비결핵항산균 폐질환의 진단과 경과의 실제

(Diagnosis and Natural history of NTM-PD)

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비결핵항산균이란?

Nontuberculous mycobacteria (NTM)

- *M. tuberculosis*, *M. leprae* 를 제외한 모든 항산균
- 토양, 물 등 자연환경에 존재
- 현재까지 190 여종 이상의 species/subspecis가 밝혀짐.
- 폐질환 (대부분, 90%이상), 림프절염, 피부/연조직/골감염증, 파종성 질환 (disseminated disease)
- 사람간 전염은 되지 않아, 격리가 필요하지 않음.

비결핵항산균 폐질환

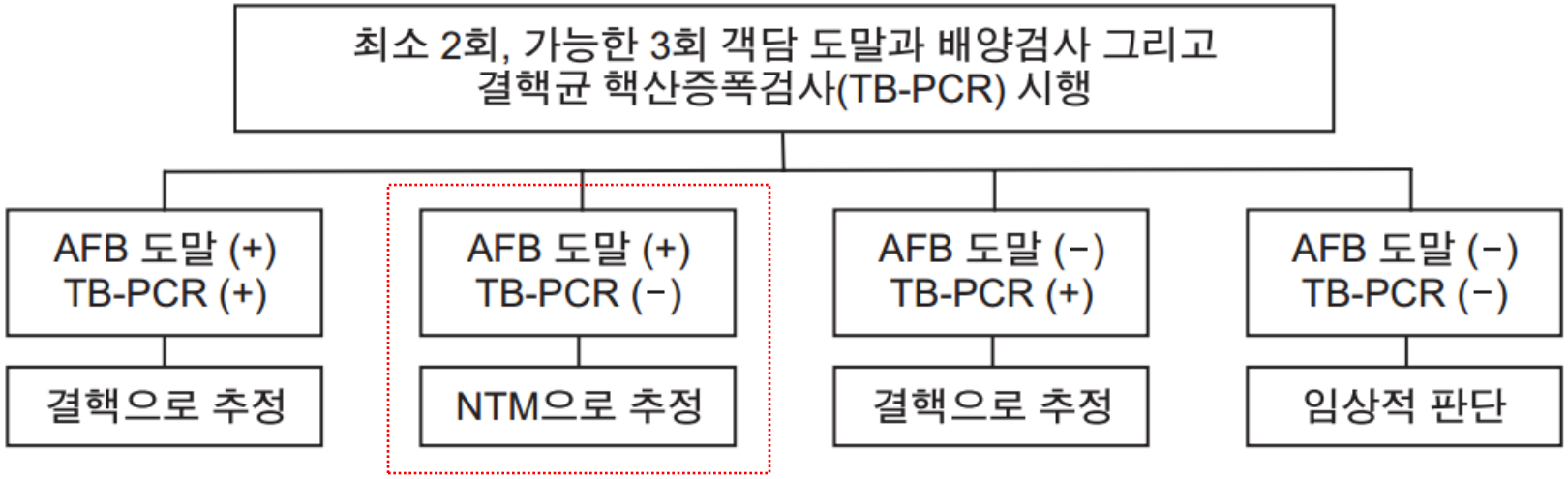
NTM-pulmonary disease (NTM-PD)

- 비결핵항산균 감염증에서 가장 흔한 임상양상
- 세계적으로 유병률, 발생률이 증가하는 추세
- 가장 흔한 원인 균종: *M. avium* complex, *M. abscessus* complex, *M. kansasii* (국내 : *M. avium* complex, *M. abscessus* complex)
- Culture (+) NTM 중 25~60%가 NTM-PD 진단 기준을 만족

폐결핵 *vs.* 비결핵항산균 폐질환

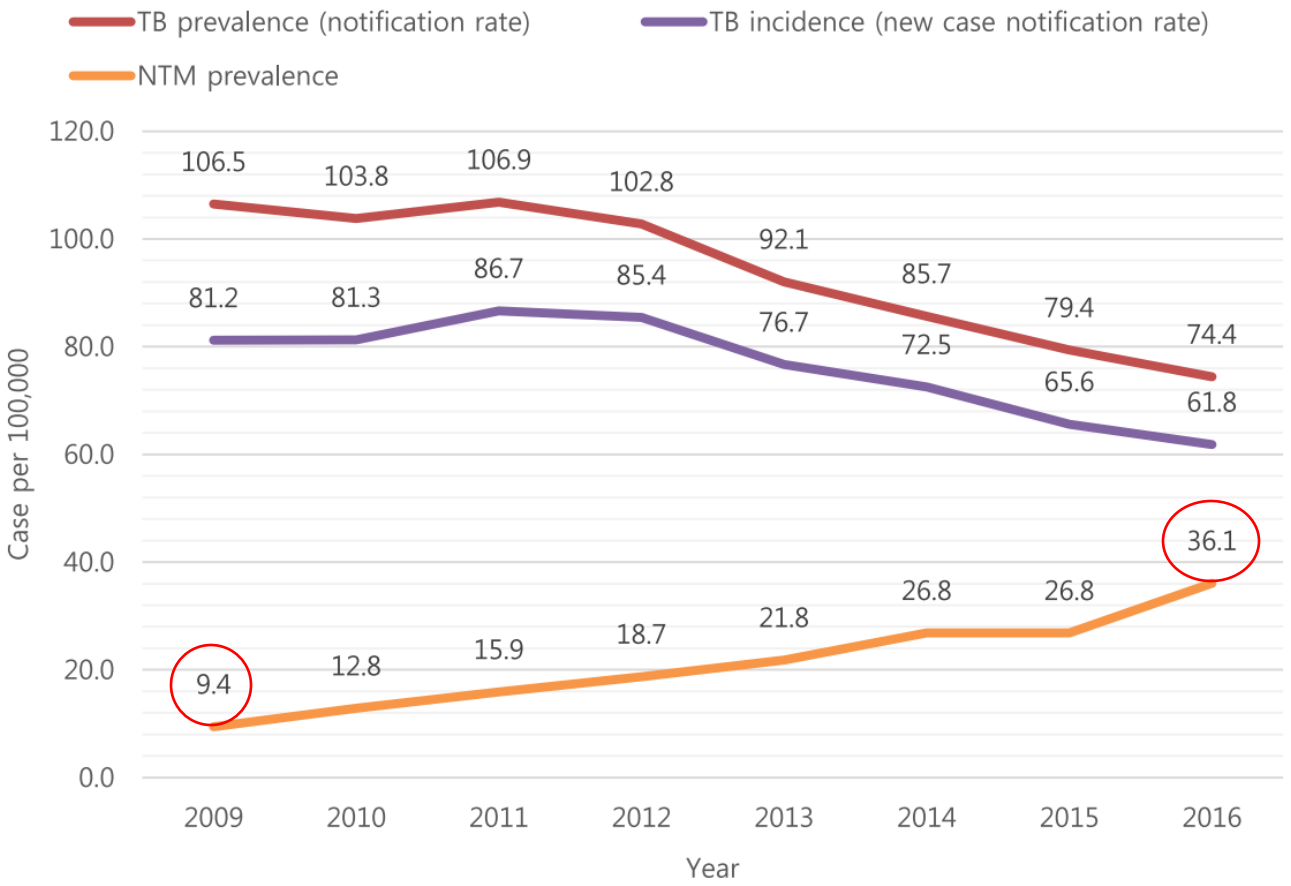
	폐결핵	비결핵항산균 폐질환
임상증상	기침, 객담, 객혈, 체중감소, 미열 등	기침, 객담, 객혈, 미열, 체중감소 등
영상검사	공동 (cavity), 중심소엽성 결절	공동 (cavity), 중심소엽성 결절
AFB 도말(smear)검사	양성	양성
핵산증폭검사 (TB-PCR)	**양성**	**음성**
AFB 배양(culture)검사	***M. tuberculosis***	**NTM species**
치료	**반드시 항결핵제 치료**	**반드시 치료를 필요하지는 않음**
전염/격리	**사람간 전염(공기전파), 격리 필요**	**사람간 전염(-), 격리 불필요**

