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MAJOR ARTICLE

Mycobacterium abscessus Infections in Solid Organ Transplant Recipients: Single-Center Experience in the United States, 2013–2018

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Background. *Mycobacterium abscessus* is increasingly recognized as a human pathogen causing life-threatening infections in immunocompromised patients. There is a paucity of data around this topic in solid organ transplant (SOT) recipients.

Methods. This work was a single-center retrospective cohort study of all SOT recipients with a positive culture for *M abscessus* between 2013 and 2018.

Results. A total of 20 patients (55% female) met inclusion criteria, including 1 kidney recipient (5.0%), 2 liver recipients (10.0%), 12 lung recipients (60.0%), 1 heart recipient (5.0%), and 4 combined organ recipients (20.0%). The median time from SOT to infection was 100 days (range, 30–431 days). Thirteen (65.0%) patients (1 kidney, 1 heart, 7 lung, 1 liver, 1 intestine, and 2 multivisceral) were treated with a median duration of 185 antibiotic days (range, 20–523 days). Among them, *M abscessus* was isolated from respiratory samples in 8 and nonrespiratory samples in 5; 4 of 13 (30.8%) patients had treatment failure and 3 of 13 (23.1%) had unrelated deaths within 1 year after diagnosis. Seven patients (5 lung transplant recipients) with the organism isolated from respiratory samples were not treated as their cultures represented airway colonization or contamination; of those, 2 (28.6%) died (unrelated to infection) and 5 (71.4%) were alive without the infection after 1 year of follow-up.

Conclusions. *Mycobacterium abscessus* infections affect SOT recipients with a high proportion of clinical failures. However, in lung recipients, not all positive cultures correlated with infection, and without treatment some patients had good clinical outcomes. Thus, differentiating colonization from infection is important, and infection prevention measures and novel therapeutic agents are needed for SOT recipients.

Keywords. lung transplant; *Mycobacterium abscessus*; *Mycobacterium abscessus* complex; solid organ transplant.

Mycobacterium abscessus complex organisms are found ubiquitously in the environment in water, soil and dust, shower heads, and ice machines [1, 2]. It is a species of rapidly growing mycobacteria, first reported by Moore and Frerichs in 1953 [3]. After it was separated from the *Mycobacterium chelonae* group, the infections caused by *M abscessus* strains were recognized to have higher fatality rates than any other rapidly growing mycobacteria [3]. *Mycobacterium abscessus* causes a wide spectrum of infections in both immunocompetent and immunocompromised patients [4, 5] and has been associated with hospital outbreaks [6].

Mycobacterium abscessus infections have been reported among lung transplant recipients as well as other solid organ transplant (SOT) recipients. The estimated reported incidence of nontuberculous mycobacterial (NTM) infection is 0.16%–0.55%, 0.04%, 2.8%, and 0.46%–4.4% in kidney, liver, heart, and lung transplant recipients, respectively [7]. Aitken et al reported the outbreak of *M abscessus* subspecies *massiliense* at a cystic fibrosis clinic and the possibility of patient-to-patient infection transmission [8]. Moreover, *M abscessus* infections are associated with high mortality among SOT recipients. Huang et al and Longworth et al suggested that early NTM infection after transplantation was related to higher mortality [9, 10]. In 2019, the guidelines for the management of NTM infection in SOT recipients were published by the Infectious Diseases Community of Practice of the American Society of Transplantation. The recommendation for *M abscessus* infection is to treat with at least 3 effective antibiotics in combination therapy including azithromycin, with caution concerning drug-drug interactions and potential drug toxicity [11].

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Although clinicians should start at least 3 antibiotics for treating this serious infection, with the risk of drug-drug interaction and potential drug toxicity, we do not have enough data about the clinical course and outcome of *M abscessus* infection among SOT recipients. Most data about *M abscessus* infection have arisen mainly from case reports, case series, and observational studies because of the rarity of this infection. For optimizing the management of *M abscessus* infection and improving the mortality among SOT recipients, we need more data about this infection.

To expand on this topic, the purpose of this study was to describe clinical characteristics and outcomes of SOT patients infected with *M abscessus* at a large transplant center in Miami, Florida.

METHODS

This is a descriptive retrospective cohort study of SOT recipients who had a positive culture for *M abscessus* group strains at the Miami Transplant Institute and Jackson Memorial Hospital, which is a 1558-licensed bed tertiary care teaching hospital located in Miami, Florida, between 1 January 2013 and 30 September 2018. The clinical samples were sent to the Mycobacterial Laboratory at National Jewish Hospital in Denver, Colorado, for susceptibility and identification. Not all *M abscessus* isolates were identified to the subspecies level, as this identification was requested by the individual treating physician. All cultures without subspecies were reported as *M abscessus* group. A list of all SOT recipients who had a positive *M abscessus* culture during the study period in our hospital was obtained from the corresponding hospital microbiology records. Data collected included patients' demographics, comorbidities (eg, cystic fibrosis, chronic bronchitis, interstitial lung disease, diabetes, and liver cirrhosis), date and type of transplantation, immunosuppressive regimen including induction therapy and maintenance therapy, history of acute rejection and treatment, site of infection, antimicrobial susceptibilities, antimicrobial therapy, and clinical outcomes via retrospective review of electronic medical records. For patients having multiple positive cultures corresponding to a single or multiple episodes of infections, only the first isolate of *M abscessus* was counted. The study was approved by the Institutional Review Board at University of Miami.

