ELSEVIER

European Journal of Cardio-thoracic Surgery 24 (2003) 601–607

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Bacterial colonization of the donor lower airways is a predictor of poor outcome in lung transplantation☆

Vassilios S. Avlonitis*, Anna Krause, Luca Luzzi, Hazel Powell, Julie A. Phillips, Paul A. Corris, F. Kate Gould, John H. Dark

Cardiopulmonary Transplantation Unit, Freeman Hospital, Newcastle upon Tyne, UK

Received 17 March 2003; received in revised form 10 July 2003; accepted 14 July 2003

Abstract

Objective: At the time of lung transplant, we routinely perform bronchoalveolar lavage (BAL) of the donor lungs on the recipient operating table immediately before implantation, for bacterial and fungal cultures. We sought to determine whether the results correlate with the outcome. **Methods**: We retrospectively analysed 115 consecutive cadaveric lung transplants (single lung: 42; bilateral lung: 63; heart–lung: 10) performed over 4 years. **Results**: Fifty-three (46%) grafts had positive BAL (bacteria: 33; fungus: 10; mixed: 10) and 62 (54%) were negative. Recipients with donor BAL culture positive for bacteria had lower mean oxygenation index in the first 6 h compared with those with negative bacterial culture (36.5 ± 14.73 vs. 44.1 ± 16.79 kPa) ($P = 0.019$). They also had longer median intensive treatment unit stay (2.5 vs. 1.5 days) ($P = 0.035$), and median time of mechanical ventilation (37.5 vs. 23.0 h) ($P = 0.008$), as well as inferior 6-month, 1-year, 2-year and 4-year cumulative survival (79, 77, 74, 60% vs. 93, 92, 88, 79% respectively) ($P = 0.04$). There was no difference in the above parameters between recipients with Gram-negative ($n = 18$) and recipients with Gram-positive bacteria ($n = 19$) in the donor BAL. Incidence of acute rejection within the first 2 weeks and time of onset of bronchiolitis obliterans syndrome (BOS) were similar in the bacteria-positive and bacteria-negative groups. Recipients with donor BAL positive for fungi alone had similar outcome with the negatives. There was no difference in the donor oxygenation index and age, recipient age, transplant type and ischaemic time between compared groups. There was a significant difference in the median length of donor mechanical ventilation between donors with Gram-positive and donors with Gram-negative bacteria in the BAL (24 vs. 48 h) ($P = 0.01$), as well as between donors with fungi alone in the BAL and donors with negative BAL (67 vs. 48 h) ($P = 0.04$). **Conclusions**: Donor lungs with lower airways colonized with bacteria result in inferior recipient outcome. Bacterial colonization of the donor lower airways could therefore be used as a marker of donor lung injury, but evidence from a prospective study is necessary.

Keywords: Lung transplantation; Bronchoalveolar lavage; Bacteria; Fungi

1. Introduction

To increase the number of donor lungs used for transplantation and improve the postoperative results, attention needs to be paid to donor selection [1]. Identification of sensitive markers of donor lung injury and accurate predictors of graft function post-transplantation has always been a challenge. One of the considerations in donor selection is the presence or absence of infection in the donor lungs. As intrapulmonary infection has been a major cause of early morbidity and mortality in lung transplant recipients, utilization of lungs from donors with a positive Gram stain of tracheal secretions has been avoided [2]. However, with the use of aggressive antibiotic treatment for donors and recipients the incidence of recipient pneumonia has recently decreased significantly [3] and the results of Gram stain of donor tracheal secretions no longer correlate with the recipient outcome [4]. Positive Gram stain of tracheal aspirates may not reflect ongoing pneumonia, but simply a collection of purulent secretions in the upper airways. Therefore, in the modern era of pulmonary

☆ Presented at the 16th Annual Meeting of the European Association for Cardio-thoracic Surgery, Monte Carlo, Monaco, September 22–25, 2002.

* Corresponding author. Department of Surgery, Medical School, University of Newcastle, Framlington Place, Newcastle upon Tyne NE2 4HH, UK. Tel.: +44-191-222-7156; fax: +44-191-222-8514.

E-mail address: avlonitis@hotmail.com (V.S. Avlonitis).

1010-7940/$ - see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/S1010-7940(03)00454-8

transplantation, the significance of organisms in the donor lungs has to be re-examined.

Bronchoalveolar lavage (BAL) is an accurate method of assessing the lungs of brain-dead donors. The results of the BAL culture have been found to correlate with the histological findings better than the results of lung tissue culture or protected specimen brush biopsy [5].

