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The role of bronchoscopic lavage culture monitoring in affecting the length of stay in intensive care unit in lung transplant patients

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ABSTRACT

Introduction: The aim of this study was to investigate whether bacterial growth detected in bronchial lavage is related to the length of stay in the intensive care unit (ICU).

Materials and Methods: A single-center retrospective cohort study was conducted, including patients who underwent lung transplantation for end-stage lung disease at a tertiary hospital between January 2017 and December 2022. Data were collected from the hospital database, comprising 86 patients admitted to the ICU for at least 24 hours postoperatively. The study focused on the first 30 days in the ICU after transplantation. Seventeen patients were excluded due to early transfer to the ward, infection developed in the ward, intraoperative mortality, or missing data.

Results: The final cohort consisted of 69 patients, with 81.2% male and a median age of 47 years (range: 32–56 years). The average waiting list duration was 3 months (range: 1–5 months). Among the patients, 44% had interstitial lung disease (ILD), followed by other conditions. Comorbidity indices showed that 30.4% had a score of 1, 46.4% had a score of 2, and 23.2% had a score of 3. No significant differences were detected in bronchoscopic lavage samples taken on days 0–3, 7, 14, and 30 post-transplantation. Additionally, bacterial culture positivity did not affect the length of stay in the ICU.

Conclusion: Postoperative mortality is highest in the months following transplantation, primarily due to complications and infections. This study found no significant relationship between bacterial culture growth and ICU stay length, likely due to effective prophylactic antibiotic strategies and diligent patient monitoring. Further multicenter studies are needed to explore potential relationships between bacterial positivity and ICU stay duration.

Keywords: Bronchial lavage culture, intensive care, lung transplantation

Introduction

Lung transplantation is an effective treatment method that improves survival and quality of life in patients with end-stage respiratory disease who do not respond to medical treatment despite optimal therapies. However, the survival rate of lung transplant recipients is the lowest among solid organ transplants, with an average of 6.5 years. This rate has been gradually improving with recent

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advancements compared to other solid organ transplants.[1] These patients are at risk of airway infections and microbial colonization due to continuous exposure to environmental factors through inhaled microorganisms, decreased ciliary transport, denervation, and a weakened cough reflex.

Although post-transplant mortality has decreased with new surgical techniques and pharmaceutical regimens, the 5-year mortality rate has been reported to be approximately 50%. Infections are the primary cause of death in the first year after lung transplantation, and among the many issues reported in the early postoperative phase, bacterial respiratory infections constitute major complications that significantly contribute to increased mortality in transplant recipients.[2–5] The etiologies of these infections are diverse, including both community-acquired and hospital-acquired microorganisms.[4–6]

After successful transplant surgery, recipients are typically transferred from the operating room to the intensive care unit (ICU). Often, recipients are still intubated, and some may require postoperative extracorporeal membrane oxygenation (ECMO) support.[7] The average duration of mechanical ventilation after lung transplantation is usually 2 to 3 days.[8] The approach to managing these patients in the early postoperative period may play an important role in their long-term morbidity and mortality.

The positive clinical outcomes of lung transplantation are increasingly threatened by the rising incidence of infections, which adversely affect both function and survival. Infections frequently occur as complications following lung transplantation, making them difficult to recognize; signs and symptoms can sometimes be misleading. Lifelong immunosuppression is necessary to prevent acute and chronic rejection, and the resulting impairment of the immune system increases patient susceptibility to infectious agents. Traditionally, recipients may host infections from a wide variety of microorganisms or become colonized by nosocomial organisms. Lung grafts can facilitate the transmission of infections from donors, and transplanted patients are prone to significant infections from agents that are relatively harmless in an immunocompetent host.[9]

Time is a determining factor in the development of infections after lung transplantation; although infections are the second leading cause of death in the first 30 days after transplantation (19.2%), they rise to first place (37.3%) between 30 days and 1 year.[10] Additionally, time affects the types of infections that can develop in the transplant patient: in the first month after surgery, the etiological cause of infection is usually associated with microbes present in the donor or recipient.[11] Perioperative deaths are correlated with longer recipient stays in the ICU. The mortality rate of patients after organ transplantation is highest in the initial months following surgery, with causes changing over time. Postoperative complications (e.g., acute rejection, bronchiolitis obliterans, and anastomotic leaks) and infections are the leading causes of death in the first year following lung transplantation.[12]

This study aims to clarify whether bacterial growth detected in bronchial lavage within the first 30 days after lung transplantation has an effect and relationship with the length of stay in the intensive care unit.

