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Association between nutritional status and clinical characteristics in nontuberculous mycobacterial pulmonary disease: preliminary results from the NTM-KOREA cohort

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Abstract

Background Evidence on the association between nutritional status and clinical characteristics in nontuberculous mycobacterial pulmonary disease (NTM-PD) remains limited. We investigated this association and its impact on longitudinal outcomes in a nationwide cohort.

Methods We analysed 627 patients from the NTM-KOREA cohort study who had initiated antibiotic therapy for NTM-PD. Baseline nutritional status was assessed using the Prognostic Nutritional Index (PNI) and Mini Nutritional Assessment Short Form (MNA-SF) tools. Clinical characteristics, physical function, and health-related quality of life (HRQOL) using Quality of Life Questionnaire–Bronchiectasis (QOL-B) were evaluated. Longitudinal analyses were performed at 6 and 12 months after therapy initiation.

Results In the baseline analysis group ($N=627$; mean age: 64.3 ± 9.7 years; females: 73.7%), 112 (17.9%) patients were classified as malnourished according to the PNI, and MNA-SF identified 319 (50.9%) patients at risk and 40 (6.4%) as malnourished. Multivariable regression analysis revealed that the PNI-defined malnutrition group was associated with increased odds (odds ratio [95% confidence interval]) of having dyspnoea (2.37 [1.34 to 4.11]), acid-fast bacilli smear positivity (2.26 [1.44 to 3.57]), and cavitary lesions (2.03 [1.25 to 3.37]). This group was also associated with higher BACES (body mass index, age, cavity, erythrocyte sedimentation rate, and sex) scores ($\beta=0.9$), shorter 6-min walking distance ($\beta=-42.1$ m), and lower QOL-B scores across physical functioning ($\beta=-10.6$), role functioning ($\beta=-7.4$), and respiratory symptoms ($\beta=-8.0$) (all $P < 0.001$).

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In the longitudinal analysis group ($n=457$), poor nutritional status reduced the likelihood of 6-month respiratory symptom improvement (0.44 [0.22 to 0.87]). In the treatment outcome analysis group ($n=119$), MNA-defined malnutrition was significantly associated with an increased risk of premature treatment discontinuation within 1 year (26.41 [2.82 to 633.89]).

Conclusions Baseline nutritional status was closely associated with disease severity and HRQOL in NTM-PD. Preliminary longitudinal data suggested that malnutrition may negatively impact symptomatic improvement and treatment adherence, highlighting the need for routine nutritional assessment.

Trial registration ClinicalTrials.gov identifier NCT03934034, Registration date May 1, 2019.

Keywords Malnutrition, Nontuberculous mycobacterium infection, Nutrition assessment, Quality of life, Treatment outcome

Background

Nontuberculous mycobacteria (NTM) are ubiquitous environmental organisms capable of causing a range of clinical diseases, including pulmonary disease (PD), lymphadenitis, and disseminated infection [1]. The global burden of NTM-PD is increasing, with a similar trend observed in South Korea [2]. Effective management of NTM-PD necessitates a multidimensional approach that extends beyond microbiological endpoints. As sputum culture conversion does not consistently reflect symptomatic or functional improvement [3], the assessment of health-related quality of life (HRQOL) has become a critical component of clinical care [4]. Within this context, nutritional status is a key—though often under-evaluated—determinant of clinical outcomes.

In NTM-PD, malnutrition—commonly indicated by body mass index (BMI) and body fat—has been associated with greater disease severity, poorer treatment tolerance, and increased mortality [5–9]. However, despite growing attention to this issue, large-scale prospective studies examining the role of nutritional status in patients with NTM-PD remain limited. In particular, its association with HRQOL and treatment outcomes has not been sufficiently investigated.

To address this gap, we conducted a comprehensive analysis of a nationwide, prospective cohort to evaluate the association of nutritional status with disease severity, symptom burden, HRQOL, physical function, and treatment outcomes in patients with NTM-PD. A clearer understanding of this relationship may support the development of more personalised management strategies, including nutritional interventions aimed at improving clinical outcomes.

Methods

Participants

NTM-KOREA is a nationwide, prospective ongoing cohort study launched on 28 February 2022 (ClinicalTrials.gov identifier: NCT03934034). This study enrolled patients who had initiated antibiotic therapy for NTM-PD at eight healthcare institutions across South Korea.

The inclusion criteria required participants to (1) be aged ≥ 19 years; (2) have a diagnosis of NTM-PD according to established guidelines [10]; (3) have one of the following causative organisms: *Mycobacterium avium* complex, *Mycobacterium abscessus* (including subspecies *abscessus* and *massiliense*), or *Mycobacterium kansasii* because these three species are the most prevalent and clinically significant causes of NTM-PD in South Korea [11, 12]; and (4) have initiated antibiotic therapy within 4 weeks. Written informed consent was obtained from all participants. The exclusion criteria comprised pregnancy and lack of informed consent. The study protocol was approved by the institutional review boards of all participating centres. To minimise selection bias, all eligible participants registered in the NTM-KOREA cohort were included in this analysis. Detailed information on the cohort design has been published previously [13]. Regarding this cohort, a previous study revealed improvements in HRQOL following antibiotic therapy [14], and another study evaluated the association of the BACES (BMI, age, cavity, erythrocyte sedimentation rate, and sex) score with HRQOL [15].

Data collection

We collected demographic and clinical data at enrolment using the NTM-KOREA database (iCreaT version 2.0 [<http://icreat.nih.go.kr>]). Baseline variables, including age, sex, BMI, smoking status, and comorbidities, were collected within 4 weeks of antibiotic therapy initiation. Microbiological details included the causative organisms and sputum acid-fast bacilli smear test results. Chest computed tomography scans were analysed by local thoracic radiologists or experienced pulmonologists, who categorised the findings as nodular bronchiectatic or fibrocavitary types. Radiological patterns that did not fit these categories—such as focal cavity, nodule, mass, or consolidation—were labelled as unclassifiable [16].

To assess NTM-PD severity, we calculated the BACES score by assigning one point for each of the following five factors: BMI < 18.5 kg/m², age ≥ 65 years, cavitary lesions, elevated erythrocyte sedimentation rate, and

male sex [17]. Based on the total score, participants were classified into three severity groups: mild (0–1 points), moderate (2–3 points), and severe (4–5 points) [18].

