Original Article

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The Relationship Between Bacterial Pathogen Presence Detected by Bronchial Lavage and Acute Rejection: 1-Year Follow-up Results Following Lung Transplantation

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Abstract

Aim: Lung transplant recipients are the highest risk group in terms of infective complications among solid organ transplants. It has improved the management of the most common infectious complications with the aid of advances in diagnostic methods, prophylaxis, and therapeutic strategies. In the present study, we evaluated the results of microbiological culture samples by the bronchoscopic method.

Methods: This retrospective cohort study included patients who were admitted between November 2016 and May 2019 in a Lung Transplantation Department. We evaluated the results of bacteria detected in the lavage fluid obtained by serial bronchoscopy in the first year after lung transplantation in lung transplant patients. We divided the patients into two groups: those with acute rejection and those without. The two groups were compared according to their culture of growth and analyzed.

Results: Of the 77 patients included in the study, 77.2% were male. In the first year after transplantation, 79 bronchoscopic lavage cultures were positive in the follow-up. While bacterial culture positivity by post-transplant bronchial lavage was found to be 62% in the first 3 months, it decreased to 43.6% between the third month and the first year. There was no significant difference between the groups with and without acute rejection of lavage culture growth.

Conclusion: This study revealed the importance of the bronchoscopic method in terms of the detection of microbiological findings and the prempitic antibiotic therapy approach in the evaluation of lung infections in lung transplant patients.

Keywords: Lung transplantation, bronchoscopy, bronchoalveolar lavage fluid

Introduction

Lung transplantation has become a curative treatment option for patients with end-stage lung diseases who have tried all treatment regimens (1). In a randomized controlled study on flexible bronchoscopy, which is a necessary procedure to ensure success after lung transplantation, they emphasized that they can make it comfortable for patients thanks to the explanation given to the recipients using a graphical expression before the procedure (2). As immunosuppressive and antibiotic therapy treatment strategies have evolved, the early signs of infections in the post-transplant period have changed. Susceptibility to infections in lung transplantation has been defined by various factors such as airway anatomy, ischemic complications, and the absence of tracheobronchial reflexes (3,4). The main causes of mortality after lung transplantation are graft failure and infectious complications (1). These should be identified to be the main causes of both the early and late post-transplant period (5,6). In the study by Büyükkale et al. (7), in which

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they presented their 3-year experience in 29 patients who underwent lung transplantation, they concluded that in selected recipients, appropriate donor and post-transplant patient management significantly improved survival.

They emphasized that, thanks to the completion of the learning process by the entire transplant team over time, it is possible to obtain satisfactory results by being organized on the basis of serious teamwork (7). It is important to know the epidemiology of post-lung transplant infections to prevent and treat infections. Although the predictive value of bronchoscopy in the detection of chronic rejection is weak, it was emphasized that it should be performed to exclude lower respiratory tract infections and acute rejection (AR) in the review of Bağ and Kıyan (8).

This study aimed to evaluate the patient population who underwent lung transplantation, the identification of the bacterial cultures, the time of infection, and the emergence of infection diagnosed using the bronchial lavage method in the 1-year period after the transplantation.

Materials and Methods

Compliance with Ethical Standards

This retrospective study was conducted in the lung transplantation department of a tertiary teaching hospital for chest diseases from November 2016, to May 2019. The study was conducted in full accordance while patients' signed informed consent was not obtained because of the retrospective nature of the study, and permission was obtained from the University of Health Sciences Turkey, Istanbul Kartal Kosuyolu Yuksek Ihtisas Training and Research Hospital Local Ethics Committee (date: 08.05.2020, decision no: 2020.4/30-335) who waived the need for patient consent to review their medical files. As informed consent from patients to review their medical records was not obtained, all patients' ID information was kept confidential.

Study Design

This study enrolled consecutive patients aged over 18 years, who underwent lung transplantation according to underlying diseases: obstructive lung disease, interstitial lung disease, end-stage infectious lung disease, lung cancer, and idiopathic pulmonary arterial hypertension (IPAH) at our institution. Cases could complete all of their routine visits planned as the clinical protocol established in our institution in the first year after transplantation were included. Patients who could not be sampled by death or bronchoscopic method for 1 year after transplantation were excluded from the study (n=8).

