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Source / Izvornik: **International Journal of Tuberculosis and Lung Disease, 2016, 20, 934 - 940**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.5588/ijtld.15.0633

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:723438

Microbiologic criteria in nontuberculous mycobacterial pulmonary disease, a tool for diagnosis and epidemiology

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Running head: microbiologic criteria in NTM-PD

Word count: 2494

Keywords: atypical mycobacteria, pulmonary mycobacteriosis, incidence, prevalence

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Summary

Setting: The value of microbiologic criteria in diagnosing nontuberculous mycobacteria pulmonary disease (NTM-PD) and monitoring its epidemiology is unknown.

Objectives: To correlate the rate of NTM-PD based on microbiologic criteria (American Thoracic Society/Infectious Diseases Society of America [ATS/IDSA] or stricter microbiologic criteria) with the full ATS/IDSA criteria, and assess the positive predictive value (PPV) of different microbiologic criteria in predicting NTM-PD. To evaluate the clinical relevance of different NTM species. Design: Retrospective study of all patients with pulmonary NTM isolates in Croatia during an eight-year period. NTM species were divided into low, intermediate, and high clinical relevance groups for additional analyses. Results: Good correlation between both microbiologic and full ATS/IDSA criteria was shown. PPV of stricter and ATS/IDSA microbiologic criteria was 93.3% and 59.8%, respectively. Usefulness of microbiologic criteria varied between groups. ATS/IDSA microbiologic criteria had a PPV of 89.8% in the high relevance group. In the intermediate relevance group, the PPV of stricter and ATS/IDSA microbiologic criteria were 94.3% and 63.4%, respectively. Conclusions: Microbiologic criteria are useful in detecting NTM-PD, allowing laboratory based monitoring. Stricter criteria should be used for species of low clinical relevance, and less stringent criteria for species of high relevance in the local setting.

INTRODUCTION

Nontuberculous mycobacteria (NTM) are ubiquitous environmental organisms with variable potential to cause disease.[1] Interest in NTM continuously grows due to reported increase in isolation frequency [1-5], particularly in countries where the incidence of tuberculosis (TB) is declining.[1,6] Diagnosis of NTM pulmonary diseases (NTM-PD) is difficult. Currently, the criteria proposed by the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) provide the best guide for the diagnosis. (Table 1).[1] Patients should have a combination of clinical, radiological and microbiological characteristics, together with the exclusion of alternative diagnoses. This approach, similar to the one recently proposed for the diagnosis and management of chronic pulmonary aspergillosis [7], a disease that can follow or occur contemporaneously with NTM-PD, further emphasizes the complexity of the disease. The epidemiology of NTM-PD is challenging to determine because reporting is not mandatory in most countries and identification of definite disease is difficoult.[1,8] Data from intermediate TB burden countries such as Croatia [9,10] are especially scarce. Laboratory-based surveillance may be the most cost-effective method for estimating the NTM disease burden over time.[11,12] Our previous study, using only ATS/IDSA microbiologic criteria or stricter microbiologic criteria estimated the incidence of NTM-PD in Croatia to 0.61 and 0.23 per 100 000 population, respectively.[13] The disease proved most prevalent in older populations with three-fold increase in NTM-PD incidence in persons older than 50 years.[13] In the current study, we sought to correlate microbiologic criteria to full ATS/IDSA diagnostic criteria and validate the use of microbiologic criteria in the estimation of NTM-PD incidence/prevalence.

METHODS

Study design and data collection

We conducted a retrospective cohort study on all Croatian residents with NTM isolated from respiratory samples in the period from January 1st 2006 to December 31st 2013. Since all NTM isolates are sent to the National Reference Mycobacteria Laboratory (NRML) at Croatian Institute of Public Health (CIPH) for species identification, we obtained patient information from the NRML archive. For each patient, we recorded age, zip code, specimen collection date, as well as source and the NTM species isolated. Samples obtained by gastric lavage were excluded from further analysis. In case of multiple isolates of one or more species, only one isolate per species per individual was taken into account when calculating NTM isolation rate. Using the zip code, patients were grouped into two larger areas according to the proximity of the sea, coastal and continental regions of Croatia.[14] The Croatian population data, including population by region, age and sex, were obtained from the statistical office of the European Union.[15] The study was approved by the Ethics Committee of the CIPH (file number 001-487/1-10).