Nutritional status assessment

Nutritional status was assessed using the Prognostic Nutritional Index (PNI) and the Mini Nutritional Assessment Short Form (MNA-SF). The PNI, calculated from serum albumin levels and lymphocyte count ($10 \times$ serum albumin [g/dL] + $0.005 \times$ total lymphocyte count [$/\text{mm}^3$]), is a simple yet valuable marker of nutritional status originally developed for perioperative risk assessment [19]. It has since been recognised as a prognostic indicator in various conditions, including respiratory diseases [20–23]. Participants with a PNI < 45 were classified as malnourished [5].

Similarly, the MNA-SF provides a complementary perspective on nutritional status. It is a survey-based tool that has been validated in respiratory diseases [24]. The MNA-SF evaluates dietary intake, recent weight loss, neuropsychological issues, and functional ability, making it suitable for assessing nutritional status in older adults and in patients with respiratory conditions, including those with NTM-PD [24–26]. Participants were classified as having normal nutritional status (MNA-SF score: 12–14), at risk of malnutrition (score: 8–11), or malnourished (score: ≤ 7) [26].

HRQOL and associated factors

HRQOL is influenced by various clinical factors, including physical activity and sarcopenia [27, 28]. To evaluate HRQOL and related health conditions, we collected the following data: (1) respiratory and constitutional symptoms; (2) self-reported information from the Quality of Life Questionnaire–Bronchiectasis (QOL-B) and the International Physical Activity Questionnaire–Short Form (IPAQ-SF); and (3) objective measurements, including the 6-minute walking test (6MWT), handgrip strength, body composition, and pulmonary function tests—forced expiratory volume in 1 s, forced vital capacity, the forced expiratory volume in 1 s and forced vital capacity ratio, and diffusing capacity of carbon monoxide.

We assessed HRQOL in patients with NTM-PD using the QOL-B questionnaire, which comprises 37 items across eight domains: respiratory symptoms, physical functioning, vitality, role functioning, health perception, emotional well-being, social functioning, and treatment burden [29]. Each domain is scored from 0 to 100, with higher scores indicating better HRQOL. Changes in HRQOL following 6 months of antibiotic therapy were evaluated using the minimal clinically important difference for each domain. The predefined minimal clinically important difference thresholds were as follows: physical function (8), role functioning (8), vitality (10), emotional functioning (7), social functioning (9), health perception (8), respiratory symptoms

(8), and treatment burden (9) [29]. The Korean-translated version of the QOL-B questionnaire was used with permission from Dr. Alexandra L. Quittner. The questionnaire was administered in paper form under the supervision of trained nurses, as previously described [14].

Anthropometric data for identifying sarcopenia were obtained via multi-frequency bioelectrical impedance analysis, which yields reliable estimates of body composition comparable with those derived from dual-energy X-ray absorptiometry [30]. Details of the devices used are listed in Additional file, Table S1. Adipopenia was defined as a fat mass index (total body fat mass/height²) of < 3.0 kg/m² for males and < 5.7 kg/m² for females [31].

Handgrip strength was measured using a Jamar® hydraulic hand dynamometer (Model 5030J1; Sammons Preston, Bolingbrook, IL, USA). Reduced handgrip strength, defined as < 28 kg for males and < 18 kg for females, was considered possible sarcopenia based on the Asian Working Group for Sarcopenia (2019) criteria [32]. Sarcopenia was diagnosed when reduced handgrip strength was accompanied by a low appendicular skeletal muscle mass index (ASMI; ASM/height²), with cut-offs of < 7.0 kg/m² for males and < 5.7 kg/m² for females [32].

Physical activity was assessed using the IPAQ-SF, which records sedentary time, walking, and moderate- and vigorous-intensity activities over the previous 7 days. The IPAQ-SF is widely used in national and regional epidemiological studies [33].

Treatment outcomes

Follow-up visits were scheduled every 6 months, and treatment outcomes were evaluated annually. Treatment status was classified as either ongoing or completed/halted. For patients who discontinued treatment, reasons were categorised as follows: completion of full therapy, adverse events, insufficient efficacy, patient preference, or other causes. Patients who discontinued treatment because of adverse events within the first year of follow-up were included in the regression analyses under the category ‘premature treatment discontinuation < 1 year’.

Culture conversion was defined as three consecutive negative sputum culture results [34]. In the regression analysis, culture conversion was assessed only among patients whose treatment status was recorded as ‘completed or halted’ at the 1-year follow-up.

Statistical analysis

Continuous variables were compared using the t-test, while one-way analysis of variance was used for comparisons involving more than two groups. To reduce the risk of Type I errors due to multiple comparisons, the Bonferroni correction was applied. The Cochran–Armitage trend test was used to assess trends in proportions across ordered groups. Associations between continuous variables were

evaluated using Pearson’s correlation analysis. Linear and logistic regression analyses were conducted to identify factors associated with PNI and the MNA-SF, as well as with HRQOL and related clinical variables.

No imputation was performed because there were minimal missing data. Case numbers are reported for each relevant variable. Most analyses were based on baseline evaluations; therefore, loss to follow-up was not applicable. For outcome analyses at 6 and 12 months, only patients with available follow-up data were included.

To test the robustness of the findings, we performed several sensitivity analyses by: (1) replacing the BACES score with an alternative ‘ACES’ score (BACES score excluding BMI) to address potential overlap between BMI and disease severity; (2) excluding patients with chronic kidney disease, chronic liver disease, or malignancy to minimise confounding by comorbidities; (3) restricting analyses to treatment-naïve patients who had

not received antibiotic therapy before enrolment; and (4) applying alternative PNI cut-off values (< 45, < 40, and < 38) to assess the consistency of the associations across different thresholds [21–23].