Microbiological Samples

Most patients underwent respiratory colonization sampling more than 6 months prior to transplantation. However, at our center, endobronchial swabs and respiratory tract samples are routinely collected from recipients just before transplantation. In the postoperative period, bronchial aspiration (BA) is performed using fiberoptic bronchoscopy every two to three days. Respiratory microbiological samples[13] obtained through BA and bronchoalveolar lavage (BAL) are processed using standard techniques. Susceptibility testing was conducted as previously described.[14]

Materials and Methods

This single-center retrospective cohort study was conducted in the Lung Transplantation Department of a tertiary hospital. Patient data were collected from the hospital database, and the identities of all patients were kept confidential. Due to the observational and retrospective nature of the study, informed consent was not required. The study received approval from the Local Ethics Committee (Date: 10.10.2023; Approval No: 2023/15/725). Between January 2017 and December 2022, 86 patients who underwent lung transplantation and were admitted to the intensive care unit (ICU) for at least 24 hours for postoperative care were included in the database. The study focused on the ICU stay during the first 30 days following transplantation. A total of 17 patients were excluded from the study: those who were transferred

from the ICU to the ward without infection, those who developed infections in the ward and were readmitted to the ICU, those who died intraoperatively, and those with missing data.

Perioperative Management

The surgical transplantation procedure was standardized according to our local policy.[15] Perioperative care, including postoperative management, followed a standardized protocol for all patients.[16] Immunosuppressive therapy consisted of a combination of a calcineurin inhibitor (tacrolimus), a cell cycle inhibitor (mycophenolate mofetil), and steroids (prednisolone),[1] with the target tacrolimus level set at 12–15 ng/mL. Antibacterial treatment was administered as perioperative prophylaxis for patients without previous respiratory tract colonization. In those with preoperative colonization, prophylaxis was tailored based on the isolated microorganisms. Antibiotic therapy is a fundamental component of postoperative care. However, there is a risk of emerging and exacerbating multidrug-resistant strains due to treatment of donors in the ICU and chronic colonization in recipients requiring frequent antibiotic use, which may lead to the selection of strains resistant to commonly used drugs. Antibiotic treatment should include broad-spectrum agents with diverse mechanisms of action. While there is no definitive recommendation for drug selection, the coverage should encompass both Gram-positive and Gram-negative bacteria, as well as methicillin-resistant Staphylococci and Pseudomonas aeruginosa.[17,18] Introducing MRSA-targeted antibiotics only after obtaining donor cultures is considered a sufficient precaution. Accordingly, patients in this study received antibiotic prophylaxis for a duration of 14 to 21 days.

Data Collection

Demographic data, including age, gender, and time of diagnosis, were extracted from patient records. In our center, diagnostic bronchoscopy is routinely performed on the 1st, 7th, and 14th days, as well as on the 1st month after lung transplantation. Additionally, bronchoscopy is conducted during other months based on clinical indications such as infection or rejection. Given the immunosuppressed status of the patients, a bacterial sample is collected during the bronchoscopy procedure as part of the microbiological testing panel, and a transbronchial biopsy is performed if necessary.

Bacterial Culture Evaluation

Bronchial lavage samples collected from patients were inoculated into solid media (5% sheep blood agar and MacConkey agar) using a quantitative method. After incubation at 37°C for 24 to 48 hours, identification and antibiotic susceptibility testing were conducted using VITEK® 2 Compact (bioMérieux, France) according to the guidelines set by the European Committee on Antimicrobial Susceptibility Testing.