In our centre, routine BAL is performed on all donor lungs when they arrive at the recipient operating theatre immediately before implantation. The fluid is sent for Gram-staining and bacterial and fungal cultures. We sought to determine whether the result of the donor BAL fluid cultures correlates with the recipient outcome.

2. Materials and methods

2.1. Study population

We retrospectively reviewed our Transplant Database, Intensive Treatment Unit (ITU) Database, Microbiology Database and the clinical notes of 115 consecutive cadaveric pulmonary transplants (single lung: 42; bilateral lung: 63; heart–lung: 10) performed in 114 patients from September 16, 1997 to August 31, 2001.

2.2. Perioperative management

2.2.1. Microbiology

All recipients received perioperative antibiotic prophylaxis with flucloxacillin for 48 h and metronidazole for 1 week. If the patient was allergic to penicillin, clindamycin was used instead. Patients with chronic bronchial sepsis also received an antibiotic active against Gram-negative organisms based on preoperative sensitivities. In addition, such patients also received nebulized colomycin, unless colonized with resistant organisms. In the case of colonization with *Aspergillus*, Itraconazole was administered for antifungal prophylaxis.

BAL was performed on all donor lungs on arrival at the recipient operating table immediately before implantation. Under sterile conditions a catheter was wedged into a segmental lower lobe bronchus through which BAL was performed with 50 ml of normal saline. The BAL fluid was sent to the microbiology department for Gram-staining and bacterial and fungal cultures. Results were available within 24–48 h post-transplantation and antibiotic treatment was adjusted accordingly.

2.2.2. Immunosuppression

Immediately preoperatively the patients received oral cyclosporine (dose adjusted according to glomerular filtration rate) and azathioprine (4 mg/kg). Intraoperatively, before graft reperfusion, 500 mg of methylprednisolone was administered intravenously, followed postoperatively by three doses of methylprednisolone 125 mg 8-hourly and then prednisolone 1 mg/kg daily reduced by 0.2 mg/kg every other day. Postoperative immunosuppression also included: rabbit anti-thymocyte globulin 2.5 mg/kg (dose adjusted to maintain absolute T-cell count $> 0.05 \times 10^9$/l) daily for the first 3 days, cyclosporin (dose adjusted to maintain serum trough level of 250–350 ng/ml) and azathioprine at a maximum dose of 4 mg/kg (dose adjusted to maintain white blood cell count $> 4.0 \times 10^9$/l). Surveillance transbronchial lung biopsy and BAL was performed on the 7th and 30th postoperative day and at regular intervals thereafter. Acute rejection was treated with intravenous methylprednisolone 10 mg/kg daily for 3 days.

2.3. Outcome variables

Recipient outcome was assessed by the following variables. (a) Mean of the recipient partial arterial oxygen pressure/inspired oxygen fraction ratios (PaO_2/FiO_2) at 1 and 6 h postoperatively. (b) Length of mechanical ventilation in hours. (c) Length of ITU stay in days. (d) Incidence of acute rejection within the first 2 weeks (grade $\geq$ A2-mild or clinical evidence of rejection treated with intravenous steroids). (e) Time of freedom from bronchiolitis obliterans syndrome (BOS) (decrease in $FEV_1 \geq 20\%$ from baseline on two measurements taken at least 3 weeks apart, in the absence of other causes). (f) Cumulative recipient survival.

2.4. Statistical analysis

Data were statistically analysed using the Statistical Package for Social Sciences v.11. Data with a normal distribution are presented as mean ± standard deviation. For data with non-parametric distribution the median and range are given. Comparisons between two independent groups of observations was performed with Student's *t*-test for parametric and the Mann–Whitney test for non-parametric distribution. Comparisons between groups for categorical variables were performed using the chi-square test. Analysis of survival and time of freedom from BOS were done with the Kaplan–Meier method and groups were compared with the log-rank test. Differences were considered significant at the level of $P < 0.05$.

3. Results

The age of the recipients ranged from 14 to 62 years (mean: 39.7 ± 14.41; median: 42.0). The donor age ranged from 9 to 61 years (mean: 35.1 ± 14.45; median: 36). The donor cause of death is shown in Table 1. The median time of donor ventilation was 48 h (range: 12–240). The mean donor PaO_2/FiO_2 was 60.7 ± 11.57 kPa (median: 60.0; range: 30–88). The mean ischaemic time was 308 ± 60.3 min. Indications for transplantation are shown in Table 2.