Bronchoscopic lavage samples were purchased from 77 lung transplant recipients. The stratification of patients was summarized in a flowchart in Figure 1. Lavage specimens by bronchoscopy are obtained routinely at 1 week, 1 month, 3 months, 6 months 9 months (as need) and 1 year post-transplant and as clinically indicated for suspected infection or rejection at this center. Whenever lavage by bronchoscopy is performed on a lung transplant recipient at this center, a bacterial specimen is performed routinely as part of a panel of microbiologic tests for immunocompromised patients, and transbronchial biopsy is also performed.

Bacterial Culture Assessment

Bronchial lavage samples taken from the patients were cultivated on solid medium (5% sheep blood agar, MacConkey agar) by a quantitative method. After incubation at 37 °C 24-48 hours, identification and antibiotic susceptibility testings were performed using VITEK® 2 Compact (bioMérieux, France) according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) (9).

Acute Rejection

AR was diagnosed and graded by the biopsies from each bronchoscopy procedure were interpreted collectively. An overall AR grade of A0 (none), A1 (minimal), A2 (mild), A3 (moderate), or A4 (severe) was assigned for the biopsies from each procedure (10,11).

Treatment of Acute Rejection

When A1 rejection accompanying clinical symptoms was detected, the typical treatment procedure was applied, while the symptomless A1 rejection episodes were not treated. A2 and higher rejection degrees are treated. 10-15 mg/kg of methylprednisolone was used for 3 days and then reduced to one mg/kg (12).

Statistical Analysis

The data were collected from patient files and hospital operating systems and analyzed with IBM SPSS Statistics for Windows v.23.0. Descriptive statistics were used to show the demographic and clinical characteristics of the patients. According to the distribution of values; median and interquartile range were used for non-parametric variables, while mean±standard deviation was used for parametric variables. Culture and biopsy samples were taken from the patient's post-transplantation routinely at the 1st week, 1st month, 3rd month, 6th month, and 1st year by the bronchoscopy method in our clinic. Discrete data is shown as percentages and absolute numbers. The results were compared using chi-square for categorical variables. Statistical significance-level p-value was taken as <0.05.

Results

In the study group of 77 patients, 77.2% were males, and the median age was 48 (34-56). The median waiting-list time was 3 (1-5) months, the median best FEV1 by