The Comorbidity Index (CCI) was utilized to predict long-term survival in individuals with cancer by assigning weights to specific diseases. Comorbid conditions with a severity score of one included congestive heart failure, myocardial infarction, peripheral vascular disease, cerebrovascular disease, dementia, gastroesophageal reflux disease, diabetes, and mild liver disease.

Statistical Analysis

Data were collected from patient files and the hospital operating system and analyzed using IBM SPSS Statistics for Windows v.23.0. Descriptive statistics were used to present demographic and clinical characteristics of the patients. For nonparametric variables, median and interquartile range were reported, while mean±standard deviation was used for parametric variables. Culture and biopsy samples were routinely collected via bronchoscopy after transplantation. Results were compared using Chi-Square tests for categorical variables, and continuous variables were analyzed among three independent groups using Kruskal-Wallis analysis of variance. A statistical significance level of $p<0.05$ was set.

Results

The study cohort comprised a total of 69 patients, with a median age of 47 years (IQR, 32–56). The majority of the patients were male (81.2%, n=56). The median duration on the waitlist was 3.5 months (range: 1–6 months). When categorized by underlying disease, 44% (n=31) of the patients had interstitial lung disease (ILD), making it the predominant group. Other groups included obstructive airway disease (OAD) and cystic fibrosis (CF) at 14.5% (n=10) each, bronchiectasis at 13% (n=9), and idiopathic pulmonary arterial hypertension (IPAH) at 2.9% (n=2). The presence of a Comorbidity Index (CCI) of 1 was noted in 30.4% (n=21) of the study population, while 46.4% (n=32) had a CCI of 2, and 23.2% (n=16) had a CCI of 3. Table 1 summarizes the demographic results of the study.

Table 1. Descriptive Values of the study

Demograhic Parameters	Lung Transplant Canditates (n=69)
Age (median,%25-75)	47 (32-56)
Male (n, %)	56 (81.2)
Underlying Diseaseas (n, %)	
OLD	10 (14.5)
ILD	31 (44.9)
CF	9 (13)
Bronchiectasis	16 (23.2)
IPAH	2 (2.9)
Adenocarsinoma	1 (1.4)
Comorbidity Index (n, %)	
1	21 (30.4)
2	32 (46.4)
3	16(23.2)
Waiting List Time, month (median, %25-75)	3 (1-5)

OLD: obstructive lung diseases; ILD: interstisial lung diseases; CF: cystic fibrosis; IPAH: idiopathic pulmonary arterial hypertension.

A total of 276 bronchoscopic lavages were performed across the 69 patients. Positive bacterial growth was observed in 33.7% (n=93) of bronchoalveolar lavage (BAL) fluid samples. The three most commonly detected bacteria in BAL samples collected within the first 30 days post-transplantation were Klebsiella pneumoniae (34.7%, n=24), Pseudomonas aeruginosa (33.3%, n=23), and Acinetobacter baumannii (24.6%, n=17). Pre-transplant sputum culture positivity among recipient candidates was 21.7% (n=15) (Table 2).

The BAL culture positivity rates, categorized by days after transplantation, were as follows: 42% (n=29) on days 0 to 3, 26% (n=18) on day 7, 34.7% (n=24) on day 14, and 23.2% (n=16) on day 30. Notably, Pseudomonas putida (n=8; 11.6%) was the most frequently isolated bacterium in sputum cultures from recipient candidates prior to transplantation. The most common bacterial species detected in BAL samples from days 0 to 3 after transplantation was methicillin-sensitive Staphylococcus aureus (n=7; 10.1%). Following transplantation, the predominant infections were Acinetobacter baumannii (n=7; 10.1%) on day 7, Klebsiella pneumoniae (n=10; 14.5%) on day 14, and Pseudomonas

Table 2. Microorganisms detected in the recipient's respiratory tract before transplantation and on days 3, 7, 14, 30 after transplantation

