

Can lungs be taken for transplantation from donors with a significant smoking history?

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Abstract

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was 'Can lungs be taken for transplantation from donors with a significant smoking history?'. Five papers were found using the reported search that represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. These studies compared the outcome and survival between patients who receive lungs from smokers with those receiving non-smoker lungs. None of these studies were randomized controlled trials. They retrospectively analysed a cohort of patients undergoing lung transplantation for the past 10 years. These studies showed worse outcomes in the early postoperative period, such as longer intensive care unit stay, longer ventilation time and higher early postoperative mortality, with lungs harvested from smokers. Two studies also demonstrated a worse long-term outcome in recipients of lungs from smokers, whereas the other two showed worse results during the early postoperative period only. These latter two studies reported similar survival rates after 3 months and up to 3 years in recipients receiving smoker vs non-smoker lungs. One study, however, showed a better 5-year survival with smoker lungs compared with non-smokers, although in this study, lungs from heavy smokers showed the worse outcome. Despite the difference in long-term results and outcome reported by these authors, all of these studies unanimously indicate that lungs from smokers should not be rejected, as survival in these patients receiving smoker lungs is still significantly higher in 3 and 5 years compared with that in those who remain on the transplant waiting list. In conclusion, the current evidence in the literature suggests that lungs from smokers can be used for transplantation. Patients should, however, be fully informed of the risks involved with these lungs and the worse outcome compared with those receiving non-smoker lungs.

Keywords: Review • Lung transplantation • Smoker donors

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in the *ICVTS* [1].

THREE-PART QUESTION

Do [patients undergoing lung transplantation] with [donor lungs from smokers] compared to [non smokers] have an equivalent [mortality].

CLINICAL SCENARIO

The transplant coordinator has contacted you regarding a 38-year old potential lung donor who was pronounced brain dead a few hours ago after a fall. All of his selection criteria match your 55-year old patient with end-stage interstitial lung disease. It has, however, been brought to your attention that the donor smoked 30 cigarettes a day for the past 12 years. You are not sure whether his lungs are suitable for transplantation and

decide to check the evidence yourself before sending the harvest team to collect the organs.

SEARCH STRATEGY

Medline 1950 to February 2013 using OVID interface [exp smoking/ OR exp tobacco use in donors.mp] AND [exp lung transplantation/OR exp lung transplantation].

SEARCH OUTCOME

Of 81 papers that were found, we excluded case reports and those that did not compare lungs from smokers with those from non-smokers as their primary or secondary outcome. We also excluded the papers that investigated the effect of extended criteria on the outcome after lung transplant as this topic had been reviewed and published previously [2].

No randomized controlled trials were identified. Overall, only five reports had analysed this topic and answered the above question. These studies are presented in Table 1.

Table 1: Papers comparing the results of using smoker donors with non-smokers

Author, year and journal Study type (level of evidence)	Patient group Recruitment years	Outcomes	Key results	Comments and limitations
Waddell <i>et al.</i> (2003), J Heart Lung Transplant, Canada [5]	SD NSD and <20 pack-year	Better results with NSD or <20 pack-year	One, 3 and 5-year mortalities significantly higher in SD	On a large number from the US organ-sharing database Only an abstract is available
Retrospective (level III)				
Oto <i>et al.</i> (2004), Transplantation, Australia [8]	SD = 77 NSD = 84	Significantly negative effect on early outcome with SD, but no effect on late outcome	Longer ventilation time, ICU stay, higher 30-day mortality ($P = S$)	Number of pack-year and cumulative dose negatively affected ICU stay and oxygenation in the SD subgroups
Retrospective (level III)	1995–2002		Hospital stay, 3-month, 1- and 3-year survival similar ($P = NS$)	
Berman <i>et al.</i> (2010), Ann Thorac Surg, UK [9]	SD = 184 NSD = 240	More deaths in early postoperative in SD, but it was not a risk factor in the long-term	Higher 3-month mortality and longer ICU stay with SD ($P = S$)	Rejection rates higher on NSDs, but results were based on a very small number The use of SD is acceptable
Retrospective (level III)	1995–2008		Infection and ventilation were similar ($P = NS$)	
Bonser <i>et al.</i> (2012), Lancet, UK [6]	SD = 510 NSD = 712	Significantly better outcome with NSD, however, patient on the list who died before transplant had worse mortality	Higher 1-, 3- and 5-year mortalities with SD ($P = S$)	SD provide 40% of available lungs
Retrospective (level III)	1999–2010			
Shigemura <i>et al.</i> (2013), Transplantation, USA [11]	SD = 293 NSD = 239	Better outcome SD compared with NSD	Five-year survival: SD = 65.8% NSD = 48.3% $P < 0.05$	The absence of smoking did not result in better outcome
Retrospective (level III)		Worse outcome with heavy smoker donors Teenage non-smoker lungs showed worse outcome compared with non-smoker adult donors		

SD: smoker donors; NSD: nonsmoker donors; S: smokers.