Definitions

Currently there is no consensus on the definition of treatment failure for *M abscessus* complex infections. In this study, we apply the definitions in the study conducted by Sfeir et al to our study [5]. We defined early treatment failure as death and/or refractory infection characterized either by persistent positive culture for *M abscessus* within 12 weeks of treatment initiation and/or lack of radiographic improvement [5]. Culture results and radiograph findings were evaluated within 12 weeks of treatment. Acute kidney injury was defined based on the RIFLE (Risk, Injury, Failure, Loss, End-Stage Renal Disease) criteria [12]. To define *M abscessus* infection, we followed the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) criteria for NTM disease during the study period for respiratory isolates [13] (Supplementary Table 1). Also, we recognized *M abscessus* cultured from sterile site with clinical syndrome as true infection. Disseminated infection was defined as the presence of at least 2 sites of *M abscessus* infection [5]. If patients had positive culture result but did not meet ATS/IDSA criteria for NTM disease, we define the patients as colonization.

Only 1 isolate per patient was included for susceptibility testing, adopting the Clinical and Laboratory Standards Institute (CLSI) guidelines [14]. Identification of *M abscessus* isolates was performed at the Mycobacteriology Laboratory at National Jewish Health in Denver, Colorado. The broth microdilution method with cation-supplemented Mueller-Hinton broth was used as recommended by the CLSI [14].

Statistical Analysis

For survival analysis, we constructed Kaplan-Meier survival curves to compare the 1-year survival of the lung transplant recipients with *M abscessus* infection and non–lung transplant recipients with *M abscessus* infection. We compared 1-year survival of the recipients with *M abscessus* infection and with *M abscessus* colonization in all SOT and lung transplantation. Statistical analysis was done with R software [15, 16].

RESULTS

Patient Characteristics in All SOT and Lung Transplant Recipients

The final study cohort included 20 SOT recipients (1 kidney, 2 liver, 12 lung, 1 heart, 2 multivisceral, 1 intestine, 1 kidney-pancreas) with positive cultures for *M abscessus*. Tables 1–3 show demographic data, medical history, site of infection, time to diagnosis from transplant, time to rejection from transplantation to *M abscessus* diagnosis, rejection after initiation of treatment, the initial treatment regimen, and clinical outcome. In this cohort, there were 9 male and 11 female patients with a median age of 61 years (range, 11–73 years). Among our 20 patients, 13 (65.0%) were treated with a median treatment duration of 185 days (range, 20–523 days); there were 4 patients who had short duration of antibiotic treatment (20–91 days); 1 patient was subsequently deemed to have colonization rather than an infection and treatment was stopped, and the other 3 patients had unrelated deaths so that they were unable to complete treatment for *M abscessus* infection. Among the 13 patients treated with antibiotics, a total of 5 (5/13 [38.5%]) patients died. All 7 patients who did not receive treatment were alive and free from *M abscessus* infection. Four patients

Table 1. Patient Characteristics

Characteristic	All Patients (n = 20)	Lung Transplant Recipients (n = 12)
Age, y, median (range)	61 (11–73)	64 (47–72)
Sex		
Male	9 (45.0)	5 (41.7)
Female	11 (55.0)	7 (58.3)
Race/ethnicity		
White	12 (60.0)	7 (58.3)
Hispanic	3 (15.0)	2 (16.7)
African American	4 (20.0)	3 (25.0)
Others	1 (5.0)	0 (0)
Time to diagnosis, d, XXX (range)	100 (0–3497)	100 (0–1382)
Site of *M abscessus* infection		
Respiratory	15 (75.0)	12 (100)
Abdominal fluid	1 (5.0)	0 (0)
Deep tissue culture	1 (5.0)	0 (0)
Blood	1 (5.0)	0 (0)
Disseminated	2 (10.0)	0 (0)
Blood + bone	1	0 (0)
Blood + pleural effusion	1	0 (0)
Organ transplant		
Kidney	1 (5.0)	0 (0)
Liver	2 (10.0)	0 (0)
Lung	12 (60.0)	12 (100)
Heart	1 (5.0)	0 (0)
Intestine/multivisceral	3 (15.0)	0 (0)
Kidney and pancreas	1 (5.0)	0 (0)
Immunosuppression induction		
Methylprednisone	10 (50.0)	8 (66.7)
ATG + methylprednisone	2 (10.0)	0 (0)
Methylprednisone + rituximab + tacrolimus	1 (5.0)	0 (0)
Methylprednisone + basiliximab	2 (10.0)	2 (16.7)
ATG + daclizumab	1 (5.0)	0 (0)
Not obtained	4 (20.0)	2 (16.7)
Immunosuppression maintenance		
MMF/MPA + prednisone + tacrolimus	11 (55.0)	9 (75.0)
MMF/MPA + methylprednisone + tacrolimus	1 (5.0)	0 (0)
MMF/MPA + tacrolimus	1 (10.0)	0 (0)
Tacrolimus + mercaptopurine	1 (5.0)	0 (0)
Prednisone + tacrolimus	2 (10.0)	2 (16.7)
Tacrolimus	2 (10.0)	0 (0)
Prednisone	1 (5.0)	1 (8.3)
No data	1 (5.0)	0
Rejection		
Rejection before the treatment[a]	3 (15.0)	2 (16.7)
Time from transplantation to rejection, d, median (range)	298 (82–343)	213 (82–343)
Rejection after *M abscessus* diagnosis[a]	7 (35.0)	3 (25.0)
Time from diagnosis to rejection, d, median (range)	59 (0–476)	59 (0–131)
Outcome		
Patients treated with antibiotics	13 (65.0)	7 (58.3)
Duration of therapy, d, XXX (range)	185 (20–523)	186 (20–296)
Treatment failure	4/13 (30.8)	3/7 (42.9)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ATG, antithymocyte globulin; *M abscessus*, *Mycobacterium abscessus*; MMF, mycophenolic mofetil; MPA, mycophenolic acid.

