Extended donor criteria for lung transplantation—a clinical reality

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Abstract

Objective: Standard lung donor criteria have been established on opinions and individual experiences rather than on existing evidence. Since the scarcity of donor organs is one of the major limitations to lung transplantation, extension of donor lung criteria might considerably increase the donor pool. This study therefore evaluates the outcome, achieved with the use of extended donors versus standard donors and aims to redefine lung donor criteria. Methods: We performed a retrospective analysis of 98 consecutive primary lung transplantations from 94 donors from 1/2001 to 12/2002. Donors were classified as extended if they fulfilled at least one criteria: age > 55 years, PaO\textsubscript{2} at FiO\textsubscript{2}/PEEP 5 < 300 mmHg, tobacco history > 20 pack years, inhalative drug abuse, presence of infiltration on chest X-ray or purulent secretions at bronchoscopy. Recipients were stratified in two groups according to whether they received a ‘standard’ or ‘extended’ organ. Postoperative complications, extubation time, ICU and hospital stay and survival were compared. Results: Twenty-three (24.5\%) donors were extended. Twenty-six recipients (26.55\%) received organs from extended donors. Differences in intubation times (12 ± 2 days standard vs. 14 ± 5 days extended, \(p = 0.70\)), ICU stay (16 ± 2 days standard vs. 18 ± 5 days extended, \(p = 0.74\)) and hospital stay (38 ± 4 days standard vs. 40 ± 6 days extended, \(p = 0.71\)) were not statistically significant. Postoperative bleeding rates were comparable (\(n = 14\) standard vs. \(n = 3\) extended) as well as bronchial anastomotic complications (\(n = 7\) standard vs. \(n = 3\) extended). Three months survival was 88.89\% in the standard group vs. 92.31\% in the extended group. One year survival is comparable as well with 81.94\% vs. 84.62\%, respectively. Conclusions: The use of lung donors who fail to meet standard criteria does not impair short and medium term results compared to standard lung donors. The impact on long term development of BOS has yet to be evaluated. The strict application of standard lung donor criteria excludes a considerable number of lungs potentially suitable for transplantation, thus liberalisation of donor criteria might help to overcome donor shortage.

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Keywords: Lung transplantation; Donors; Presumed consent

1. Introduction

The quality of donor organs undeniably has a significant impact on early and long term outcome after transplantation. Existing standard lung donor criteria have been established in an earlier period of lung transplantation based mainly on opinions and individual experiences rather than on existing evidence \cite{1}. Since scarcity of donor organs is one of the major limitations to lung transplantation, the extension of donor lung criteria has the potential to considerably increase the donor pool. Beside the sole donor-specific criteria, re-evaluation of matching criteria might have a similar effect. Due to the constantly increasing use of marginal donor lungs, this study evaluates the outcomes achieved with the use of extended donors versus standard donors and aims to redefine lung donor criteria.

2. Patients and methods

Ninety-eight consecutive primary lung transplantations from 94 lung donors from 1/2001 to 12/2002 were retrospectively reviewed. Donors were evaluated according to age, available medical record, blood gas analysis, available laboratory values, chest X-ray and findings during bronchoscopy and harvesting. Blood group compatibility as a prerequisite, donor/recipient matching was based primarily on size (with the predicted total donor lung capacity compared to the recipient’s predicted and real total lung capacity as the primary method), age and urgency of the recipient. Additionally the estimated ischemic time was taken into account.

Donors were classified as extended if they fulfilled at least one of the following criteria: age > 55 years, PaO\textsubscript{2} at
Mean age at transplantation was 45 years.

Swyer–James–Syndrom (each n=1), chronic thromboembolic pulmonary hypertension and the extended group (n=11 extended donor group), pulmonary fibrosis (n=15 vs. 6), primary or secondary pulmonary hypertension (n=7 vs. 5), cystic fibrosis (n=13 vs. 3), bronchiectasia (n=1 vs. 1), chronic thromboembolic pulmonary hypertension and Swyer–James Syndrom (each n=1 standard group) (Fig. 1). Mean age at transplantation was 45±16 years in the standard group compared to 45±15 years in the extended group. Gender distribution was 26 females and 46 males in the standard group compared to 20 females and six males in the extended group (P<0.01).

