



Impact of Donor Lung Pathogenic Bacteria on Patient Outcomes in the Immediate Post-transplant Period



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Introduction

Lung transplantation is an effective treatment for advanced pulmonary diseases refractory to medical therapy. However, patient outcomes after lung transplantation are suboptimal compared to other solid organs. In fact, the median survival for all adult recipients is only 5.7 years (1).

A major cause of death within the first 30 days post-transplant is the graft failure-mediated acute lung injury known as primary graft dysfunction (PGD). PGD has been associated with increased mortality, a longer duration of mechanical ventilation, and poor functional outcomes (2). Additionally, acute kidney injury (AKI) is a common consequence of lung transplantation. Associated with increased morbidity and mortality, it has been known to prolong both hospitalization as well as the need for mechanical ventilation postoperatively (3). Finally, the need for mechanical ventilation in the immediate postoperative period exposes lung transplant patients to the various risks associated with positive pressure ventilation – such as gastrointestinal hemorrhage, neuromuscular dysfunction, and ventilator associated pneumonia (4,5,6).

Given the detrimental effects of PGD, AKI, and extended mechanical ventilation, we investigated whether the presence of potentially pathogenic bacteria (PPB) in perioperative donor lung bronchial cultures was associated with said occurrences in the immediate post-transplant period. We also investigated whether PPB affected 30-day postoperative mortality rates.

References

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Methods

All adult patients hospitalized at the University of Kentucky Medical Center who underwent lung transplantation between August 1, 2015 and April 30, 2017 were identified. Patients who either underwent retransplant, were diagnosed with Cystic Fibrosis, or received organ(s) from DCD donors were excluded. Patients in whom donor lung bronchial cultures were not obtained were excluded as well. The remaining subjects underwent retrospective review.

Perioperative donor lung bronchial cultures were reviewed, and patients were subdivided into two groups: those with donor lung cultures positive for PPB, and those whose cultures either returned negative for pathogenic bacteria or were sterile. PaO₂/FiO₂ ratios were calculated at 24 and 72 hours postoperatively for all subjects. Chest x-ray findings were reviewed at said time periods also. Serum creatinine values of all patients were recorded in the perioperative period, as well as 24 and 72 hours postoperatively. The number of days patients required mechanical ventilation postoperatively was additionally documented. Finally, 30-day postoperative mortality rates were calculated.

PGD was graded according to the International Society for Heart and Lung Transplantation criteria for all participants at 24 and 72 hours postoperatively – and the presence or absence of grade 3 PGD was documented. Additionally, the occurrence of AKI at 24 and 72 hours postoperatively based on Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) criteria was recorded.

Table 1. Patient demographics

Patient Characteristics	Overall cohort n = 32	Patients with PPB n = 20	Patients without PPB n = 12
Age Mean (SD) Median (min, max)	60.0 (7.8) 61 (41, 75)	59.5 (7.9) 60 (41, 75)	60.8 (7.8) 62 (49, 70)
Gender, n (%) Male Female	13 (40.6) 19 (59.4)	7 (35.0) 13 (65.0)	6 (50.0) 6 (50.0)
Type of transplant, n (%) Bilateral lung Single lung	20 (62.5) 12 (37.5)	14 (70.0) 6 (30.0)	6 (50.0) 6 (50.0)
Underlying illness, n (%) COPD ILD	8 (25.0) 24 (75.0)	5 (25.0) 15 (75.0)	3 (25.0) 9 (25.0)

Results

32 patients ultimately comprised our study population. Table 1 details the overall cohort's patient characteristics as well as the demographics of each subset.

Twenty subjects (63%) were found to have PPB on donor lung cultures. Table 2 details the particular organisms discovered. Overall, 39 isolates were recovered, including methicillin-sensitive and methicillin-resistant Staphylococcus aureus, Enterobacter cloacae, Enterobacter aerogenes, and Acinetobacter baumannii. Of the remaining 12 patients (37%) who were found to have either nonpathogenic bacteria or absent growth on donor lung cultures, 10 subjects' respiratory cultures returned sterile. Of note, the 2 nonpathogenic bacteria isolated were Corynebacterium tuberculostearicum and Propionibacterium acnes.

Table 2. PPB recovered from donor cultures

Pathogenic Bacteria	Number of isolates recovered, n (%) ^a Total n = 39
Methicillin-sensitive Staphylococcus aureus	15 (38.5)
Enterobacter cloacae	5 (12.8)
Streptococcus agalactiae	4 (10.3)
Methicillin-resistant Staphylococcus aureus	3 (7.7)
Enterobacter aerogenes	3 (7.7)
Acinetobacter baumannii	2 (5.1)
Burkholderia gladioli	2 (5.1)
Klebsiella pneumoniae	1 (2.6)
Haemophilus influenzae	1 (2.6)
Escherichia coli	1 (2.6)
Peptostreptococcus magnus	1 (2.6)
Streptococcus anginosus	1 (2.6)

Table 3. Patient outcomes

Patient Outcomes	Overall cohort n = 32	Patients with PPB n = 20	Patients without PPB n = 12
Days on ventilator Mean Median	9.3 4.5	11.3 5.0	5.8 3.0
AKI 24 hours, n (%) 72 hours, n (%)	6 (18.8) 4 (12.5)	4 (20.0) 3 (15.0)	2 (16.7) 1 (8.3)
PGD 24 hours, n (%) 72 hours, n (%)	3 (9.4) 1 (3.1)	3 (15.0) --	-- 1 (8.3)
30-day mortality rate	3%	5%	--

Outcomes

The summation of our study's findings is outlined in Table 3. AKI occurred in 4 of the 20 patients with PPB, and in 2 of the 12 patients without PPB at 24 hours post-transplant. This corresponded with incidence rates of 20% and 17%, respectively. AKI was additionally seen in 3 of the 20 patients with PPB, and in 1 of the 12 patients without PPB at 72 hours post-transplant. This amounted to incidence rates of 15% and 8%, respectively. Neither difference was found to be statistically significant, however.

Three of the 20 patients with PPB were diagnosed with Grade 3 PGD at 24 hours post-transplant versus none of the 12 patients without PPB – resulting in incidence rates of 15% and 0%, respectively. Additionally, 1 of the 12 patients without PPB suffered from Grade 3 PGD at 72 hours postoperatively compared to none of the 20 patients with PPB – leading to respective incidence rates of 8% and 0%. Neither difference was again determined to be statistically significant, however.

In terms of the 30-day postoperative mortality rate among the two patient populations, 19 of the 20 subjects with PPB survived 30 days post-transplant compared to all 12 patients without PPB. This corresponded to mortality rates of 5% and 0%. The difference was deemed to not be statistically significant.

That being said, patients whose donor lung cultures grew PPB were found to require a significantly longer duration of mechanical ventilation postoperatively compared to those with no isolated PPB (mean = 11.3, median = 5.0 vs mean = 5.8, median = 3.0, respectively) (p = 0.0232).

Conclusion

In our study, the presence of PPB in donor lung bronchial cultures correlated with a longer duration of mechanical ventilation in patients post-lung transplantation. This was in comparison to those subjects whose bronchial cultures either returned negative for PPB or were sterile.. Given the incidence of prolonged mechanical ventilation post-transplant in patients with PPB in their respiratory flora, it is not unreasonable to advocate for broad spectrum or at least targeted antibiotics in all potential lung donors at the time of declaration of brain death.