The donor BAL culture was positive in 53 (46%) and negative in 62 (54%) transplants. Thirty-three (29%) were

Table 1
Cause of death in 115 donors

Cause of death	No. of donors (%)
Traumatic	41 (35.7)
Primary traumatic head injury	41 (35.7)
Non-traumatic	65 (56.5)
Subarachnoid haemorrhage	34 (29.6)
Intracerebral haemorrhage	17 (14.8)
Primary cerebral tumour	2 (1.74)
Overdose	1 (0.9)
Carbon monoxide poisoning	1 (0.9)
Acute hydrocephalus	1 (0.9)
Hypoxic brain injury	2 (1.7)
Primary intracranial infection	4 (3.5)
Cerebral infarct	3 (2.6)
Unknown	9 (7.8)

positive for bacteria, 10 (9%) for fungi and 10 (9%) for both (Table 3).

3.1. Positive (n = 53) vs. negative (n = 62)

The recipient PaO_2/FiO_2 was lower in the positive group (36.9 ± 13.92 vs. 44.8 ± 17.53 kPa) ($P = 0.01$). There was no difference in median ITU stay (2.5 days; range:0.5–61.0 vs. 1.5 days; range:0.5–46.0) ($P = 0.1$), median time of ventilation (30.8 h; range:1–1392 vs. 24.0 h; range:1–1020) ($P = 0.18$), incidence of early acute rejection (32 vs. 39%) ($P = 0.6$) and time of onset of BOS ($P = 0.3$) between the positive and the negative groups. Cumulative survival was also similar for both groups ($P = 0.15$) (Fig. 1).

3.2. Bacteria-positive (n = 43; 33 positive for bacteria plus 10 mixed) vs. bacteria-negative (n = 72)

Recipients of lungs with donor BAL culture positive for bacteria had significantly lower PaO_2/FiO_2 compared with recipients of lungs negative for bacteria (36.5 ± 14.73 vs. 44.1 ± 16.79 kPa) ($P = 0.019$). They also had longer median ITU stay (2.5 days; range:0.5–61.0 vs. 1.5 days; range:0.5–46.0) ($P = 0.035$) and median time of mechanical ventilation (37.5 h; range:1–1392 vs. 23.0 h; range:1–1020) ($P = 0.008$), as well as inferior 6-month, 1-year, 2-year and 4-year cumulative survival (79, 77, 74 and 60% vs. 93, 92, 88 and 79%) ($P = 0.04$) (Fig. 2). There was no significant difference in the outcome for the above parameters between recipients with Gram-negative ($n = 18$) and recipients with Gram-positive bacteria ($n = 19$) in the donor BAL (Table 4) (Fig. 3). Incidence of early acute rejection (31 vs. 38%) ($P = 0.5$) and time of onset of BOS ($P = 0.8$) were similar in the bacteria-positive and bacteria-negative groups.

Table 2
Indication for transplantation in 115 pulmonary transplants

Indication	No. of transplants (%)
Cystic fibrosis	44 (38)
Emphysema	24 (21)
Interstitial lung disease	16 (14)
Bronchiectasis	8 (7)
Primary pulmonary hypertension	6 (5)
Obliterative bronchiolitis	5 (4)
Histiocytosis X	3 (3)
Congenital anomaly	3 (2)
Lymphangioleiomyomatosis	2 (2)
Sarcoidosis	2 (2)
Asthma	1 (1)
Bronchoalveolar carcinoma	1 (1)

Table 3
Organisms isolated in bronchoalveolar lavage cultures from 53 donors

Organism	No. of donors (% out of positives)
Staphylococcus aureus	21 (40)
[Methicillin-resistant]	[2 (4)]
Haemophilus influenzae	13 (25)
Streptococcus pneumoniae	5 (9)
Escherichia coli	3 (6)
Pseudomonas aeruginosa	2 (4)
Haemophilus parainfluenzae	2 (4)
β-Haemolytic *Streptococcus* spp.	2 (4)
α-Haemolytic *Streptococcus* spp.	1 (2)
Pseudomonas spp.	1 (2)
Klebsiella pneumoniae	1 (2)
Serratia marcescens	1 (2)
Enterobacter cloacae	1 (2)
Candida albicans	19 (36)
Aspergillus fumigatus	1 (2)

3.3. Positive for fungi alone (n = 10) vs. negative (n = 62)

The recipients with donor BAL culture positive only for fungi ($n = 10$) had similar PaO_2/FiO_2 (39.1 ± 9.06 vs. 44.8 ± 17.53 kPa) ($P = 0.37$), median ITU stay (1.25 days; range: 1–7 vs. 1.5 days; range: 0.5–46.0) ($P = 0.82$) and median time of ventilation (16.5 h; range: 2–123 vs. 24 h; range: 1–1020) ($P = 0.12$), as well as similar incidence of early acute rejection (40 vs. 39%) ($P = 1.0$), time of onset of BOS ($P = 0.16$) and survival ($P = 0.62$) with the negative patients (Fig. 4).

