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Natural course of untreated nontuberculous mycobacterial pulmonary disease according to microbiologic diagnostic method

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임상의과학과

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Master of Science in Clinical Medical Science

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Abstract

Natural course of untreated nontuberculous mycobacterial pulmonary disease according to microbiologic diagnostic method

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Background:

Microbiologic diagnosis of nontuberculous mycobacterial pulmonary disease (NTM-PD) can be achieved by at least two positive sputum cultures or by one positive culture from bronchial washing, lavage, or lung tissue. However, to date, there is a lack of evidence on the difference in the natural course and prognosis of NTM-PD diagnosed by sputum culture or by other methods.

Methods:

This study assessed data from patients from the retrospective NTM cohort at Seoul National University Bundang Hospital, from January 2005 to December 2016. All patients were categorized into three groups: 1) The NTM colonizer group in which NTM was isolated only once, 2) The NTM-PD group in which NTM was isolated from respiratory specimens other than sputum, and 3) The NTM-PD group in which NTM was isolated from two separate cultures of expectorated sputum. The patients who were treated for NTM-PD within one year from the time of NTM isolation were excluded. The proportion of patients with radiographic aggravation and those who initiated therapy were compared between the groups. Kaplan-Meier analysis was also performed taking into consideration the duration from the time of NTM isolation to the time of deterioration of each patient.

Results:

In total, 669 patients (239 [35.7%] male; median age, 61 years; range, 23–88 years) were included in the study. Of the patients, 124 patients were in the NTM colonizer group, 112 patients were in the NTM-PD group diagnosed by other methods (i.e., other than sputum culture) and, 433 patients were in the NTM-PD group diagnosed by sputum culture. There were significant

differences in the proportion of patients with radiographic aggravation and those who initiated therapy between groups ($p < 0.001$ for both). The NTM-PD group diagnosed by sputum culture showed a significantly higher proportion of patients with deterioration when compared with the other two groups in the post-hoc analysis. However, there were no significant differences between the NTM-PD group diagnosed by other methods and the NTM colonizer group. Furthermore, there were significant differences in the duration from the time of NTM isolation to radiographic aggravation (Log rank $p = 0.019$) and to initiation of therapy (Log rank $p = 0.003$) between the NTM-PD groups.

Conclusion:

The prognosis of untreated NTM-PD diagnosed by bronchoscopic specimens or lung tissue was similar to that observed in the NTM colonizer group but better than that of the NTM-PD group diagnosed by sputum culture.

Keywords: Nontuberculous mycobacterial pulmonary disease; Microbiologic diagnosis; Bronchoscopy; Natural course; Prognosis

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Introduction

Recently, the worldwide prevalence and mortality of nontuberculous mycobacterial pulmonary disease (NTM-PD) have increased worldwide (1-3). Therefore, accurate diagnosis of NTM-PD and treatment according to the diagnosis are becoming more important. However, pulmonary infection with nontuberculous mycobacteria (NTM) is challenging to diagnose and treat. According to the 2007 American Thoracic Society guidelines for the diagnosis of NTM-PD, microbiologic diagnosis of NTM-PD is typically based on positive results from at least two separate sputum cultures. Alternatively, NTM-PD could be microbiologically diagnosed by obtaining positive cultures from bronchoscopic specimens or lung tissue in cases where NTM-PD is suspected even if sputum culture is negative or the patients have no sputum (4). Patients diagnosed with NTM-PD who meet all the diagnostic criteria including the microbiologic criteria can be considered for initiation of treatment; however, not all patients need treatment. On the other hand, it is suggested that the respiratory tract can be infected with NTM without causing disease; this is referred to as “colonization.” Treatment is usually considered unnecessary for colonization, although the reason for this is not fully understood. Moreover, NTM is well-known for its ubiquitous nature; therefore,

a one-time detection of NTM in a subject's sputum is not sufficient for a definitive microbiologic diagnosis (4, 5).

It has been proven once in 1991 that patients with more than one positive sputum culture showed the typical clinical course of a pulmonary disease when compared to patients with only one positive sputum culture (6). Also, the diagnostic yield of sputum culture and other microbiologic methods for diagnosing NTM-PD has been investigated in several previous studies (7-10). However, no study has investigated whether the isolation of NTM from bronchoscopic specimens or lung tissue can discriminate NTM-PD from colonization. Considering these, to date, the quality of evidence of microbiologic criteria for NTM-PD is poor, and it remains to be clarified whether NTM-PD diagnosed by microbiologic criteria other than those based on sputum culture has a prognosis similar to that for the clinical course of a pulmonary disease. Therefore, in this study, we compared the prognosis of NTM-PD diagnosed by other methods (i.e., other than sputum culture) with that of NTM-PD diagnosed by sputum culture and that of NTM colonization.