NTM 감별



대한결핵 및 호흡기학회 2017 결핵진료지침 3판

Prevalence of NTM



Patients with NTM infection, 2009-2016

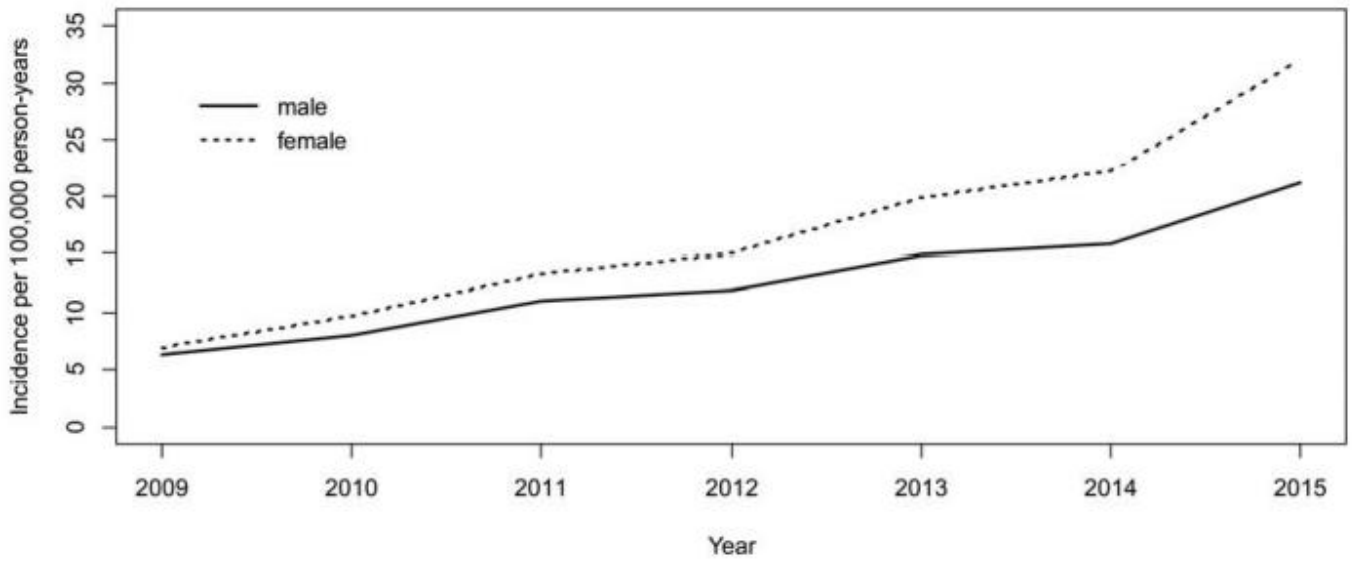
National claims data for HIRA database

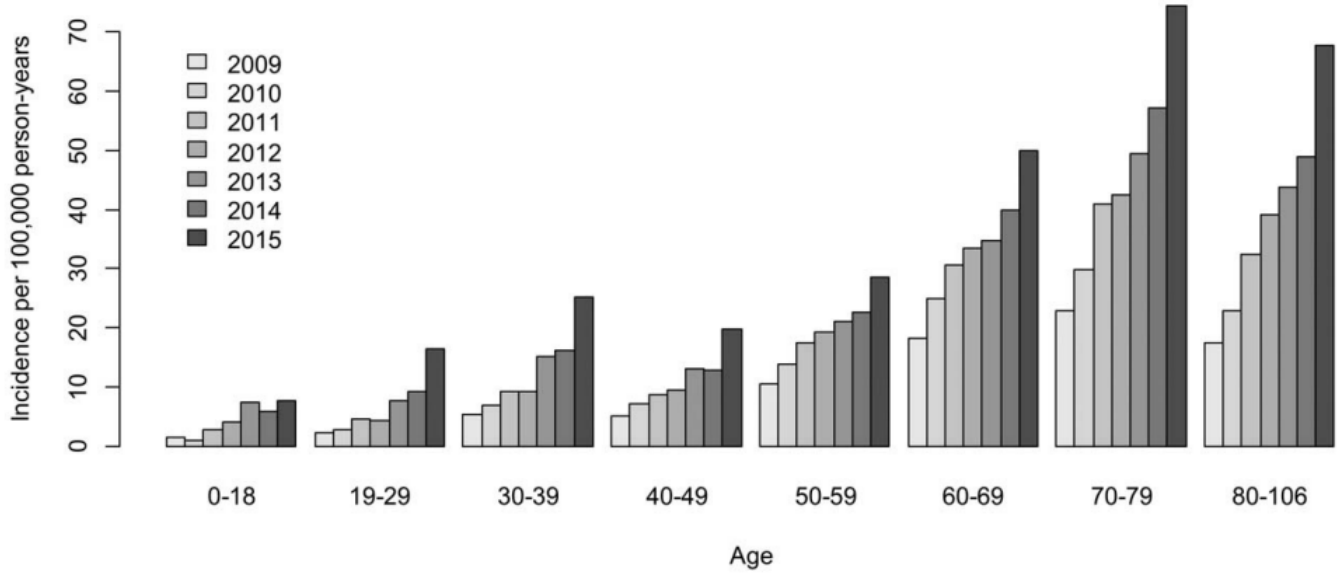
(ICD-10: A31)

The age- and sex- adjusted prevalence of NTM per 100,000 population increased between **2009 (9.4)** and **2016 (36.1)**.

BMC Infect Dis. 2017 Jun 15;17(1):432.

Prevalence of NTM





52,511 patients with NTM-PD, 2009-2015

National claims data for HIRA database

ICD-10: A31 codes

(excluding A31.1 cutaneous mycobacterial infection)

Medicine . 2019 Nov;98(45):e17869.

NTM is increasing

Table 2. Changes in the proportions of nontuberculous mycobacteria among mycobacterial isolates from clinical respiratory specimens in South Korea

Study	Hospital	Study period	Proportion of nontuberculous mycobacteria	
			Start of study period	End of study period
Park et al. (2010)[53]	Seoul National University Hospital	2002–2008	427/1,921 (22%)	781/1,701 (46%)
Lee et al. (2012)[54]	Severance Hospital	2006–2010	268/1,041 (26%)	970/2,064 (47%)
Yoo et al. (2012)[55]	Asan Medical Center	2002–2010	403/1,921 (21%)	1,530/2,648 (59%)
Koh et al. (2013)[56]	Samsung Medical Center	2001–2011	548/1,283 (43%)	3,341/4,800 (70%)
Kim and Rheem (2013)[57]	Dankook University Hospital	2005–2011	26%	44%
Lee et al. (2014)[58]	Ulsan University Hospital	2010–2013	25%	38%
Kim et al. (2017)[59,*]	Pusan National University Hospital	2009–2015	24.8%	44.8%

*This study included both respiratory and non-respiratory specimens.

Tuberc Respir Dis. 2019 Apr;82(2):94-101

NTM species

TABLE 1 Classification of NTM commonly causing human disease

Slowly growing mycobacteria	Rapidly growing mycobacteria
Runyon group I, photochromogens	Runyon group IV
M. kansasii	*M. abscessus* complex
M. marinum	*M. chelonae*
M. simiae	*M. fortuitum* complex
Runyon group II, scotochromogens	*M. peregrinum*
M. scrofulaceum	
M. szulgai	
M. gordonae	
Runyon group III, nonchromogens	
M. avium complex	
M. ulcerans	
M. xenopi	
M. malmoense	
M. terrae complex	
M. haemophilum	
M. genavense	

TABLE 2 Pulmonary and extrapulmonary disease caused by NTM

Disease	Common etiology
Pulmonary disease	*M. avium* complex
	M. abscessus complex
	M. kansasii
	M. malmoense
	M. xenopi
Lymphadenitis	*M. avium* complex
	M. scrofulaceum
	M. malmoense
	M. hemophilum
Skin, soft tissue infecton	*M. abscessus* complex
	M. chelonae
	M. fortuitum complex
	M. marinum
	M. ulcerans
Bone infection	*M. avium* complex
	M. xenopi
	M. marinum
	M. kansasii
	M. abscessus complex
	M. fortuitum complex

* Rapidly growing: 7일 이내

Microbiol Spectr. 2017 Jan;5(1)

Causative species of NTM-PD

Table 3. Etiologic species of nontuberculous mycobacterial lung disease in South Korea

	Koh et al. (2006)[63]	Park et al. (2010)[53]	Lee et al. (2012)[54]	Jang et al. (2014)[64]	Lee et al. (2014)[58]	Kim et al. (2014)[65]	Yoon et al. (2017)[60]
Study period	2002–2003	2002–2008	2006–2010	2012	2010–2013	2007–2011	2011–2016
No. of patients	195	651	345	111	245	90	64
Mycobacterium avium complex	94 (48)	NA (63)	263 (76)	73 (66)	132 (54)	61 (68)	29 (45)
M. avium	38	NA	141	32	39	42	13
M. intracellulare	56	NA	122	41	93	19	16
M. abscessus complex	64 (33)	NA (27)	63 (18)	32 (29)	22 (9)	15 (17)	27 (42)
M. abscessus	NA	NA	NA	21	NA	11	NA
M. massiliense	NA	NA	NA	11	NA	4	NA
M. kansasii	7 (4)	NA	7 (2)	1 (1)	80 (33)	1 (1)	4 (6)
Others	30 (15)	NA (10)	12 (3)	5 (5)	11 (4)	13 (14)	4 (6)

Values are presented as number (%).
NA: not available.

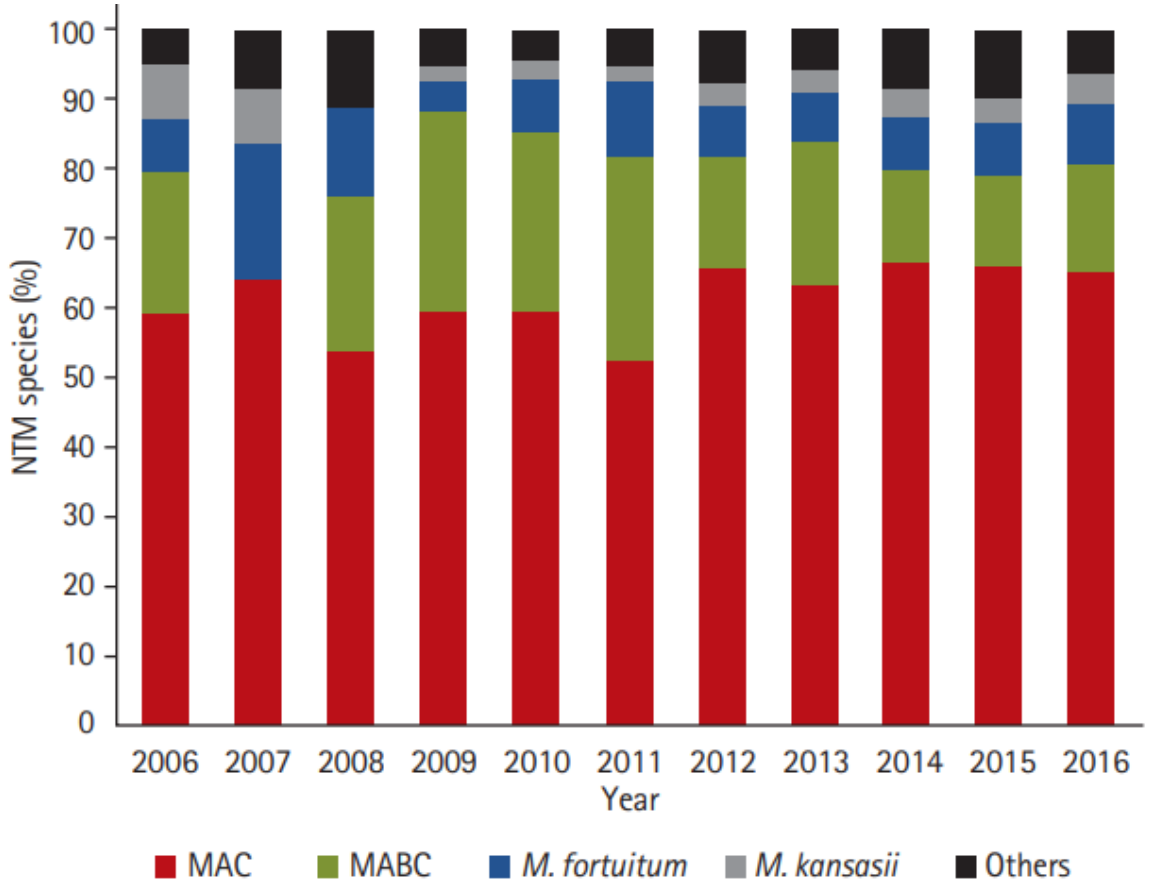
Ulsan

Tuberc Respir Dis. 2019 Apr;82(2):94-101

Causative species of NTM-PD

1017 cases with NTM-PD, 2006-2016

Severance hospital, South Korea



Koren J Intern Med. 2020 Nov;35(6):1424-1431

Pathogenicity of NTM-PD

- Pathogenicity of NTM varies.