[a]Patients who had rejection on the day when *Mycobacterium abscessus* infection was diagnosed were categorized in "rejection during *M abscessus* treatment."

(20.0%) had treatment failure, 2 of whom (50.0%) died subsequently. Among our 20 patients, the infectious disease (ID) service was consulted in 17 cases (85.0%); the 3 cases without ID consult were lung transplant recipients, and all were alive without infection.

Lung transplant recipients included 5 males and 7 females with a median age of 60 years (range, 47–70 years). Seven patients (58.3%) were treated with antibiotics with a median treatment duration of 186 days (range, 20–296 days); 2 (16.7%) had unrelated deaths. Three (25.0%) patients had treatment failure, 1 of whom died. Five patients (41.7%) were not treated and were alive without evidence of *M abscessus* infections within 1 year of follow-up. In lung transplant recipients, 8 of 12 patients (66.7%) met the ATS/IDSA criteria for diagnosis of NTM infection and only 6 of 8 patients (75.0%) who met the criteria were treated with antibiotics. The 2 patients who met ATS/IDSA criteria were not treated by their transplant pulmonary team and were never referred to ID.

Antibiotic Treatment in All SOT Recipients

Initial antibiotic management of all our patients is summarized in Table 3. The combination of azithromycin, cefoxitin and tigecycline was prescribed in 6 patients (46.2%). All patients tolerated azithromycin, clarithromycin, cefoxitin, and imipenem-cilastatin. Tigecycline use was frequently associated with adverse effects such as gastrointestinal upset (2/6 [33.3%]), transaminitis (4/6 [66.7%]), and pancreatitis (2/6 [33.3%]), and amikacin caused acute kidney injury (1/3 [33.3%]) and hearing loss (1/3 [33.3%]). The 1 patient who had a linezolid-based regimen developed thrombocytopenia.

Rejection in All SOT and Lung Transplant Recipients

In our cohort, a total 8 of 20 (40.0%) patients had rejection with a median time from transplantation to rejection of 192 days (range, 63–594 days); 3 (15.0%) patients had rejection prior to *M abscessus* diagnosis, and 7 (35.0%) patients had it after *M abscessus* diagnosis (2 patients had rejection twice, before and after the diagnosis). The median time from transplantation to rejection in the 3 patients was 298 days (range, 82–343 days) and the median time from diagnosis to rejection in the 7 patients was 59 days (range, 0–476 days). In lung transplant recipients, a total 4 of 12 (33.3%) patients had rejection after transplantation with a median time from transplantation to rejection of 192 days (range, 82–343 days); 2 (16.7%) patients had rejection before the *M abscessus* diagnosis in a median of 213 days (range, 82–343 days) from the transplantation, and 3 (25.0%) patients had rejection after the diagnosis at a median of 59 days (range, 0–131 days) from the diagnosis (1 patient had rejection before and after the diagnosis).