Methods

Study design and population

This study is a retrospective cohort study based on the NTM cohort at Seoul National University Bundang Hospital, which enrolled 1531 patients from whom NTM was isolated from January 2005 to December 2016. From this cohort, we designated patients with a one-time NTM isolation from sputum as the NTM colonizer group. Patients with positive NTM isolation from bronchoscopic specimens (i.e., from bronchial washing or bronchoalveolar lavage) or lung tissue and patients who showed negative results on at least two sputum cultures were included in the NTM-PD group diagnosed by methods other than sputum culture. In addition, patients in whom NTM was isolated at least two times from separately expectorated sputum samples were designated as the NTM-PD group diagnosed by sputum culture.

Among the eligible patients, the following antimycobacterial therapies were administered: (1) macrolide plus ethambutol and rifamycin for *Mycobacterium avium* complex (MAC) pulmonary disease (2) amikacin plus cefoxitin or imipenem for *Mycobacterium abscessus* pulmonary disease (3) rifampin, ethambutol, and isoniazid for *Mycobacterium kansasii* pulmonary disease, for at least 30 days within 1 year from the time of NTM isolation were

excluded. Additionally, those without baseline radiography or follow-up radiography for comparison and those with a follow-up period of less than one year were excluded. Additionally, patients diagnosed with active pulmonary tuberculosis within 1 year before or after the time of NTM isolation (first isolation in the NTM colonizer group and the NTM-PD group diagnosed by methods other than sputum culture and second isolation in the NTM-PD group diagnosed by sputum culture) were excluded; those diagnosed with a malignancy in lung or interstitial lung disease during the follow-up period were also excluded since these comorbidities also affect the review of radiography.

Of the patients in the NTM cohort, 277 patients were included in the NTM colonizer group, 235 patients in the NTM-PD group diagnosed by methods other than sputum culture and, 934 patients in the NTM-PD group diagnosed by sputum culture. Of all the included patients, 777 patients, including 382 patients who received medical treatment within a year from the isolation of NTM were excluded according to the exclusion criteria. Accordingly, the following number of patients were finally included in each group in our study: 124 in the NTM colonizer group, 112 in the NTM-PD group diagnosed by methods other than sputum culture, and 433 in the NTM-PD group diagnosed

by sputum culture (Figure 1).

This study was approved by the Institutional Review Board of the Seoul National University Bundang Hospital (IRB No. B-1812-511-102) and conformed to the tenets of the Declaration of Helsinki.

Data collection

We reviewed all subjects' results of acid-fast bacilli (AFB) staining and culture from January 2005 to December 2016. The time of NTM isolation from sputum was set as the baseline time for the NTM colonizer group and the time of first NTM isolation from other specimens (i.e., other than sputum) was set as the baseline time for the NTM-PD group diagnosed by methods other than sputum culture. In the NTM-PD group diagnosed by sputum, the time of second NTM isolation from sputum was set as the baseline time. Retrospective data including baseline (± 3 mo from the baseline time) demographics, comorbidities, smoking history, and respiratory symptoms were collected using electronic medical records (EMR) search. Additionally, we reviewed all the chest radiography reports (chest CT and X-ray images) and medical records including prescription during each patient's follow-up period.

Outcomes

Radiographic aggravation and initiation of treatment for NTM-PD were the two established outcomes we used for comparing the disease prognosis between groups. Therefore, follow-up radiographs were compared with the baseline and previous radiographs in each patient to evaluate whether there was an aggravation. Aggravation of radiographic features was limited to the appropriate features for NTM-PD specified in the ATS/IDSA guideline (4). Chest X-ray image was used for evaluation if there was no baseline CT (± 3 months from the baseline time) or follow-up CT. In addition, we reviewed medical records to identify the patients who started treatment for NTM-PD after 12 months from the baseline time regardless of the treatment period.

The proportion of the patients with radiographic aggravation and initiation of treatment were compared between groups. Furthermore, the duration from the baseline time to the time of radiographic aggravation and to that of treatment initiation was also compared between groups.

Statistical analyses

A one-way ANOVA test was used for between-group comparisons of

demographics involving continuous variables and the Chi-square test and Bonferroni's correction for multiple testing were used for between-group comparisons of demographics involving categorical variables. We also performed Kaplan–Meier analysis with log-rank testing to compare outcomes according to groups. P-values less than 0.05 were considered statistically significant. Data analyses were conducted using the STATA 13 software (Stata Corp, College Station, Texas).

Result

Patient characteristics

At baseline, the median (range) age of overall patients was 61 (23–88) years and 239 (35.7%) patients were males. The median (IQR) observation time for all patients was 49.6 months (IQR 31.1-78.5).