There was significant difference in the median length of donor mechanical ventilation between donors with Gram-positive (24 h; range: 12–192) and donors with Gram-negative bacteria (48 h; range: 24–240) in the BAL ($P = 0.01$), as well as between donors with fungi alone in the BAL (67 h; range: 24–120) and donors with negative BAL (48 h; range: 12–168) ($P = 0.04$). Otherwise, there was no difference in the recipient age, donor age, donor cause of death (traumatic vs. non-traumatic), donor PaO_2/FiO_2, donor length of mechanical ventilation, transplant type and ischaemic time between compared groups (data not shown).

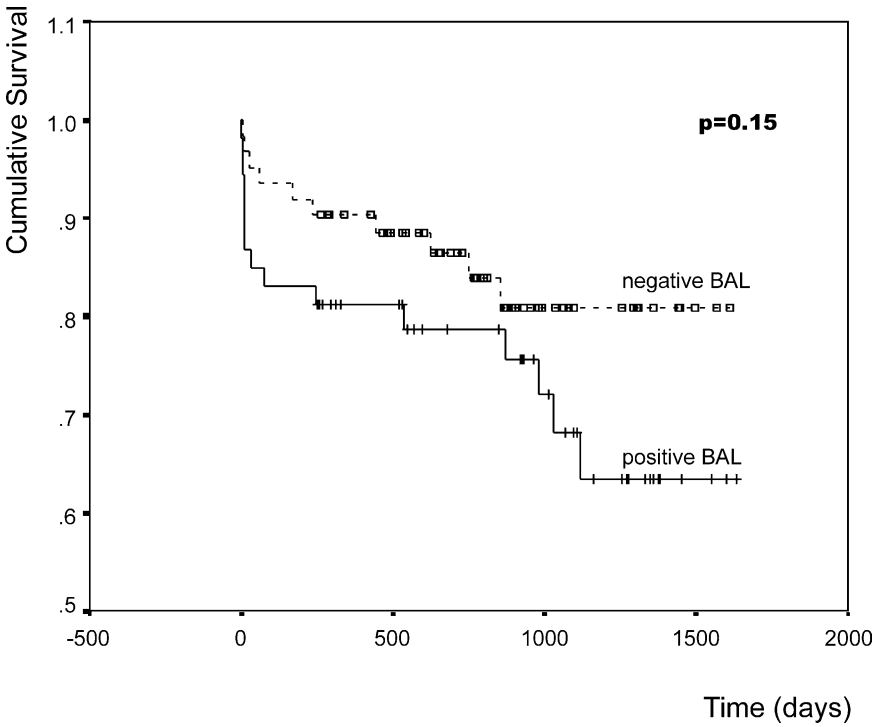

Fig. 1. Kaplan–Meier survival curves for the groups with positive and negative donor BAL. □ and + mark censored cases.

Initial perioperative antibiotic prophylaxis had covered the organisms in the donor BAL culture in 79% of the cases with positive bacterial culture and in 15% of the cases with positive fungal culture. After the donor BAL culture result was available, adjusted antimicrobial treatment covered 93% of the patients with positive bacterial culture and 65% of the patients with positive fungal culture.

From the recipients of lungs with a positive BAL culture, 13 (21%) patients had growth of the donor organism in at least one postoperative culture of tracheal aspirates, sputum,