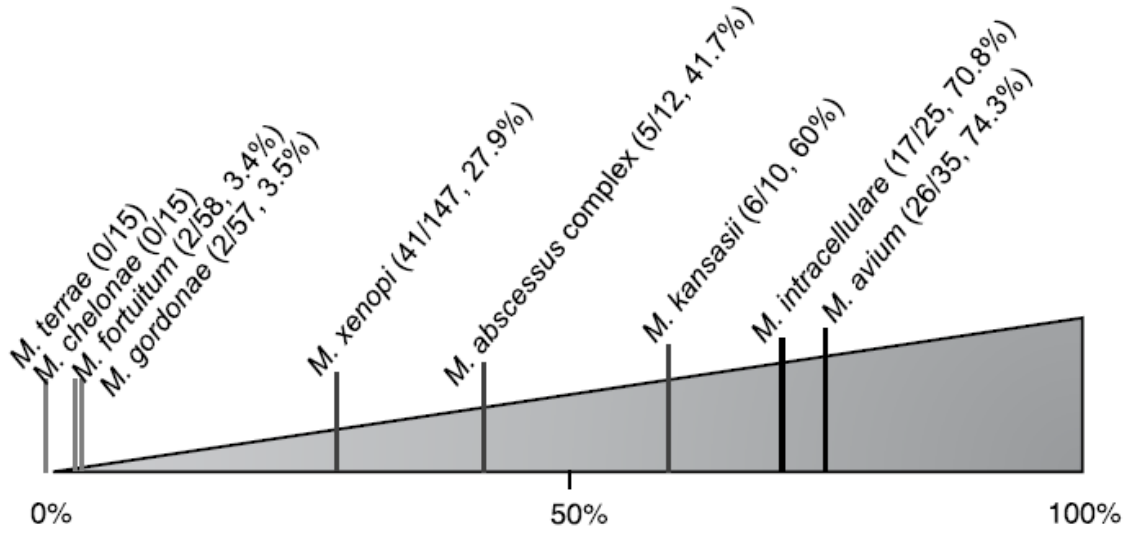


Figure Clinical relevance of non-tuberculous mycobacteria isolated from respiratory samples according to the percentage of patients meeting the full ATS/IDSA diagnostic criteria.[1] ATS/IDSA = American Thoracic Society/Infectious Diseases Society of America.

Table 3. Risk Factors Associated With Progression of Nontuberculous Mycobacterial Pulmonary Disease

• Host/demographic
– Male sex
– Younger age
– Presence of comorbidities
– Low body mass index
• Radiographic
– Fibrocavitary disease
– Extent of disease
• Laboratory
– Elevated inflammatory indices (ESR, CRP)
– Anemia
– Hypoalbuminemia
• Microbial
– Bacterial load
– Species

Int J Tuberc Lung Dis . 2016 Jul;20(7):934-40.
J Infect Dis 2020;222:S199-S211

Infection sources





Table 1. Source of nontuberculous mycobacteria

Natural environment
Natural water in lakes, rivers, streams, and swamps
Soils and dust from soils
Household environment
Household plumbing systems
Drinking water and distribution systems
Shower heads and faucets
Hot tubs, spas, hydrotherapy pools, and footbaths
Humidifiers
Refrigerator water and ice
Garden and potting soils
Hospital environment
Hospital plumbing systems
Hospital water and distribution system
Contaminated medical device: heater-cooler devices
Filter and ice machines

Tuberc Respir Dis. 2019 Apr;82(2):94-101

NTM 폐질환의 진단

ATS/ERS/ESCMID/IDSA Guideline (2020)

임상적 (Clinical)	호흡기 또는 전신증상 + 다른 질환의 배제
영상학적 (Radiologic)	결절 또는 공동 (Chest X-ray) Or 기관지확장증에 동반된 다발성 작은 결절들 (HRCT)
	AND
미생물학적 (Microbiologic)	(1주 이상 간격) 객담 배양 (+) ≥ 2 Or Bronchial washing 또는 BAL 검체 배양 (+) ≥ 1 Or 합당한 조직학적 소견* + 객담/washing 또는 조직 배양 (+) ≥ 1

* Granulomatous inflammation or AFB

Eur Respir J. 2020 Jul 7;56(1):2000535

NTM 폐질환의 영상학적 분류

(1) 섬유공동형, Fibrocavitary (FC) form

(2) 결절 기관지확장증형, Nodular bronchiectatic (NB) form

- Non-cavitary nodular bronchiectatic (NC-NB) form
- Cavitary nodular bronchiectatic (C-NB) form

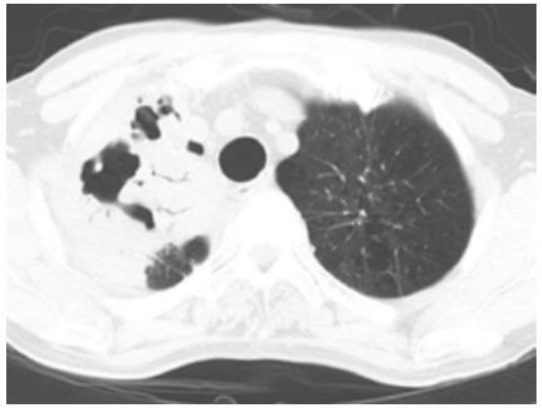
NTM 폐질환의 영상학적 분류

섬유공동형 (FC form)	결절 기관지확장증형 (NB form)
오랜 기간 흡연력과 음주력이 있는 중년 이상의 남성	비흡연자 중년 이상 여성
대부분 만성폐쇄성폐질환, 기존의 폐결핵 등 **기저질환 동반**	**기저질환 X**
상엽의 공동 **(폐결핵과 유사)**	상엽의 공동 X 주로 **우중엽과 좌상엽의 설상엽**을 침범 **양측 하부에 결절과 침윤**
림프절 비대와 흉수는 드물다.	CT에서 기관지확장증에 동반된 **다발성 중심소엽성 결절(centrilodular nodule)**
MAC-PD 치료하지 않으면, 1-2년이내 광범위한 폐 실질의 파괴와 사망	NB form 증가추세

대한결핵 및 호흡기학회 2020 결핵진료지침 4판

NTM 폐질환의 영상학적 분류

(1) 섬유공동형, Fibrocavitary (FC) form



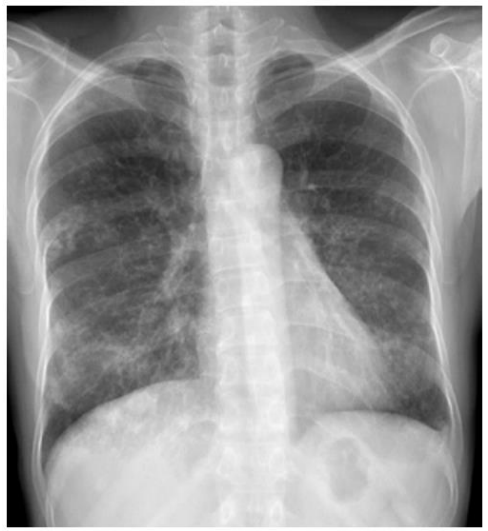

- 고령의 남성
- 기저 폐질환 동반
- 대개 상엽의 공동과 증가된 폐음영 (폐결핵과 유사)

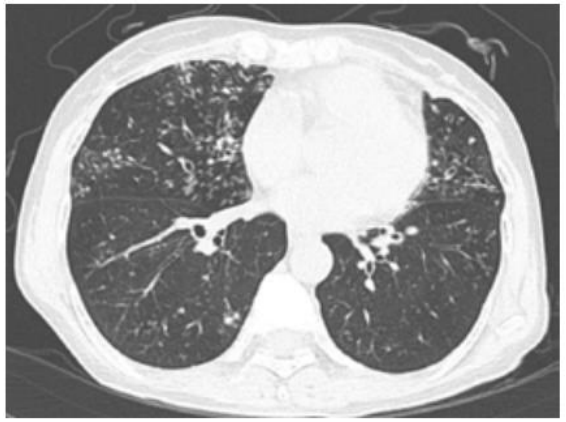
Tuberc Respir Dis 2016;79:74–84

NTM 폐질환의 영상학적 분류

(2) 결절 기관지확장증형, Nodular bronchiectatic (NB) form

Non-cavitary NB (NC-NB) form





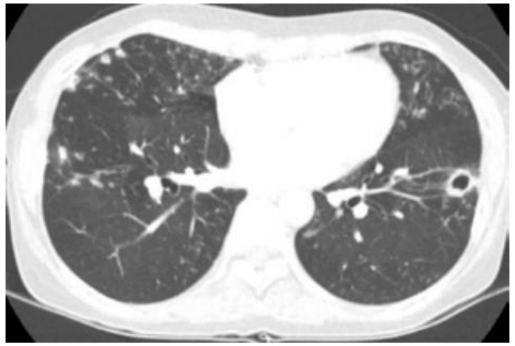
- 중년 여성, 비흡연자
- 기저질환이 없음
- 주로 우중엽과 좌상엽의 설상엽을 침범하는 양측 기관지확장증 (bronchiectasis)을 동반한 다발성 중심소엽성 결절(multiple centrilobular nodules)