RESULTS

The standard lung transplant donor criteria include age <55, ABO blood group compatibility, a clear chest X-ray, $\text{PaO}_2 \geq 300$ mmHg on fractional inspired oxygen of 1.0 l, positive end-expiratory pressure >5 cm H_2O , ≤ 20 pack-year smoking history, absence of chest trauma, no aspiration or sepsis, and sputum sample free of bacteria and significant number of WBC. However, due to the shortage of donors in recent years, in most centres extended or marginal criteria are being used. In a best-evidence topic, Schiavon *et al.* compared the results of 14 studies that used extended criteria donors with donors from standard criteria and concluded that the current evidence shows no contraindications for the use of lung transplantation from marginal or extended criteria. However, in his best-evidence topic, the influence of smoking as a separate factor was not taken into consideration. In those cases, one or more of the above factors does not apply to the donor, and current evidence shows that there are no contraindications to the use of such extended donor criteria for lung transplantation [2]. Studies have

also developed a lung donor score based on the results of the use of extended/marginal criteria and in Eurotransplant, there are already well-established definitions of an extended criteria donor [3, 4].

However, the effect of smoking as a single factor on the outcome post-transplantation has been investigated by a few authors only. Waddell *et al.* [5] retrospectively reported their analysis from the US organ-sharing database and divided the patients into two categories of smokers; those who smoked >20 per day and a group of donors who were non-smokers or smoked <20 per day. The results showed a significantly higher mortality rate at 1, 3 and 5 years in patients who receive lungs from smokers. Similarly, Bonser *et al.* [6] analysed the UK transplant registry and showed a significantly high mortality rate at 1, 3 and 5 years when lungs were obtained from donors who smoked compared with non-smokers. The poor results with smoker lungs in the long term was mainly due to respiratory complications, and interestingly, a case of cancer 1 year after transplantation in a patient receiving smoker lungs has been reported. This resulted in end-stage lung cancer in the recipient [7].

Moreover, Bonser *et al.* demonstrated that 40% of the available donor lungs were harvested from smokers and more importantly, he showed that, despite the high mortality rate with lungs from smokers, survival remains significantly better in patients who receive these lungs compared with those for whom a suitable donor is not found.

The effect on outcome following transplantation using lungs from smokers has been shown to be more prominent in the early, but not late, postoperative period in two other studies. Oto *et al.* [8] also showed longer ventilation time, intensive care unit (ICU) stay and higher 30-day mortality with smokers' lungs, but mortality at 1 and 3 years was found to be similar to that of the patients transplanted with non-smokers' lungs. They also showed that the number of pack-years and cumulative dose negatively affect the outcome. Similar to Oto, Berman *et al.* [9] also showed a worse outcome up to 3 months after transplantation with smokers' lungs, but this was not maintained in the long term. That study demonstrated that the rejection rate was higher with non-smoker lungs compared with the smokers. It has been shown previously that smoking negatively affects the immune system [10].

On the other hand, a recent study by Shigemura *et al.* showed a better long-term survival rate in recipients of lungs from donors with a smoking history compared with those who received non-smoker lungs, although patients who received lungs from heavy smokers still showed higher short- and long-term mortalities. They also demonstrated a higher incidence of mortality and morbidity in recipients of lungs from teenaged donors with no smoking history than in those with lungs from adult non-smokers [11].

CLINICAL BOTTOM LINE

Lung transplantation from smokers affects both short- and long-term survivals postoperatively. However, the worse outcome is expected during the early postoperative period than in the long term. Despite worse outcomes post-transplant in patients receiving smoker lungs compared with those receiving non-smoker lungs, due to the shortage of donors, smoker lungs should be

considered in patients requiring (urgent/early) transplant, as delay can result in death from the original lung pathology prior to finding a suitable match in these patients, and patients should also fully be informed about the risks of using smokers' lungs in the long term.

Conflict of interest: none declared.

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