Identification of NTM and NTM pulmonary disease case definition

All NTM species were identified by molecular methods (GenoType® CM/AS; Hain Lifescience GmbH) supplemented with phenotypic methods, using previously published guidelines.[16] NTM unidentifiable to species level were sent to the Supranational Reference Laboratory (Forschungszentrum Borstel, Germany or Emerging Pathogens Institute, Milan, Italy) for further identification by 16S rDNA gene sequencing.

We used the ATS/IDSA microbiologic criteria (Table 1) [1] and stricter microbiologic criteria (more than two positive sputum samples or one positive BAL/ brush and one or more positive sputum samples) [13] to establish a laboratory-based diagnosis of NTM-PD. Furthermore, clinical and radiological data were gathered in order to evaluate whether patients had symptoms and radiological findings compatible with the diagnosis of NTM-PD according to the full ATS/IDSA criteria.[1] In case of concurrent active respiratory disease more likely to be the cause of symptoms (i.e. active tuberculosis, concomitant isolation of significant respiratory pathogens such as *Streptococcus pneumoniae* and resolution of symptoms/radiological findings after the appropriate treatment), NTM were ruled out as a

cause of the disease. For calculating disease incidence, we took into account the first time that NTM-PD criteria were met. For individuals meeting these criteria, patients with NTM isolated in 2005 were excluded from disease incidence calculation.

Clinical relevance of NTM species and criteria correlations

For NTM species with more than 10 isolates with available complete patient's medical records, clinical relevance was evaluated based on the percentage of patients meeting the full ATS/IDSA criteria. Based on that percentage, NTM species were divided into three groups: „low relevance" (<25% of isolates meeting full criteria), „intermediate relevance" (25-70% of isolates meeting full criteria) and „high relevance" (>70% meeting full criteria). NTM-PD diagnosis based on ATS/IDSA or stricter microbiologic criteria were correlated with the rate of diagnosis based on full ATS criteria. Correlation of the criteria was also calculated for the three groups.

Data analysis

Microsoft Excel (Microsoft, Redmond, WA, USA) was used to calculate frequencies, percentages, median age, and crude and standardized rates. The $\chi 2$ and $\chi 2$ test for trend, correlation coefficients as well as rate comparisons were done using MedCalc (MedCalc Software, Ostend, Belgium)

RESULTS

During the study period, the NRML identified a total of 2105 pulmonary NTM isolates from 1841 patients. Average annual NTM isolation incidence amounted to 5.21 per 100 000 population. The most frequently isolated NTM species, percentage of patients meeting at least one microbiologic criterion, and percentage of patients with available medical records per species are shown in Table 2.

The species distribution differed between coastal and continental Croatia: *M. gordonae* (OR 1.62, 95% confidence interval (CI) 1.25 to 1.97; p<0.0001), *M. terrae* (OR 2.72, 95% CI 1.86 to 6.51; p<0.0001,) and *M. chelonae* (OR 2.11, 95% CI 1.10 to 4.23; p=0.022) were significantly more frequently isolated in continental Croatia, whereas *M. avium* (OR 0.35, 95% CI 0.19 to 0.58; p<0.0001), *M. kansasii* (OR 0.45, 95% CI 0.19 to 0.96; p=0.033), and *M. xenopi* (OR 0.27, 95% CI 0.22 to 0.38; p<0.0001) were more frequent in the coastal region. Of 1841 patients with NTM isolates, 58.6% were male (median age 65), and 41.6% female (median age 66 years).

NTM pulmonary disease and clinical relevance of NTM species

Out of 1841 patients, 370 (20.1%) and 111 (6%) met ATS/IDSA and stricter microbiologic criteria, respectively. The demographic characteristics of these patients are shown in Table 3. Medical records were available for 411 (22.34%) patients. Out of 411 patients, 278 (67.6%) had no disease, while 105 (25.6%) had NTM-PD according to the full ATS/IDSA criteria. For 28 (6.8%) patients, the available data were highly suggestive of NTM-PD, but the disease couldn't bee definitively confirmed due to not fulfilling the microbiologic part of the ATS/IDSA criteria (usually because of only single sputum culture taken). Thus, although those patients had a probable NTM-PD, they were excluded from further analyses.