Statistical significance was defined as $P < 0.05$. All analyses were conducted using R software (version 4.4.2; The R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

From 28 February 2022 to 31 March 2024, a total of 666 individuals were enrolled in this ongoing prospective cohort study (Fig. 1). Of these, 627 patients with complete data for baseline PNI, MNA-SF, and BACES score were included in the present analysis. Baseline characteristics of the participants are presented in Table 1. The mean age of the study cohort was 64.3 ± 9.7 years, and 73.7% were females. The most common etiologic

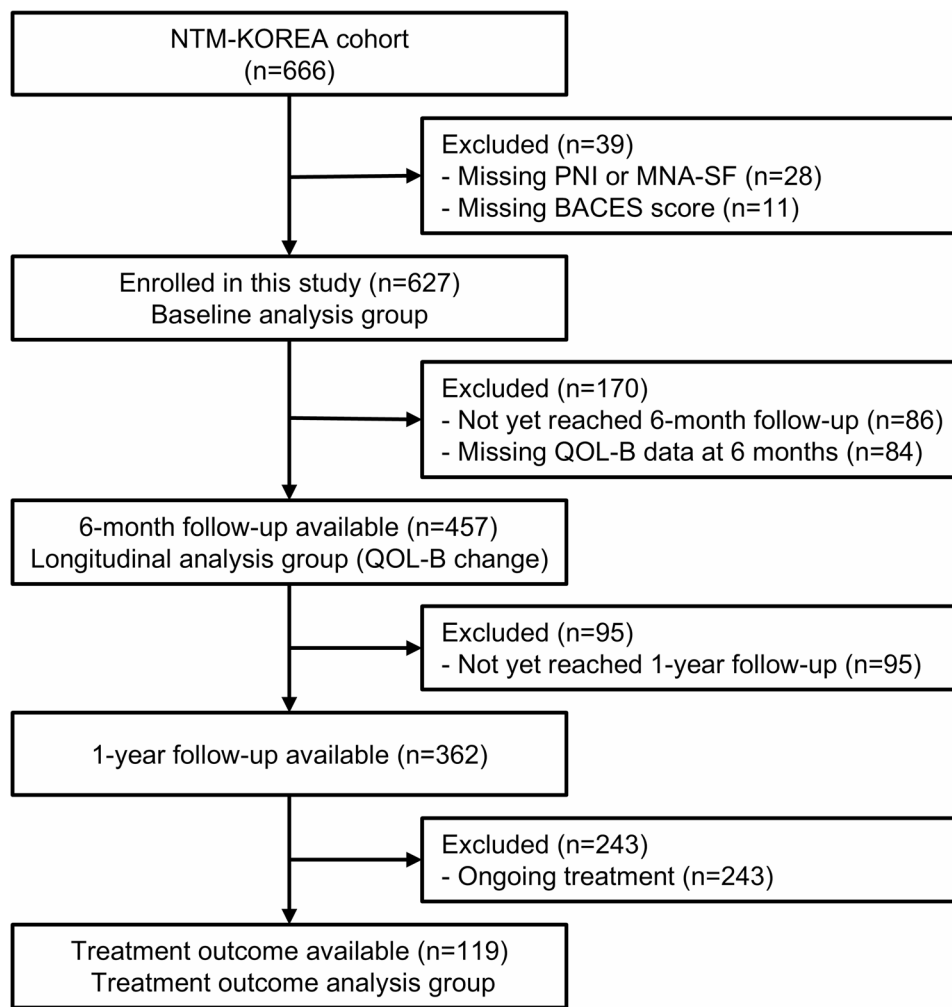


Fig. 1 Study flow diagram. Study flow diagram defining the baseline cohort and the sub-cohorts for longitudinal (6-month) and treatment outcome (12-month) analyses. Abbreviations: PNI, Prognostic Nutritional Index; MNA-SF, Mini Nutritional Assessment Short Form; QOL-B, Quality of Life Questionnaire–Bronchiectasis

Table 1 Baseline characteristics by PNI at treatment initiation (Baseline analysis group)

Characteristics	Total (N = 627)	PNI-defined normal nutrition (n = 515)	PNI-defined malnutrition (n = 112)	P-value
Age, year	64.3 ± 9.7	63.3 ± 9.6	69.0 ± 8.9	< 0.001
Females	462 (73.7)	402 (78.1)	60 (53.6)	< 0.001
Height, cm	160.9 ± 7.7	160.9 ± 7.5	161.0 ± 8.4	0.881
Weight, kg	52.9 ± 9.0	53.7 ± 9.0	49.6 ± 8.6	< 0.001
BMI, kg/m ²	20.4 ± 2.7	20.7 ± 2.6	19.1 ± 2.9	< 0.001
BMI < 18.5 kg/m ²	147 (23.4%)	99 (19.2)	48 (42.9)	< 0.001
Ever smoker	127 (20.3)	85 (16.5)	42 (37.5)	< 0.001
History of tuberculosis	176 (28.1)	137 (26.6)	39 (34.8)	0.101
History of NTM treatment	209 (33.3)	171 (33.2)	38 (33.9)	0.971
Respiratory comorbidity	424 (67.6)	346 (67.2)	78 (69.6)	0.695
Bronchiectasis	385 (61.4)	325 (63.1)	60 (53.6)	0.077
COPD	29 (4.6)	20 (3.9)	9 (8.0)	0.099
Asthma	15 (2.4)	9 (1.7)	6 (5.4)	0.054
Interstitial lung disease	12 (1.9)	8 (1.6)	4 (3.6)	0.302
Chronic pulmonary aspergillosis	9 (1.4)	3 (0.6)	6 (5.4)	< 0.001
Lung cancer	18 (2.9)	12 (2.3)	6 (5.4)	0.154
Non-respiratory comorbidity				
Diabetes mellitus	53 (8.5)	44 (8.5)	9 (8.0)	1.000
Rheumatologic diseases	14 (2.2)	12 (2.3)	2 (1.8)	1.000
Chronic liver disease	14 (2.2)	12 (2.3)	2 (1.8)	1.000
Chronic kidney disease	4 (0.6)	2 (0.4)	2 (1.8)	0.304
Cardiovascular disease	54 (8.6)	45 (8.7)	9 (8.0)	0.957
Malignancy	55 (8.8)	44 (8.5)	11 (9.8)	0.803
Mycobacterial species				< 0.001
<i>M. avium</i> complex	509 (81.2)	445 (86.4)	64 (57.1)	
<i>M. abscessus</i>	112 (17.9)	66 (12.8)	46 (41.1)	
<i>M. kansasii</i>	6 (1.0)	4 (0.8)	2 (1.8)	
AFB Smear positivity	223 (35.6)	163 (31.7)	60 (53.6)	< 0.001
Presence of cavity	379 (60.4)	294 (57.1)	85 (75.9)	< 0.001
Radiography				< 0.001
Fibrocavitary	86 (13.7)	55 (10.7)	31 (27.7)	
Nodular bronchiectatic	484 (77.2)	417 (81.0)	67 (59.8)	
Unclassified	57 (9.1)	43 (8.3)	14 (12.5)	
BACES score				< 0.001*
Mild (0–1)	173 (27.6)	161 (31.3)	12 (10.7)	
Moderate (2–3)	358 (57.1)	304 (59.0)	54 (48.2)	
Severe (4–5)	96 (15.3)	50 (9.7)	46 (41.1)	

Data are presented as numbers (%) or mean ± SD. P-values were calculated using Student's t-test or χ^2 test, unless otherwise indicated

Abbreviations: AFB Acid-fast bacillus, COPD Chronic obstructive pulmonary disease

*P-value from the Cochran–Armitage Trend Test

organism was *Mycobacterium avium* complex, accounting for 81.2% of cases. Furthermore, 77.2% of patients exhibited the nodular bronchiectatic radiologic type.