Tuberc Respir Dis 2016;79:74–84

NTM 폐질환의 영상학적 분류

(2) 결절 기관지확장증형, Nodular bronchiectatic (NB) form

Cavitary NB (C-NB) form



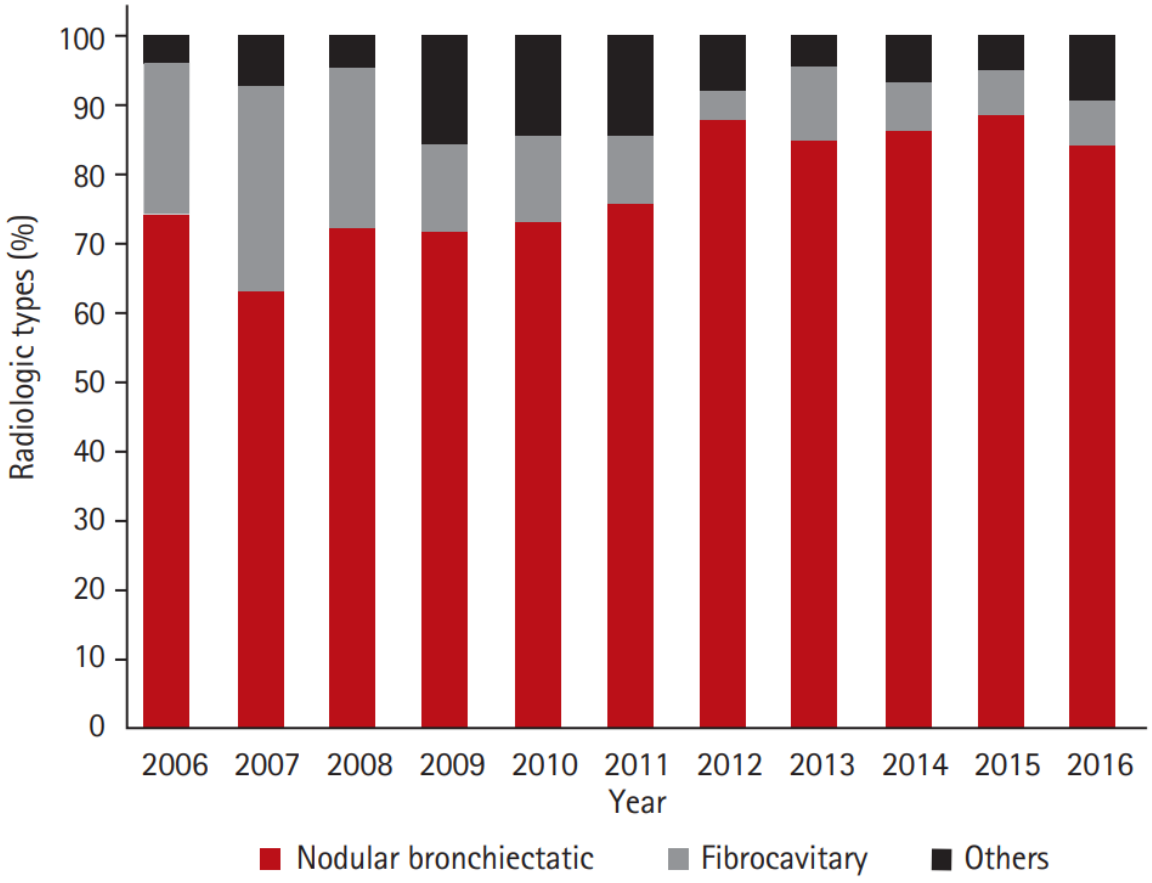
- 결절 기관지확장증형이 우세함
- 1개 이상 공동이 있음

Eur Respir J. 2017 Sep 27;50(3):1602503

NTM 폐질환의 영상학적 분류

1017 cases with NTM-PD, 2006-2016

Severance hospital, South Korea



Koren J Intern Med. 2020 Nov;35(6):1424-1431

Cavitary diseases

566 cases with MAC-PD, 2002-2013

Samsung Medical Center, South Korea

- **Favorable outcome***

  Noncavitary disease (88%)

  Cavitary disease (76 FC 76%, C-NB 78%)

- **Cavitary disease** was independently associated with **unfavorable outcomes**.

TABLE 3 Risk factors for unfavourable outcomes in the study population

	Favourable	Unfavourable	Univariable analysis		Multivariable analysis	
			OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Subjects	402 (84)	79 (16)				
Male	153 (38)	43 (54)	1.94 (1.20–3.16)	<0.001	1.80 (1.07–3.02)	0.027
Age years	58 (50–67)	61 (52–70)	1.02 (1.00–1.04)	0.055		
BMI kg·m^{-2}	20.2 (18.8–21.9)	19.5 (17.8–21.7)	0.97 (0.89–1.05)	0.440		
Mycobacterium intracellulare	183 (46)	43 (54)	1.43 (0.88–2.32)	0.148		
Sputum smear positivity	215 (54)	55 (70)	1.99 (1.19–3.35)	0.009		
COPD	64 (16)	14 (18)	1.14 (0.60–2.15)	0.691		
Concurrent CPA	14 (4)	6 (8)	2.28 (0.85–6.12)	0.103		
Previous lung resection	23 (6)	6 (8)	1.35 (0.53–3.44)	0.524		
Type of disease						
Noncavitary NB	246 (61)	32 (41)	1.00	Ref.	1.00	Ref.
Cavitary NB	62 (15)	18 (23)	2.23 (1.07–4.65)	0.014	2.36 (1.24–4.52)	0.009
Fibrocavitary	94 (23)	29 (37)	2.37 (1.26–4.48)	0.002	1.99 (1.11–3.54)	0.020
Use of streptomycin	169 (42)	41 (52)	1.49 (0.98–2.41)	0.108		
Surgical resection	32 (8)	4 (5)	0.62 (0.21–1.80)	0.375		

Data are presented as n (%) or as median (interquartile range), unless otherwise stated. n=481. BMI: body mass index; COPD: chronic obstructive pulmonary disease; CPA: chronic pulmonary aspergillosis; NB: nodular bronchiectatic form of *Mycobacterium avium* complex lung disease.

*Favorable outcome was defined as sputum culture conversion after initiation of treatment and maintenance of a negative culture for ⩾12 months on treatment

Eur Respir J 2017;50:1602503

Cavitary NTM-PD (FC and C-NB form)	Non-cavitary NTM-PD (NC-NB form)
- Usually require immediate treatment - The presence of cavity is associated with higher mycobacterial burden and mortality.	- Indolent course, often progress slowly - Early treatment of mild NC-NB NTM-PD may not be advisable. - Adverse effects of the long-term use of multiple antibiotics

J Korean Med Sci 2016;31:649–659
Int J Infect Dis 2016;45:123–134
Eur Respir J 2017;50:1602503

NTM 폐질환의 자연경과

1) Spontaneous culture conversion

   Stable course without progression

2) Disease progression leading to treatment

3) Reversion or redevelopment after conversion

4) Recurrence after treatment success

NTM 폐질환의 자연경과

1) Spontaneous culture conversion

   Stable course without progression

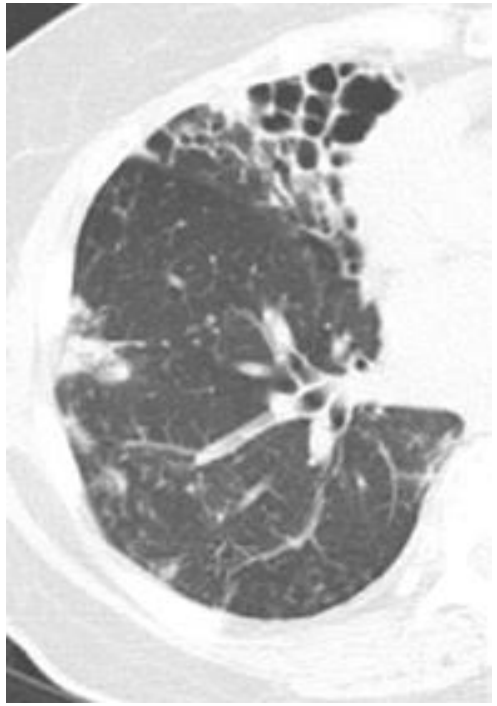
2) Disease progression leading to treatment

3) Reversion or redevelopment after conversion

4) Recurrence after treatment success

Spontaneous culture conversion

F/62, Cough/sputum for 1 year



2 years later

증상 호전

Sputum AFB: *M. avium* (3차례)

Sputum AFB: no growth

Spontaneous culture conversion

F/80, Cough for 5 months

Never-smoker, TB history (-), Lt.breast cancer s/p op (2014) - NED

1 year later

2 years later

PCNBx; Chronic granulomatous inflammation

NTM-PCR (+)

Spontaneous culture conversion

NC-NB form NTM-PD, 2003-2013

Samsung Medical Center, South Korea

- Of 459 patients who did not initiate treatment, **157 (34%)** showed spontaneous sputum culture conversion.

Respir Med 2019;150:45–50

Spontaneous culture conversion

NC-NB form MAC-PD, 2000-2013

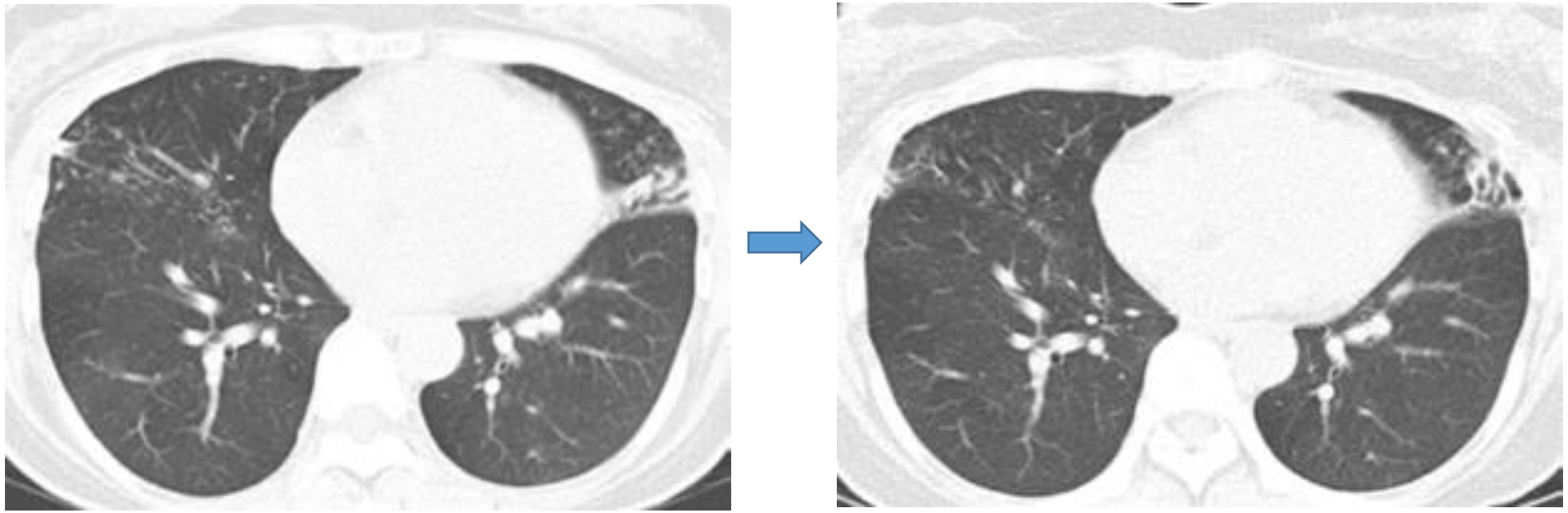
Asan Medical Center, South Korea

- During the median of 5.0 years of follow-up, 203 patients who received no treatment during the study period showed that spontaneous sputum conversion occurred in **106** (**52.2%**).