Microorganism	Recipient Swabs-Sputum Pretransplant	Day 1 to 3	Day 7	Day 14	Day 30	Total after transplantation n,%
Gram-positive						
MSSA	2 (2.6)	7 (10.1)	0	0	2 (2.9)	9 (13)
MRSA	0	0	1 (1.3)	0	0	1 (1.4)
Streptococcus pneumonia	0	1 (1.3)	0	0	0	1 (1.4)
Coagulase-negative staphylococci	0	0	0	0	1 (1.3)	1 (1.4)
Gram-negative						
Escherichia coli	0	1 (1.3)	0	0	0	1 (1.4)
Proteus mirabilis	0	0	1 (1.3)	1 (1.3)	0	2 (2.9)
Enterobacter cloaca	1 (1.3)	0	0	3 (3.9)	0	3 (4.3)
Enterobacter aerogenes	0	2 (2.6)	0	0	0	2 (2.9)
Pseudomonas aeroginosa	0	6 (8.7)	4 (5.8)	6 (7.2)	7 (10.1)	23 (33.3)
Pseudomonas putida	8 (11.6)	0	0	0	0	0
Acinetobacter baumannii	2 (2.6)	5 (7.2)	7 (10.1)	4 (5.8)	1 (1.4)	17 (24.6)
Serratia rubidaea	0	0	1 (1.4)	0	0	1 (1.4)
Stenotrophomonas maltophilia	1 (1.4)	2 (2.8)	0	0	0	2 (2.9)
Klebsiella pneumonia	1 (1.4)	5 (7.2)	4 (5.8)	10 (14.5)	5 (7.2)	24 (34.7)
Total (n,%)	15 (21.7)	29 (42)	18 (26)	24 (34.7)	16 (23.1)	87

MSSA: methicillin-sensitive Staphylococcus aureus; MRSA: Methicillin-resistant Staphylococcus aureus.

aeruginosa (n=7; 10.1%) on day 30. There was no significant difference in the bronchoscopic lavage samples collected on days 0–3, 7, 14, and 30 post-transplantation.

Discussion

In this study, the predominant bacterial species detected within the first 30 days post-lung transplantation were Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, and methicillin-sensitive Staphylococcus aureus. Previous studies have also identified Enterobacteriaceae, Streptococcus spp., and Pseudomonas aeruginosa as dominant species in similar patient populations.[2,5] A key finding of our study was that bacterial culture positivity in bronchial lavage samples taken in the ICU after transplantation did not significantly correlate with the length of ICU stay. Notably, perioperative mortality is often linked to extended ICU stays, with the highest mortality rates occurring in the first months following transplantation. Postoperative complications, particularly infections, are leading causes of death within the first year, followed by chronic lung allograft dysfunction in subsequent years.[12]

Infectious complications contribute to significant morbidity and mortality at all stages post-transplantation and are responsible for the majority of deaths among lung transplant recipients.[19] Bacterial infections (BIs) represent the most common type of infectious complication. Despite advancements in immunosuppressive therapy and antimicrobial prophylaxis, opportunistic pathogens continue to pose a risk, particularly in the first year following solid organ transplantation, including lung transplants.[20] The Swiss Transplant Cohort Study reported that 55% of lung transplant recipients developed infections within the first year, with 63% of these infections being bacterial.[19] Another study indicated that 69% of lung transplant recipients experienced BIs, predominantly due to Gram-negative bacteria.[21] Generally, 50–85% of lung transplant recipients encounter at least one episode of BI,[22] with bacterial pneumonia accounting for a significant proportion of early infection-related deaths.[23]

In our center, we perform regular bronchoalveolar lavage in lung transplant patients during the first year post-transplantation to monitor for infections. This procedure is conducted every 2–3 days in the immediate post-transplant period to assess anastomotic healing and to collect samples for microbiological testing. The graft mucosa undergoes a healing process lasting about three weeks post-transplant, during which purulent discharge is a crucial indicator of infection. Consistent with our findings, Charlson et al.[24] reported that lung transplant recipients exhibit higher bacterial loads in BAL samples compared to healthy controls, regardless of the underlying indication for transplantation.

