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► **To cite this version:**

E. Atchade, M. Desmard, E. Kantor, C. Genève, G. Tebano, et al.. Fungal Isolation in Respiratory Tract After Lung Transplantation: Epidemiology, Clinical Consequences, and Associated Factors. *Transplantation Proceedings*, 2020, 52, pp.326 - 332. 10.1016/j.transproceed.2019.10.031 . hal-03489599

**HAL Id: hal-03489599**

**<https://hal.science/hal-03489599v1>**

Submitted on 7 Mar 2022

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TEXT: 2484 words

ABSTRACT: 231 words

**FUNGAL ISOLATION IN RESPIRATORY TRACT AFTER LUNG  
TRANSPLANTATION: EPIDEMIOLOGY, CLINICAL CONSEQUENCES AND  
ASSOCIATED FACTORS**

E. ATCHADE<sup>1</sup>, M. DESMARD<sup>2</sup>, E. KANTOR<sup>1</sup>, C. GENÈVE<sup>1</sup>, G. TEBANO<sup>1</sup>, C. DE  
TYMOWSKI<sup>1,3</sup>, A. TRAN-DINH<sup>1,4</sup>, N.ZAPPELLA<sup>1</sup>, S. HOUZÉ<sup>5</sup>, H. MAL<sup>6</sup>, Y. CASTIER<sup>7</sup>, S.  
TANAKA<sup>1,8</sup>, P. MONTRAVERS<sup>1,9</sup>

Affiliations:

1. APHP, CHU Bichat-Claude Bernard, Département d'Anesthésie Réanimation, 46 rue Henri Huchard, 75018 Paris, France
2. Département d'Anesthésie, Centre Hospitalier Sud Francilien, Corbeil-Essonnes, France
3. INSERM UMR 1149, Immunorecepteur et immunopathologie rénale, Paris, France
4. INSERM U1148 LVTS, Paris, France
5. AP-HP, CHU Bichat-Claude Bernard, Laboratoire de Mycologie Parasitologie, Paris, France
6. APHP, CHU Bichat-Claude Bernard, Service de Pneumologie B et Transplantation Pulmonaire, Paris, France
7. APHP, CHU Bichat-Claude Bernard, Service de Chirurgie Thoracique et Vasculaire, Paris, France
8. Université de la Réunion, INSERM UMR 1188, Diabète Athérombose Réunion Océan Indien (DÉTROU), Saint-Denis de la Réunion, France
9. INSERM UMR 1152, Physiopathologie et Epidémiologie des maladies respiratoires, Paris France

Corresponding author: Enora Atchade, phone number +33140258117, email:

[enora.atchade@aphp.fr](mailto:enora.atchade@aphp.fr)

Key words: Lung transplantation, fungal isolation, respiratory tract

## **ABBREVIATIONS**

AFT: Antifungal therapy

APACHE II: Acute Physiology And Chronic Health Evaluation II

BA: Bronchial aspiration

BAL: Bronchoalveolar lavage

CFU: Colony forming unit

COPD: Chronic obstructive pulmonary disease

FI: Fungal infections

ICU: Intensive care unit

IPF: Idiopathic pulmonary fibrosis

ISHLT: International society of heart and lung transplantation

LT: Lung transplantation

LRTI: Lower respiratory tract infection

MV: Mechanical ventilation

OR: Odds ratio

SAPS II: Simplified Acute Physiology Score II

SOFA: Sequential organ failure assessment

WBC: White blood cell

## INTRODUCTION

Fungal infections (FI) are common after LT and are associated with high morbidity and mortality rates (2–5). The most life-threatening issue is obviously related to invasive aspergillosis (6,7) but epidemiological and clinical studies report the emergence of molds other than *Aspergillus*, as well as resistant *Candida* strains. Interestingly, most published studies have focused on late invasive infections, while the early post-transplant period in the Intensive Care Unit (ICU) setting is rarely assessed.

Although recent guidelines have defined bacterial pneumonia, tracheobronchitis and colonization after lung and heart transplantation (8), no consensus has been reached concerning initiation of antifungal therapy (AFT) for patients with early postoperative fungus-positive respiratory samples. The criteria usually proposed for AFT remain controversial, resulting in a risk of both overtreating some colonized patients or missing pneumonia in these immunocompromised patients. Some centers initiate systematic AFT from the first day after LT. Our local policy is to restrict AFT to *Aspergillus*-positive samples and to initiate anti-candida regimens for patients with suspected *Candida* tracheobronchitis, even in the absence of criteria of pneumonia.