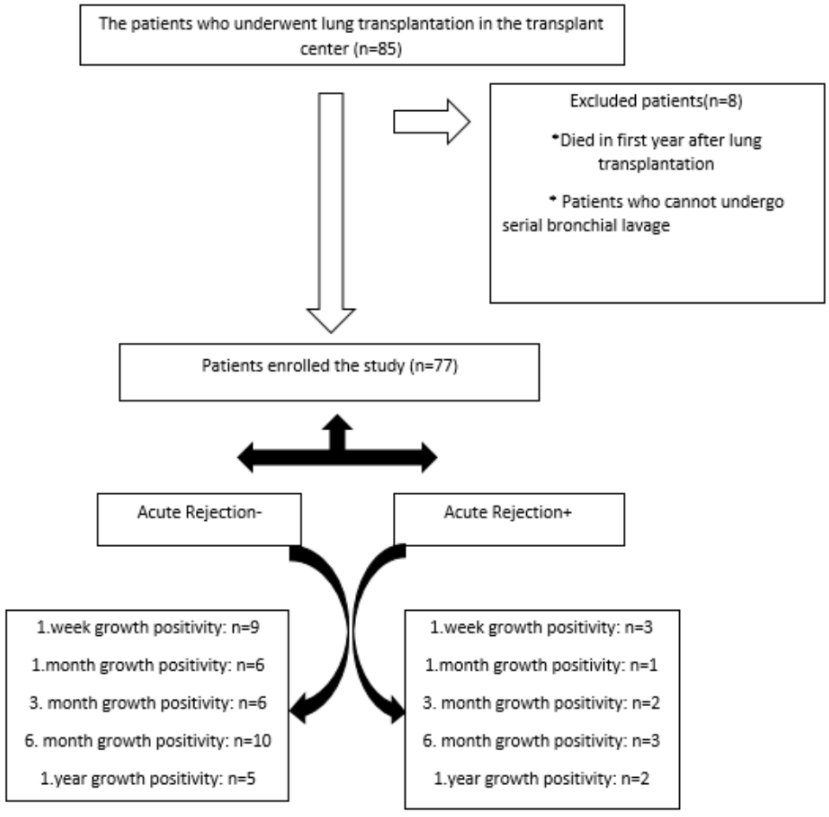

Figure 1. Flow chart of patients distribution

pulmonary function test was 2.52 (1.69-2.71) lt, the median duration of mechanical ventilation was 2 (1-8.5) days, the median length of ICU stay was 5 (3-13) days, and the median length of hospital day was 19 (16.4-19) days (Table 1).

According to the Charlson comorbidity index, 31.2% of the study population (n=24) was calculated as having 1 score, 46.8% (n=36) had 2 scores, and 22.1% (n=17) had 3 scores.

Fifty-nine (73.7%) bacterial isolates were in the first 3 months, 13 (16.2%) bacterial growth in the sixth month, and 8 (10%) in the first year (Table 2). The culture positivities of serial bronchial lavage samples are shown in Figure 2. Between the third month and the first year, the incidence of bacterial growth decreased drastically to 86.4%. Eighty isolates were recovered: *Methicillin-sensitive staphylococcus aureus* (n=11), *Streptococcus pneumonia* (n=2), *Klebsiella pneumoniae* (n=21), *Enterobacter cloacae* (n=2), *Acinetobacter baumannii* (n=9), *Extended spectrum beta-lactamase escherichia coli* (n=2), *Pseudomonas aeruginosa* (n=28), *Stenotrophomonas maltophilia* (n=2), *Staphylococcus haemolyticus* (n=1), *Escherichia coli* (n=2), *Proteus miriabilis* (n=2).