The landscape of bacterial infections has evolved with the introduction of routine postoperative antimicrobial therapy.[4,22,25] Recent studies have shown bacterial microbes isolated in up to 80% of transplant recipients.[4,22,25] A multicenter prospective Spanish study involving 236 lung transplant recipients with a mean follow-up of 180 days documented 72 pneumonia cases per 100 recipients annually, with two-thirds (57 cases) identified with microbiological etiology and 82% being bacterial infections. Notably, Pseudomonas aeruginosa was isolated in 24.6% (n=14) of cases, along with Acinetobacter baumannii and Staphylococcus aureus at 14% each, and various other bacteria at lower frequencies.[4]

In a study by Raviv et al.[26], 52 positive culture episodes for K. pneumoniae were reported among 136 recipients. The acquisition of carbapenem-resistant K. pneumoniae (CRKP) and extended-spectrum beta-lactamase K. pneumoniae (KP-ESBL) was linked to decreased survival rates among lung transplant recipients. Rodrigo-Troyano et al.[27] highlighted the significant threat posed by multidrug-resistant (MDR) Gram-negative bacteria in respiratory infections, underscoring a critical concern for managing these infections in solid organ transplant patients.

The early postoperative period, particularly the first three months post-surgery, has been identified as a critical timeframe for bacterial infections in lung transplant patients. The anatomical structure and functions of transplanted lungs may make them more susceptible to colonization than other organs. Secretions in the distal bronchi can serve as reservoirs for pathogenic flora, and mucus biofilm production can provide resistance against mechanical factors and antibiotics.[28] In our study, mucopurulent discharge was observed in 70% of recipients, yet positive culture rates were only 33.7%. Tanaka et al.[29] demonstrated that purulent discharge was present in 89% of pneumonia cases and 25% of tracheobronchitis cases.[29]

While our study found K. pneumoniae to be the most common bacterial species detected in the early postoperative period, it did not significantly affect the length of ICU stay.

Lung transplant recipients may be particularly vulnerable to severe K. pneumoniae infections due to multiple factors, including intense immunosuppression, limited ability to clear airway secretions, and potential malnutrition.[30,31] Pseudomonas aeruginosa was the second most frequently detected bacterium, yet it too did not significantly influence ICU length of stay.

It's important to note that our study did not classify bacteria by primary disease. Recipients with cystic fibrosis (CF) have a higher susceptibility to Pseudomonas aeruginosa colonization and infection compared to non-CF recipients.[3,32,33] The persistence of Pseudomonas colonization can be linked to chronic graft rejection and may increase the incidence of infection-related death.[34]

In conclusion, while our study identified significant bacterial infections, it did not find a substantial relationship between bacterial culture growth and the length of ICU stay. Frequent bronchoscopy and laboratory follow-ups are crucial for the early diagnosis of infections and for the development of effective antibiotic regimens. Due to the small sample size of our study, multicenter analyses with larger cohorts are recommended to further elucidate the impact of bacterial infections on ICU stay and patient outcomes. Limitations of our study include its retrospective nature, the preference for sputum sampling over BAL before transplantation, and the lack of evaluation of cold ischemia time, radiological findings, and parenchymal lesions.

Conclusions

The highest mortality rates following organ transplantation occur in the initial months after surgery, with postoperative complications and infections being the primary contributors. In our study, we found no significant correlation between bacterial culture growth and the length of ICU stay. This may be attributed to individualized preoperative prophylactic antibiotic treatments and the development of tailored antibiotic regimens. Additionally, regular bronchoscopy procedures, along with timely imaging and laboratory follow-ups based on the patients' clinical courses in the ICU, likely play a beneficial role in patient management.

To better understand the relationship between culture positivity and ICU length of stay, we advocate for multicenter studies with larger patient populations that compare different bacterial groups.

Disclosures

Ethichs Committee Approval: The study received approval from the Koşuyolu Higher Specialization Training and Research Hospital Local Ethics Committee (Date: 10.10.2023; Approval No: 2023/15/725).

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Conflict of Interest: None declared.

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