The primary objective of this study was to assess the epidemiology of fungus-positive respiratory samples in the ICU during the first month post-LT, in the absence of systematic antifungal prophylaxis in our unit. The secondary objectives were to determine factors associated with the presence of fungi in the respiratory tract and to evaluate the outcome on ICU stay, and Day-28 survival and 1-year survival after LT in patients with fungus-positive respiratory samples.

## **MATERIALS AND METHODS**

### ***Study population***

This observational, retrospective, single-center study included all consecutive patients who underwent LT at Bichat-Claude Bernard Hospital, Paris, from January 2006 to December 2012. The study period included all ICU stays during the first 28 days post-LT. According to French law, no informed consent was required in view of the observational and retrospective nature of this study. The study was approved by the Paris-North-Hospitals Institutional Review Board (Paris Diderot University, AP-HP, IRB No. 00006477).

### ***Perioperative management***

Perioperative care, including postoperative management, was standardized for all patients according to our standard protocol (9,10). Immunosuppressive therapy was based on a combination of prednisolone, cyclosporine and azathioprine, subsequently replaced by mycophenolate mofetil (9).

Perioperative antibacterial prophylaxis consisted of cefamandole at induction of anesthesia and continued for 48 hours, while prophylaxis in patients with preoperative colonization was adapted to the micro-organisms isolated. Our center's policy does not include digestive or bronchial bacterial or fungal decontamination prior to LT.

### ***Microbiologic samples and anti-infective therapy***

Donor airway samples were obtained by bronchial aspiration during the surgical procedure before transplantation to assess pre-transplant tracheal colonization. In the postoperative period, fiberoptic bronchoscopy was performed daily with invasive respiratory tract samples collected by bronchial aspiration (BA) or protected bronchial samples every two or three days completed by bronchoalveolar lavage (BAL) in the case of suspected viral or fungal infection

(11). Additional samples were obtained in the case of suspected pneumonia. Bacterial and mycological identification and susceptibility testing were performed on all respiratory tract samples according to the usual techniques. Pneumonia was defined as positive culture of BA samples yielding  $\geq 10^5$  colony-forming units (CFU)/mL combined with new or persistent lung infiltrate on chest X-ray, and two or more of the following criteria: temperature  $\geq 38.4^\circ\text{C}$  or  $< 36^\circ\text{C}$ , WBC count  $> 11,000/\text{mm}^3$  or  $< 4,000/\text{mm}^3$ , decreased  $\text{PaO}_2/\text{FiO}_2$  ratio, and purulent secretions (12). Lower respiratory tract infection (LRTI) was defined as positive culture of microbiological samples, at least one or more of the aforementioned clinical signs and radiological signs of new-onset pneumonia.

In the case of positive bacterial cultures of donor samples, empirical antibacterial therapy was initiated, secondarily targeted according to susceptibility testing and continued for seven days. If the donor developed pneumonia prior to transplantation, targeted antibiotic therapy was administered to the recipient for seven days. Similarly, every case of suspected lower respiratory tract infection in the post-LT period was treated by empirical antibiotic therapy followed by targeted antibiotics according to susceptibility testing for a total duration of seven days. Antibiotic therapies targeting *Pseudomonas aeruginosa* or methicillin-resistant *Staphylococcus aureus* were considered to be broad-spectrum antibiotic therapies. Antifungal therapy was initiated in the case of respiratory samples yielding *Aspergillus* or in the case of *Candida* species recovered from respiratory samples associated with fiberoptic abnormalities suggestive of tracheobronchitis, such as ischemic bronchitis, bronchial necrosis, or pseudomembranes in the bronchial tree (8). The Candida Colonization Index was not monitored during ICU stay, and fungal biomarkers were not routinely assayed.