Clinical characteristics of patients who met full ATS/IDSA NTM-PD criteria and those who did not are shown in Table 4. The two groups were similar regarding age and medical comorbidities, but some differences have been found (Table 4). Among patients with NTM-PD, females were significantly older compared to males (70 vs. 63 yr; t-test p=0.015), less likely to present with cavitary disease (OR 0.39, CI 0.16 to 0.98; p=0.04), more likely to have bronchiectasies (OR 3.21, CI 1.36 to 7.6; p=0.007), and more likely to be a nonsmoker (OR 19.63, CI 7.12 to 54.09; p<0.0001).

Estimated clinical relevance of isolates according to the percentage of patients meeting full ATS/IDSA criteria is shown in Figure 1. On the basis of this percentage, we classified NTM species into three groups: „low relevance"- *M. terrae*, *M. fortuitum*, *M. gordonae* and *M. chelonae*; „intermediate relevance"- *M. kansasii*, *M. xenopi*, and *M. abscessus complex* (MABSC); „high relevance"– *M. avium* complex (MAC).

Criteria correlation and NTM pulmonary disease incidence

The phi coefficient for correlation between different microbiologic criteria and full ATS/IDSA criteria is shown in Table 5. Positive predictive values (PPV) of ATS/IDSA microbiologic criteria and stricter microbiologic criteria were 59.3% and 93.2%, respectively. While ATS/IDSA microbiologic criteria had a PPV of 89.8% in the high relevance group, in the intermediate relevance group, the PPV of stricter microbiologic criteria was considerably higher in comparison to ATS/IDSA microbiologic criteria (94.3 vs. 63.4%).

Based on ATS/IDSA and stricter microbiologic criteria, we estimated the average annual NTM-PD incidence at 1.07/100 000 and 0.32/100 000, respectively (Table 3). Incidence was higher in the coastal compared to the continental region, with no significant increase of incidence over the studied period. On the basis of patients with available medical records, the estimated average annual incidence of the NTM-PD was 0.29/100 000.

DISCUSSION

This population-based study addresses the usefulness of microbiologic laboratory data in the monitoring of NTM-PD prevalence, and the PPV of microbiologic criteria in the detection of NTM-PD. The retrospective design and reliance on complex ATS/IDSA criteria for establishing NTM-PD represent potential limitations in the interpretation of the study results. Still, these criteria are currently the best available tool and the most widely used method for diagnosing NTM-PD.

Criteria correlation

Overall, we have shown moderate to good correlation between both microbiologic criteria, and full ATS/IDSA criteria. Still, PPV of stricter microbiologic criteria was considerably higher when compared to ATS/IDSA microbiologic criteria (93.3% vs. 59.8%). Furthermore, different microbiologic criteria perform differently in predicting NTM-PD for various NTM species. Stricter criteria, when compared to ATS/IDSA microbiologic criteria, show significantly higher PPV for NTM-PD caused by species of intermediate clinical relevance. On the other hand, the ATS/IDSA microbiologic criteria have very high PPV for detecting NTM-PD caused by NTM species of high clinical relevance, and the usage of stricter criteria in this group likely underestimates the disease incidence. Our overall result appears to be in disagreement with Winthrop et al. who showed the PPV of 86% for ATS/IDSA microbiologic criteria in predicting NTM-PD.[12] The proportion of patients with NTM-PD caused by MAC in Winthrop's study was significantly higher (88% vs. 43% in the current study). The discrepancy in MAC incidence could explain the significant difference between PPV of ATS/IDSA microbiologic criteria in the two studies. The PPV for NTM species of high clinical relevance (89.8%), which in our setting comprises members of MAC, is in agreement with their finding. Several studies showed higher PPV (70-90%) of ATS/IDSA microbiologic criteria in predicting NTM-PD, but the studied cohorts mostly comprised patients with NTM isolates of significant or, at least, intermediate clinical relevance (MAC, *M. xenopi*, MABSC).[4,17,18] Thus, to prevent unwarranted diagnoses and treatment of NTM disease, as well as unnecessary diagnostic delay, it could be helpful to use separate, more stringent criteria for species of low relevance, and less stringent criteria for species considered to be of high clinical relevance in the local setting. This aspect should be covered in the upcoming diagnostic criteria. However, such stratified system further complicates the diagnostic criteria,

and requires users' awareness of species distribution and clinical relevance in their local area.[19]