There were no significant differences in baseline characteristics of BMI, smoking status, history of pulmonary tuberculosis, comorbidities such as malignancy, diabetes mellitus, chronic renal disease, hypertension, cardiovascular disease, and respiratory symptoms such as dyspnea, and weight loss between groups. However, the NTM colonizer group had a high proportion of female patients and had fewer complaints of hemoptysis when compared with the other groups. In addition, the NTM-PD group diagnosed by methods other than sputum culture was younger, had fewer comorbidities such as chronic obstructive pulmonary disease or asthma, and less complains of cough or sputum when compared with the other groups. Patients with a history of pulmonary tuberculosis were 24 (19.4%), 26 (23.2%), and 122 (28.2%) in the NTM colonizer group, the NTM-PD group diagnosed by methods other than sputum culture, and the NTM-PD group diagnosed by sputum culture, respectively. Likewise, patients with bronchiectasis were 70

(56.5%), 67 (59.8%), and 315 (72.7%) in the NTM colonizer group, the NTM-PD group diagnosed by methods other than sputum culture, and the NTM-PD group diagnosed by sputum culture, respectively (Table 1). The median (IQR) observation time was 37.5 months (IQR 22.7-57.4) for the NTM colonizer group, 35.8 months (IQR 22.8-59.7) for the NTM-PD group diagnosed by methods other than sputum culture and, 42.2 months (IQR 26.7-68.5) for the NTM-PD group diagnosed by sputum culture.

Characteristics of isolated NTM

Among the 112 patients in the NTM-PD group diagnosed by methods other than sputum culture, 92 (82.1%) patients had a positive NTM isolation from bronchial washing, 15 (13.4%) patients had a positive isolation from bronchoalveolar lavage, and 5 patients (4.5%) had a positive isolation from percutaneous needle aspiration of lung tissue. MAC was most frequently isolated in all groups. Patients in the NTM-PD group diagnosed by methods other than sputum culture showed more frequent isolation of *Mycobacterium abscessus* than those in other groups (27.7% versus 4.2% in the NTM colonizer group and 12.5% in the NTM-PD group diagnosed by sputum culture) and less frequent isolation of the other NTM strains with unspecified

names than those in other groups (0.9% versus 9.7% in the NTM colonizer group and 8.5% in the NTM-PD group diagnosed by sputum culture) (Table 2). The other NTM strains with unspecified names included *Mycobacterium chelonae, Mycobacterium gordonae, Mycobacterium phocaicum, Mycobacterium margeritense, Mycobacterium septicum, Mycobacterium terrae*, and *Mycobacterium lentiflavum*.

Outcomes

Among the NTM colonizer group, 44 (35.5%) patients showed radiographic aggravation during the follow-up period compared with 38 (33.9%) patients in the NTM-PD group diagnosed by methods other than sputum culture and 259 (59.8%) patients in the NTM-PD group diagnosed by sputum culture. The proportions of radiographic aggravation were significantly different between groups ($P<0.001$). In addition, post-hoc analysis showed a significant difference between the NTM-PD group diagnosed by sputum culture and the other groups, but there was no significant difference between the NTM colonizer group and the NTM-PD diagnosed by methods other than sputum culture. In the same way, 3 (2.4%), 7 (6.3%), and 101 (23.3%) patients initiated therapy for NTM-PD in the NTM colonizer group, the NTM-PD

group diagnosed by methods other than sputum culture, and the NTM-PD group diagnosed by sputum culture, respectively. Additionally, the proportions of initiation of therapy were significantly different between the groups ($P<0.001$) and post-hoc analysis showed a significant difference between the NTM-PD group diagnosed by sputum culture and the other two groups, but no significant difference between the NTM colonizer group and NTM-PD diagnosed by methods other than sputum culture.

The time to radiographic aggravation and initiation of therapy for NTM-PD from baseline time was significantly different between the groups (Log rank $P = 0.027$ and <0.001, respectively) (Figure 2 and Figure 3). The median time duration to the radiographic aggravation was 60.5 months in the NTM colonizer group, 79.4 months in the NTM-PD group diagnosed by methods other than sputum culture, and 44.8 months in the NTM-PD group diagnosed by sputum culture.

Table 1. Baseline demographics and clinical features of patients.

Variables	NTM colonizer group (n = 124)	NTM-PD group diagnosed by methods other than sputum culture (n = 112)	NTM-PD group diagnosed by sputum culture (n = 433)	P-value
Age, years	63.5 ± 11.2	58.1 ± 12.3	64.3 ± 10.8	<0.001
Sex, male, n (%)	57 (46.0)	41 (36.6)	141 (32.6)	0.023
BMI, kg/m2	21.8 ± 3.1	21.5 ± 2.6	21.5 ± 2.7	0.579
Smoking, n (%)				0.002
Never	94 (75.8)	88 (78.6)	351 (81.1)	
Ex-smoker	22 (17.7)	14 (12.5)	75 (17.3)	
Current smoker	8 (6.5)	10 (8.9)	7 (1.6)	
History of pulmonary TB	24 (19.4)	26 (23.2)	122 (28.2)	0.113
Comorbidities, n (%)				
Bronchiectasis	70 (56.5)	67 (59.8)	315 (72.7)	<0.001