### ***Data collection and statistical analysis***

Demographic characteristics, underlying diseases and clinical data were recorded at the time of ICU admission. Severity scores (APACHE II, SAPS II and SOFA) were assessed on ICU

admission. Clinical characteristics (purulent secretions, abundance of secretions, temperature), laboratory parameters (WBC count, PaO<sub>2</sub>), chest X-ray imaging and results of microbiologic cultures were collected at the time of respiratory samples. Microbiological results of respiratory samples were collected during the whole ICU stay or for the first 28 postoperative days. Non-respiratory mycological samples (blood cultures, urine samples, vascular device cultures, peritoneal fluid cultures) were also collected. The clinical appearance of the bronchial tree recorded during fiberoptic bronchoscopy were noted in patients with fungus-positive respiratory samples: presence of airway ischemia, anastomotic dehiscence, bronchial mucosal necrosis and pseudomembranes. Presence of fungi in pre-transplantation samples, lung donor respiratory samples, and timing of antifungal therapy in ICU, were also collected. Type and duration of antifungal therapy were also collected. ICU length of stay, duration of mechanical ventilation, need of tracheostomy for ventilation weaning were assessed at Day-28. One-year mortality was assessed. The use of renal replacement therapy and episodes of acute rejection during the ICU stay were also recorded.

Qualitative data are expressed as numbers and proportions. Quantitative data are expressed as the median and interquartile range. Qualitative data were analyzed by a Chi-square test or Fisher's exact test and Mann-Whitney and Kruskal-Wallis tests were used for quantitative data. The level of statistical significance was set at 5% and odds ratios (OR) with 95% confidence intervals (95%CI) were reported.

Multivariate models were developed to identify risk factors for fungus-positive respiratory samples. Fisher's exact tests and Wilcoxon tests were used in univariate analysis for these models, and unadjusted ORs were calculated. Variables with a p-value less than 0.2 on univariate analysis were entered into a multivariate logistic regression model. Logistic models were evaluated for discrimination with the c-statistic and for calibration with the Hosmer-Lemeshow test.



Prism (version 5.0, GraphPad Software, Inc), R (version 2.15.0, The R foundation statistical computing) and SAS 9.E (SAS© Institute, Inc, Cary, NC, USA) statistical software were used for statistical analyses.

## RESULTS

### *General characteristics of the study population*

Overall, 176 LT recipients were included in the analysis over a 6-year period. General characteristics are presented in Table 1. Overall, 1,525 respiratory samples were performed during the ICU stay (BA (93% of samples), protected bronchial samples (4%) and BAL (3%)). For each patient, a median of 7 samples [5-13] was performed during the ICU stay.

### *Mycological status before lung transplantation*

In the pre-transplantation period, *Candida*- and *Aspergillus*-positive samples were observed in 30 (17%) and 8 (4%) patients, respectively (Table 2). In the early postoperative period, none of the preoperative *Candida* strains was treated by AFT, while AFT targeting a preoperative *Aspergillus*-positive sample was administered to 4 patients. Only 5 (3%) respiratory samples cultured from donors yielded fungi, including *Candida albicans* in three cases, while culture of the preservation fluid did not recover any fungi. AFT was administered to 2 patients with donor positive respiratory samples (azole in 100% of cases).

### *Mycological status in post-transplantation period*

Fungi were cultured from 682 samples (45% of samples), in 122 (69%) patients, including two strains in 36 (2.4%) samples and mixed bacterial/fungal isolates in 403 (26.4%) samples (Table 2). *Aspergillus* spp. were identified in 21 (1.4%) samples, while *Candida* spp. were isolated from 646 (42%) samples.

AFT therapy was administered to 77/122 LT recipients during their ICU stay (63% of cases).

Among the patients with pre-transplantation cultures positive for *Aspergillus* spp., no *Aspergillus*-positive respiratory sample was reported after LT. No *Aspergillus* was recovered from any of the donor respiratory samples. After LT, *Aspergillus* strains were cultured in 12

(7%) patients a median of 5 days [3-14] after LT. AFT was administered in 8 (75%) cases, a median of 12 days [9-16] after LT (voriconazole in every case, and a combination of liposomal amphotericin B and posaconazole in one case as second-line treatment). No significant association was observed between *Aspergillus*-positive respiratory sample and the presence of any type of bacteria. Among the patients who did not receive AFT for *Aspergillus*-positive respiratory samples, two (67%) patients died in ICU with no subsequent *Aspergillus* detection on their last respiratory samples.