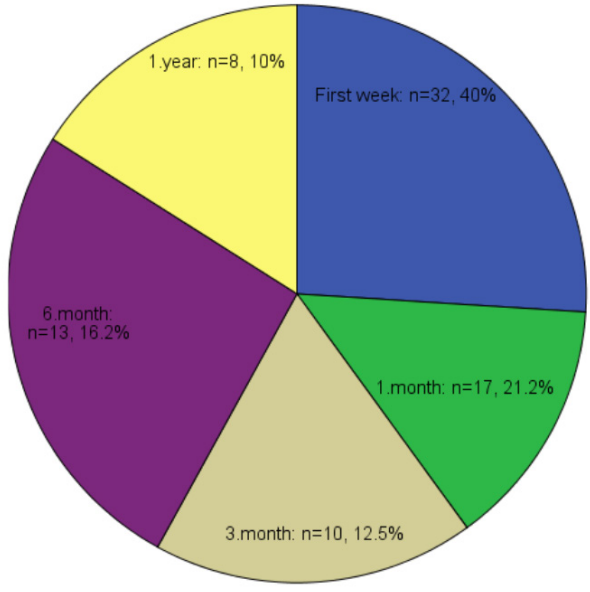

Figure 2. Culture positivities of serial bronchial lavage samples were showed

Table 1. Demografic and clinical parameters of the study

Variables	Total Patients (n=77)	OLD	ILD	EILD	Lung cancer	IPAH
Gender, male, n (%)	61 (77.2%)	15 (24.6%)	25 (41%)	21 (34.4%)	1 (1.6%)	1 (1.6%)
Age, median, IQR	48 (34-56)	55 (50-57)	51 (44-58)	33 (24-55)	43 (43-43)	25 (25-25)
Waiting list time, month, median, IQR	3 (1-5)	2 (1-6)	2 (1-5)	4 (2-6)	1 (1-1)	2 (2-2)
CRP (1st-3rd day), median, IQR	8.7 (2.8-19.6)	9.57 (1.67-21.15)	9.57 (3.02-19.60)	6.95 (3.13-15.10)	15 (15-15)	124 (124-124)
WBC (1st-3rd day), median, IQR	12200 (8550-18550)	9100 (7700-16805)	11850 (7650-16650)	14900 (9200-19000)	19100 (19100-19100)	29300 (29300-29300)
FEV_1 (lt) values						
Post-transplant best FEV_1 (lt), median, IQR	2.52 (1.69-2.71)	2.51 (1.88-3.08)	2.32 (1.76-2.78)	2.04 (1.61-2.38)	2.00 (2.00-2.00)	1.88 (1.88-1.88)
1. visit FEV_1 (lt), median, IQR	2.03 (1.58-2.52)	1.87 (1.76-2.67)	2.06 (1.64-2.55)	1.60 (1.33-2.15)	1.76 (1.76-1.76)	1.85 (1.85-1.85)
2. visit FEV_1 (lt), median, IQR	2.05 (1.46-2.44)	2.18 (1.78-2.61)	2.04 (1.49-2.54)	1.55 (1.26-2.26)	2.44 (2.44-2.44)	1.78 (1.78-1.78)
3. visit FEV_1(lt), median, IQR	2.14 (1.56-2.57)	2.40 (1.98-2.57)	2.28 (1.56-2.57)	1.73 (1.30-2.31)	2.01 (2.01-2.01)	1.98 (1.98-1.98)
4. visit FEV_1(lt), median, IQR	2.10 (1.54-2.75)	2.46 (2.16-2.68)	2.01 (1.61-2.76)	1.74 (1.38-2.50)	2.16 (2.16-2.16)	-
Duration of mechanical ventilation, day, median, IQR	2 (1-8.5)	2 (1-5)	4 (1-9)	2 (1-9)	14 (14-14)	2 (2-2)
Length of ICU stay, day, median, IQR	5 (3-13)	5 (3-13)	5 (3-16)	4 (3-11)	14 (14-14)	9 (9-9)
Length of hospital stay, day, median, IQR	19 (16.4-19)	14 (11-21)	17 (9-35)	22 (16-36)	24 (24-24)	30 (30-30)
Acute rejection, n (%)	8 (10.1%)	1 (16.7%)	4 (28.6%)	3 (23.1%)	0 (0%)	0 (0%)
BOS, n (%)	3 (3.8%)	1 (16.7%)	1 (7.7%)	1 (7.7%)	0 (0%)	0 (0%)

OLD: Obstructive Lung Disease, ILD: Interstitial Lung Disease, EILD: End-Stage Infectious Lung Disease, IPAH: Idiopathic Pulmonary Arterial Hypertension, CRP: C-reactive protein, WBC: White blood cell, FEV_1: Forced expiratory volume in 1 second, ICU: Intensive Care Unit, BOS: Bronchiolitis obliterans syndrome, IQR: Interquartile Ratio

Table 2. Bacterial growths obtained with serial bronchial lavage samples in the post-transplant period

Etiology	1st week	1st month	3st month	6st month	1st year	Total (n)
Acinetonobacter baumanii, n (%)	6 (7.6%)	1 (1.3%)	1 (1.3%)	1 (1.3%)	-	9
Enterobacter clocacae, n (%)	2 (2.5%)	-	-	-	-	2
ESBL + *E. coli*, n (%)	1 (1.3%)	-	-	-	-	1
Klebsiella pneumonia, n (%)	5 (6.3%)	6 (7.6%)	4 (5.1%)	5 (6.3%)	1 (1.3%)	21
Pseudomonas aeroginosa, n (%)	7 (8.9%)	7 (8.9%)	3 (3.8%)	5 (6.3%)	6 (7.6%)	28
Staf. aureus, n (%)	8 (10.1%)	2 (2.5%)	-	1 (1.3%)	-	11
Stenotrophomonas maltophilia, n (%)	2 (2.5%)	-	-	-	-	2
Streptococcus pneumonia, n (%)	1 (1.3%)	-	-	-	1 (1.3%)	2
Staphylococcus haemolyticus, n (%)	-	1 (1.3%)	-	-	-	1
E. coli, n (%)	-	-	1 (1.3%)	1 (1.3%)	-	2
Proteus miriabilis, n (%)	-	-	1 (1.3%)	-	-	1
Total	32	17	10	13	8	80

Data are presented as percentages and absolute numbers n (%).
ESBL: Extended spectrum beta-lactamase, *E. coli*: *Escherichia coli*

There was no difference in bronchoscopic lavage cultures on the first-third day after lung transplantation between with/without AR. The first month of culture positivity was higher in the AR-negative group than in the AR-positive group, but it was not statistically significant (n=6, 85.7%, n=1, 14.3%). In the six-month period, culture positivity was found to be lower in the group with AR, but it was not significant (n=5, 25%, n=15, 75%). Summarily, serial bronchoscopic lavage culture positivity during post-transplantation was not found to be significant when patients with and without AR were compared (Table 3).