Respir Med. 2019 May;151:1-7.

Spontaneous culture conversion

- A significant proportion of patients with MAC-PD (**approximately 40%–60%**) remain without disease progression for several years after diagnosis, even without treatment.



3 years later

Tuberc Respir Dis. 2019 Jan;82(1):15-26.

Spontaneous culture conversion

- 비결핵항산균 폐질환 진단만으로 즉각적인 치료를 시작할 필요는 없다.

- Indolent and mild NC-NB form의 NTM-PD 의 경우, **“Watchful waiting”**

NTM 폐질환의 자연경과

1) Spontaneous culture conversion

   Stable course without progression

2) **Disease progression leading to treatment**

3) Reversion or redevelopment after conversion

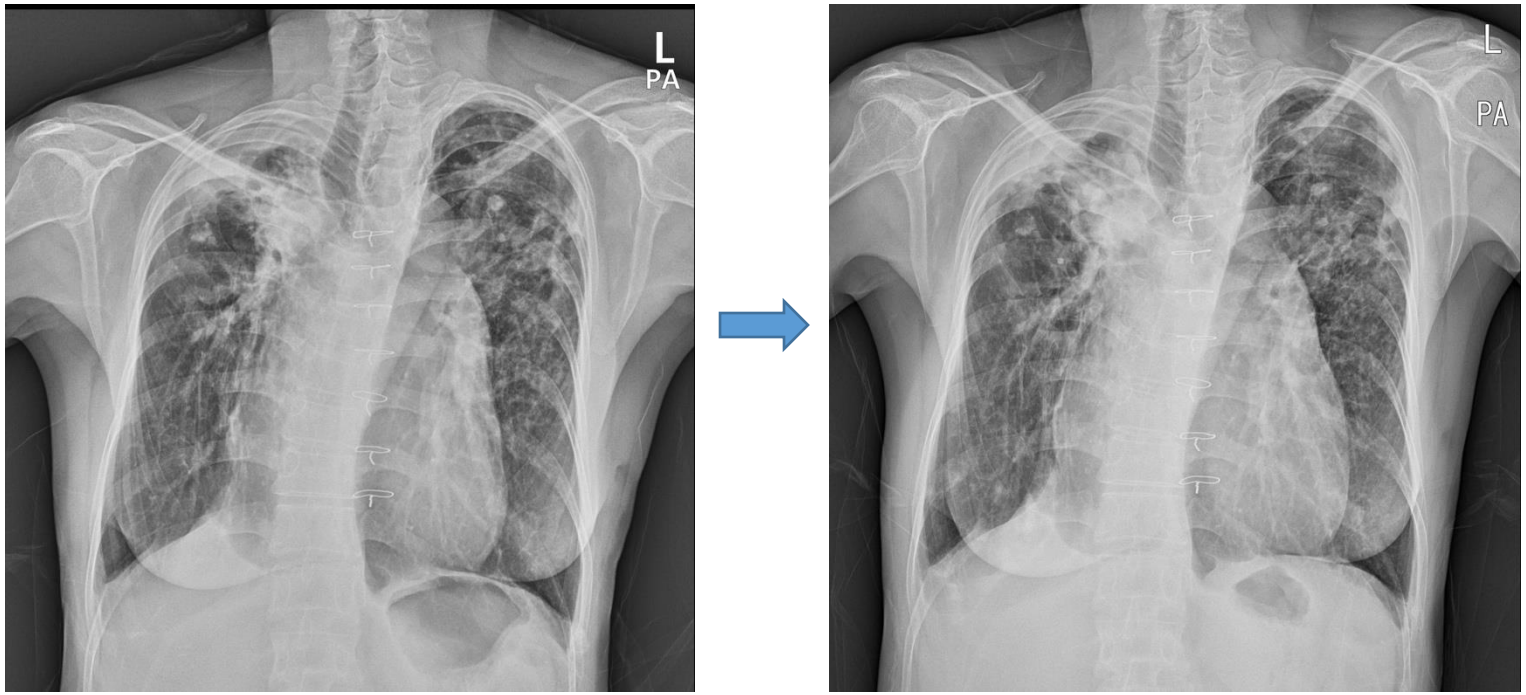
4) Recurrence after treatment success

Disease progression

F/63, Dyspnea and cough/purulent sputum for 6 months

Never-smoker, h/o pul.TB (2011)

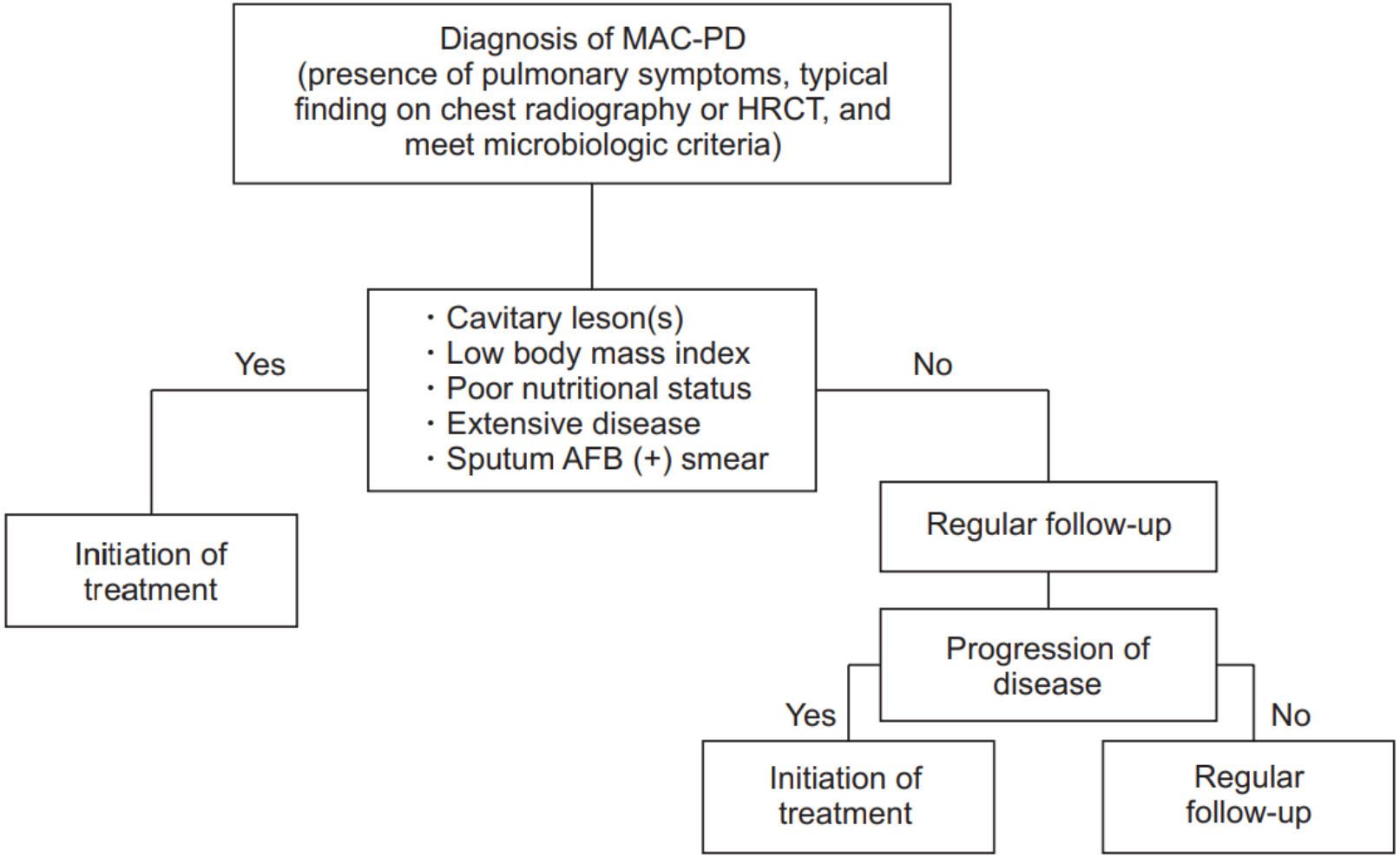
BMI: 17.4 kg/m^2



1 year later

Positive AFB smear, Sputum AFB culture: *M. ab subsp. abscessus*

Disease progression



Tuberc Respir Dis. 2019 Jan;82(1):15-26.

Disease progression

Table 3. Risk Factors Associated With Progression of Nontuberculous Mycobacterial Pulmonary Disease

• Host/demographic
– Male sex
– Younger age
– Presence of comorbidities
– Low body mass index
• Radiographic
– Fibrocavitary disease
– Extent of disease
• Laboratory
– Elevated inflammatory indices (ESR, CRP)
– Anemia
– Hypoalbuminemia
• Microbial
– Bacterial load
– Species

J Infect Dis 2020;222:S199-S211

Disease progression

- BMI was inversely related to development of NTM-PD.
- Weight loss increased the risk of NTM-PD.

BMI	NTM-PD incidence	
	HR	Adjusted HR*
<18.5 kg/m^2	(reference)	(reference)
18.5–22.9 kg/m^2	0.25	0.38
23.0–24.9 kg/m^2	0.10	0.17
25.0–29.9 kg/m^2	0.06	0.10
≥30 kg/m^2	0.06	0.10

*: adjusted for age, sex, residence, income, diabetes, respiratory disease, solid cancer, haematologic malignancy, transplantation, AIDS, GERD, smoking status, number of hospital visits and chest radiograph findings during health screening

Eur Respir J. 2021 Feb 4;57(2):2000454.