Based on the PNI classification, 99% ($n=112$) of patients were categorised as malnourished. According to the MNA-SF, the at-risk group comprised 50.9% ($n=319$) of the study population, and the malnutrition group comprised 6.4% ($n=40$) (Additional file, Table S2).

Correlation among nutritional indices

Figure 2 presents the distributions of baseline BMI, PNI, and MNA-SF scores, alongside correlation coefficients and scatter plots illustrating the relationships between these indices. Statistically significant positive correlations were observed between PNI and MNA-SF ($r=0.205$), PNI and BMI ($r=0.244$), and MNA-SF and BMI ($r=0.508$), all with $P < 0.001$.

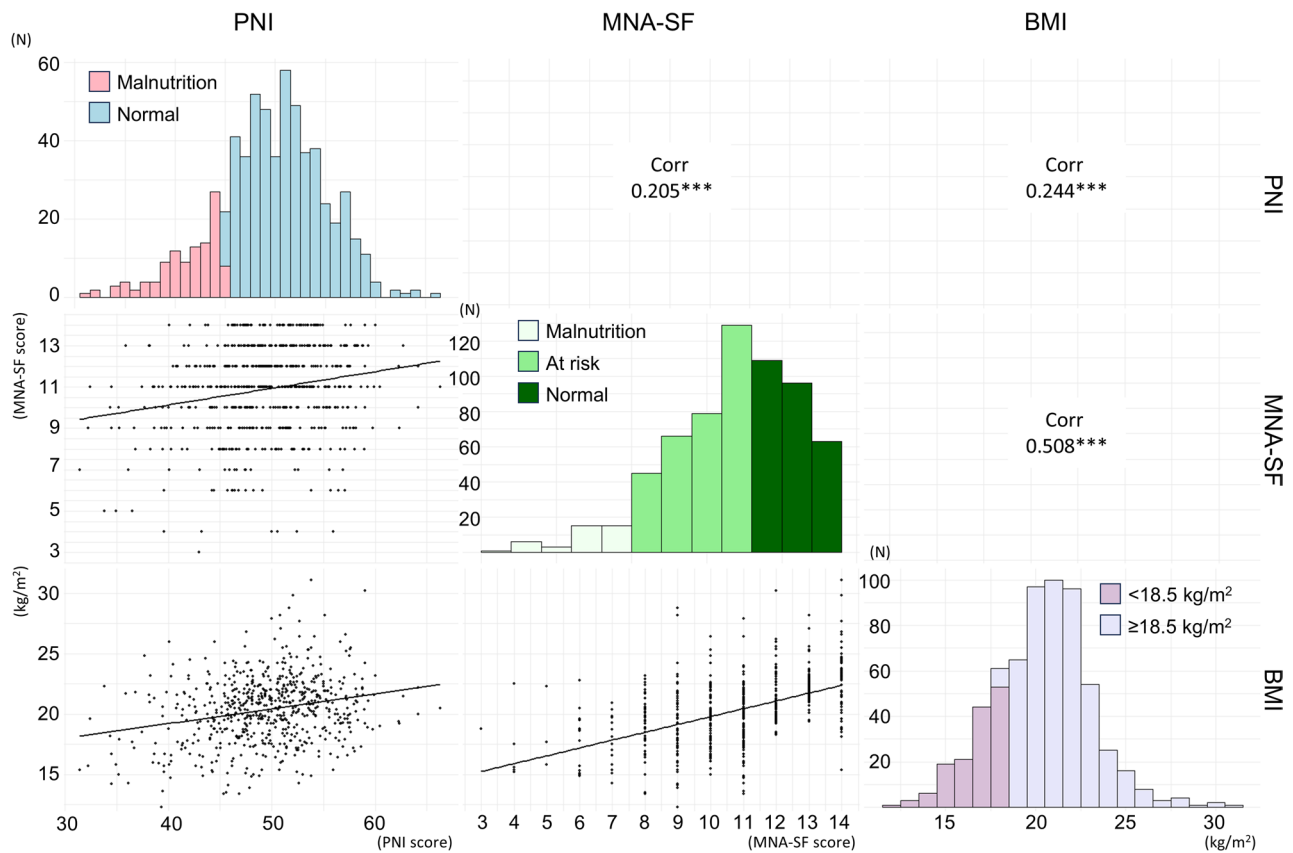


Fig. 2 Distribution and correlation of baseline nutritional indices. Pairwise scatter plots and histograms depicting the relationships among PNI, MNA-SF, and BMI. The upper triangle displays Pearson correlation coefficients between the indices, with asterisks denoting statistical significance (***) $p < 0.001$). Histograms along the diagonal show the distributions of each index, stratified by corresponding nutritional risk categories: PNI-defined malnutrition (score < 45 ; pink) and normal (score ≥ 45 ; blue); MNA-defined malnutrition (score ≤ 7 , light green), at-risk (score 8–11; green), and normal (score 12–14; dark green); and BMI $< 18.5 \text{ kg/m}^2$ (purple) versus $\geq 18.5 \text{ kg/m}^2$ (lavender). Scatter plots in the lower triangle visualise the linear associations between each pair of indices, with fitted regression lines overlaid. Abbreviations: PNI, Prognostic Nutritional Index; MNA-SF, Mini Nutritional Assessment Short Form; BMI, body mass index; Corr, correlation

Nutritional status and HRQOL and related factors

Table 2 summarises the comparisons of HRQOL and associated factors according to nutritional status in patients with NTM-PD. Patients categorised as malnourished according to the PNI exhibited significantly higher frequencies of symptoms, including cough (68.8% vs. 57.3%, $P = 0.033$), dyspnoea (29.5% vs. 10.3%, $P < 0.001$), and weight loss (22.3% vs. 10.3%, $P < 0.001$). These individuals also demonstrated lower QOL-B scores across multiple domains, including physical functioning (53.6 ± 29.9 vs. 67.9 ± 22.6 , $P < 0.001$), role functioning (65.2 ± 24.0 vs. 76.8 ± 19.4 , $P < 0.001$), vitality (47.6 ± 23.4 vs. 53.7 ± 20.9 , $P = 0.012$), treatment burden (59.5 ± 29.0 vs. 67.6 ± 26.0 , $P = 0.018$), health perception (30.2 ± 22.7 vs. 36.8 ± 22.5 , $P = 0.006$), and respiratory symptoms (70.9 ± 17.0 vs. 80.0 ± 16.0 , $P < 0.001$). Moreover, these patients had shorter 6MWT distances (428.1 ± 102.9 vs. $496.7 \pm 88.4 \text{ m}$, $P < 0.001$) and significantly lower physical activity levels, as assessed by the IPAQ-SF ($P < 0.001$) (Table 2).