*Candida* spp. were cultured in 118/176 (67%) patients a median of 2 days after LT. Pre-transplantation cultures positive for *Candida* spp. were reported in 27 of these patients (23% of cases). Overall, 20/27 (67%) patients with *Candida*-positive samples during the pre-transplantation period had *Candida*-positive respiratory samples after LT (the same organism in all cases, in association with another strain in 4 (20%) cases). Cultures of *C. albicans* and non-*albicans* species were positive after a median of 4 days [1-7], and 4 days [2-10], respectively. Among the patients with post-transplantation *Candida*-positive respiratory samples, 8 (7%) had a *Candida*-positive sample in another site (candidemia in 2 cases (2%), intra-abdominal *Candida* peritonitis in one case (1%), vascular device infection in 2 cases (2%), urinary tract colonization in one case (1%), cutaneous colonization in 2 cases (2%)). No extrapulmonary *Candida* isolates were detected among the patients without post-transplantation *Candida*-positive respiratory samples,.

The association between fungi and bacteria is presented in Table 3. The presence of *Candida* spp. In the respiratory tract was not significantly associated with the presence of any type of bacteria. AFT was administered in 68/118 (58%) cases (azole in 62 (91%) patients, caspofungin in 7 (6%) patients) a median of 7 days [4-14] after LT, including 46 patients (67% of cases) presenting fiberoptic abnormalities such as ischemic bronchitis, necrosis, pseudomembranes or anastomotic leaks.

Factors associated with fungus-positive respiratory samples are presented in Tables 4 and 5.

***Relationship between mycological status and outcome***

The presence of *Candida* spp. in postoperative respiratory samples was not associated with increased morbidity or mortality (Table 4). No significant difference in terms of survival time was observed between patients with *Candida*-positive respiratory samples and the other patients (Figure 1a). No significant difference in terms of survival time was observed among the patients with *Candida*-positive respiratory samples, regardless of the presence or absence of antifungal therapy (Figure 1b).

## DISCUSSION

While fungal infections after LT have been extensively described in the late post-transplantation period (3–5), to the best of our knowledge, the epidemiology of early fungal colonization and infection has not been previously assessed. We report herein the epidemiology of early fungal samples and their therapeutic consequences in a retrospective cohort of 176 LT recipients.

A specificity of our unit's practice is the absence of systematic antifungal prophylaxis. In a worldwide study, only 5% of LT centers declared that they did not administer antifungal prophylaxis (13). Antifungal prophylaxis was administered systematically to LT recipients in 58 to 69% of LT centers (6,13). In the absence of controlled clinical trials and clear guidelines, we chose to administer antifungal therapy to all patients with *Aspergillus*-positive samples, and to limit antifungal therapy in the presence of *Candida* spp. to patients with signs suggestive of invasive infection (candidemia, fiberoptic abnormalities such as ischemic bronchitis). This policy could explain the short median time to positive fungal cultures in this study population

In the post-transplantation period, the overall incidence of positive fungal cultures in this cohort was similar to that reported in previous published studies, regardless of whether or not antifungal prophylaxis was administered, with colonization rates of 76 to 86% for *Candida* spp. (14,15), and 23 to 35% for *Aspergillus* spp. (15,16). The main fungal pathogen reported in another study describing invasive candidiasis after heart and lung transplantation was *C. albicans* (17). *A. fumigatus* was the main *Aspergillus* species, as reported in previous published studies (18). While an increasing prevalence of “emerging fungi” (*Scedosporium*, *Fusarium*, *Zygomycosis*) has been reported by several studies (19,20), the prevalence of these organisms remained low in this postoperative cohort, which could be explained by the short follow-up period and the small sample size.

In the present study, postoperative positive fungal cultures were not associated with increased ICU mortality or morbidity, suggesting that systemic antifungal therapy should be avoided in patients with fungus-positive samples with no obvious sign of invasive fungal infection. *Candida* colonization in the post-transplantation period was only associated with an increased ICU length of stay, raising the question of the relevance of *Candida*-positive samples. Positive *Candida* cultures can be considered to be a surrogate of prolonged ICU stay rather than the cause of prolonged ICU stay.

Risks factors for *Candida*-positive samples in the post-transplantation period were double-lung transplantation, use of broad-spectrum antibiotic therapy after LT, and SOFA score > 6 on univariate analysis, and only double-lung transplantation on multivariate analysis. In previous studies, single-lung transplantation has been reported to be a risk factor for aspergillosis after LT (3), as the presence of the native lung predisposes to graft infection. These differences compared to published data could be related to the specificities of our cohort and our antifungal prophylaxis strategies.