COPD	14 (11.3)	3 (2.7)	36 (8.3)	0.044
Asthma	21 (16.9)	5 (4.5)	56 (12.9)	0.011
Malignancy	18 (14.5)	12 (10.7)	63 (14.5)	0.565
Diabetes mellitus	12 (9.7)	13 (11.6)	45 (10.4)	0.887
Chronic renal disease	2 (1.6)	4 (3.6)	8 (1.8)	0.443
Hypertension	24 (19.4)	19 (17.0)	98 (22.6)	0.370
Cardiovascular	8 (6.5)	2 (1.8)	36 (8.3)	0.051
Symptoms, n (%)				
Cough	50 (40.3)	27 (24.1)	160 (37.0)	0.018
Sputum	52 (41.9)	16 (14.3)	158 (36.5)	<0.001
Hemoptysis	15 (12.1)	30 (26.8)	95 (21.9)	0.015
Dyspnea	9 (7.3)	8 (7.1)	46 (10.6)	0.351
Fever	13 (10.5)	8 (7.1)	14 (3.2)	0.004
Weight loss	2 (1.6)	1 (0.9)	6 (1.4)	1

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; NTM, nontuberculous

mycobacteria; NTM-PD, nontuberculous mycobacterial pulmonary disease; TB, tuberculosis

Table 2. Methods of identifying NTM and characteristics of isolated NTM.

	NTM colonizer group (n = 124)	NTM-PD group diagnosed by methods other than sputum culture (n = 112)	NTM-PD group diagnosed by sputum culture (n = 433)
Isolated specimen			
Sputum, n (%)	124 (100)	-	433 (100)
Bronchial washing	-	92 (82.1)	
BAL	-	15 (13.4)	
PCNA	-	5 (4.5)	
Positive AFB smear, n (%)	1 (0.8)	10 (8.9)	39 (9.0)
Isolated organism, n (%)			
Mycobacterium avium	63 (43.8)	47 (42.0)	228 (52.7)
Mycobacterium intracellulare	15 (10.4)	19 (17.0)	86 (19.9)
Mycobacterium abscessus	6 (4.2)	31 (27.7)	54 (12.5)

Mycobacterium kansasii	2 (1.4)	0 (0)	5 (1.2)
Mycobacterium massiliense	3 (2.1)	4 (3.6)	18 (4.2)
Others	14 (9.7)	1 (0.9)	37 (8.5)

Abbreviations: AFB, acid-fast bacilli; BAL, bronchoalveolar lavage; PCNA, percutaneous needle aspiration; NTM, nontuberculous mycobacteria; NTM-PD, nontuberculous mycobacterial pulmonary disease

Table 3. Proportions of outcomes

	NTM colonizer group (n = 124)	**NTM-PD group diagnosed by methods other than sputum culture (n = 112)**	**NTM-PD group diagnosed by sputum culture (n = 433)**	**P-value***			
				Overall	NTM colonizer group vs. NTM-PD group diagnosed by methods other than sputum culture	NTM colonizer group vs. NTM-PD group diagnosed by sputum culture	NTM-PD group diagnosed by methods other than sputum culture vs. NTM-PD group diagnosed by sputum culture
Radiographic aggravation, n (%)	44 (35.5)	38 (33.9)	259 (59.8)	<0.001	0.802	<0.001	<0.001
Initiation of treatment, n (%)	3 (2.4)	7 (6.3)	101 (23.3)	<0.001	0.199	<0.001	<0.001

Abbreviations: NTM, nontuberculous mycobacteria; NTM-PD, nontuberculous mycobacterial pulmonary disease

*P values for the overall comparisons were calculated with the Chi-square analysis. P-values for the comparisons between two groups of each three groups were calculated with Chi-square analysis and Bonferroni's correction for multiple testing in post hoc analyses.

Figure 1. Flow diagram of the study population.