Similarly, patients with poorer nutritional status based on the MNA-SF reported more frequent respiratory symptoms, lower QOL-B scores across multiple domains, and shorter 6MWT distances (Additional file, Table S3).

Spirometry results, body composition metrics, and handgrip strength were further analysed and stratified by sex (Additional file, Table S4). Poor nutritional status, as defined by the PNI, was associated with reduced forced vital capacity ($67.4 \pm 16.0\%$ predicted vs. $82.3 \pm 15.5\%$ predicted, $P < 0.001$ in males; $80.4 \pm 20.8\%$ predicted vs. $88.8 \pm 45.0\%$ predicted, $P = 0.026$ in females), forced expiratory volume in 1 s ($73.8 \pm 20.8\%$ predicted vs. $87.9 \pm 17.9\%$ predicted, $P < 0.001$ in males), and diffusing capacity of carbon monoxide ($68.8 \pm 22.5\%$ predicted vs. $88.0 \pm 20.0\%$ predicted, $P < 0.001$ in males; $71.1 \pm 18.6\%$ predicted vs. $83.3 \pm 15.9\%$ predicted, $P < 0.001$ in females). Body composition also varied significantly according to nutritional status. Sarcopenia was more prevalent among PNI-defined malnourished group (31.9% vs. 8.3% in males, $P < 0.001$; 35.2% vs. 15.2% in females, $P = 0.001$).

Table 2 Health-related quality of life and associated factors by PNI at treatment initiation (Baseline analysis group)

	Total (N=627)	PNI-defined normal nutrition (n=515)	PNI-defined malnutrition (n=112)	P-value
Symptom				
Cough	372 (59.3)	295 (57.3)	77 (68.8)	0.033
Sputum	430 (68.6)	348 (67.6)	82 (73.2)	0.292
Haemop- tysis	130 (20.7)	102 (19.8)	28 (25.0)	0.271
Dyspnoea, mMRC ≥ 2	86 (13.7)	53 (10.3)	33 (29.5)	< 0.001
Weight loss > 10% in the past 1 yr	78 (12.4)	53 (10.3)	25 (22.3)	< 0.001
QOL-B				
Physical functioning	65.3 ± 24.6	67.9 ± 22.6	53.6 ± 29.9	< 0.001
Role functioning	74.7 ± 20.7	76.8 ± 19.4	65.2 ± 24.0	< 0.001
Vitality	52.6 ± 21.5	53.7 ± 20.9	47.6 ± 23.4	0.012
Emotional functioning	76.1 ± 22.2	76.0 ± 22.0	76.5 ± 23.0	0.850
Social functioning	70.0 ± 24.4	70.6 ± 24.0	67.1 ± 26.0	0.189
Treatment burden (n=415)	65.8 ± 26.9	67.6 ± 26.0	59.5 ± 29.0	0.018
Health perception	35.6 ± 22.7	36.8 ± 22.5	30.2 ± 22.7	0.006
Respirato- ry symptoms	78.4 ± 16.6	80.0 ± 16.0	70.9 ± 17.0	< 0.001
Physical activity (n=602)				
IPAQ_MET, min/week	1963.0 ± 2607.5	2044.6 ± 2578.1	1601.7 ± 2716.6	0.121
IPAQ, Kcal	1751.3 ± 2442.0	1854.9 ± 2504.7	1292.8 ± 2091.7	0.015
IPAQ category				< 0.001*
High	110 (18.3)	96 (19.5)	14 (12.7)	
Moderate	316 (52.5)	269 (54.7)	47 (42.7)	
Low	176 (29.2)	127 (25.8)	49 (44.5)	
6-minute walking distance, m	485.5 ± 94.3	496.7 ± 88.4	428.1 ± 102.9	< 0.001

Data are presented as numbers (%) or mean ± SD. P-values were calculated using Student's t-test or χ^2 test, unless otherwise indicated

Abbreviations: MET, metabolic equivalent of task; mMRC, modified Medical Research Council dyspnoea scale

*P-value from the Cochran–Armitage Trend Test

Similarly, the MNA-defined at-risk and malnutrition groups had comparable results (Additional file, Table S5).

Regression analyses

Multivariable regression analyses were conducted to examine the associations between nutritional status, HRQOL, and relevant clinical parameters, adjusting for potential confounding variables.

At baseline, patients with PNI-defined malnutrition had higher odds of dyspnoea (adjusted odds ratio [95% confidence interval]: 2.37 [1.34 to 4.11]), smear positivity (2.26 [1.44 to 3.57]), and cavitory lesion (2.03 [1.25 to 3.37]) compared with those in the well-nourished group. Likewise, individuals classified as at risk or malnourished according to the MNA-SF showed progressively higher odds of dyspnoea (at risk: 3.71 [1.93 to 7.51]; malnutrition: 5.75 [2.12 to 15.54]) compared with those in the well-nourished group (Table 3).

Patients in the PNI-defined malnutrition group had lower baseline QOL-B scores than those in the normal nutrition group: physical functioning ($\beta = -10.6$, $P < 0.001$), role functioning ($\beta = -7.4$, $P < 0.001$), treatment burden ($\beta = -9.8$, $P = 0.005$), and respiratory symptoms ($\beta = -8.0$, $P < 0.001$). Moreover, this group demonstrated higher disease severity, as indicated by higher BACES scores ($\beta = 0.9$, $P < 0.001$) and shorter 6MWT distance ($\beta = -42.1$ m, $P < 0.001$). When the ACES score was used instead of the original BACES score, the association between poor nutritional status and disease severity remained consistent ($\beta = 0.6$, $P < 0.001$), indicating that these relationships were not solely driven by BMI. Similar trends were observed in the MNA-defined at-risk and malnutrition groups (Table 4).