NTM species distribution differs by region

Most species isolated in continental region were of low clinical relevance. *M. gordonae* was the most commonly isolated NTM species, with a peak isolation frequency in 2009 (data not shown) that can be explained by contamination of tap water with *M. gordonae* in one hospital.[20] In contrast, clinically relevant NTM species were more common in the coastal region. Some of the factors that might promote these regional differences include the climate, the rate of urbanization and different rates of TB incidence. The more urbanized coastal region [14] has a more humid, warmer climate and relies on larger municipal water supplies. Furthermore, the incidence of TB was lower in the coastal region than in the continental region (21.2 vs. 30.1/100 000 in 2006).[9] The observation that species distribution differs by region mirrors findings from the recent NTM-NET study, which also showed major differences between and within countries.[21] The association between difference in species distribution and disease prevalence between coastal and continental regions has not been previously shown in other settings. A recent study from USA showed that regional environmental factors related to soil and differences in daily evapotranspiration levels are associated with NTM-PD, but that both the host susceptibility and environmental factors should be considered in explaining disease development.[22]

Clinical relevance differs by NTM species

Medical records were available for a total of 22.3% patients, but the percentage of patients with evaluated records reached over 60% in case of NTM species of presumably higher clinical interest (i.e. MAC, *M. xenopi*). Also, we managed to evaluate a significant number of medical records from patients with NTM species considered to be of low clinical relevance in order to have comparable groups (Table 2).

Although *M. xenopi* was the primary cause of NTM-PD, only around 25% of patients with *M. xenopi* isolates had the disease according to the full ATS/IDSA criteria. MAC was found to be clinically the most relevant species, while *M. gordonae*, *M. terrae*, *M. chelonae* and *M. fortuitum* showed very low or no clinical significance. *M. kansasii* and MABSC were infrequently isolated, and around 60% and 42% of patients with these isolates met the disease

criteria, respectively. These findings differ from observations in the Netherlands where clinical relevance for *M. kansasii* and *M. xenopi* exceeded that of MAC.[3,23] Also, in a study from Korea, MABSC *was* among the most frequently isolated NTM species with considerably higher clinical relevance compared to our results.[24] The exact reason for such apparent regional differences remains unknown. However, the limited significance of *M. kansasii* in our study may result from its infrequent isolation and the fact that many patients had a concomitant disease (i.e. active tuberculosis) which was a more plausible cause of the symptoms. In addition, we haven't performed sub-typing, and it has been shown that some subtypes of *M. kansasii* are typically environmental microorganisms of little or no clinical significance.[25]

Incidence and prevalence of NTM-PD in Croatia

Based on full ATS/IDSA criteria, our calculated NTM-PD annual incidence of 0.29/100 000 mirrors the incidence previously calculated using stricter microbiologic criteria (0.23/100 000).[13] Use of ATS/IDSA microbiologic criteria (0.61/100 000) overestimated disease incidence. This overestimation results from a relatively high proportion of clinically insignificant NTM species (such as *M. gordonae*, *M. terrae and M. fortuitum*) meeting the ATS/IDSA microbiologic criteria. Both incidence and prevalence of NTM-PD are higher in coastal than continental region which might reflect the NTM species distribution in these regions. NTM-PD incidence in Croatia is low compared to TB incidence as well as to NTM-PD incidence in North-Western Europe [4,26-28], North America [11,17,22,29,30], Australia [31] and Japan.[32] Similar disease incidence was recorded in Greece [33,34] and Sao Paulo region, Brasil.[35] Generally, the prevalence of NTM-PD in Europe is substantially lower than in North America, Australia and Japan.[5] The exact reasons for such apparent differences remain to be elucidated in future studies.

CONCLUSION

We have shown that microbiologic criteria are useful in detecting NTM-PD, but that more stringent criteria should be used for species of low relevance, and less stringent criteria for species considered to be of high clinical relevance in the local setting. Microbiologic criteria used to define NTM-PD can be helpful to monitor the epidemiology of NTM-PD in settings

where notification of cases is not obligatory. Still, usage of ATS/IDSA microbiologic criteria alone, in our setting, overestimates the disease prevalence. In our setting, stricter microbiologic criteria should be used in a laboratory based surveillance of NTM-PD.