Our clinical practices may change in the near future in the light of recent international guidelines (8) and the results of this study. Aerosolized amphotericin B could be used as postoperative antifungal prophylaxis, possibly resulting in a change in epidemiology of fungal cultures and susceptibility.

This study presents several limitations. Interpretation of the results is limited by the retrospective and single-center design. In addition, single-lung transplantations were predominantly performed in our center, while double-lung transplantations are mainly performed worldwide (21). Moreover, the main indications for LT during the study period were COPD and IPF, with only a small proportion of CF cases in our cohort, while CF represents 17% of all LT indications worldwide (21), with a high prevalence (up to 70%) of pre-transplantation fungal colonization (22,23) A major limitation to interpretation of this

study is the absence of distinction between fungal colonization and infection. In the absence of systematic transbronchial biopsies, use of biomarkers ((1-3)- $\beta$ -D-Glucan, Galactomannan antigen), and missing data concerning fiberoptic abnormalities, colonization cannot be distinguished from infection, which explains our use of the term “positive samples”.

## **CONCLUSION**

A high prevalence of fungus-positive respiratory samples was observed during the early postoperative period after lung transplantation. Most of these samples were positive for *Candida* spp., mainly *C. albicans*. The lack of association between post-LT *Candida*-positive respiratory samples and increased ICU, 28-day and one-year mortality rates, is suggestive of colonization. Based on these observations, it seems reasonable to avoid systemic antifungal therapy in the absence of signs suggestive of invasive infection. In the light of these findings and the recent ISHLT guidelines, a new AFT policy may be initiated for our patients.

**ACKNOWLEDGEMENT**

None

**FUNDING**

None

**CONFLICTS OF INTEREST**

Dr. Mal reports personal fees from Chiesi, personal fees from Roche, personal fees from Boehringer, personal fees from gilead, outside the submitted work.

Dr. MONTRAVERS reports personal fees and non-financial support from Pfizer, personal fees and non-financial support from MSD, personal fees and non-financial support from Menarini, personal fees and non-financial support from Paratek, outside the submitted work.