Discussion

The primary finding of this article was that the bacterial growth numbers obtained from post-transplant periodic bronchoscopic lavage were not predictive of AR in lung transplant patients. AR remains a significant cause of morbidity after lung transplantation and can range from mild to severe. Even a single episode of AR is a risk factor for developing bronchiolitis obliterans syndrome, which is the cause of a progressive decline in lung function and the cause of death in most patients. Despite the critically important importance of AR, the risk factors have not been fully defined. To date, adequate data on the role of lung bacterial load in post-transplant AR has not been presented. Culture-dependent studies have shown that colonization with pseudomonas aeruginosa is a risk factor for chronic lung allograft dysfunction (CLAD) development (13). However, recent studies have suggested that lung bacteria are a key factor in post-transplant pulmonary inflammation and allograft dysfunction, independent of acute infections. Based on post-lung transplant BAL growth results in 134 healthy lung transplant recipients, Combs et al. (14) demonstrated that the lung microbiome was a new risk factor for the development of CLAD. However, in the same study, they found that bacteria isolated with BAL were not associated with host dysfunctions such as AR, consistent with the primary findings of our study. Furthermore, they proposed that the bacteria isolated from the lung reflect the underlying host detoriation (14).

In the early days of post-transplant, lower airway growth with bacteria is recognized as one of the major causes of recipient mortality, but with the use of aggressive antibiotic therapy for recipients, the incidence of recipient pneumonia has recently decreased significantly (15). In this study, it has been shown that the bacterial growth detected in the early period according to the serial bronchoscopic control culture results from the first week of lung transplantation gradually decreases in long-term follow-ups after appropriate antibiotic therapy modalities targeting pathogens.

In 1998, Fishman and Rubin (16), two of the first clinicians to deal with the infection status of transplant patients, drew attention to 3 periods of infection after solid organ transplantation: These are nosocomial infections up to 1 month after transplantation; opportunistic infections in the 1-to 6-month period; and community-acquired or persistent infections 6 months later. This important timeline has guided the appropriate design of empirical treatments. Six months after transplantation, community-acquired pathogens were found to be a major problem (16).

It was shown that infection rates were highest in the first month post-transplant and decreased after 6-12 months. The cumulative incidence of infection reached 62% at 12 months post-transplant. Bacterial infections caused 63% of all infections. Of the bacterial infections identified, 54% belonged to Enterobacteriaceae infections, with *Escherichia coli* and *Klebsiella* spp. (47%) predominant. Bacterial infections predominated during the first year post-transplant. Infections with Enterobacteriaceae were common, especially in the first 180 days after transplantation, and non-fermenting gram-negative bacteria appeared frequently in the first 150 days after transplantation. After that, it decreased but still continued at a regular rate. Pseudomonas aeruginosa and enterobacteriaceae occurred throughout the post-transplant first year. The most frequent pathogens infecting lung transplant recipients include gram-negative rods such as pseudomonas aeruginosa and enterobacteriaceae (17).

Table 3. Comparison of bacterial growth numbers in post-transplantation periods between presence of acute rejection and absence

	Acute rejection (+)	Acute rejection (-)	p-value
FOB 1st-3rd day culture, n (%)	3 (25%)	9 (75%)	0.827
FOB 1st month culture, n (%)	1 (14.3%)	6 (85.7%)	0.546
FOB 3rd month culture, n (%)	2 (25%)	6 (75%)	0.869
FOB 6th month culture, n (%)	3(23.1%)	10 (76.9%)	0.961
Culture positivity in the six-month period, n (%)	5 (25%)	15 (75%)	0.809
FOB 12th month culture, n(%)	2 (28.6%)	5 (71.4%)	0.724