ACKNOWLEDGEMENTS

This research was supported by the Croatian National Institute of Public Health and University Hospital Centre Zagreb, without any additional funding.

Conflict of interest: none declared.

Table 1

ATS/IDSA criteria for diagnosing nontuberculous mycobacterial (NTM) pulmonary disease [1]

Clinical criteria	Respiratory or constitutional symptoms, and
	Appropriate exclusion of other diagnoses, and
Radiological criteria	reticular, interstitial, nodular infiltrate, or cavitation on chest radiograph, or high-resolution computed tomography scan that shows multifocal bronchiectasies with multiple small nodules, and
Microbiological criteria	Positive culture results from at least 2 separate expectorated sputum samples, or
	Positive cultures from at least 1 bronchial wash or lavage*, or
	Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid-fast bacilli) and positive culture for NTM, or biopsy showing mycobacterial histopathologic features and one sputum sample or bronchial washing/lavage that is culture positive for NTM

*applies to patients incapable of producing sputum samples

ATS/IDSA – American Thoracic Society/Infectious Diseases Society of America

Table 2. Nontuberculous mycobacteria isolation frequency in Croatia according to the geographic region, sex, and microbiologic criteria [1,13]

		Gender		Region			Meeting the microbiologic criteria			
NTM	Total	M n (%)	F n (%)	Inland n (%)	Coast n (%)	Unknown n (%)	Only ATS/IDSA n (%)	Strict n (%)	Not satisfied n (%)	Medical records evaluated (%)
M. gordonae	760	443 (58.3)	317 (41.7)	618 (81.3)	140 (18.4)	2 (0.3)	78 (10.3)	13 (1.7)	669 (88)	59 (7.8)
M. xenopi	288	190 (66)	98 (34)	153 (53.1)	133 (46.2)	2 (0.7)	71 (24.6)	33 (11.5)	184 (63.9)	167(58)
M. fortuitum	229	141 (61.6)	88 (38.4)	186 (81.2)	43 (18.8)	0 (0)	29 (12.7)	6 (2.6)	194 (84.7)	61 (26.6)
M. terrae	132	71 (53.8)	61 (46.2)	118 (89.4)	14 (10.6)	0 (0)	8 (6.1)	2 (1.5)	122 (92.4)	13 (9.8)
MAC	101	50 (49.5)	51 (50.5)	63 (62.4)	38 (37.6)	0 (0)	34 (33.66)	31 (30.7)	36 (35.6)	63 (62.4)
M. avium	57	28 (49.1)	29 (50.9)	31 (54.4)	26 (45.6)	0 (0)	23 (40.35)	16 (28.1)	18 (31.6)	38 (66.7)
M. intracellulare	41	22 (53.7)	19 (46.3)	29 (70.7)	12 (29.3)	0 (0)	11 (26.83)	15 (36.6)	15 (36.59)	25 (61)
MAC-X	3	0 (0)	3 (100)	3 (100)	0 (0)	0 (0)	0 (0)	0 (0)	3 (100)	(0)
M. chelonae	85	49 (57.7)	36 (42.3)	74 (87.1)	11 (12.9)	0 (0)	16 (18.8)	4 (4.7)	65 (76.5)	15 (17.7)
MABSC	47	26 (55.3)	21 (44.7)	41 (87.2)	6 (12.8)	0 (0)	5 (10.6)	10 (21.3)	32 (68.1)	12 (25.5)
M. kansasii	26	15 (57.69)	11 (42.31)	15 (57.69)	10 (38.46)	1 (3.85)	7 (26.92)	5 (19.23)	14 (53.85)	12 (46.2)
Other	173	91 (52.6)	82 (47.4)	138 (79.77)	34 (19.65)	1 (0.58)	11 (6.36)	7 (4.05)	155 (89.6)	9 (5.2)
Total	1841	1076 (58.4)	765 (41.6)	1406 (76.4)	429 (23.3)	6 (0.3)	259 (14.1)	111 (6)	1471 (79.9)	411 (22.3)