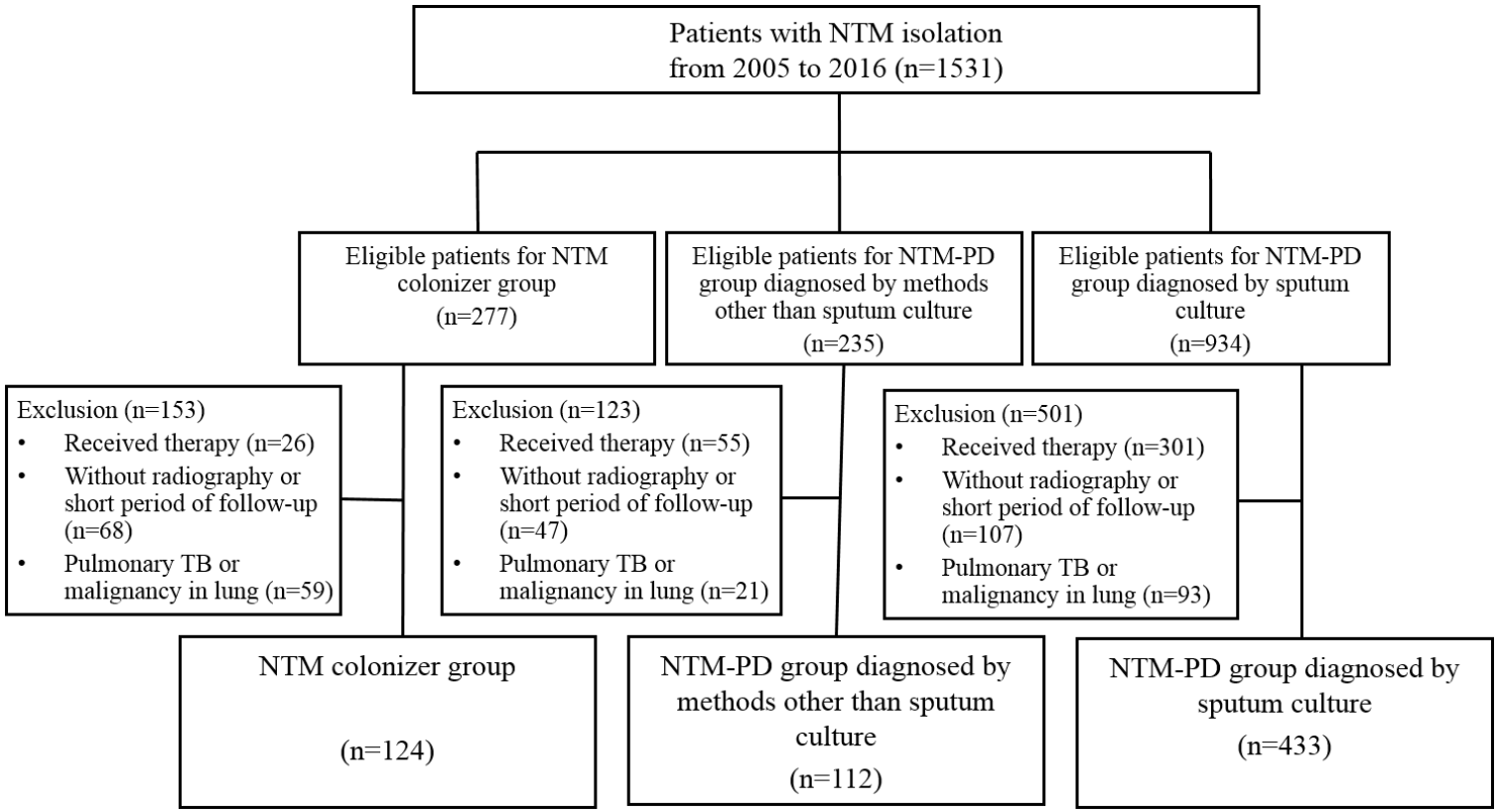

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Figure 2. Time to radiographic aggravation of the groups.