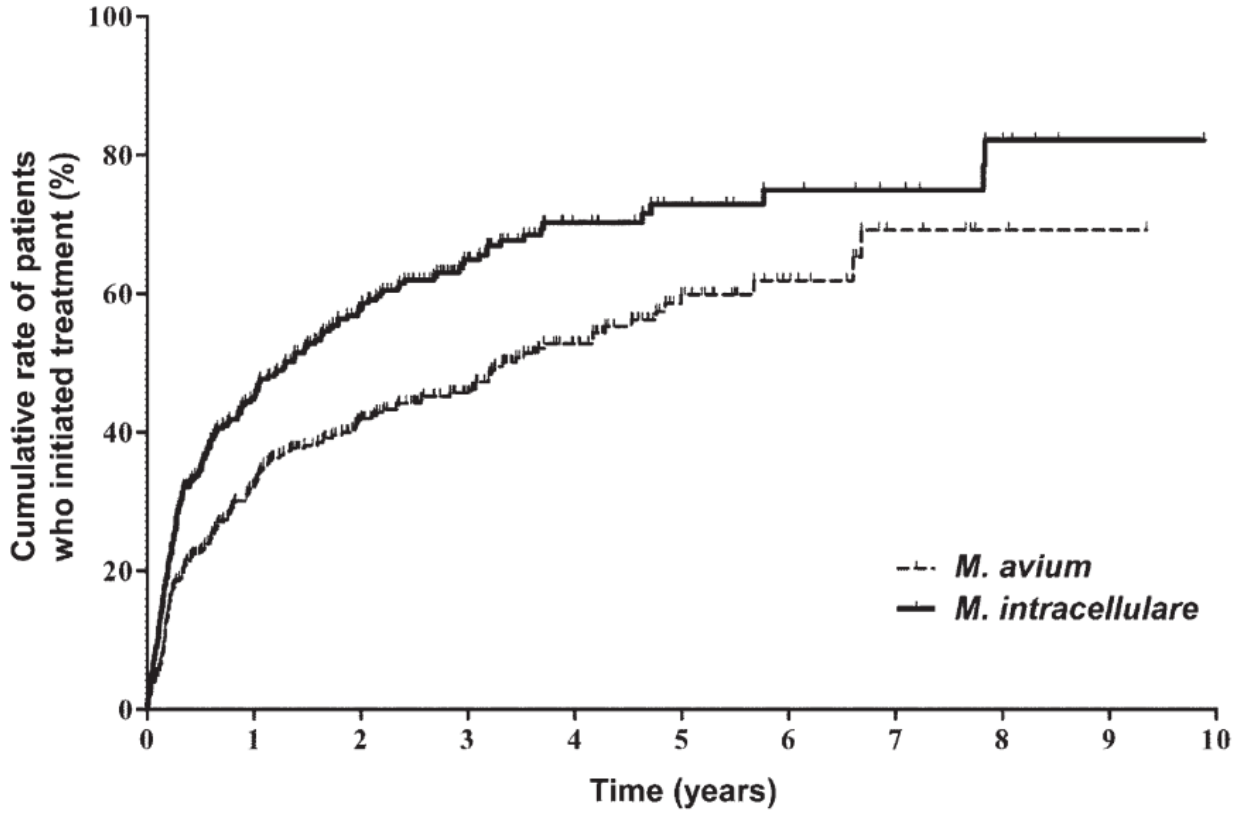
Disease progression

590 patients with MAC-PD, 2000-2009

Samsung Medical Center, South Korea

M. avium (n = 323)

M. intracellulare (n = 267)



Chest. 2012 Dec;142(6):1482-1488.

Disease progression

110 patients with MABC-PD, 2006-2015

Seoul National University Hospital, South Korea

M. abscessus (n = 56)

M. massiliense (n = 54)

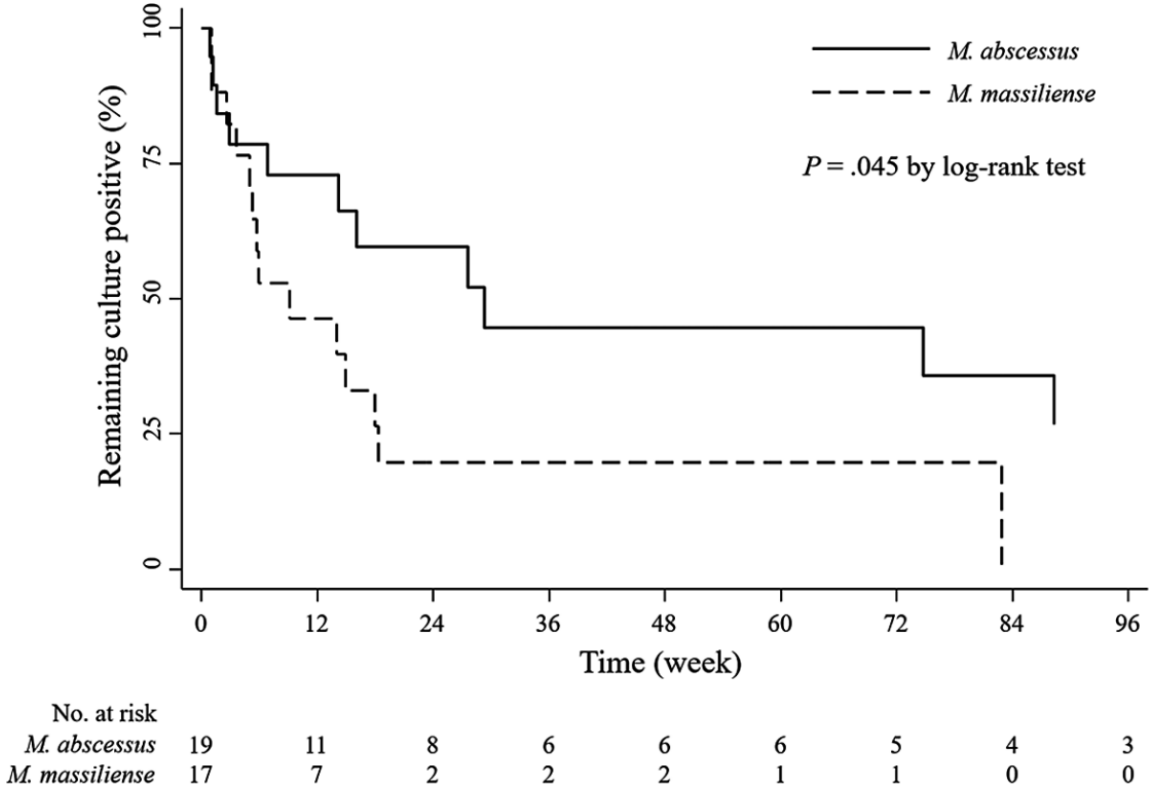


Table 3. Clinical Characteristics Associated With Disease Progression Requiring Treatment Among 110 Patients With *Mycobacterium abscessus* or *Mycobacterium massiliense* Lung Disease

Variable	Unadjusted Odds Ratio (95% CI)	*P* Value	Adjusted[a] Odds Ratio (95% CI)	*P* Value
NTM species				
M. abscessus	1.00	.881	1.00	.435
M. massiliense	1.06 (.49–2.29)		1.46 (.57–3.74)	

Clin Infect Dis. 2017 Feb 1;64(3):301-308.

Disease progression

Indicators for the initiation of treatment for MAC-PD

Table 1 Indicators for the initiation of treatment for *Mycobacterium avium* complex (MAC)—lung disease.

Indicators & timing	Patient related factors	Chest radiographic features	Microbiological features
At initial visits	Severe symptoms[a], low BMI, and immunocompromised conditions (on TNF-α inhibitors)	Fibrocavitary lesion, cavitary nodular bronchiectasis, and extensive involvement	AFB smear positive and virulent MAC subspecies
During follow-up	Worsening symptoms even on symptomatic therapy[a]	New or worsening lung cavitation, new foci of consolidation/tree-in-bud opacity, increased size/number of nodules, and worsening extent and/or severity of bronchiectasis	Persistent culture positivity, increase in grade of AFB smear positivity and number of positive MAC cultures

AFB, acid-fast bacilli; BMI, body mass index; TNF-α, tumor necrosis factor-α.
[a] Other diseases must be excluded as the cause of symptoms.

J Formos Med Assoc. 2020 Jun;119 Suppl 1:S67-S75

NTM 폐질환의 자연경과

1) Spontaneous culture conversion

   Stable course without progression

2) Disease progression leading to treatment

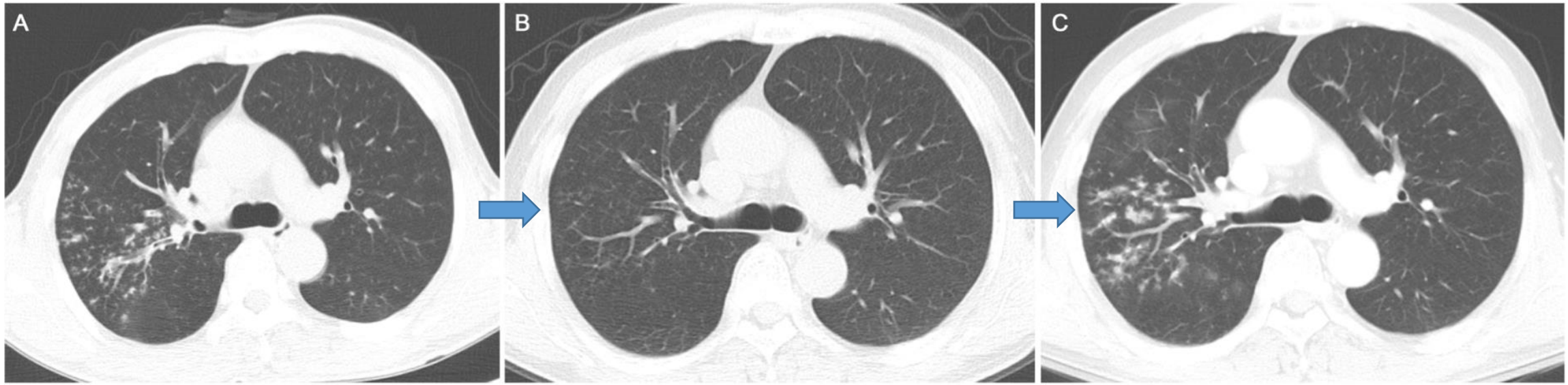
3) **Reversion or redevelopment after conversion**

4) Recurrence after treatment success

Reversion or redevelopment after conversion

F/55, *M. abscessus* complex PD

- The changes in radiological imaging of one patient who experienced spontaneous conversion and reversion.