MAC – *Mycobacterium avium* complex; MABSC – *M. abscessus* complex; ATS/IDSA microbiologic criteria - two positive sputum samples or one positive bronchoalveolar lavage (BAL) or brush); Strict microbiologic criteria - more than two positive sputum samples or one positive BAL/ brush and one or more positive sputum samples)

Table 3. Demographic characteristics of patients meeting the ATS/IDSA microbiological criteria and strict microbiologic criteria for nontuberculous mycobacterial pulmonary disease in Croatia

	Strict microbiologic criteria			ATS/IDSA **microbiologic criteria only**			
Cases	**Value (%)**	**Median age**	**Average incidence (per 100.000)**	**Value (%)**	**Median age**	**Average annual incidence (per 100.000)**	**Average population**
All cases	111 (100)	67	0.32	259 (100)	67	0.75	4 297 326
Gender							
Female	46 (41.4)	67	0.26	95 (36.7)	66	0.53	2 226 568
Male	65 (58.6)	67	0.39	164 (63.3)	67.5	0.99	2 070 758
Age							
0-49	15 (13.5)	38	0.07	44 (17)	34	0.21	2 657 136
50-69	51 (46)	62	0.58	103 (39.8)	62	1.16	1 094 909
70+	45 (40.5)	77	1.04	110 (42.5)	78	2.46	542 867
50+	96 (86.5)	68.5	0.73	213 (82.2)	70	1.60	1 637 776
Unknown	0 (0)			2 (0.7)			
Geographic location							
Continental	64 (57.7)	65.5	0.28	173 (66.8)	67	0.75	2 887 134
Coastal	47 (42.3)	69	0.42	85 (32.8)	68	0.75	1 410 192
Unknown	0 (0)			1 (0.4)			

ATS – American Thoracic Society; IDSA – Infectious Diseases Society of America; ATS/IDSA microbiologic criteria - two positive sputum samples or one positive bronchoalveolar lavage (BAL) or brush); Strict microbiologic criteria - more than two positive sputum samples or one positive BAL/ brush and one or more positive sputum samples)

Table 4. Characteristics of patients with clinically evaluable records that met full ATS/IDSA NTM pulmonary disease criteria [1] compared with patients with respiratory NTM isolates who did not meet criteria

Characteristics	Confirmed case (n=105)	Did not meet full ATS/IDSA criteria (n=278)	P value
Demographics:			
Age (median, range)	66 (16-90)	66 (14-90)	
Female sex	51 (48.6%)	80 (28.8%)	0.0004
Chest radiographic abnormalities:			
Infiltrate	74 (70.5%)	16 (5.8%)	<0.0001
Cavity	28 (26.7%)	11 (4%)	<0.0001
Pleural effusion	5 (4.8%)	30 (10.8%)	0.07
Concurrent and predisposing conditions			
COPD	48 (45.7%)	112 (40.3%)	0.34
Bronchiectasis	34 (32.4%)	21 (7.6%)	<0.0001
Prior tuberculosis	28 (26.7%)	49 (17.6%)	0.068
Diabetes mellitus	15 (14.3%)	32 (11.5%)	0.46
Below normal BMI	37 (35.2%)	19 (6.8%)	<0.0001
GERD	5 (4.8%)	15 (5.4%)	0.8
Lung cancer*	3 (2.9%)	34 (12.2%)	0.01
Alcohol abuse	5 (4.8%)	22 (7.9%)	0.28
Current smoker	29 (27.6%)	73 (26.3%)	0.79
Past smoker	29 (27.6%)	97 (34.9%)	0.18
Nonsmoker	45 (42.9%)	93 (33.5%)	0.09
Signs and symptoms			
Productive cough	78 (74.3%)	173 (62.2%)	0.017
Malaise	66 (62.9%)	86 (30.9%)	<0.0001
Apetite loss	37 (35.2%)	78 (28.1%)	0.17
Fever	34 (32.4%)	93 (33.5%)	0.84
Hemoptysis	28 (26.7%)	27 (9.7%)	<0.0001
Increased sweating	10 (9.5%)	21 (7.6%)	0.53