Both groups were compared with regard to postoperative complications, time until extubation, ICU and hospital stay, survival and incidence of BOS.

### 3. Results

Results are described as mean±SD unless otherwise indicated.

Twenty-three (24.5%) donors were extended according to the above mentioned criteria. Eight donors had a reduced arterial oxygenation, five donors were older than 55 years, in three donors pathologies on chest X-ray were detected, one donor had a smoking history of more than 20 pack-years and in one donor active cocaine abuse was known. Five donors presented with various combinations of two extended factors.

Twenty-six recipients (26.55%) received organs from extended donors. Mean waiting list time was 87±90 days in the standard group versus 101±87 days in the extended group (P=0.21). In the standard group, 58 bilateral and 14 single lung transplantations were performed compared to 18 double and eight single in the extended group. Twenty-nine patients in the standard group and six patients in the extended group were transplanted with ECMO support. In one patient in the extended group cardiopulmonary bypass was required due to a concomitant ventricular septum defect repair. In 36 patients (27 in the standard group, nine in the extended group) ischemic time was prolonged more than 6 h. Mean ischemic time was 6.1±1.0 h in the standard group compared to 6.1±1.9 h in the extended group (P=0.9). Additional downsizing of the donor lung due to a size mismatch was required in 10 recipients in the extended group and 17 recipients in the standard group. If matching criteria like extended graft ischemic time of more than 6 h and/or size mismatch requiring downsizing of the donor lung are also taken into account then 61 (62.2%) recipients received non-guideline donor organs.

Intubation time (12±2/median 3 days standard vs. 14±5/median 4 days extended, P=0.70), intensive care unit stay (16±2/median 8 days standard vs. 18±5/median 9 days extended, P=0.74) and hospital stay (38±4/median 25 days standard vs. 40±6/median 31 days extended, P=0.71) was slightly, but not statistically significant longer in the extended group. Postoperative bleeding rates requiring operative revision were comparable in both groups (n=14 standard vs. n=3 extended, P=0.36) as well as bronchial anastomotic complications (n=7 standard (5.4% of 130 anastomoses at risk) vs. n=3 (6.8% of 44 anastomoses at risk)) extended, P=0.79). Three months survival was 88.89% in the standard group vs. 92.31% in the extended group.

<table>
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<td>Chest X-ray</td>
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Fig. 1. Indications for lung transplantation.

FiO2/PEEP 5 < 300 mmHg, tobacco history > 20 pack years, inhalative drug abuse, presence of infiltration on chest X-ray or purulent secretions at bronchoscopy.

The lungs were harvested en-bloc after perfusion with a high molecular low potassium dextrane (LPD) solution and 0.5 mg epoprostenol, separated at the back-table and stored separately in perfusion solution. Surgical approach for transplantation was either gained by uni- or bilateral anterolateral thoracotomy or bilateral transternal thoracotomy (clamshell incision). If intraoperative cardiopulmonary support was required, extracorporeal membrane oxygenation (ECMO) was routinely used instead of cardiopulmonary bypass.

Recipients were stratified in two groups according to whether they received a ‘standard’ or ‘extended’ organ. Recipient diagnoses were COPD (n=33 standard group vs. n=11 extended donor group), pulmonary fibrosis (n=15 vs. 6), primary or secondary pulmonary hypertension (n=7 vs. 5), cystic fibrosis (n=13 vs. 3), bronchiectasia (n=1 vs. 1), chronic thromboembolic pulmonary hypertension and Swyer–James Syndrom (each n=1 standard group) (Fig. 1). Mean age at transplantation was 45±16 years in the standard group compared to 45±15 years in the extended group. Gender distribution was 26 females and 46 males in the standard group compared to 20 females and six males in the extended group (P<0.01).
Patient details for 30 day mortality are given in Table 1. After a mean follow up of 697 ± 343 days (range 0–1268 days) actuarial survival is 68.35% in the standard group compared to 75.21% in the extended group (Fig. 2).

