in the annual number of transplantations and the utilization of extended donors has led to an improvement in the deceased donor lung retrieval rate to about 25%–30% in recent years.[7,8,15]

In this study, 29.1% and 63.6% of the participants were eligible for lung donation using the ideal and extended

criteria, respectively. When the extended criteria were applied, a significant proportion of the participants with higher age, insignificant abnormalities in chest radiograph, and minor sepsis, but otherwise with an acceptable $PaO_2$:$FiO_2$ ratio was considered suitable for donating their lungs. Nearly one-fourth of our participants had to be excluded solely because their age was ≥55 years when the ideal criteria were applied. With the use of the extended criteria, all these participants could be considered for lung transplantation. In fact, several studies have shown that lungs from older donors can be used safely for transplantation.[22-24] Another common reason for exclusion of donors for lung transplantation with the ideal criteria is an abnormal chest radiograph. Up to 41%–61% of lung donors can have abnormal chest radiographs.[17,25] However, these opacities could be because of several noninfectious conditions such as mucus plugging, pulmonary edema, aspiration pneumonitis, and lung contusion which may resolve with appropriate management.[25] In this study, the inclusion of lungs of participants with minor opacities in the chest radiograph with preserved oxygenation reduced the donor exclusion rate from 27.3% to 14.5%. In recent years, participants with minor sepsis are included if the $PaO_2$:$FiO_2$ ratio is acceptable.[17] The inclusion of participants with good oxygenation capacity despite sepsis scaled down our donor exclusion rate from 25.5% to 14.5%. Colonization of the respiratory tract with bacteria is common, and about 30%–90% of lungs from deceased organ donors are reported to have positive cultures.[26-28] However, donor lung colonization has not been shown to predict posttransplant pneumonia.[26,27] In this study, the donor lung colonization was only 7.3%, possibly because of the short mean hospital stay (4 days).

Although nearly one-third to two-third of the brain-dead participants may be eligible for lung donation, it may not be possible to harvest lungs from all the potential lung donors, even in the ideal setting. This is because lung retrieval is affected by several other factors, including the availability of suitable recipient with a compatible blood group and body size. In addition, in the absence of a robust nationwide organ-sharing network akin to the United Network for Organ Sharing of the United States, donor-recipient matching is not possible for all organs, resulting in wastage of precious organs. Moreover, the status of the donor's lungs might change during the reassessment, which is usually performed before harvesting, if sufficient time elapses after the initial assessment.

Finally, this study is not without limitations. It has a retrospective study design with its inherent limitations. The eligible lung donor population described in this study may not be a true representation of the actual lung retrieval rate because it is affected by several factors as discussed above. Only one lung transplantation could be performed during the study period, and the lungs from the rest of the brain-dead donors could not be utilized due to several logistic and patient-related factors despite their suitability and availability.[1,3]

## CONCLUSION

The results of this study indicate that even in a developing country like India with poor deceased organ donation rates, a significant proportion of the brain-dead participants, whose families are willing for donation have lungs suitable for donation. A majority of the eligible lung donors are nevertheless unutilized. Improving the awareness regarding lung transplantation and a better organ-sharing network among centers performing lung transplantation can help in better utilization of these potential lung donors.

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### Conflicts of interest
There are no conflicts of interest.

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