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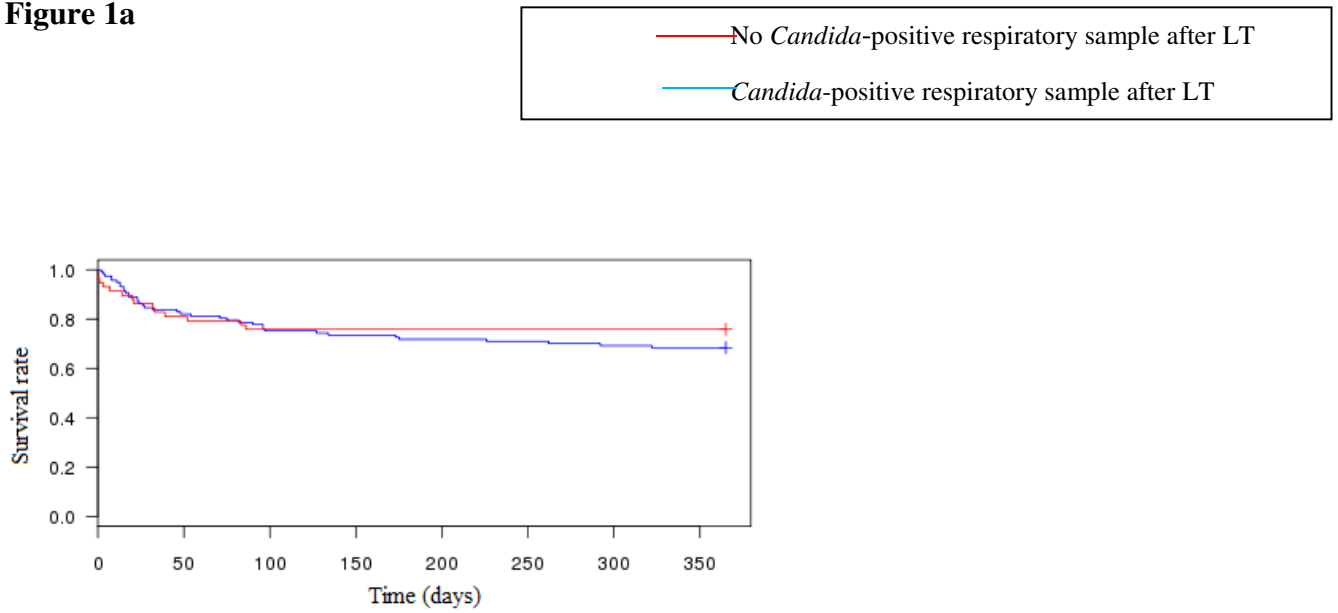
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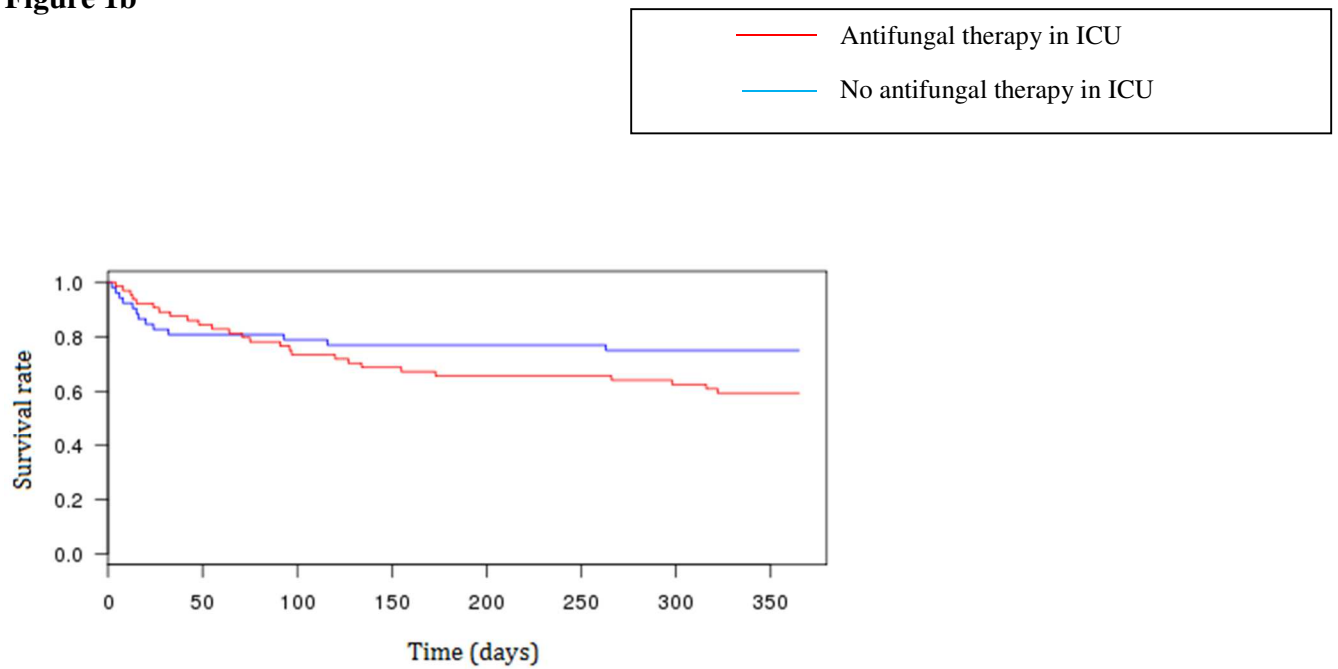
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**Figure 1a**



*Candida*-positive respiratory sample versus no *Candida*-positive respiratory sample: log rank  $p= 0.405$

**Figure 1b**



AFT versus no AFT in patients with *Candida*-positive respiratory samples: log rank  $p= 0.138$

**Figure 1a:** Long-term mortality in patients with and without *Candida*-positive respiratory samples after lung transplantation

**Figure 1b:** Long-term mortality in patients with *Candida*-positive respiratory samples with and without administration of antifungal therapy.

Table 1. Clinical characteristics of the study population in patients in whom *Candida* spp. or *Aspergillus* spp. were cultured after LT (SAPSII: Simplified Acute Physiology Score II; APACHE II: Acute Physiologic And Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment).