Table 2. Summary of 20 Cases

No.	Age/ Sex	Diseases	Transplant	Site of Infection (Culture)	No. of Culture Positivity	Finding in Chest Imaging	ATS/IDSA Diagnostic Criteria	Time to Diagnosis, d	Rejection Before Treatment	ID Consult
1	48/M	End-stage intestinal failure, liver failure, chronic pancreatitis, enterocutaneous fistula	Multivisceral	Bacteremia (blood culture)	1	NA	NA	17	No	Yes
2	63/F	Bronchiectasis, GERD	Lung (double)	BAL culture	1	Abnormal findings in CXR	No	470	Yes	No
3	63/F	Cirrhosis due to chronic hepatitis C, HCC, DM, and GERD	Liver	Wound infection (deep wound culture)	1	NA	NA	31	No	Yes
4	73/M	ESRD due to hypertension	Kidney	Pneumonia (sputum culture)	1	Multiple nodular lesions in chest CT	No	2158	No	Yes
5	48/M	Stage 4 sarcoidosis, bronchiectasis	Lung (double)	NA (BAL culture)	5	Abnormal findings in CXR	Yes	24	No	Yes
6	11/F	Cystic fibrosis	Liver	NA (sputum culture)	2	Pulmonary nodule in chest CT	Yes	3497	No	Yes
7	69/M	Pulmonary fibrosis, GERD	Lung (double)	Pneumonia (BAL culture)	3	Worsening opacifications in CXR	Yes	0	No	Yes
8	53/F	Short bowel syndrome, DM	Intestine	Intra-abdominal infection (abdominal fluid culture)	1	NA	NA	118	No	Yes
9	70/M	Pulmonary fibrosis, DM	Lung (double)	NA (BAL culture)	1	No acute cardiopulmonary issues in CXR	No	281	No	No
10	60/F	COPD	Lung (double)	NA (BAL culture)	1	Worsening consolidation in right upper lung	Yes	44	No	Yes
11	68/F	COPD, DM	Lung (double)	Pneumonia (BAL culture)	3	No acute cardiopulmonary issues in CXR	No	242	No	Yes
12	65/F	Primary sarcoidosis and COPD, GERD	Lung (single)	Disseminated infection (BAL culture/pleural effusion culture)	1	Consolidation, bronchopleural fistula, and hemopneumothorax, anastomosis breakdown in chest CT	Yes	11	No	Yes
13	34/M	Dilated cardiomyopathy, GERD	Heart	Bacteremia (blood culture)	12	NA	NA	314	Yes	Yes
14	60/M	Pulmonary fibrosis	Lung (single)	Pneumonia (BAL culture)	2	Postsurgical change and pulmonary nodules in chest CT	Yes	82	Yes	Yes
15	61/M	Pulmonary fibrosis, GERD	Lung (double)	Pneumonia (BAL culture)	8	Mild perihilar density in CXR	Yes	66	No	Yes
16	47/F	Lymphangioleiomyomatosis	Lung (double)	Pneumonia (BAL culture)	1	Tree-in-bud and ground glass opacity in chest CT	Yes	195	No	Yes
17	65/F	COPD	Lung (double)	Pneumonia (BAL culture)	9	Consolidations in CXR	Yes	56	No	Yes
18	55/F	Short bowel syndrome, pseudo-obstruction and DM	Multivisceral	Disseminated infection (blood culture/bone culture)	1	NA	NA	56	No	Yes

Table 2. Continued

No.	Age/ Sex	Diseases	Transplant	Site of Infection (Culture)	No. of Culture Positivity	Finding in Chest Imaging	ATS/IDSA Diagnostic Criteria	Time to Diagnosis, d	Rejection Before Treatment	ID Consult
19	72/F	Pulmonary fibrosis, bronchiectasis, DM, and GERD	Lung (single)	NA (BAL culture)	1	NA	NA	1382	No	No
20	56/M	DM (type 1), ESRD	Kidney and pancreas	NA (throat swab culture)	1	NA	NA	1690	No	Yes

Abbreviations: ATS/IDSA, American Thoracic Society/Infectious Diseases Society of America; BAL, bronchoalveolar lavage; COPD, chronic obstructive pulmonary disease; CT, Computerized Tomography; CXR, chest radiograph; DM, diabetes mellitus; ESRD, end-stage renal disease; GERD, gastroesophageal reflex disease; HCC, hepatocellular carcinoma; ID, infectious diseases; NA, not applicable.

Survival in All SOT and Lung Transplant Recipients

There was no significant difference in survival during the first year after the diagnosis among lung transplant recipients and non–lung transplant recipients (0.833 and 0.875, respectively; Figure 1*B*). The patients with *M abscessus* colonization had better survival than those with infection in all SOT recipients (1.0 and 0.786, respectively) and lung transplant recipients (1.0 and 0.786, respectively), but it was not statistically significant (Figure 1*C* and 1*D*).

Microbiology

In our facility, not all of the isolates were sent for subspecies identification or susceptibilities identification as the laboratory protocol depends upon each provider's request and clinical decision. Among our 20 cases, 12 had the subspecies identification (Supplementary Table 2) of *M abscessus massiliense* (n = 7), *M abscessus bolletii* (n = 4), *and M abscessus abscessus* (n = 1). Susceptibilities were available for 14 cases (Supplementary Table 3). Based on these results, we calculated the proportion of susceptible isolates as (number of cases with *M abscessus* susceptible to the specific antibiotic) / (number of cases that have the antibiotic susceptibility test result for the specific antibiotic). Amikacin, azithromycin, clarithromycin, kanamycin, and tigecycline were the most active antibiotics against *M abscessus* infection in our facility (100% for each agent). Other drugs such as clofazimine, linezolid, cefoxitin, imipenem-cilastatin, ciprofloxacin, and moxifloxacin were more likely to be resistant in vitro (percentage susceptible: 92.0%, 36.3%, 9.1%, 7.1%, 0%, and 0%, respectively).