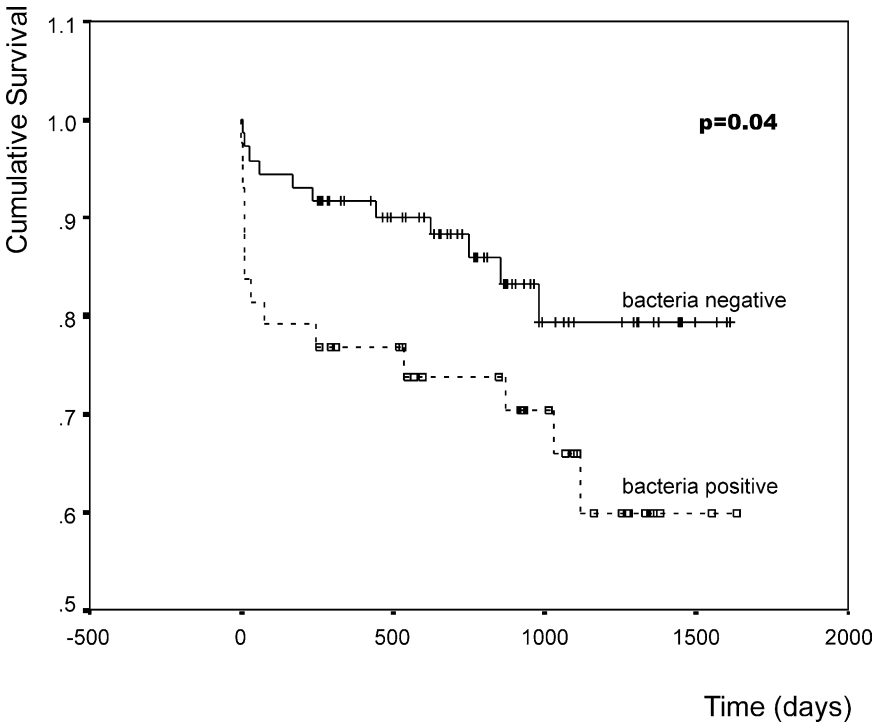

Fig. 2. Kaplan–Meier survival curves for the groups with donor BAL positive and negative for bacteria. □ and + mark censored cases.

Table 4
Comparison of recipient outcome between groups with Gram-positive and Gram-negative bacteria in the donor BAL culture

Bacteria in BAL culture	Gram-positive ($n = 19$)			Gram-negative ($n = 18$)			P-value
	Range	Median	Mean ± SD	Range	Median	Mean ± SD	
Recipient PaO_2/FiO_2 (kPa)	16.6–62.5	39.1	40.4 ± 13.85	10.9–61.8	34.8	35.8 ± 15.11	0.2
Recipient ITU stay (days)	0.5–61	2.0	6.0 ± 13.51	0.5–20.5	5.0	5.7 ± 5.56	0.3
Recipient length of ventilation (h)	6–1392	28.0	118.4 ± 312.65	1–440	55.0	106.3 ± 120.30	0.2

BAL or intrathoracic collection. Only one patient developed clinical intrathoracic infection due to the donor BAL organism proven with cultures, but was treated successfully. None of the patients died of an infection from the donor BAL organism. Early causes of death in patients with a positive donor BAL bacterial culture were: primary graft failure ($n = 4$); infection ($n = 3$); pulmonary embolism ($n = 1$); technical/surgical complications ($n = 1$). Late causes of death were: non-specific graft failure ($n = 1$); BOS ($n = 4$).

4. Discussion

Selection of suitable lung donors in pulmonary transplantation has always been a major challenge. The criteria used for donor selection are rather weak in predicting graft function post-transplantation [6]. Most transplant units have 'relaxed' their selection criteria, as there is growing evidence that lungs considered as 'marginal' can be transplanted with good results [7,8]. Expansion of the donor pool by such means is desirable, as the availability of lungs cannot meet the demand [1].

Currently, one of the donor selection issues that remains controversial, is the significance of the presence of organisms in the donor lungs. In the early days of pulmonary transplantation, early intrathoracic infection was recognized as one of the major causes of recipient mortality [9]. Studies had shown that the presence of organisms in donor tracheal cultures was associated with early infection and decreased survival in the recipient [9]. Transplantation from donors with a positive Gram stain of tracheal secretions was strongly discouraged [2]. Subsequent clinical use of combined intravenous and aerosolized antibiotics in donors and recipients reduced the incidence of recipient pneumonia dramatically [3]. Recent studies have now shown that a positive Gram stain of donor upper airway secretions does not predict recipient outcome [4]. An Australian study provides evidence that even utilization of donors with pulmonary infection has no adverse effect on the transplant outcome [8].