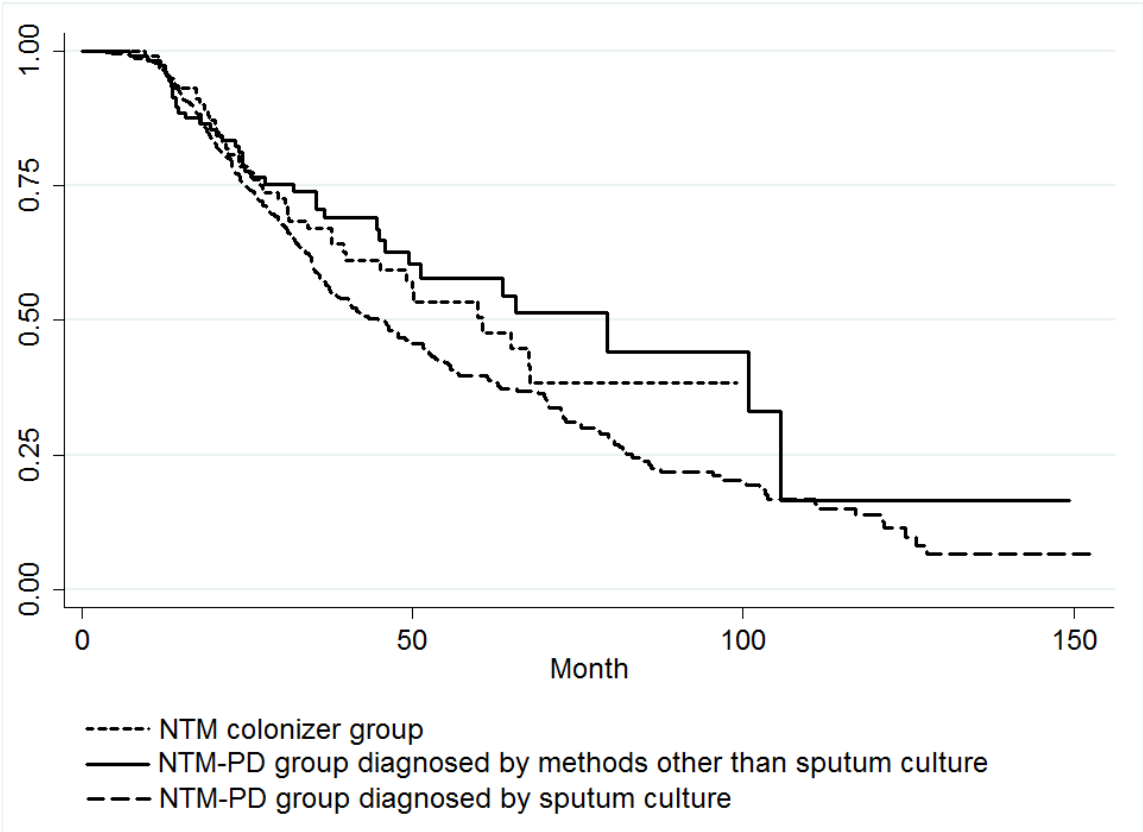

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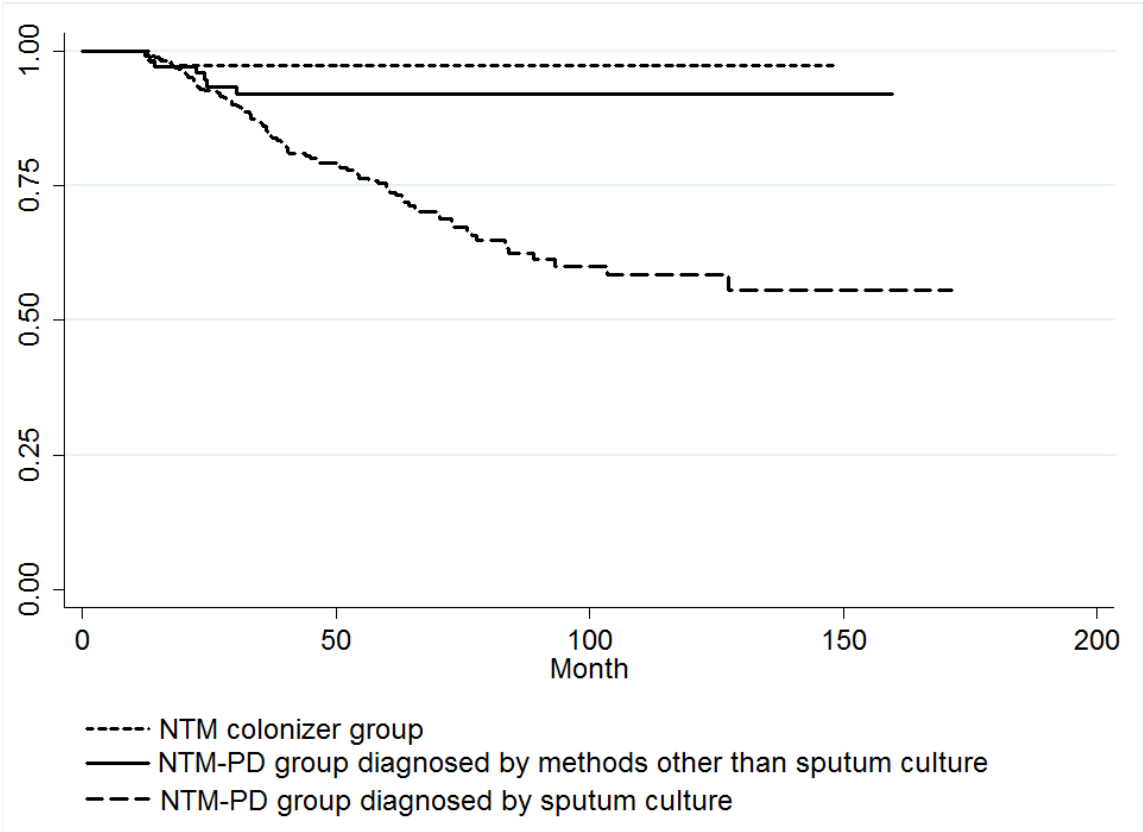
Figure 3. Time to initiation of treatment of the groups.