The best lung function tests achieved after transplantation were also comparable in both groups. (FEV1% 73.5 ± 20.8 vs. 75.1 ± 22.8, P = 0.77; TLC% 91.3 ± 17.4 vs. 99.6 ± 19.7, P = 0.10)

During the observation period, eight patients in the standard group developed bronchiolitis obliterans syndrome 0p, whereas, all of the patients in the extended group are in either BOS 0 or 0p. Mean time to onset of BOS was 223 ± 198 days (Fig. 3).

4. Discussion

In order to accept an organ donor, several criteria need to be taken into account (Table 2). Besides general donor criteria which might avert organ donation at all, lung specific criteria have been defined in an attempt to deduce the functional capacity of a donor lung and exclude organs likely to provide unsatisfying results. However, those criteria are based mainly on opinions and individual experiences rather than on existing evidence [1]. Several reports have been published that the use of lung donors who fail to meet all standard criteria does not significantly impair results compared to standard lung donors [2–4]. Even after refinement of guidelines [5], they still do not reflect clinical reality.

Besides the sole donor criteria obviously the organisational background of a transplant program is an important factor. The Vienna lung transplant programme is established in the Austrian legal framework of ‘presumed consent’ organ donation and center orientated allocation. This results in a relatively high organ donation rate and a short waiting list with low waiting list mortality. Additionally the organ can be allocated by the center to the most suitable recipient not only by strict waiting time or size matching criteria but also according to the current medical status of the patient. Even in this setting every fourth donor accepted does not meet the standard lung donor criteria. If matching criteria like extended graft ischemic time of more than 6 h and/or size mismatch requiring downsizing of the donor lung are also taken into account then 61 (62.2%) recipients received non-guideline organs. In transplant centers with long waiting lists and a high mortality rate on the waiting list, the pressure to accept marginal donor organs might be even more prevalent.

Several criteria are mentioned in the recommendations. One criterion which needs critical reflection in each individual case is the arterial oxygenation. If arterial oxygenation in an otherwise acceptable donor is reduced, potential reasons have to be scrutinized. To give an example we encountered distinct reduced arterial oxygenation in a severely obese donor. At harvesting almost total atelectasis of the lower lobe was observed, yet the lung was after full inflation completely unimpaired. Overall there is inadequate data regarding the risk/benefit ratio for the lower limit of acceptability for donor arterial blood gases [6].

The current guidelines for upper age limit suggest 55 years as maximum age. While in kidney transplantation in the framework of Eurotransplant an old-to-old program has been successfully established [7], no such efforts have been undertaken in lung transplantation. In our patients, donors up to the age of 61 have been used. A thorough evaluation of these donors, especially for malignancy and other potentially undiagnosed diseases has to be undertaken. Although smaller studies have not shown a survival disadvantage with

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**Table 2**

Current standard donor lung criteria

| Age < 55 years |
| ABO blood group compatibility |
| Clear chest radiography |
| Arterial oxygen pressure > 300 mm mercury on fractional inspired oxygen of 1.0 and positive end-expiratory pressure on 5 cm H2O |
| < 20 pack-year smoking history |
| Absence of chest trauma |
| No aspiration or sepsis |
| Sputum gram stain sample free of bacteria, fungus and significant number of white blood cells |

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Fig. 2. Kaplan–Meier survival.

Fig. 3. Donor chest X-ray. Partial clouding of the right hemithorax due to iatrogenic pleural fluid instillation by a misplaced subclavian catheter. Upon harvesting of the lungs the parenchyma was completely unimpaired and both lungs successfully transplanted.
the application of standard lung donor criteria excludes a considerable number of lungs potentially suitable for transplantation, thus liberalisation of donor criteria might help in overcoming donor shortage.

### References


### Appendix A. Conference discussion

**Dr N. van der Kaay (Rotterdam, Netherlands):** Were there patients in your study which had combined donor extended criteria among them, or did they just have one extended criterion?