Data are presented as descriptive analyze (percentages and absolute numbers) n (%) and chi-square test.
FOB: Fiberoptic bronchoscopy

Infections are most common in the first year after lung transplantation. Predominantly, bacterial infections occur in the first 3 months post-transplant (18). The most common bacterial infection in the first six months after lung transplantation was pseudomonas aeruginosa (19). Stjärne Aspelund et al. (20) found that bronchoalveolar lavages have a high bacterial load. The most commonly detected bacterial infection was pseudomonas aeruginosa. In the same study, the incidence of lung infections decreased over time (20). In addition, we also found pseudomonas aeruginosa (35.4%) as the vast majority of pathogens in findings similar to the studies mentioned in the 6-month period following transplantation. Among solid organ transplants, the lung is the only organ with direct external exposure. Additionally, the lower respiratory tract is susceptible to pathogens in the first months due to impaired mucociliary clearance and denervation that inhibit the cough reflex in the early post-transplantation period (18).

In this study, 91.1% of bacterial growth was detected in the first 6 months, and 10.1% of growth was detected after 6 months, and we found a gradual decrease within a year. We also reported similar results in other studies where the first three months after surgery were defined as the critical period for infections, especially for bacterial etiology (20,21).

It was thought that although survival increased thanks to the development of the immunosuppressive protocol and the increased bacterial load, the middle-low income of the country where the study was conducted contributed to the risk of pulmonary infection in the study in which pulmonary infections were investigated in the kidney transplant patient group.

Infections occurred in the early months after transplantation, whereas in this study the timeline had shifted to later months. We believe that this may be even stronger in geography, where the general exposure to infections in the population is high and population density increases the risk even in the late post-transplant period (22).

Potent immunosuppressive strategies have been developed to reduce the post-transplant rejection rate, however, alter the recipients' susceptibility to infections. Additionally, with the contribution of effective and modern antibiotics, the frequency and schedule of post-transplant infections may have changed (23). Additionally, rapid and effective diagnostic detection of potential pathogens, keeping in mind geographical conditions and epidemiological exposures, is vital in establishing prevention strategies to further reduce the morbidity and mortality associated with post-transplant infections. For this reason, we believe that each center must have its own unique aspects in the treatment schemes. The common goal of pulmonologists and doctors treating infections specializing in lung transplantation is to determine patient-specific prophylactic and empirical antibiotic therapies. Thus, it minimizes the possibility of AR or chronic rejection, which shortens post-transplant survival. In this study, we attributed the absence of AR in the group with more bacterial growth to the development of appropriate strategies against pathogens detected early with close follow-up of the patients.

Study Limitations

One of the most important limitations of our study was that the underlying patient group was not homogeneous: there was a large group of patients with suppurative pulmonary diseases and IPAH patients. Secondly, we excluded comorbidities of the patient population due to a lack of data. Thirdly, we included all of the bronchoscopic lavage growth results without distinguishing between colonization and infection, especially in the patient groups such as bronchiectasis or cystic fibrosis. We can explain this situation. We also designed the current study to present a timeline of the main bacterial infections after transplantation in this specific population.

Conclusion

Microbiological culture samples obtained using bronchoscopy after serial lung transplantation are an important method that helps predict the patient's preemptive antibiotic treatment. Although we could not find a significant relationship between AR and microbiological culture growth, we believe that more prospective studies are needed to clarify this ambiguous situation.

Ethics

Ethics Committee Approval: The ethical approval was obtained from the University of Health Sciences Turkey, Istanbul Kartal Kosuyolu Yuksek Ihtisas Training and Research Hospital Local Ethics Committee (date: 08.05.2020, decision no: 2020.4/30-335).

Informed Consent: Informed consent was not obtained because of the retrospective nature of the study.

Peer-reviewed: Internally and externally peer-reviewed.