To our knowledge, no previous studies have been published reporting routine use of BAL on the donor

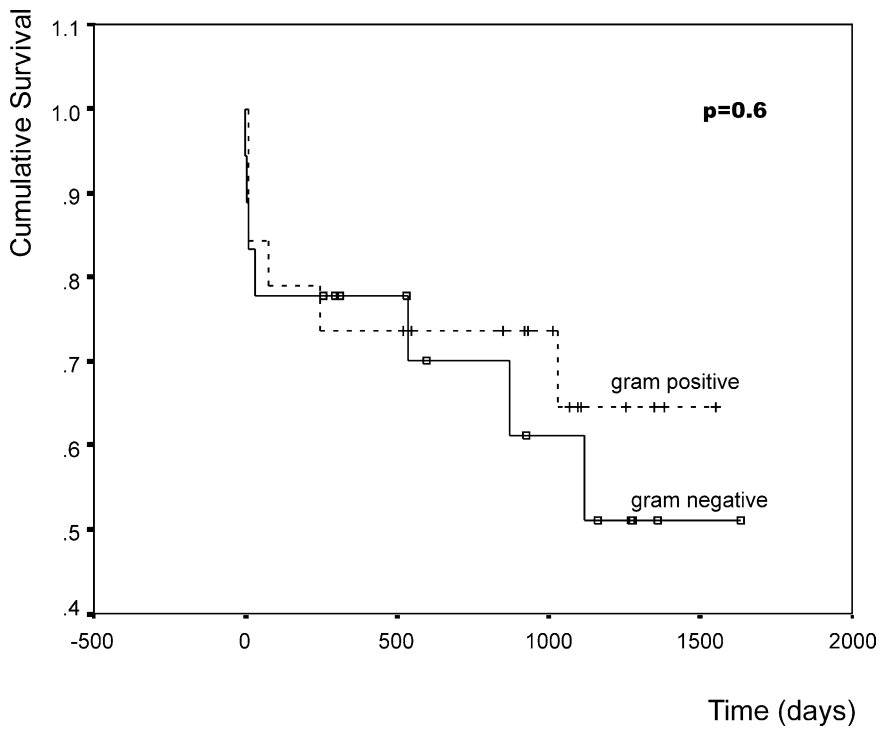

Fig. 3. Kaplan–Meier survival curves for the groups with Gram-negative and Gram-positive bacteria in the donor BAL. □ and + mark censored cases.

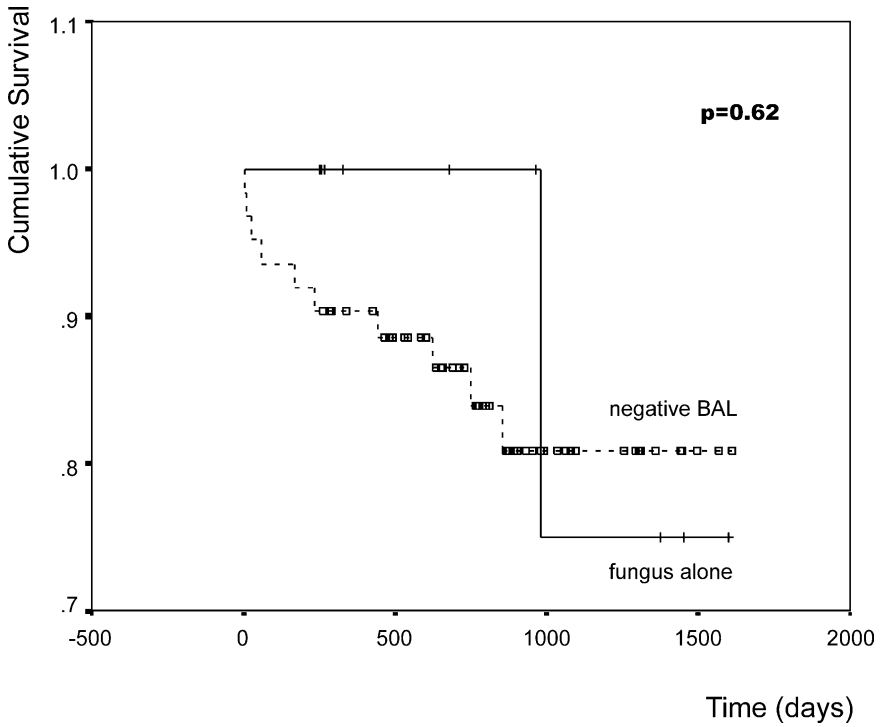

Fig. 4. Kaplan–Meier survival curves for the group with donor BAL positive for fungus alone and the group with negative donor BAL. □ and + mark censored cases.

lungs before implantation. As a result, our study gives a different dimension to the significance of donor organisms. The advantage of BAL is that it provides information about the microorganisms colonizing the lower airways of the donor, as opposed to tracheal aspirates, which are obtained from the upper airways. The upper airways of the intubated and mechanically ventilated donor are prone to contamination and their microbiological status may not reflect the condition of the lung parenchyma.