Changes in HRQOL after 6 months

At 6 months after therapy, QOL-B scores were available for 457 participants (longitudinal analysis group, Fig. 1). While the patients in this sub-cohort were slightly younger and had lower BACES scores than those in the remainder of the cohort, the baseline nutritional profile—our primary exposure of interest—remained consistent between the two groups (Additional file, Table S6).

Table S7 presents the number of patients achieving clinically meaningful improvement in QOL-B scores at 6 months. Patients in the PNI-defined malnutrition group had lower odds of achieving a clinically meaningful improvement in the QOL-B respiratory symptoms domain (0.44 [0.22 to 0.87]) (Table 5). Similarly, patients in the MNA-defined malnutrition group had lower odds of improvement across multiple QOL-B domains, including physical functioning (0.32 [0.10 to 0.94]), role functioning (0.22 [0.06 to 0.70]), vitality (0.25 [0.09 to 0.69]), and emotional functioning (0.33 [0.11 to 0.96]).

Treatment outcomes at 1 year

At 1 year, follow-up data were available for 362 patients. Among them, 243 were still receiving treatment, and 119 had either completed or halted therapy, comprising the treatment outcome analysis group (Fig. 1). While this sub-cohort had a lower proportion of patients with BMI < 18.5 kg/m² than did the remainder of the cohort (n = 508), no significant differences were observed in the

Table 3 Association between nutritional status and baseline symptoms and disease severity (Baseline analysis group)

Dependent variables	PNI-defined malnutrition		MNA-defined at-risk		MNA-defined malnutrition	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Cough	1.52 (0.95 to 2.45)	0.084	1.34 (0.91 to 1.97)	0.139	1.88 (0.87 to 4.26)	0.118
Sputum	1.16 (0.72 to 1.92)	0.550	1.16 (0.77 to 1.74)	0.479	0.96 (0.44 to 1.16)	0.916
Haemoptysis	1.26 (0.73 to 2.13)	0.392	1.03 (0.63 to 1.67)	0.910	1.57 (0.67 to 3.60)	0.289
Dyspnoea, mMRC \geq 2	2.37 (1.34 to 4.11)	0.003	3.71 (1.93 to 7.51)	<0.001	5.75 (2.12 to 15.54)	0.001
Weight loss > 10% in the past 1yr	1.35 (0.73 to 2.44)	0.329	2.58 (1.28 to 5.46)	0.010	12.09 (4.63 to 32.64)	< 0.001
Sputum AFB smear positivity	2.26 (1.44 to 3.57)	< 0.001	1.22 (0.82 to 1.81)	0.331	1.35 (0.62 to 2.88)	0.440
Presence of cavity	2.03 (1.25 to 3.37)	0.005	1.12 (0.77 to 1.64)	0.552	1.48 (0.68 to 3.41)	0.332

Data are presented as odds ratios (95% confidence interval)

Models were calculated using the well-nourished group as the reference and adjusted for age, sex, BMI, smoking status, history of tuberculosis, and respiratory comorbidity

Abbreviations: mMRC Modified Medical Research Council dyspnoea score, NA Not available

prevalence of malnutrition as defined by PNI or MNA-SF (Additional file, Table S8).

Of the 119 patients in the treatment outcome analysis group, 45 (37.8%) discontinued treatment prematurely within 1 year (Additional file, Table S9). Regarding microbiological outcomes, sputum culture conversion data were available for 118 patients; of these, 62 (52.5%) achieved successful conversion. Multivariable regression analyses revealed that sputum culture conversion rates did not significantly differ by nutritional status. However, the odds of premature treatment discontinuation within 1 year were significantly higher in the MNA-defined malnutrition group (OR 26.41; [2.82 to 633.89]), although the 95% confidence interval was wide (Additional file, Table S10).

Sensitivity analyses

Overall, the results of sensitivity analyses were consistent with the primary findings. The direction and magnitude of associations between poor nutritional status and clinical characteristics remained similar across models when the ACES scores were used instead of the BACES scores, chronic comorbidities were excluded, and analysis was restricted to patients who were treatment-naïve. Analyses using alternative PNI thresholds (< 45, < 40, and < 38) also yielded comparable results, although smaller subgroup sizes led to wider confidence intervals. Detailed results are provided in the Additional files, Table S11–S13.

Discussion

This study primarily focused on the baseline association between nutritional status and clinical characteristics in the NTM-KOREA cohort, while providing preliminary longitudinal data at 6 and 12 months as exploratory assessments. We observed a substantial burden of malnutrition among patients with NTM-PD, with nutritional status closely linked to multiple dimensions of the disease, including symptom burden, disease severity, physical function, and HRQOL. Notably, suboptimal baseline

nutritional status was associated with a lower likelihood of achieving clinically meaningful improvement in QOL-B domain scores after 6 months of antibiotic therapy. Furthermore, it was associated with an increased risk of premature treatment discontinuation within 1 year. Collectively, these findings highlight the critical importance of nutritional assessment in NTM-PD management and highlight its potential as a modifiable factor influencing treatment outcomes.

The clinical significance of nutritional status in respiratory diseases is increasingly recognised. In chronic obstructive pulmonary disease, nutritional status influences not only disease onset but also its progression and prognosis, highlighting the importance of phenotype-specific, individualised interventions [35]. In bronchiectasis, immunonutrients—particularly vitamin D and zinc—may contribute to immune modulation and reduce susceptibility to infection [36]. Tuberculosis is both a cause and a consequence of malnutrition, which impairs treatment responsiveness and highlights the necessity for systematic nutritional support [37]. Comparable associations have been observed in NTM-PD, where malnutrition has been associated with increased disease severity and worse clinical outcomes [5–9]. In our nationwide cohort, a substantial proportion of participants were identified as being at risk of malnutrition or already malnourished. Given the demonstrated associations with disease severity and treatment response, routine nutritional assessment should be considered an integral component of NTM-PD management.