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Discussion

The present study is the first to investigate whether NTM-PD diagnosed by a positive result using diagnostic methods other than sputum culture in accordance with the ATS/IDSA guidelines has typical natural course of NTM-PD. To clarify this, we compared the prognosis of these NTM-PD patients diagnosed with other methods with the prognosis of (1) patients diagnosed by separately expectorated sputum (with at least two separate positive isolations) who are generally considered to have pulmonary disease and (2) patients considered to be NTM colonizer whose risk of progression to pulmonary disease is regarded to be minimal. Consequently, we found that there were significant differences in the progression of pulmonary disease, represented by radiographic aggravation and initiation of treatment, between the NTM-PD group diagnosed by methods other than sputum culture and the NTM-PD group diagnosed by sputum culture, but there were no significant differences between the NTM-PD group diagnosed by methods other than sputum culture and the NTM colonizer group. In addition, our study showed that it took a long time (median of 79.4 months) for radiographic aggravation to be observed and the proportion of patients who received therapy for NTM-PD was very low (6.3%) in the NTM-PD group diagnosed by methods other than sputum culture.

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The proportion of patients who received treatment in NTM-PD group diagnosed by sputum culture in other studies investigating the natural course of NTM-PD is in line with our data (11, 12). Our results suggest that among patients diagnosed with NTM-PD in accordance with current guidelines, those diagnosed only by isolation of NTM from bronchoscopy or lung tissue biopsy may have very slowly progressive disease or may even be over-diagnosed as having NTM-PD. The usefulness of bronchoscopy in detecting NTM or tuberculosis in respiratory specimens was shown to be superior to sputum culture in several studies (8, 9, 13, 14). In support of these previous studies, our data suggest that bronchoscopy is likely more sensitive to detect NTM strains compared with sputum culture regardless of bacterial burden. It is well-known that colonization of lower respiratory tract by various microorganisms occurs through diverse mechanisms including defected immunity in patients with underlying lung disease such as cystic fibrosis, bronchiectasis, or non-cystic fibrosis bronchiectasis (15, 16). Previous studies have also shown that NTM was isolated in a significant proportion of these patients (17-20). Therefore, the isolation of NTM from bronchial washing or bronchoalveolar lavage may indicate colonization especially in patients with underlying lung disease. Furthermore, patients with underlying lung diseases frequently have symptoms and radiographic findings that are difficult to distinguish from

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NTM-PD. Therefore, such patients are more likely to be mistaken for NTM-PD. In fact, the patients in the NTM-PD group diagnosed by methods other than sputum culture also satisfied the clinical and radiological criteria in present study.

In the present study, patients who received treatment for NTM-PD within a year from the isolation of NTM were excluded because their responses to treatment were inconsistent and, therefore, it could have complicated the analysis and interpretation of the natural course of the disease. The proportion of those who received treatment within a year from the isolation of NTM was significantly higher in the NTM-PD group diagnosed by methods other than sputum culture than in the NTM colonizer group (32.9% versus 17.3%, Chi-square test P = 0.002). However, the initiation of treatment of suspected NTM-PD patients depends on the subjective decision of the clinician and the clinician's decision can be greatly influenced by the official diagnosis according to the current guidelines, therefore, considering this, a high proportion of patients with treatment in the NTM-PD group diagnosed by methods other than sputum culture may not indicate a more severe disease state than the NTM colonizer group. Rather the majority of patients enrolled in the present study had a history of pulmonary TB or an underlying lung

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disease such as bronchiectasis which is difficult to differentiate from NTM-PD that these patients could have been diagnosed and treated for NTM-PD. Consequently, some of them might not have been treated without an official diagnosis of NTM-PD.

There is a lack of data regarding the long-term prognosis of NTM-PD. Moreover, to our knowledge, there is no data evaluating the prognosis of NTM-PD microbiologically diagnosed by other methods (i.e., other than sputum culture). In the present study, for the first time, we investigated the prognosis of untreated NTM-PD diagnosed by bronchoscopy or lung tissue biopsy. Furthermore, our study included a relatively large number of patients with NTM-PD diagnosed by bronchoscopy or lung tissue biopsy.

There are several limitations to our study. First, owing to the retrospective design of our study, a considerable number of patients could not be followed for longer time or evaluated for disease progression. In addition, there was a lack of standardization in the radiologic evaluation methods and protocols used for microbiologic confirmation. For example, some patients were evaluated using CT scans with diverse vendors while other patients were evaluated using X-ray images. Additionally, different number of sputum cultures were carried out for different patients during the follow-up period.