DISCUSSION

The incidence, risk factors, and outcome of NTM infection in SOT recipients are not fully defined, and the incidence is still uncertain. The purpose of the present study was to reveal the clinical course and outcomes of *M abscessus* infection. We demonstrated that both treatment failure rate and mortality rate were high in *M abscessus* infection; treatment failure rate was 4 of 13 (30.8%) and 3 of 7 (42.9%) in all SOT recipients and lung transplant recipients, respectively, and 1-year survival was 85.0% and 83.3% in in all SOT recipients and lung transplant recipients, respectively. Five of 12 lung transplant recipients with positive respiratory culture with *M abscessus* were not treated. Further review revealed that all of them were alive and free from *M abscessus* infection at a median of 818 days after positive culture (range, 228–1910 days).

There was a high treatment failure rate in our cohort, which was related to the concomitant infections and immunosuppression as the previous studies addressed [9, 10, 17]. We also found that more patients had adverse events from the initial antibiotic regimens (Supplementary Table 4). Regarding mortality, Longworth et al reported that NTM infection after SOT

Table 3. Summary of Initial antibiotic therapy and clinical outcomes in 20 Cases

No.	Initial Regimen	Comment	Duration of Therapy, d	Treatment Failure	Rejection After Treatment	Outcome
1	Clarithromycin, levofloxacin, and tigecycline	After initial treatment, tigecycline caused transaminitis and levofloxacin was stopped based on susceptibility result. But treatment was terminated in about 25 d because it was thought that *M abscessus* was contaminated.	25	No	Yes	Alive
2	Not treated	Not treated	Not treated	No	Yes	Alive
3	Azithromycin, cefoxitin, and tigecycline	Initial regimen was continued for 3 mo, and then it was stepped down to azithromycin and tigecycline.	297	No	Yes	Dead
4	Azithromycin, imipenem-cilastatin, and tigecycline	After the initial treatment was started, imipenem-cilastatin was switched to cefoxitin 2 d later. Then the patient was discharged to other facility and there was no further follow-up in our system.	NA	NA	NA	NA
5	Not treated	Not treated	Not treated	No	No	Alive
6	Not treated	Not treated	Not treated	No	No	Alive
7	Azithromycin, cefoxitin, and tigecycline	Initial treatment was continued without any significant side effect.	20	No	No	Dead
8	Azithromycin, cefoxitin, and tigecycline	Initial regimen was switched to azithromycin, imipenem-cilastatin, and cefoxitin because of transaminitis. The patient had been on the 3 medications for 8 mo and then azithromycin and imipenem-cilastatin were continued additional 10 mo for relapse.	523	No	Yes	Alive
9	Not treated	The patient was not treated as infection. Azithromycin was given as prophylaxis.	202	No	Yes	Alive
10	Not treated	Not treated	Not treated	No	Yes	Alive
11	Azithromycin, cefoxitin, and tigecycline	The initial regimen was switched to azithromycin, imipenem-cilastatin, and linezolid in 4 d. But the further information was missing.	NA	No	No	Alive
12	Azithromycin, imipenem-cilastatin, and cefoxitin	The initial regimen was switched to azithromycin, tigecycline, and amikacin. The patient died of the event not related to *M abscessus* infection.	87	Yes	No	Dead
13	Azithromycin, cefoxitin, and amikacin	After the initial treatment, amikacin was stopped in 1 mo, then the regimen was switched to azithromycin, cefoxitin, and tigecycline. The treatment was stopped in 4 mo. After the treatment, the infection relapsed.	136	No	Yes	Dead
14	Azithromycin, cefoxitin, and tigecycline	The initial treatment was switched to azithromycin, imipenem-cilastatin, and inhaled amikacin because tigecycline caused transaminitis and imipenem-cilastatin was started for treating *Achromobacter* infection.	184	Yes	No	Alive
15	Azithromycin, cefoxitin, and amikacin	The initial treatment was switched to azithromycin, cefoxitin, and tigecycline because amikacin caused hearing loss. After that, tigecycline caused transaminitis and it was switched to inhale amikacin. Inhale amikacin was complicated with bronchospasm.	186	No	No	Alive
16	Azithromycin, cefoxitin, and tigecycline	The initial regimen was continued, but tigecycline caused nausea and vomiting. Then the dose of tigecycline was decreased, but it caused transaminitis. The regimen was switched to azithromycin, cefoxitin, and inhaled amikacin.	220	No	Yes	Alive
17	Azithromycin, imipenem-cilastatin, and tigecycline	The initial regimen was complicated with transaminitis likely due to azithromycin and/or tigecycline, and it was switched to inhaled amikacin, imipenem-cilastatin and linezolid. After that, inhaled amikacin was stopped because of worsening respiratory status, and linezolid caused thrombocytopenia. Imipenem-cilastatin and azithromycin were continued.	296	Yes	No	Alive
18	Clarithromycin, tigecycline, and amikacin	After the initial treatment, clarithromycin was switched to azithromycin and tigecycline was switched to cefoxitin due to pancreatitis. And amikacin was stopped because of acute kidney injury. Meantime cefoxitin was initiated but finally clofazimine and imipenem-cilastatin were continued.	91	Yes	No	Dead
19	Not treated	Not treated	Not treated	NA	No	Alive
20	Not treated	Not treated	Not treated	NA	No	Alive