Variables	All patients N=176	<i>Candida</i> spp. N=118	Patients without <i>Candida</i> spp. N=58	<i>Aspergillus</i> spp. N=12	Patients without <i>Aspergillus</i> spp. N=164
Age, years, median [IQR]	57 [50-60]	56 [50-59]	58 [50-61]	58 [55-59]	56 [50-60]
Male gender, n (%)	119 (68)	79 (67)	40 (69)	9 (75)	110 (67)
Indication for lung transplantation					
Chronic obstructive pulmonary disease, n (%)	70 (40)	51 (43)	19 (33)	6 (50)	64 (39)
Idiopathic pulmonary fibrosis, n (%)	66 (37)	39 (33)	27 (47)	2 (17)	64 (39)
Others, n (%)	40 (23)	28 (24)	12 (21)	4 (33)	36 (22)
Fungal colonization before transplantation, n (%)	38 (22)	28 (24)	10 (17)	3 (25)	35 (21)
Transplantation procedure					
Single-lung transplantation, n (%)	126 (72)	75 (64)	51 (88)	9 (75)	117 (71)
Double-lung transplantation, n (%)	50 (28)	43 (36)	7 (12)	3 (25)	47 (29)
Donor with positive respiratory sample, n (%)	5 (3)	4 (3)	1 (2)	1 (8)	4 (2)
Severity score on the day of admission					
SAPS II, median [IQR]	35 [29-43]	35 [29-43]	35 [27-41]	45 [40-48]	34 [27-41]
APACHE II, median [IQR]	16 [13-21]	17 [13-21]	15 [12-19]	20 [15-25]	16 [13-20]
SOFA, median [IQR]	5 [3-8]	5 [3-8]	5 [3-8]	8 [6-9]	5 [3-7]
Renal replacement therapy, n (%)	39 (22)	31 (26)	8 (14)	2 (17)	37 (23)
Broad-spectrum antibiotic therapy, n (%)	159 (90)	91 (77)	32 (55)	10 (83)	149 (91)
Acute cellular rejection, n (%)	15 (9)	10 (8)	5 (9)	1 (8)	14 (9)
Acute antibody-mediated rejection, n (%)	8 (5)	7 (6)	1 (2)	0 (0)	8 (5)
Duration of mechanical ventilation, days, median [IQR]	3 [2-14]	4 [2-16]	3 [2-28]	14 [4-23]	3 [2-11]
Mechanical ventilation >3 days, n (%)	87 (49)	64 (54)	23 (40)	9 (75)	78 (48)
Tracheostomy, n (%)	33 (19)	25 (21)	8 (14)	3 (25)	30 (18)
ICU length of stay, days, median [IQR]	17 [9-25]	16 [11-30]	10 [8-20]	23 [20-34]	14 [9-24]
ICU mortality rate, n (%)	43 (24)	31 (26)	12 (21)	4 (33)	39 (24)
28-day mortality rate, n (%)	22 (13)	15 (13)	7 (12)	2 (17)	20 (12)
One-year mortality rate, n (%)	52 (30)	39 (33)	13 (22)	4 (33)	48 (29)

**Table 2:** Epidemiology of pre-transplantation and post-transplantation fungus-positive fungal respiratory samples

	Pre-transplantation N=176	Post-transplantation N=176
No fungal colonization, n (%)	138 (78)	54 (31)
Candida, n (%)	30 (17)	118 (67)
<i>C. albicans</i> , n (%)	26 (15)	58 (49)
<i>C. glabrata</i> , n (%)	-	6 (5)
<i>C. parapsilosis</i> , n (%)	-	3 (3)
<i>C. tropicalis</i> , n (%)	-	4 (3)
<i>C. krusei</i> , n (%)	1 (1)	5 (4)
<i>C. dubliniensis</i> , n (%)	2 (1)	3 (3)
<i>C. lusitaniae</i> , n (%)	1 (1)	-
<i>C. kefyr</i> , n (%)	-	1 (1)
<i>C. famata</i> , n (%)	-	1 (1)
Aspergillus, n (%)	8 (4)	12 (7)
<i>A. fumigatus</i> , n (%)	5 (3)	8 (5)
<i>A. niger</i> , n (%)	1 (1)	2 (1)
<i>A. nidulans</i> , n (%)	1 (1)	-
Geotrichum, n (%)	1 (1)	-
Fusarium, n (%)	-	1 (1)
Zygomycosis, n (%)	-	1 (1)