**Dr Aigner:** No, there were 5 donors who had 2 criteria extended, as I mentioned in the beginning.

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#### Table 3

| Donor lung criteria applied at Vienna lung transplant program |
|-------------|----------------|
| Age <65 years |
| No proven impairments after smoking history > 20 pack years |
| No extensive parenchymal destruction after chest trauma |
| Unilateral infiltrate, aspiration or extensive trauma → use of contralateral lung possible |
| Positive sputum gram stain → adequate prophylaxis (except multiresistant bacteria) |
| Reduced arterial oxygenation → evaluation of potential non-pulmonary causes (obesity, pleural effusions, malnutrition, ...). |
| Clarify possibility of improvements with active donor management |

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#### Ascertainment ofDonor Lung Criteria

- **Consensus:**
  - Age ≤ 70 years
  - No acute lung injury
  - No apparent infectious diseases
  - No evidence of pulmonary embolism
  - No malignant disease

- **Donor Lung Criteria applied at Vienna lung transplant program**
  - Age ≤ 70 years
  - No acute lung injury
  - No apparent infectious diseases
  - No evidence of pulmonary embolism
  - No malignant disease

- **References**
Dr van der Kaay: And was there a result which was different than in the other group?

Dr Aigner: No, there was no difference in the results between the donors who had 2 extended criteria compared to those who had only 1 criterion extended.

Dr van der Kaay: Then I missed it.

Dr M. Strueber (Hannover, Germany): I have a couple of problems with the criteria used to establish the term 'extended donor'. and this applies to both presentations.

I think it’s very hard to establish a proper smoking history of a donor. Most of the time we do not know if the smoking history is more or less than 20 pack years. We just know it’s a smoker or not, or heavy or not. And so this, in my opinion, is a very weak criteria.

The second is PO2: It is also a weak criterion to decide. Because in case you have a donor arterial blood gas analysis at 40%, which appear to have 130 mmHg, and then you get a bad PO2 at 100% fiO2, you don’t worry anymore. But this is labeled 'extended donor'.

And with purulent secretions, this is also a weak factor, because what is somebody calling purulent secretions and what is not? So my question is, why are you not using more standard criteria like extended ventilation time of the donor?

Dr Aigner: Well, we were referring to the ideal donor criteria mentioned in the beginning which are published by the ISHLT, as you know. And I certainly agree with you that the PO2 is a weak criterion. There are many factors why a PO2 can be decreased like, say, an obese donor who has massive basal atelectasis or there might be a malintubation or anything. But nevertheless, we needed some reference to compare and a way to define the extended donor criteria. We considered this the best way to do it according to the ISHLT criteria.

And I also agree with you that, for example, that smoking history in most cases is not exactly known. So we only classify the donors as extended if it was really known that the smoking history was definitely more than 20 pack years, which was the case in only one donor as you would have noticed.

Dr D. Van Roemdonck (Leuven, Belgium): In those donors with bad oxygenation, did you correlate the PO2 at the time of organ offer versus the PO2 during the retrieval when the lung was completely ventilated with open chest?

Dr Aigner: No, we did not do that.

Dr L. Mueller (Innsbruck, Austria): These are very important results and they also meet our results mainly. But I have two questions.

Your mean recipient age was 45 years which seems quite young. Did you analyze your results regarding the effect or the acceptability of the extended donor lungs per age group, young and older recipients? Do you have different, maybe worse results, in the older recipients?

And second question is, was it a printing mistake that you have median intubation time of 12 and 14 days?

Dr Aigner: No, the median intubation time was 4 days and 3 days. The first one was mean. There were a few recipients with very long intubation times which made up for a very long mean intubation. But the median was 4 days in the extended group and 3 days in the standard recipient group.

Dr Mueller: Okay.

Dr Aigner: And no, we did not stratify the results according to age. But the low mean age might come due to a relatively high rate of cystic fibrosis in young patients with primary pulmonary hypertension which make up the low mean age.

Dr Mueller: Do you have a feeling about the results in the older age recipient group regarding extended donors?

Dr Aigner: I think that age itself does not make so much difference. It’s the stage of disease which makes more difference, whether it’s a very advanced stage of disease, and it doesn’t matter that much whether this is in a young CF recipient or in an old CF recipient.