At diagnosis **16 months later** **2 years later**

PLoS One. 2020 Apr 27;15(4):e0232161.

Reversion or redevelopment after conversion

NC-NB form NTM-PD, 2003-2013

Samsung Medical Center, South Korea

- After spontaneous culture conversion, **26** of 157 **(17%)** showed redeveloped NTM-PD caused by a species different from the original species

Redevelopment of NTM lung disease caused by a different NTM species after spontaneous culture conversion.

Initial Species	Subsequent Species After Spontaneous Culture Conversion				
	M. avium	*M. intracellulare*	*M. abscessus*	*M. massiliense*	Total
M. avium	—	8	0	4	12
M. intracellulare	5	—	0	0	5
M. abscessus	5	0	—	0	5
M. massiliense	3	1	0	—	4
Total	13	9	0	4	26

NTM, nontuberculous mycobacteria.

Respir Med 2019;150:45–50

Reversion or redevelopment after conversion

126 patients MABC-PD, 2012-2018

Asan Medical Center, South Korea

- Spontaneous culture conversion:

  24 (25.8%), mean follow-up 3.7 years after diagnosis

- Reversion:

  27.8%, median 18.2 months after conversion

PLoS One. 2020 Apr 27;15(4):e0232161.

Reversion or redevelopment after conversion

- 비결핵항산균 폐질환은 spontaneous sputum conversion이 있더라도 **지속적인 추적관찰**이 필요하다.

NTM 폐질환의 자연경과

1) Spontaneous culture conversion

   Stable course without progression

2) Disease progression leading to treatment

3) Reversion or redevelopment after conversion

4) **Recurrence after treatment success**

Recurrence after treatment success

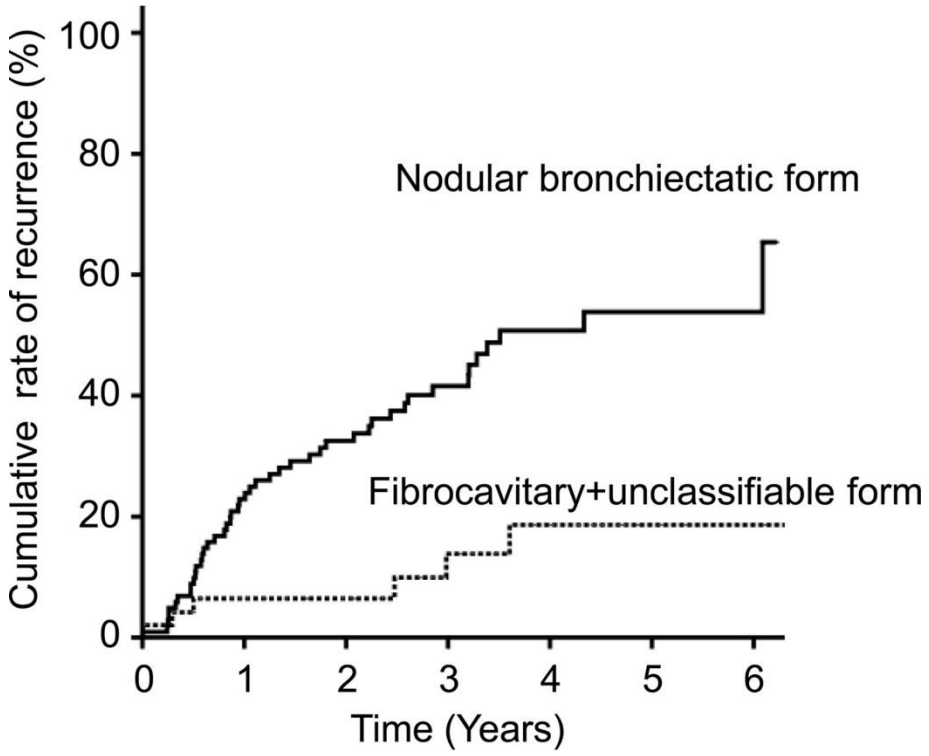
158 patients successfully treated MAC-PD, 2000-2009

Asan Medical Center, South Korea

- 31.6% recurrence

  (Median follow-up: 43.8 months)

- Recurrence rate: **NB form** > other form



Antimicrob Agents Chemother. 2015;59(6):2972-7.

Recurrence after treatment success

46 patients completed the recommended antibiotics for MAC-PD, 2000-2012

Northwestern Memorial Hospital, Chicago, Illinois

- 25 (**54%**) – True relapse (median time: **210 days**)
- 21 (**46%**) – Reinfection (median time: **671 days**)

Ann Am Thorac Soc. 2016 Nov;13(11):1956-1961.

Recurrence after treatment success

Patients with MAC-PD, 2002-2013

Samsung Medical Center, South Korea

- Of the 402 patients who completed treatment, **118 (29%)** redeveloped NTM lung disease.
  (Median follow-up period: 13.6 months)

TABLE 4 Redevelopment of nontuberculous mycobacterial (NTM) lung disease in 118 patients after successful treatment of *Mycobacterium avium* complex (MAC) lung disease

Initial disease	Subjects	Redevelopment of NTM lung disease	Subjects
M. avium	65	*M. avium*	31 (48)
		M. intracellulare	15 (23)
		M. abscessus complex	14 (22)
		Others[#]	5 (7)
M. intracellulare	53	*M. intracellulare*	34 (64)
		M. avium	9 (17)
		M. abscessus complex	7 (13)
		M. kansasii	1 (2)
		Others[#]	2 (4)

Data are presented as n or n (%). [#]: including mixed infections.

Eur Respir J. 2017 Sep 27;50(3):1602503

Recurrence after treatment success

Patients with MAC-PD, 2002-2013

Samsung Medical Center, South Korea

TABLE 6 Genotyping results of paired clinical isolates from patients with recurrent *Mycobacterium avium* complex (MAC) lung disease[#]

	Total	Reinfection[¶]	Relapse[¶]	p-value
Subjects	27 (100)	20 (74)	7 (26)	
Type of disease				0.091
NB	22 (81)	18 (82)	4 (18)	
Noncavitary NB	17	14	3	
Cavitary NB	5	4	1	
Fibrocavitary form	5 (19)	2 (40)	3 (60)	
Aetiology				0.091
M. avium	12 (44)	11 (92)	1 (8)	
M. intracellulare	15 (56)	9 (60)	6 (40)	
Time interval between treatment completion and recurrence months	10.6 (5.5–18.3)	13.0 (6.0–23.7)	6.0 (4.8–8.5)	0.040

Data are presented as n (%), n or median (interquartile range), unless otherwise stated. NB: nodular bronchiectatic form. [#]: "recurrent MAC lung disease" only includes cases where MAC lung disease redeveloped due to the same species; [¶]: repetitive sequence-based PCR profiles indicated that genotypes differed from the original isolates (reinfection) or were identical to the initial genotype (relapse).

Eur Respir J. 2017 Sep 27;50(3):1602503

NTM 폐질환의 자연경과

1) Spontaneous culture conversion

   Stable course without progression

2) Disease progression leading to treatment

3) Reversion or redevelopment after conversion

4) Recurrence after treatment success

Mortality

Pulmonary Nontuberculous Mycobacteria–Associated Deaths, Ontario, Canada, 2001–2013

Theodore K. Marras, Michael A. Campitelli, Hong Lu, Hannah Chung, Sarah K. Brode, Alex Marchand-Austin, Kevin L. Winthrop, Andrea S. Gershon, Jeffrey C. Kwong,[1] Frances B. Jamieson[1]

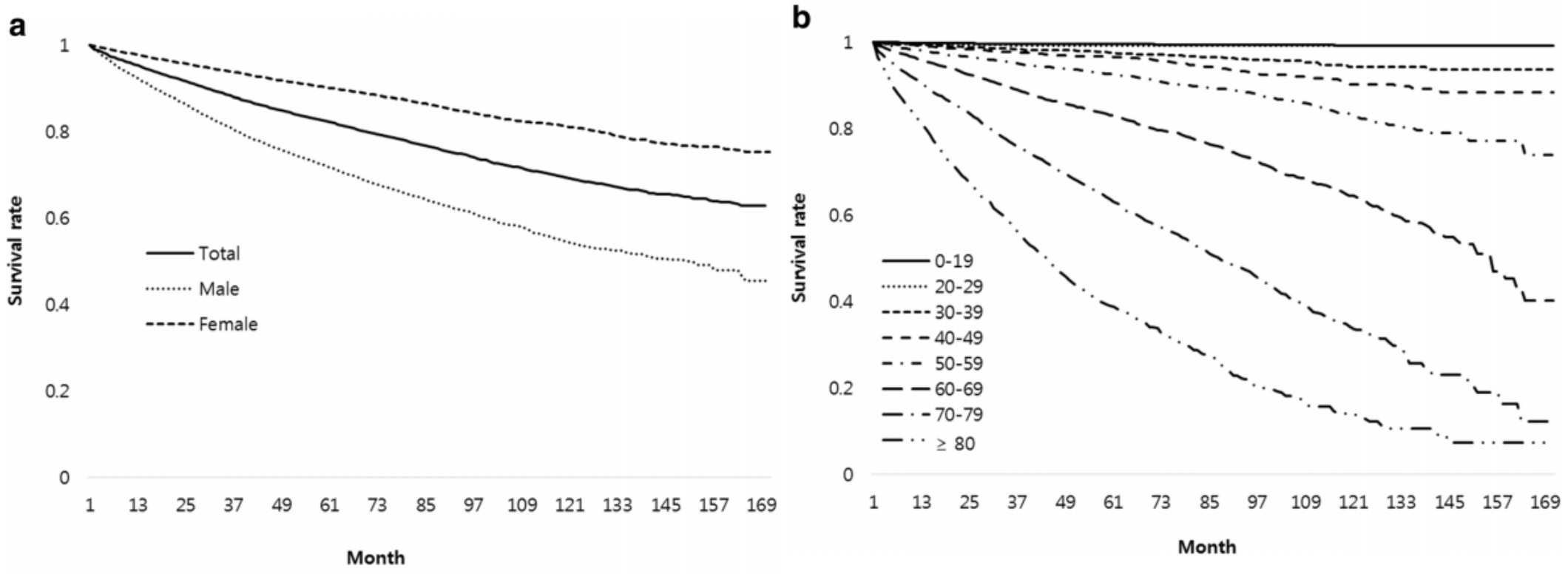
in patient selection (*7*,*8*,*10*). Although our 5-year mortality estimates (26.6% for NTM-PI and 36.9% for NTM-PD) were of generally similar magnitude to prior studies (*7*–*11*),