**Table 3:** Co-pathogens in post-LT respiratory samples

	Candida			Aspergillus		
	OR	95% CI	p	OR	95% CI	p
<i>Enterobacteriaceae</i>	1.85	0.94-3.69	0.076	2.40	0.57-14.25	2.40
<i>Pseudomonas aeruginosa</i>	0.94	0.45-2.01	0.86	2.00	0.47-7.77	0.31
<i>Acinetobacter</i> spp.	1.24	0.20-13.38	1	2.38	0.05-22.57	0.39
<i>Staphylococcus aureus</i>	2.10	0.92-5.18	0.069	0.56	0.06-2.81	0.73
Enterococci	2.42	0.74-10.33	0.15	3.77	0.76-15.81	0.05
<i>Stenotrophomonas maltophilia</i>	2.07	0.53-11.89	0.39	2.31	0.22-12.69	0.27
Streptococci	1.01	0.50-2.11	1	0.66	0.11-2.79	0.75

**Table 4:** Univariate and multivariate analysis of factors associated with *Candida*-positive respiratory samples after lung transplantation, (*LT*: lung transplantation, *MV*: mechanical ventilation; *ICU*: intensive care unit; *SOFA*: sequential organ failure assessment)

	Univariate analysis			Multivariate analysis		
	OR	95% CI	<i>P</i> -value	aOR	95% CI	<i>P</i> -value
Male gender	0.91	0.43-1.88	0.86	-	-	-
Chronic Obstructive Pulmonary Disease	1.56	0.77-3.021	0.19	-	-	-
Idiopathic Pulmonary Fibrosis	0.57	0.28-1.14	0.10	-	-	-
Double-lung transplantation	4.15	1.67-11.80	0.0007	3.790	1.51-9.51	0.004
Fungal colonization of recipient before LT	1.49	0.64-3.74	0.44	-	-	-
Fungus-positive respiratory sample of the donor	1.99	0.19-100	1	-	-	-
Renal replacement therapy after LT	2.21	0.91-6.03	0.08	1.88	0.69-5.14	0.22
Broad-spectrum antibiotic therapy after LT	2.72	1.32-5.66	0.005	1.01	0.48-2.15	0.98
Acute cellular rejection	0.98	0.29-3.85	1	-	-	-
Acute antibody-mediated rejection	3.57	0.44-164.7	0.27	-	-	-
SOFA score > 6	2.64	1.21-5.83	0.01	0.49	0.22-1.12	0.09
ICU mortality	1.36	0.61-3.20	0.46	-	-	-
1-year mortality	1.70	0.79-3.86	0.16	-	-	-
28-day mortality	1.06	0.38-3.28	1	-	-	-
MV > 3 days	1.80	0.91-3.60	0.08	1.29	0.54-3.07	0.57
Tracheotomy	1.88	0.76-5.13	0.17	0.82	0.48-2.15	0.75
ICU length of stay < 17 days	0.43	0.21-0.89	0.015	-	-	-

Notes: Statistical performance: C-index for the model: 0.67, 95% CI: [0.59-0.75], Hosmer-Lemeshow test *p*-value: 0.634.

**Table 5:** Factors associated with *Aspergillus*-positive respiratory samples after lung transplantation (*LT*: lung transplantation, *MV*: mechanical ventilation; *ICU*: intensive care unit; *SOFA*: Sequential Organ Failure Assessment)

	OR	95% CI	p
Male gender	1.47	0.35-8.78	0.75
Chronic Obstructive Pulmonary Disease	1.56	0.40-6.11	0.55
Idiopathic Pulmonary Fibrosis	0.31	0.03-1.54	0.21
Double-lung transplantation	0.86	0.14-3.63	1
Fungal colonization of recipient before LT	1.23	0.20-5.23	0.72
Fungus-positive respiratory sample of the donor	2.25	0.04-25.6	0.43
Renal replacement therapy after LT	0.69	0.07-3.44	1
Broad-spectrum antibiotic therapy after LT	0.51	0.09-5.17	0.33
Acute cellular rejection	0.97	0.02-7.69	1
Acute antibody-mediated rejection	-	-	-
SOFA score > 6	4.46	0.96-27.98	0.037
ICU mortality	1.55	0.32-6.15	0.5
1-year mortality	1.21	0.25-4.77	0.75
28-day mortality	1.29	0.13-6.67	0.67
MV > 3 days	9.16	2.15-55.1	0.0006
Tracheotomy	1.61	0.26-7.02	0.44