Our main finding is that transplantation of lungs with donor BAL positive for bacteria results in poor outcome, with poor early graft function and inferior survival. These results suggest that donor lungs with lower airways colonized with bacteria are of inferior quality.

One possible explanation for our findings is that bacteria initiate subclinical infection and local injury in the donor lung, which is amplified by the process of ischaemia-reperfusion and results in poor recipient outcome. Previous investigators found that although the risk of recipient pneumonia is high when the donor lungs are colonized with bacteria, the recipient infection is usually by different organisms [9,10]. They suggested that subclinical donor infection results in lung injury, which makes the lung prone to infection by different organisms in the recipient. In our study also only one patient developed an infection by the donor organism and therefore donor-transmitted infection cannot be the cause of poor outcome in the recipients with donor BAL positive for bacteria. The explanation of lung injury associated with bacteria-induced subclinical donor infection is more likely.

A second explanation is that bacteria tend to grow in donor lungs, which are injured by other causes and therefore become a marker of donor lung injury. It has been observed that patients with acute lung injury/acute respiratory distress syndrome are prone to nosocomial pneumonia [11]. In vitro studies triggered by these observations confirmed that bacterial growth is enhanced by the presence of cytokines at high concentrations [12]. *Staphylococcus aureus* is one of the organisms reported to show enhanced growth in the presence of cytokines [12]. As in previous studies [9,15–17], *S. aureus* was the most common organism also isolated from our donors. The presence of injury and proinflammatory cytokines in some donor lungs is highly likely. The donor is at high risk of lung injury due to trauma, mechanical ventilation, aspiration, infection, but also due to the process of brain death. Brain death causes a systemic inflammatory response with up-regulation of cytokines in peripheral organs including the lung [13,14]. Cytokine levels in the BAL were not routinely measured in our donors.

Recipient and donor age, donor PaO_2/FiO_2, donor length of mechanical ventilation, transplant type and ischaemic time were similar between the bacteria-positive and bacteria-negative groups in our study. The BAL culture result was the only obvious difference between these groups. Bacteria in BAL culture may be a sensitive marker of subclinical donor lung injury and an accurate predictor of graft outcome post-transplantation.

Donors with Gram-negative bacteria in the BAL culture had been ventilated for longer than those with Gram-positive bacteria. Donors with fungus had also been

ventilated for longer than those with a negative BAL culture. The finding of a positive association between longer donor mechanical ventilation and colonization with Gram-negative bacteria and fungus is expected, as these organisms are known to colonize patients ventilated in ITU. However, no difference in the outcome was found between the recipients of these donor subgroups.

In this study, patients who received lungs with fungus alone in the donor BAL had similar outcome to those who received lungs with sterile BAL. Because of this, no statistical differences were found in the outcome between the positive and negative groups, as the fungus subgroup reduced the differences created by the positive for bacteria subgroup. The good results in the fungus subgroup could be explained by our policy to administer antifungal treatment to the recipients, if there is significant growth of fungus in the donor BAL. However, the number of recipients with donor BAL positive for fungus alone is too small to make any definite conclusions.

Our study has the limitations of retrospective data collection and analysis. We did not determine the incidence of early recipient pneumonia. To do this we would have had to set criteria such as white cell count in the blood, chest X-ray findings and sputum or BAL culture results. However, in a retrospective study, the collection of such data from the case notes and databases could lead to inaccurate conclusions. The difficulty in distinguishing between different pathologic processes in lung transplant recipients is well-recognized [16]. For these reasons, we chose to set objective outcome measures i.e. oxygenation index, length of ITU stay and ventilation, incidence of acute rejection, time of onset of BOS, as well as survival.

The finding of poor early oxygenation index, prolonged mechanical ventilation and ITU stay and inferior survival in patients who received lungs with lower airways colonized with bacteria, indicates that these organs could have been injured in the donor. Our study, although retrospective, contributes to the generation of new hypotheses regarding the relevance of the donor organisms to the donor lung injury and the transplant outcome. We believe that further research is worthwhile in order to determine: (a) whether bacterial colonization of the donor lower airways correlates with cytokine levels in the donor BAL and whether these lungs have true histopathological evidence of injury; and (b) whether bacteria are the cause of the injury or simply a marker. An answer to these questions could have a significant impact on donor management and selection and could be given by a prospective study.