Abbreviations: *M abscessus*, *Mycobacterium abscessus*; NA, not applicable.

transplantation decreased 3-year survival after transplantation and there was no difference in mortality between lung transplant recipients and non–lung transplant recipients with NTM infection [10]. In our study, we calculated 1-year survival and there was no significant difference between lung transplant recipients and non–lung transplant recipients (Figure 1*B*). It is possible that some of lung transplant included in our cohort had colonization, not infection, overestimating better survival

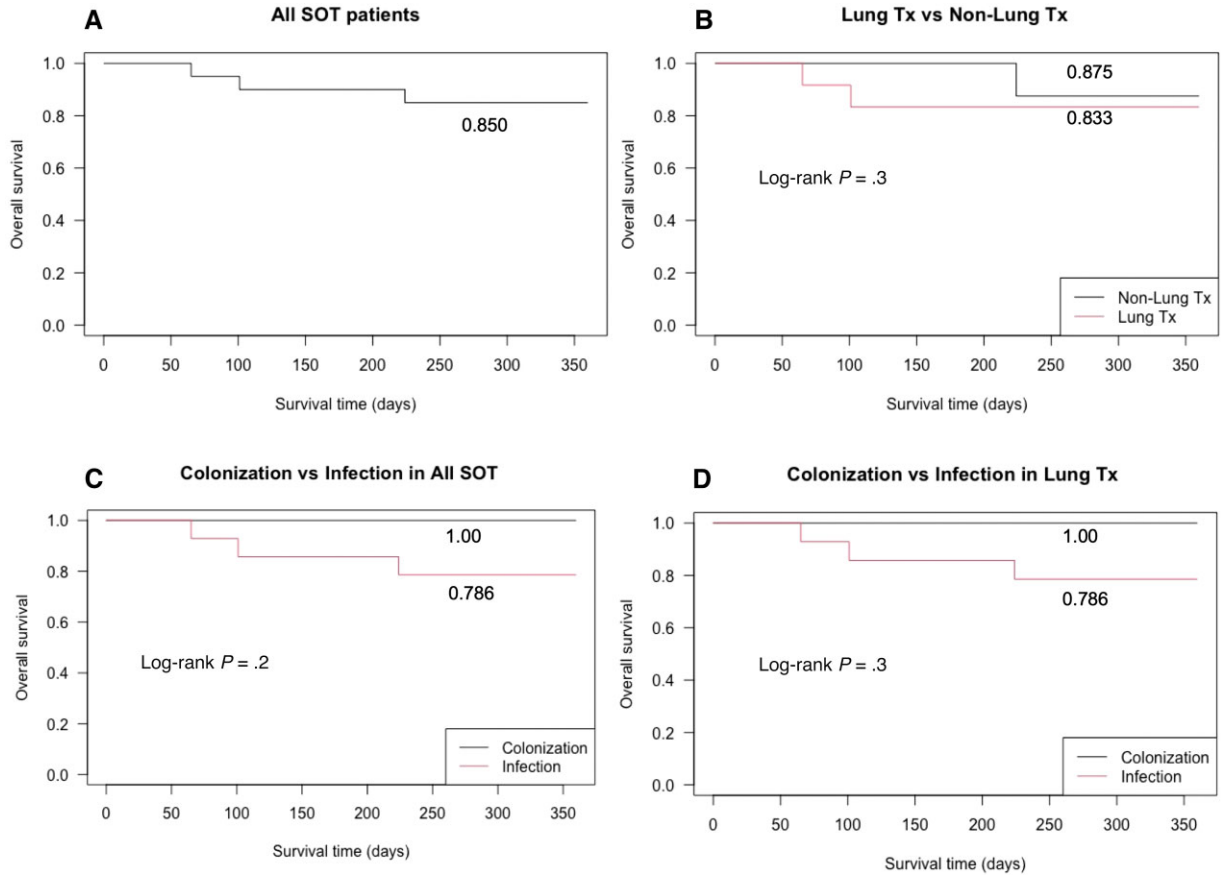

Figure 1. One-year survival after transplantation. *A*, One-year survival in all solid organ transplant (SOT) recipients with *Mycobacterium abscessus* infection. *B*, One-year survival in *M abscessus* infection, lung transplant (Tx) recipients vs non–lung Tx recipients. *C*, One-year survival in *M abscessus* infection, colonization vs infection in all SOT recipients, We defined colonization as the patients who had positive *M abscessus* culture but did not meet American Thoracic Society/Infectious Diseases Society of America criteria. *D*, One-year survival in *M abscessus* infection, colonization vs infection in lung Tx recipients.