Table 4. Survival estimates for patients with incident pulmonary NTM disease and with NTM isolation, Ontario, Canada, 2001–2013*

Species, group	Total	1-y survival, %	5-y survival, %	SMR† (95% CI)	Crude HR (95% CI)	Adjusted‡ HR (95% CI)
All						
Disease	9,681	84.4	63.1	2.83 (2.74–2.92)	1.49 (1.42–1.56)	1.23 (1.17–1.28)
Isolation	10,936	89.7	73.4	2.30 (2.22–2.38)	1.00 (ref)	1.00 (ref)
MAC						
Disease	6,323	85.7	64.7	2.59 (2.49–2.69)	1.40 (1.32–1.49)	1.16 (1.09–1.24)
Isolation	5,756	89.5	73.2	2.27 (2.16–2.38)	1.00 (ref)	1.00 (ref)

Emerg Infect Dis. 2017 Mar; 23(3): 468–476

Mortality



- Mortality ratio of NTM to general population: **2.16** (95% CI: 2.10 to 2.22)
- 5-year mortality : 17.8% for NTM infection
  [26.6% Marras TK et al.(Ontario, Canada), 35.1% Novosad SA et al.(Oregon,USA)]

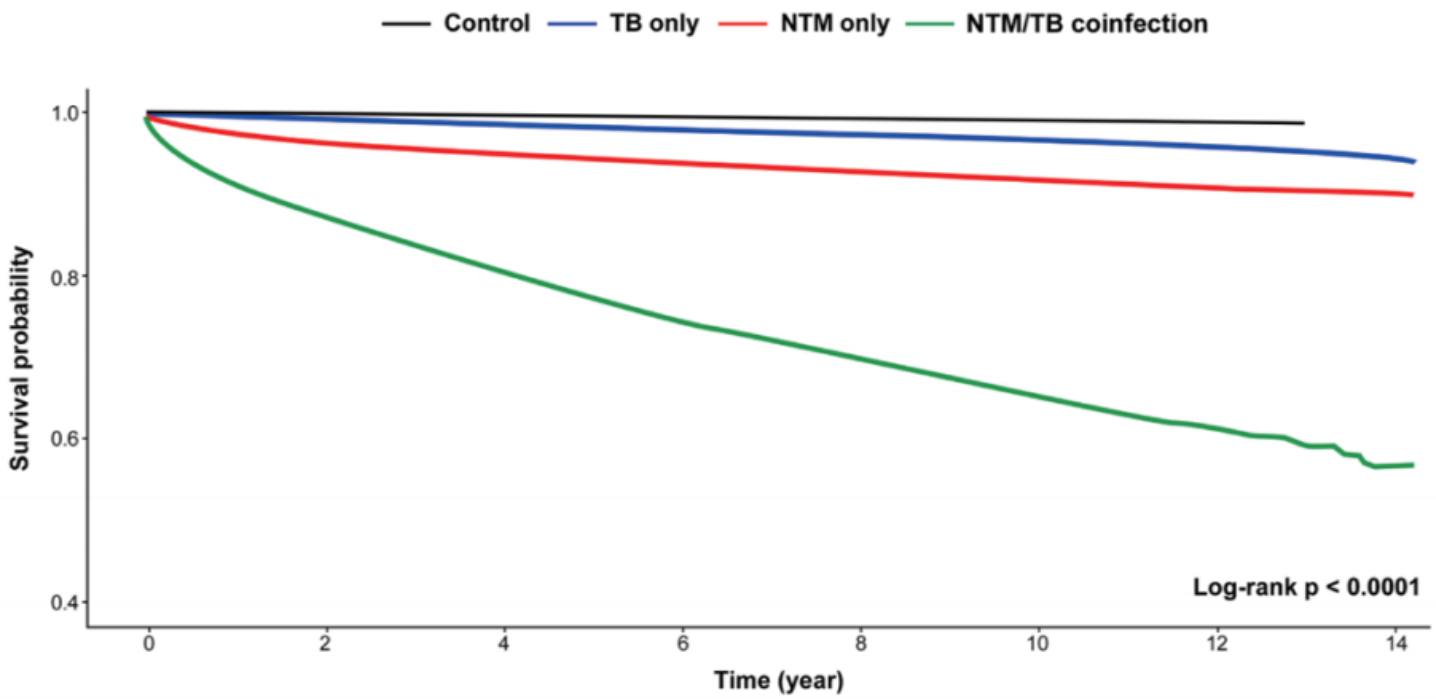
BMC Pulm Med. 2019 Aug 1;19(1):140

Mortality

Table 2 Cause of death in patients with NTM infection

Causes of death	Number of patients (%)
Tuberculosis	509 (10.0)
Pneumonia	424 (6.0)
CLRD	725 (8.3)
Lung cancer	369 (14.2)
Other cancers	769 (7.2)
CDVD	300 (15.0)
CBVD	155 (5.9)
DM	99 (3.0)
Hypertension	34 (1.9)
Others	1,392 (27.2)
Unknown	29 (0.6)
Total	5,112 (100.0)

CLRD chronic lower respiratory disease, *CDVD* cardiovascular disease, *CBVD* cerebrovascular disease, *DM* diabetes mellitus



BMC Pulm Med. 2019 Aug 1;19(1):140
Clin Infect Dis. 2020 Sep 14;ciaa1381.

Mortality

Novel scoring system to predict mortality in NTM-PD

- **1,181 Derivation cohort**

(Samsung Medical Center)

- **377 Validation cohort**

(Seoul National University Hospital)

Table 2. Factors Associated with Time to Mortality among Patients with Nontuberculous Mycobacterial Pulmonary Disease in the Derivation Cohort

Variables	Unadjusted HR	Adjusted HR in the Final Model	β Coefficient in the Final Model	Score
Age ⩾65 yr	4.42 (3.39–5.75)	3.31 (2.52–4.36)	1.20	1
Sex, M	3.56 (2.75–4.61)	2.29 (1.75–3.00)	0.83	1
Body mass index, <18.5 kg/m^2	3.53 (2.75–4.53)	2.25 (1.73–2.91)	0.81	1
Ever-smoker*	2.77 (2.15–3.56)	—	—	—
History of tuberculosis	2.25 (1.74–2.90)	—	—	—
Acid-fast bacillus smear positivity	2.43 (1.85–3.20)	1.38 (1.03–1.86)	0.32	0
Mycobacterial species				
M. avium	Reference	—	—	—
M. intracellulare	2.13 (1.60–2.83)	—	—	—
M. abscessus subsp. *abscessus*	1.41 (0.90–2.21)	—	—	—
M. abscessus subsp. *massiliense*	0.84 (0.52–1.35)	—	—	—
Elevated erythrocyte sedimentation rate†	3.88 (2.63–5.72)	2.38 (1.60–3.54)	0.87	1
Cavity on chest computed tomography	2.62 (2.82–4.66)	2.41 (1.82–3.18)	0.88	1

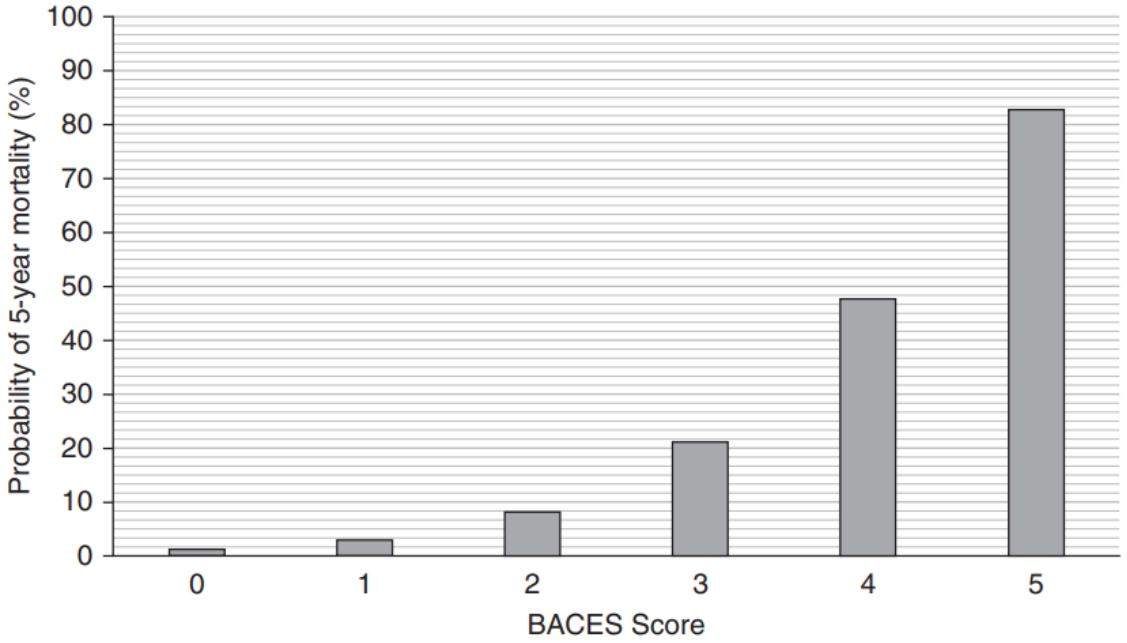
Definition of abbreviation: HR = hazard ratio.
Numbers are presented as HR (95% confidence interval), unless otherwise specified.
*Includes current and former smokers.
†Men >15 mm/h, women >20 mm/h.

Am J Respir Crit Care Med. 2021 Jan 15;203(2):230-236.

Mortality

BACES scoring system

- **B**MI
- **A**ge
- **C**avity
- **E**SR
- **S**ex



Am J Respir Crit Care Med. 2021 Jan 15;203(2):230-236.

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Q & A

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