Acknowledgements

We thank Andrew Sims, Department of Medical Physics, Freeman Hospital, Newcastle upon Tyne, UK, for his assistance with the intensive treatment unit database.

References

[1] Fisher AJ, Dark JH, Corris PA. Improving donor lung evaluation: a new approach to increase organ supply for lung transplantation. Thorax 1998;53(10):818–20.
[2] Zenati M, Dowling RD, Armitage JM, Kormos RL, Dummer JS, Hardesty RL, Griffith BP. Organ procurement for pulmonary transplantation. Ann Thorac Surg 1989;48:882–6.
[3] Dowling RD, Williams P, Zenati M, Griffith BP, Hardesty RL. Infections and pathologic factors in the donor lung. J Thorac Cardiovasc Surg 1995;109(6):1263–4.
[4] Weill D, Dey GC, Hicks RA, Young KR, Zorn GL, Kirklin JK, Early L, McGiffin DC. A positive donor gram stain does not predict outcome following lung transplantation. J Heart Lung Transplant 2002;21(5):555–8.
[5] Sole-Violan J, de Castro FR, Rey A, Freixinet J, Aranda A, Caminero J, Bolanos J. Comparison of bronchoscopic diagnostic techniques with histological findings in brain dead organ donors without suspected pneumonia. Thorax 1996;51(9):929–31.
[6] Ware LB, Wang Y, Fang X, Warnock M, Sakomu T, Hall TS, Matthay MA. Assessment of lungs rejected for transplantation and implications for donor selection. Lancet 2002;360(9333):619–20.
[7] Shumway SJ, Hertz MI, Petty MG, Bolman III RM. Liberalization of donor criteria in lung and heart–lung transplantation. Ann Thorac Surg 1994;57:92–5.
[8] Gabbay E, Williams TJ, Griffiths AP, MacFarlane LM, Kotsimbos TC, Esmore DS, Snell GI. Maximizing the utilization of donor organs offered for lung transplantation. Am J Respir Crit Care Med 1999;160:265–71.
[9] Zenati M, Dowling RD, Dummer JS, Paradis IL, Arena VC, Armitage JM, Kormos RL, Hardesty RL, Griffith BP. Influence of the donor lung on development of early infections in lung transplant recipients. J Heart Transplant 1990;9:502–9.
[10] Dowling RD, Zenati M, Yousem SA, Pasculle AW, Kormos RL, Armitage JA, Griffith BP, Hardesty RL. Donor-transmitted pneumonia in experimental lung allografts. Successful prevention with donor antibiotic therapy. J Thorac Cardiovasc Surg 1992;103:767–72.
[11] Delclaux C, Roupie E, Blot F, Brochard L, Lemaire F, Brun-Buisson C. Lower respiratory tract colonization and infection during severe acute respiratory distress syndrome. Incidence and diagnosis. Am J Respir Crit Care Med 1997;156:1092–8.
[12] Meduri GU. Clinical review: a paradigm shift: the bidirectional effect of inflammation on bacterial growth. Clinical implications for patients with acute respiratory distress syndrome. Crit Care 2002;6(1):24–9.
[13] Takada M, Nadeau KC, Hancock WW, Mackenzie HS, Shaw GD, Waaga AM, Chandraker A, Sayegh MH, Tilney NL. Effects of explosive brain death on cytokine activation of peripheral organs in the rat. Transplantation 1998;65(12):1533–42.
[14] Fisher AJ, Donnelly SC, Hirani N, Burdick MD, Strieter RM, Dark JH, Corris PA. Enhanced pulmonary inflammation in organ donors following fatal non-traumatic brain injury. Lancet 1999;353(9162):1412–3.
[15] Low DE, Kaiser LR, Haydock DA, Trulock E, Cooper JD. The donor lung: infectious and pathologic factors affecting outcome in lung transplantation. J Thorac Cardiovasc Surg 1993;106:614–21.
[16] Deusch E, End A, Grimm M, Graninger W, Klepetko W, Wolner E. Early bacterial infections in lung transplant recipients. Chest 1993;104:1412–6.
[17] Ciulli F, Tamm M, Dennis C, Biocina B, Mullins P, Wells FC, Large SR, Wallwork J. Donor-transmitted bacterial infection in heart–lung transplantation. Transplant Proc 1993;25(1):1155–6.