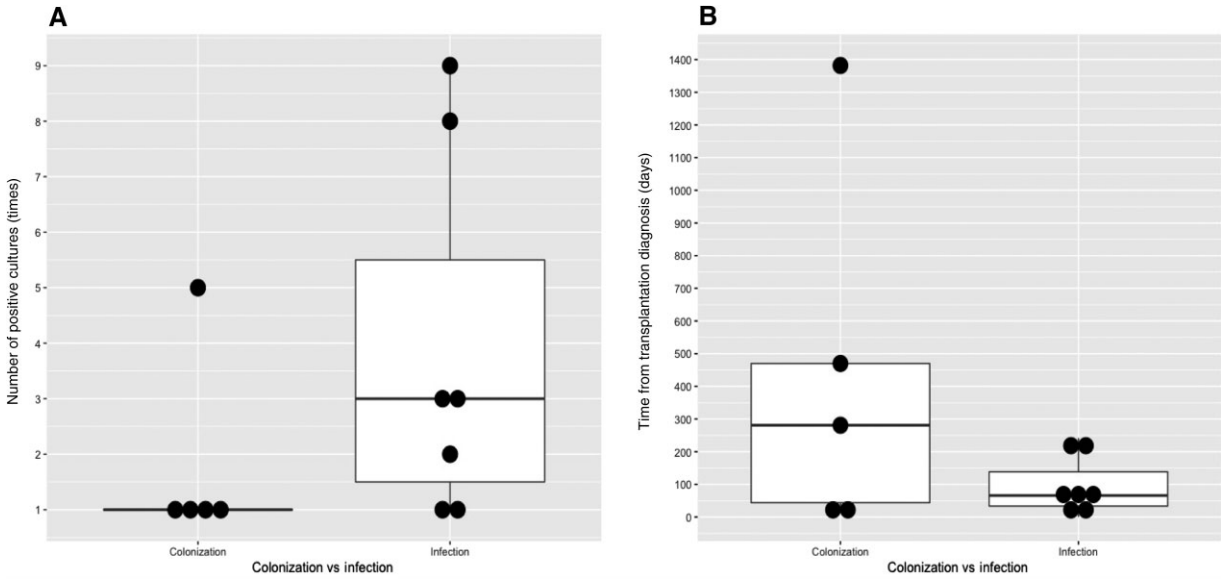

Figure 2. Colonization vs infection in lung transplant recipients. *A*, Number of positive cultures. *B*, Time from transplantation to diagnosis.

Table 4. *Mycobacterium abscessus* Infection and Outcome

Study	Study Design	No. of Patients	Age/Sex and Type of Transplantation (Indication for Transplantation)	Site of Infection	Time from Transplantation to Infection	Clinical Course/ Treatment Failure	Mortality
Cherneko et al [17]	Survey	17	17 Lung 57/F (bronchiectasis) 29/M (CF) 33/M (PAH) 49/M (COPD) 65/M (IPM) 38/M (CF) 37/M (CF) 40/F (Ei) 48/M (COPD) 66/M (IPF) 53/M (COPD) 60/M (A) 25/F (IPF) 39/M (CF) 54/F (Sclero) 42/F (benign metastasizing leiomyoma) 66/M (IPF)	Lung Cut lesion Lung Lung Lung Lung Lung Cut lesion Lung Lung Lung Lung Lung Lung Lung Lung Lung Lung	18.5 mo (range, 1–111 mo)	One patient was not treated. Among the treated 16 patients, 1 patient did not respond to the treatment.	58.8% (10/17) were alive and cured, and 41.2% (7/17) have died. Median follow-up after identification of an organism was 835 d. Mean follow-up was 1207.1 d.
Garrison et al [18]	Case series	3	73/F kidney 35/M kidney 28/F multivisceral	SSTI PD catheter-related infection SSTI, and septic arthritis at sternoclavicular joint	12 wk after Tx 2 mo after Tx 9 mo after Tx	Recurrence of infection in 20 mo after completion of therapy No recurrence, but the patient was back to hemodialysis 11 mo after *M abscessus* infection. Clinical course was complicated with varicella zoster infection, intestinal graft rejection, and multiorgan failure, and finally died 14 mo after transplantation.	Alive Alive, but graft loss Dead
Morales et al [19]	Case series	7	4 Lung 15/F (CF) 19/M (CF) 57/M (COPD) 54/M (pulmonary fibrosis) 2 Kidney 61/F (polycystosis) 58/M (renal failure) 1 Heart 69/M (DCM)	4 Lung Nodules in both knees SSTI and disseminated infection Stenosis in LMB and pneumonia Pneumonia 2 Kidney Panniculitis SSTI 1 Heart Pneumonia	24 mo (range, 7 d–276 mo)	Not reported	Not reported
Huang et al [20]	Retrospective cohort	4	49/F lung 56/F lung 33/M lung 57/M lung	Lung infection	614 d 487 d 583 d 83 d	NTM clearance by 3 mo, progressive graft dysfunction NTM clearance by 6 mo, complete resolution Unknown NTM clearance, progressive graft dysfunction NTM clearance by 3 mo, progressive graft dysfunction	Dead/postoperative day 1161 Alive/ postoperative day 2109 Dead/ postoperative day 612 Dead/ postoperative day 436
Richey et al [21]	Case report	1	1 Heart 49/M (nonischemic cardiomyopathy)	Lead infection	<3 mo	No treatment failure	Alive at 18 mo after diagnosis