Authorship Contributions

Concept: M.E.C., E.S., Design: P.A.G., Data Collection and/or Processing: M.V., S.C., Analysis and/or Interpretation: P.A.G., A.E.T., Literature Research: Y.U.K., A.N.H., Writing: P.A.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult lung and heart-lung transplant report: 2014; focus theme: retransplantation. J Heart Lung Transplant 2014;33:1009-24.
2. Seeliger B, Kayser MZ, Drick N, et al. Graphic narrative based informed consent for bronchoscopy improves satisfaction in patients after lung-transplantation: A randomized controlled trial. Patient Educ Couns 2022;105:949-55.
3. Garrido RS, Aguado JM, Díaz-Pedroche C, et al. A review of critical periods for opportunistic infection in the new transplantation era. Transplantation 2006;82:1457.
4. Rubin RH, Wolfson JS, Cosimi AB, Tolkoff-Rubin NE. Infection in the renal transplant recipient. Am J Med 1981;70:405-11.
5. de Perrot M, Chaparro C, McRae K, et al. Twenty-year experience of lung transplantation at a single center: influence of recipient diagnosis on long-term survival. J Thorac Cardiovasc Surg 2004;127:1493-501.
6. Zander DS, Baz MA, Visner GA, et al. Analysis of early deaths after isolated lung transplantation. Chest 2001;120:225-32.
7. Büyükkale S, Çıtak N, İşgörücü Ö, et al. Early period lung transplantation results of Yedikule Organ Transplantation Center: our three-year experience. Turk J Thorac Cardiovasc Surg 2017;25:86-95.
8. Bağ R, Kıyan E. Lung Transplantation in Idiopathic Pulmonary Fibrosis. Current Chest Diseases Series 2017;5:72-92.
9. Leclercq R, Cantón R, Brown DF, et al. EUCAST expert rules in antimicrobial susceptibility testing. Clin Microbiol Infect 2013;19:141-60.
10. Yousem SA, Berry GJ, Cagle PT, et al. Revision of the 1990 working formulation for the classification of pulmonary allograft rejection: Lung Rejection Study Group. J Heart Lung Transplant 1996;15:1-15.
11. Khalifah AP, Hachem RR, Chakinala MM, et al. Minimal acute rejection after lung transplantation: a risk for bronchiolitis obliterans syndrome. Am J Transplant 2005;5:2022-30.
12. Chakinala MM, Trulock EP. Acute allograft rejection after lung transplantation: diagnosis and therapy. Chest Surg Clin N Am 2003;13:525-42.
13. Vos R, Van Herck A. Seudomonas aeruginosa and chronic lung allograft dysfunction: does evading an iceberg prevent the ship from sinking?. Eur Respir J 2021;58:2100041.
14. Combs MP, Wheeler DS, Luth JE, et al. Lung microbiota predict chronic rejection in healthy lung transplant recipients: a prospective cohort study. Lancet Respir Med 2021;9:601-12.
15. Anesi JA, Blumberg EA, Abbo LM. Perioperative antibiotic prophylaxis to prevent surgical site infections in solid organ transplantation. Transplantation 2018;102:21-34.
16. Fishman JA, Rubin RH. Infection in organ-transplant recipients. N Engl J Med 1998;338:1741-51.
17. van Delden C, Stampf S, Hirsch HH, et al. Burden and Timeline of Infectious Diseases in the First Year After Solid Organ Transplantation in the Swiss Transplant Cohort Study. Clin Infect Dis 2020;71:159-69.
18. McCort M, MacKenzie E, Pursell K, Pitrak D. Bacterial infections in lung transplantation. J Thorac Dis 2021;13:6654-72.
19. Påhlman LI, Manoharan L, Aspelund AS. Divergent airway microbiomes in lung transplant recipients with or without pulmonary infection. Respir Res 2021;22:118.
20. Stjärne Aspelund A, Hammarström H, Inghammar M, et al. Microbiological findings in bronchoalveolar lavage fluid from lung transplant patients in Sweden. Transpl Infect Dis 2018;20:e12973.
21. Jacob M, Damas C. Lung transplantation for Interstitial Lung disease, the experience of an outpatient clinic. Sarcoidosis Vasc Diffuse Lung Dis 2020;37:e2020007.
22. 22 Mangalgi S, Madan K, Das CJ, et al. Pulmonary infections after renal transplantation: a prospective study from a tropical country. Transpl Int 2021;34:525-34.
23. Timsit JF, Sonneville R, Kalil AC, et al. Diagnostic and therapeutic approach to infectious diseases in solid organ transplant recipients. Intensive Care Med 2019; 45:573-91.