Various tools have been employed to evaluate nutritional status in patients with NTM-PD. BMI is a simple and widely used indicator; however, it lacks sensitivity and fails to reflect the metabolic or immunological dimensions of malnutrition [38]. In contrast, the PNI and MNA-SF offer more comprehensive evaluations. PNI, which is calculated from routine laboratory parameters, has been associated with various clinical outcomes in

Table 4 Association between nutritional status and QOL-B, BACES score, and 6MWT distance at treatment initiation (Baseline analysis group)

Dependent variables	PNI-defined malnutrition		MNA-defined at-risk		MNA-defined malnutrition	
	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value
QOL-B						
Physical functioning	-10.6 (-15.8 to -5.5)	< 0.001	-8.9 (-13.2 to -4.6)	< 0.001	-20.5 (-28.9 to -12.1)	< 0.001
Role functioning	-7.4 (-11.7 to -3.1)	< 0.001	-9.2 (-12.7 to -5.6)	< 0.001	-19.3 (-26.3 to -12.3)	< 0.001
Vitality	-4.3 (-8.9 to 0.4)	0.071	-9.1 (-12.9 to -5.3)	< 0.001	-19.8 (-27.3 to -12.3)	< 0.001
Emotional functioning	0.3 (-4.4 to 5.0)	0.903	-7.0 (-10.9 to -3.1)	< 0.001	-17.8 (-25.5 to -10.2)	< 0.001
Social functioning	-3.7 (-9.0 to 1.6)	0.170	-8.3 (-12.7 to -3.9)	< 0.001	-13.8 (-22.5 to -5.2)	0.002
Treatment burden (n = 415)	-9.8 (-16.5 to -3.0)	0.005	-6.0 (-12.0 to 0.1)	0.055	-14.0 (-26.1 to -2.0)	0.023
Health perception	-4.8 (-9.6 to 0.1)	0.055	-11.0 (-15.0 to -7.0)	< 0.001	-19.4 (-27.2 to -11.5)	< 0.001
Respiratory symptoms	-8.0 (-11.5 to -4.5)	< 0.001	-7.8 (-10.7 to -4.9)	< 0.001	-19.1 (-24.7 to -13.4)	< 0.001
BACES score*	0.9 (0.7 to 1.1)	< 0.001	0.6 (0.4 to 0.8)	< 0.001	1.0 (0.6 to 1.3)	< 0.001
6 min walking distance, m	-42.1 (-61.9 to -22.3)	< 0.001	-13.5 (-29.7 to 2.7)	0.104	-58.8 (-91.8 to -25.9)	< 0.001

Models were calculated using the well-nourished group as the reference and were adjusted for age, sex, BMI, smoking status, and history of tuberculosis and bronchiectasis, unless otherwise indicated

*Adjusted for smoking status, history of tuberculosis, and bronchiectasis; age, BMI, and sex were excluded due to collinearity with the BACES score

patients with NTM-PD [5, 6]. Similarly, the MNA-SF has demonstrated utility in identifying individuals at nutritional risk and in predicting disease severity [26]. Our findings further corroborate the clinical value of these indices, as they showed correlations with BMI and various clinical parameters.

The PNI was calculated using serum albumin levels and lymphocyte counts. Hypoalbuminemia is indicative of malnutrition; however, it may also signify a state of pronounced systemic inflammation [8]. Inflammatory conditions suppress appetite, reduce energy intake, and impair protein metabolism, thereby exacerbating nutritional deterioration. As a marker of catabolic stress, serum albumin has been consistently associated with adverse clinical outcomes [39]. Similarly, lymphopenia serves as an indicator of both compromised nutritional status and immune dysfunction. Malnutrition interferes with apoptotic regulation and immune homeostasis, while reduced lymphocyte counts compromise antibody production and cytokine signalling [40, 41]. Such immune dysregulation may contribute to the poor prognosis observed in malnourished individuals.

Sarcopenia, a known determinant of HRQOL, may mediate the association between poor nutritional status and functional impairment. Takayama et al. [7] reported that diminished skeletal muscle mass and lower concentrations of nutritional biomarkers were independently associated with greater disease severity in female patients with NTM-PD. In our cohort, sarcopenia was more prevalent among malnourished individuals than among the well-nourished group, with observed rates exceeding national prevalence estimates for all age and sex categories in South Korea (13.1–14.9% in males aged ≥ 65 years, 11.4% in females aged ≥ 65 years, and 13.4% in females aged 50–64 years) [42, 43]. This elevated prevalence may partially account for the differences in physical performance observed between groups: patients with malnourishment exhibited significantly shorter 6MWT distances than did their well-nourished counterparts. A validated minimal clinically important difference for 6MWT has not been established in NTM-PD; however, prior studies have proposed clinically meaningful thresholds of 22.3–24.5 m in bronchiectasis and 30 m in chronic obstructive pulmonary disease [44, 45]. These reference values support the clinical significance of the intergroup differences observed in our study. Taken together, these findings suggest that malnutrition-related muscle loss may contribute to both impaired physical function and reduced HRQOL, highlighting the importance of timely nutritional and functional assessments in clinical care.

Interestingly, prior findings from the NTM-KOREA cohort indicated that patients presenting with more severe baseline respiratory symptoms tended to experience greater symptomatic improvement following treatment [14]. However, this pattern was not observed

Table 5 Association between nutritional status and clinically meaningful improvement in QOL-B scores after 6-month antibiotic therapy (Longitudinal analysis group, $n = 457$)

QOL-B domains	PNI-defined malnutrition		MNA-defined at-risk		MNA-defined malnutrition	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Physical functioning (MCID=8)	0.64 (0.31 to 1.24)	0.198	0.65 (0.38 to 1.11)	0.116	0.32 (0.10 to 0.94)	0.045
Role functioning (MCID=8)	0.61 (0.30 to 1.21)	0.167	0.55 (0.30 to 0.93)	0.029	0.22 (0.06 to 0.70)	0.014
Vitality (MCID=10)	0.66 (0.34 to 1.22)	0.190	0.56 (0.33 to 0.92)	0.024	0.25 (0.09 to 0.69)	0.008
Emotional functioning (MCID=7)	0.65 (0.33 to 1.26)	0.210	0.70 (0.40 to 1.19)	0.188	0.33 (0.11 to 0.96)	0.046
Social functioning (MCID=9)	0.81 (0.39 to 1.63)	0.566	0.82 (0.47 to 1.44)	0.495	0.76 (0.24 to 2.22)	0.621
Treatment burden (MCID=9) ($n = 288$)	0.41 (0.18 to 0.90)	0.029	0.69 (0.35 to 1.34)	0.270	0.97 (0.24 to 3.78)	0.968
Health perception (MCID=8)	0.76 (0.42 to 1.36)	0.357	0.86 (0.53 to 1.40)	0.553	0.62 (0.24 to 1.58)	0.314
Respiratory symptoms (MCID=8)	0.44 (0.22 to 0.87)	0.020	1.00 (0.57 to 1.76)	0.991	0.47 (0.15 to 1.39)	0.183

Data are presented as odds ratios with 95% confidence intervals. Models were adjusted for age, sex, BMI, smoking status, history of tuberculosis, bronchiectasis, and baseline QOL-B score, using the well-nourished group as the reference

Abbreviation: MCID Minimal clinically important difference

among malnourished individuals in the present study, suggesting that poor nutritional status may attenuate treatment responsiveness, even in those with a substantial symptom burden.