Table 4. Continued

Study	Study Design	No. of Patients	Age/Sex and Type of Transplantation (Indication for Transplantation)	Site of Infection	Time from Transplantation to Infection	Clinical Course/ Treatment Failure	Mortality
Osamani et al [22]	Case series	9	9 Lung 76/M (IPF) 69/M (IPF) 40/F (CF) 53/M (IPF) 43/M (IPF) 68/M (COPD) 70/M (IPF) 72/F (IPF) 65/F (COPD)	Pneumonia (*M abscessus* was isolated from respiratory samples)	7.5 mo (range, 3 d–13 mo)	4/9 (44.4%)	Median survival 39 mo (range, 11–96 mo)
Ose et al [23]	Case series	2	2 Lung 38/F (bronchial ectasia) 39/F (lymphangioleiomyomatosis)	2 Lung Pneumonia Pneumonia	82 mo after transplantation 58 mo after transplantation	No treatment failure	Alive at 22 mo after treatment Alive at 12 mo after treatment

We performed a literature review of *Mycobacterium abscessus* infection and summarized the findings: age, site of infection, time from transplantation to infection, outcome, and mortality.

Abbreviations: A, α1-antitrypsin deficiency; CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy; Ei, xxx; IPF, idiopathic pulmonary fibrosis; IPAH, idiopathic pulmonary arterial hypertension; IPM, xxx; LMB, xxx; NTM, nontuberculous mycobacteria, PD, peritoneal dialysis, Sclero, scleroderma; SSTI, skin and soft tissue infection; Tx, transplantation.

outcomes because our data support that patients with *M abscessus* colonization had better survival than those with the infection and we cannot perfectly differentiate *M abscessus* colonization from the infection at the first evaluation (Figure 1*C* and 1*D*). And lung transplant recipients are clinically diagnosed earlier as there is a low threshold to perform diagnostic bronchoscopies in these patients. In this regard, this practice can cause lead time bias and we need to interpret the survival outcome carefully.

It must be emphasized that in lung transplant recipients whose respiratory culture showed *M abscessus*, 41.7% of patients were free from *M abscessus* infection without treatment. As we mentioned above, our study and the previous study by Osmani et al applied ATS/IDSA criteria of NTM infection for diagnosis [13, 22]. In our study, 5 lung transplant recipients with positive *M abscessus* respiratory culture did not receive treatment, but all of them were alive. And 2 of them did meet the ATS/IDSA criteria but did not receive the treatment because the patients were clinically stable when the ID physicians evaluated them several days after the organism grew from the culture. These 2 patients were alive and free from *M abscessus* infection. The fact may suggest that the current ATS/IDSA criteria of NTM infection were not applicable in lung transplant recipients and that lung transplant recipients who have positive respiratory cultures with *M abscessus* do not always need treatment because *M abscessus* growing in respiratory samples just means its colonization, not infection. In lung transplant recipients, it was difficult to differentiate true infection from colonization, especially early after lung transplantation. Considering the high treatment failure rate and mortality rate, aggressive treatment is recommended, but the combination therapy against *M abscessus* can cause drug-drug interaction and adverse events simultaneously. Therefore, clinical decision making in some of these cases is not always straightforward, and it should be done on a case-by-case basis weighing risks and benefits as well as evidence of infection vs colonization. Better diagnostic criteria are required to optimize the chance of cure and lower the adverse events. In our cohort, the lung transplant recipients with *M abscessus* colonization tended to have a lower number of positive culture and shorter time from transplantation and the first positive culture result (Figure 2), although the data were preliminary and need to be confirmed by larger studies.

It is also important to highlight that 8 of 20 (40.0%) patients had rejection after the diagnosis of *M abscessus* infection. We speculate that the infection itself and/or lowering the level of immunosuppression—due to dose reduction for managing the infection or drug-drug interaction with antibiotics—could have triggered rejection. Further investigations are needed to evaluate the relationship between *M abscessus* infections and rejection.

Our study has limitations. First, our cohort had more patients with *M abscessus* infection compared with other studies, but the number of patients was still small. And the clinical course, treatment failure rate, and mortality rate varied widely between these studies (Table 4), so our data including treatment failure rate and mortality rate can be under- or overestimated. Second, there is no validated diagnostic criteria in SOT recipients, especially in lung transplant recipients, for *M abscessus* infection and we may treat the patients with *M abscessus* colonization, not *M abscessus* infection, which might result in a lower mortality rate. Although our data had these limitations, we identified important implications for the diagnosis of *M abscessus* infections in transplant recipients. Taken all together, culture positivity in respiratory samples does not always suggest infection. In this regard, we recommend caution and

thoughtful criteria to confirm the diagnosis of the lung infection and not based on a single respiratory culture balancing the risks and benefits in each individual patient.

In conclusion, our data showed that *M abscessus* infections are associated with a high number of treatment failures and potentially increased mortality in SOT recipients. Further studies are needed to improve infection prevention strategies, develop better diagnostic criteria to distinguish colonization vs infection in lung transplant recipients, design novel agents to improve clinical outcomes, and minimize adverse events in this challenging patient population.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Patient consent. This research project was approved and conducted under the local institutional review board approval; written consent was waived due to practical issues.

Potential conflicts of interest. All authors: No reported conflicts of interest.

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