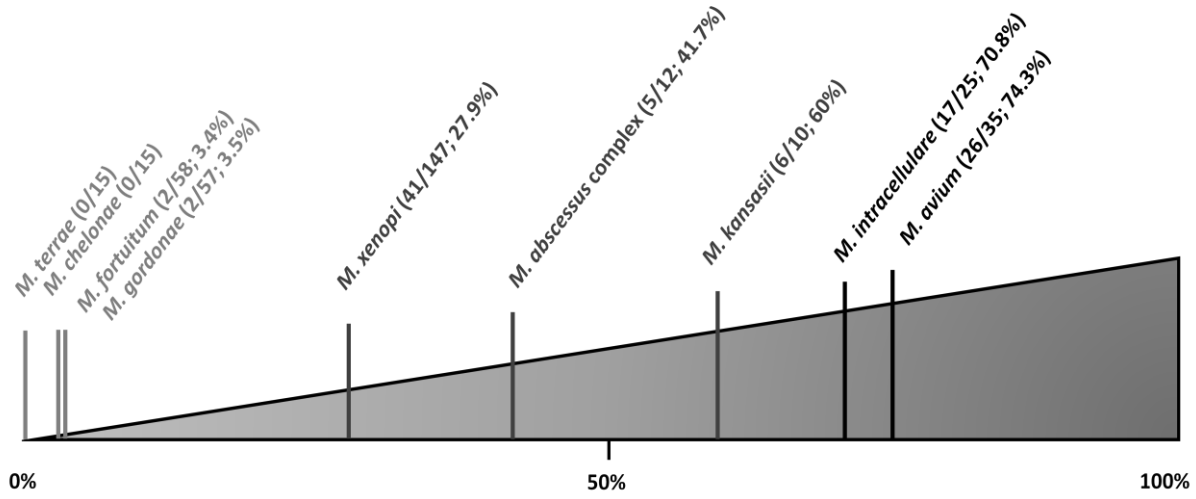
ATS/IDSA – American Thoracic Society/Infectious Diseases Society of America; BMI – body mass index; COPD – chronic obstructive pulmonary disease; GERD – gastroesophageal reflux disease; Tx – therapy; * active disease or surgically resected within the last year

Table 5. Correlation of NTM pulmonary disease diagnosed according to the different microbiologic and full ATS/IDSA criteria, and positive predictive value for the use of microbiologic criteria in establishing NTM-PD diagnosis.

NTM species*	Phi coefficient of correlation of ATS/IDSA microbiologic criteria with the whole ATS/IDSA criteria	PPV for ATS/IDSA microbiologic criteria	Phi coefficient of correlation of stricter microbiologic criteria with the whole ATS/IDSA criteria	PPV for stricter microbiologic criteria
All species	**0.66** (95% CI 0.60-0.72; p<0.0001)	**59.3%** (95% CI 51.7 - 66.6)	**0.73** (95% CI 0.68-0.77; p<0.0001)	**93.2%** (95%CI 84.9 - 97.8)
Low relevance	**0.28** (95% CI 0.12-0.43; p=0.001)	**10.5%** (95%CI 2.9-25.1)	**0.6** (95% CI 0.48-0.7; p<0.0001)	**50%** (95%CI 9.4-90.6)
Intermediate relevance	**0.69** (95% CI 0.6-0.76; p<0.0001)	**63.4%** (95% CI 52.0-73.8)	**0.7** (95%CI 0.62-0.77; p<0.0001)	**94.3%** (95% CI 80.6-99.3)
High relevance	**0.77** (95% CI 0.64-0.86; p<0.0001)	**89.8%** (95% CI 77.2-96.6)	**0.57** (95% CI 0.37-0.72; p<0.0001)	**100%** (95% CI 87.2-100)

PPV – positive predictive value; ATS – American Thoracic Society; IDSA - Infectious Diseases Society of America; * - „low relevance“: <25% of isolates meeting full ATS/IDSA criteria; „intermediate relevance“: 25-70% of isolates meeting full criteria; “high relevance“: >70% of isolates meeting full criteria.

Figure 1. Clinical relevance of nontuberculous mycobacteria isolated from respiratory samples according to the percentage of patients meeting the full ATS/IDSA diagnostic criteria [1]



ATS – American Thoracic Society; IDSA - Infectious Diseases Society of America;

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