Our study possesses several strengths. This was a large-scale, multi-centre study with longitudinal data obtained through regular follow-up assessments, facilitating the evaluation of disease trajectory and treatment outcomes across the course of therapy. The study findings may be generalised to the broader population of patients with NTM-PD in the country because the study enrolled patients from eight major university hospitals across South Korea.

Some limitations must be acknowledged. First, as an observational study, our findings cannot establish causality. Although more advanced or prolonged NTM-PD could have contributed to poorer nutritional status, sensitivity analyses restricted to treatment-naïve patients yielded consistent results, suggesting that disease chronicity alone does not fully explain the observed associations. Second, outcome-related analyses—particularly those involving culture conversion and premature treatment discontinuation—were limited by the small number of eligible participants in the treatment outcome analysis group ($n = 119$), resulting in wide confidence intervals. Notably, none of the participants in the MNA-defined malnutrition group ($n = 6$) achieved culture conversion, precluding further statistical analysis. These results should be interpreted as exploratory and preliminary, and larger samples with longer follow-up are required to validate these findings. Third, in the absence of validated gold standards for interpreting disease indicators in NTM-PD—such as 6MWT performance—we referenced comparative thresholds from other pulmonary conditions. Finally, although both the PNI and MNA-SF showed reasonable correlations with BMI and clinical outcomes,

a universally accepted definition of malnutrition in NTM-PD is still lacking. The PNI may be influenced by factors, such as immune dysfunction or systemic inflammation, other than nutritional status, potentially limiting its accuracy in reflecting the true impact of malnutrition on treatment outcomes. To address this limitation, we included the MNA-SF as a complementary assessment tool. Although originally validated for geriatric populations, its applicability has been supported in younger adults as well, albeit with some limitations in precision [46–48]. Discrepancies between the two instruments—whereby some patients classified as malnourished by PNI fell within the normal range of nutritional status according to MNA-SF, and vice versa—highlight the variability among screening methods and the urgent need for further validation in the context of NTM-PD.

Conclusions

In the overall cohort, baseline nutritional status assessed by PNI and MNA-SF was associated with disease severity, symptom burden, physical function, and HRQOL. Furthermore, exploratory sub-group analyses suggested that malnutrition may influence 6-month symptomatic improvement and 1-year treatment outcome. These findings highlight the potential value of integrating routine nutritional assessments into clinical care and underscore the need for further research to confirm the impact of nutritional interventions on long-term outcomes.

Abbreviations

NTM	Nontuberculous mycobacteria
PD	Pulmonary disease
HRQOL	Health-related quality of life
BMI	Body mass index
PNI	Prognostic Nutritional Index
MNA-SF	Mini Nutritional Assessment Short Form
QOL-B	Quality of Life Questionnaire–Bronchiectasis
IPAQ-SF	International Physical Activity Questionnaire–Short Form
6MWT	6-minute walking test

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12931-026-03579-5>.

Additional File 1. Table S1. Models of multi-frequency bioelectrical impedance analysis used in each institution. Table S2. Baseline characteristics by MNA at treatment initiation. Table S3. Health-related quality of life and associated factors by MNA at treatment initiation (Baseline analysis group). Table S4. Pulmonary function, body composition, and handgrip strength by PNI at treatment initiation (Baseline analysis group). Table S5. Pulmonary function, body composition, and handgrip strength by MNA at treatment initiation (Baseline analysis group). Table S6. Comparison of baseline characteristics between the longitudinal analysis group (n=457) and the remainder of the cohort (n=170). Table S7. Number of participants achieving clinically meaningful improvement in QOL-B after 6 months of antibiotic therapy (Longitudinal analysis group, n=457). Table S8. Comparison of baseline characteristics between the treatment outcome analysis group (n=119) and the remainder of the cohort (n=508). Table S9. Comparison of 1-year treatment outcomes according to baseline nutritional status (Treatment outcome analysis group, n=119). Table S10. Association between baseline nutritional status and 1-year treatment outcomes: multivariable logistic regression analysis (Treatment outcome analysis group, n=119). Table S11. Sensitivity analyses evaluating the impact of chronic comorbidities on the association between nutritional status and clinical characteristics (Baseline analysis group, n=627). Table S12. Sensitivity analyses comparing the associations between PNI-defined malnutrition and clinical characteristics across different cutoff values (PNI < 45, < 40, and < 38; Baseline analysis group, n=627). Table S13. Sensitivity analysis of associations between PNI-defined malnutrition and clinical parameters in the overall (n=627) and treatment-naïve (n= 418) cohorts.

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Authors' contributions

Study design: NK, J-JY, YP, YAK. Data acquisition: YP, YAK, HH, J-YK, H-JK, NK, BWJ, K-WJ, Y-SK, J-JY, DJ, TSS, JHL, JM, HS, JW, and GIL. Data management: YRK, JK, and NP. Formal analysis: SY and YP. Writing Draft: SY and YP. All authors read and approved the final manuscript.

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Data availability

De-identified clinical data can be shared with qualified researchers. Proposals for data usage will be reviewed by the NTM-KOREA Committee. Upon obtaining ethics approval, data can be shared through a secure online platform contingent on signing a data access agreement. Such proposals should be submitted to Jae-Joon Yim (yimjj@snu.ac.kr).

Declarations

Ethics approval and consent to participate

The study protocol was approved by the institutional review boards of all participating institutions prior to participant enrolment:

- Seoul National University Hospital (IRB No. H-1903-021-1015, approved on March 19, 2019)
- Pusan National University Hospital (IRB No. 1911-005-084, approved on November 14, 2019)
- Samsung Medical Center (IRB No. SMC 2019-06-030, approved on June 13, 2019)
- Asan Medical Center (IRB No. 2019-0638, approved on May 9, 2019)
- Severance Hospital, Yonsei University College of Medicine (IRB No. 4-2019-0297, approved on May 20, 2019)

- Pusan National University Yangsan Hospital (IRB No. 05-2019-081, approved on May 22, 2019)
 - Chonnam National University Hospital (IRB No. CNUH-2019-179, approved on June 25, 2019)
 - Seoul National University Bundang Hospital (IRB No. B-2111-722-402, approved on November 3, 2021)
- Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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