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Nevertheless, the median follow-up period was long in our study compared with other studies. Second, since this study was conducted in a single tertiary referral center, the population in our study is not representative of the nationwide population. Third, our study included various NTM strains. Because each NTM strain is known to exhibit different virulence and prognosis (5, 21), the results of present study might be a mix of various NTM strains. However, with the exception of some strains such as *Mycobacterium abscessus*, the proportions of most strains were not different between groups. Moreover, *Mycobacterium abscessus* is not known to be an indolent pathogen; rather, it is known to be rapidly growing and a treatment-refractory pathogen (22, 23), such that a higher proportion of the strain in the NTM-PD group diagnosed by methods other than sputum culture than in the other groups might not underestimate the outcomes.

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Conclusion

In the current study, we evaluated the long-term prognosis of untreated NTM-PD patients microbiologically diagnosed by other methods (i.e., other than sputum culture) and compared it with the NTM colonizers and the untreated NTM-PD patients diagnosed by sputum culture. The patients diagnosed with NTM-PD by bronchoscopic specimens or lung tissue showed no significant differences in the radiographic aggravation and initiation of therapy when compared with the patients with a one-time positive sputum NTM isolation. However, the patients diagnosed with NTM-PD by bronchoscopic specimens or lung tissue showed significantly better prognoses when compared with the patients diagnosed with NTM-PD by sputum culture. This suggests that the natural course of the patients diagnosed with NTM-PD by methods other than sputum culture may not be similar to that of a pulmonary disease. Further multicenter prospective studies are needed to investigate the long-term prognosis of NTM-PD according to microbiologic diagnosis methods. This may lead to a revision of the guidelines for the microbiologic diagnosis of NTM-PD.

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요약 (국문초록)

서론

비결핵 항산균 폐질환의 미생물학적 진단은 객담에서 2회 이상 배양 양성을 보이거나 기관지세척액에서 1회 이상 배양 양성, 혹은 폐조직에서 조직배양이 양성일 경우 이루어진다. 그러나 객담배양과 객담 외 배양에 의해 진단된 질환의 경과 및 예후의 차이에 대해서는 연구가 부족하다.

방법

본 연구는 분당서울대학교병원에서 2005년 1월에서 2016년 12월 사이의 후향적 비결핵 항산균 코호트를 바탕으로 설계되었다. 연구에 포함된 환자들은 단 한번 객담에서 비결핵 항산균이 배양되어 비결핵 항산균 폐질환의 미생물학적 진단조건을 충족하지 않는 '동정' 군과 기관지 내시경 검체나 폐 조직 검체에서 비결핵 항산균이 배양되어 비결핵 항산균 폐질환의 진단조건을 충족시키는 객담 외 방법으로 진단된 '질병' 군, 그리고 객담에서 2회 이상 배양되어 비결핵 항상균 폐질환의 진단조건을 충족시키는 객담으로 진단된 '질병' 군으로 나누어 졌다. 대상 환자 중 균

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배양 1년 내에 비결핵 항산균 폐질환에 대한 약물치료를 받은 환자를 제외한 나머지 환자에서 영상학적인 악화와 비결핵 항상균 폐질환 치료력을 조사하였고, 세 군 간의 차이를 비율에 대한 분석과 시간 변수를 고려한 카플란-마이어 분석을 이용하여 비교하였다.

결과

최종적으로 669명의 환자가 (239 [35.7%] 남자; 중앙연령 61세; 범위 23-88세) 분석되었고, '동정' 군 124명과 객담 외 방법으로 진단된 '질병' 군 112명, 객담으로 진단된 '질병' 군 433명이 포함되었다. 영상의학적 악화가 발생한 비율과 치료를 시작한 비율은 세 군간 유의미한 차이가 있었고 ($p<0.001$), 사후분석 결과 '동정' 군과 객담 외 방법으로 진단된 '질병' 군 간의 유의미한 차이는 없었으나, 객담으로 진단된 '질병' 군과 나머지 두 군 간에는 유의미한 차이가 확인되었다. 또한 카플란-마이어 분석 결과 객담 외 방법으로 진단된 '질병' 군과 객담으로 진단된 '질병' 군 간에 영상학적인 악화에서 유의미한 차이가 확인되었고 (Log rank $p=0.019$), 치료시작에 대한 분석에서는 객담으로 진단된 '질병' 군과 나머지 두 군 간 유의미한 차이가 확인되었다 ('동정' 군과 Log rank $p<0.001$, 객담 외 방법으로 진단된 '질병' 군과 Log rank $p=0.003$).

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결론

기관지 내시경 검체나 폐 조직 검체로부터 진단된 비결핵 항산균 폐질환은 영상학적 악화 및 치료시작과 관련한 예후에서 비결핵 항산균 보유군과 비교하였을 때 차이를 보이지 않으나 객담에서 2회 이상 비결핵 항산균이 배양된 비결핵 항산균 폐질환보다 좋은 예후를 보인다.

주요어 : 비결핵 항산균 폐질환; 미생물학적 진단 방법; 기관지 내시경; 자연 경과; 예후

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