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BACES score: a predictor of health-related quality of life and associated factors in patients with nontuberculous mycobacterial pulmonary disease

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The evaluation of health-related quality of life (HRQOL) is gaining importance among patients with nontuberculous mycobacterial pulmonary disease (NTM-PD). We assessed whether the BACES score reflects HRQOL and associated factors in these patients. Data were collected from the nationwide NTM-KOREA prospective cohort of patients with NTM-PD who started antibiotic treatment and included symptoms, Quality of Life–Bronchiectasis (QOL-B) questionnaire, nutritional status using the Mini Nutritional Assessment–Short Form (MNA-SF) and Prognostic Nutritional Index (PNI), physical activity, body composition, spirometry, handgrip strength, and 6-min walking distance. Multivariate linear and logistic regressions were used for analysis. As the BACES score increased, so did the odds (adjusted odds ratio [95% confidence interval]) of cough (1.24 [1.04–1.48]), dyspnea (1.69 [1.28–2.27]), weight loss (1.78 [1.36–2.36]), and malnutrition, defined as MNA-SF score ≤ 7 (1.71 [1.21–2.45]), and PNI < 45 (2.14 [1.66–2.81]). The QOL-B respiratory symptom score (estimate: −2.259, $P = 0.002$) and 6-min walking distance (estimate: −18.015, $P < 0.001$) were negatively associated with the BACES score. Moreover, the odds of adipopenia (1.08 [1.03–1.13]), possible sarcopenia (1.80 [1.35–2.45]), and sarcopenia (2.09 [1.48–3.03]) increased in women. The BACES score can estimate HRQOL and associated conditions at antimicrobial treatment initiation in patients with NTM-PD.

Keywords Nontuberculous mycobacteria, Nutritional status, Physical activity, Quality of life, Sarcopenia

Abbreviations

aOR	Adjusted odds ratio
ASMI	Appendicular skeletal muscle index
CI	Confidence interval
HRQOL	Health-related quality of life
MNA-SF	Mini Nutritional Assessment–Short Form
PNI	Prognostic nutritional index

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Nontuberculous mycobacteria (NTM) are ubiquitous organisms prevalent in natural, household, and hospital environments[1]. NTM can cause chronic infections that manifest as pulmonary disease (PD), lymphadenitis, and disseminated disease in humans[2]. In recent decades, the global burden of NTM-PD has been increasing, including that in South Korea, where the annual prevalence rate has increased five-fold between 2010 and 2021[3].

From diagnosis to treatment, NTM-PD often presents challenges to clinicians. Diagnosis of NTM-PD requires fulfillment of clinical, radiological, and microbiological criteria[4]. After diagnosis, current guidelines recommend 'watchful waiting' in some cases rather than immediate treatment because the pathogenicity of NTM significantly varies[4]. Once treatment is initiated, ≥ 12 months of treatment post-culture conversion with a combination of multiple antibiotics is recommended. A longer treatment period could result in better treatment outcomes[5]; however, it is often accompanied by high rates of adverse drug reactions, aggravating burdens for patients and practitioners[6]. Moreover, favorable microbiological outcomes do not guarantee symptom improvement[7].

Consequently, integrated management strategies that extend beyond antibiotic therapy, including the assessment and enhancement of health-related quality of life (HRQOL), have been emphasized in the management of NTM-PD[8,9]. Further, the United States Food and Drug Administration recently determined patient-reported outcomes, which measure symptoms and HRQOL, as an alternative primary endpoint in treating NTM-PD, alongside the microbiological response[10]. The BACES score is a recently developed clinical severity index for NTM-PD that incorporates five baseline factors: body mass index (BMI), age, presence of cavity on imaging, erythrocyte sedimentation rate, and sex[11]. A higher BACES score can reflect more severe symptoms, impaired lung function, faster disease progression, and poorer treatment response in patients with NTM-PD[12–15]. In this study, we aimed to evaluate whether the BACES score at the initiation of antibiotic treatment can also reflect HRQOL and associated factors in patients with NTM-PD.

Results

Baseline characteristics

Between February 28, 2022, and August 23, 2023, 419 individuals consented to participating in the current study. We used the data of 409, excluding 10 with missing baseline BACES score information. Table 1 presents the baseline characteristics of the study population. The median age was 64.0 (interquartile range, 58.0–71.0) years, and 27.6% were men. *M. avium* complex was the dominant causative species (80.0%), and 75% of participants had the nodular bronchiectatic type. According to the BACES severity classification, the mild group (score: 0–1) comprised 28.3% ($n = 116$) of the study population, with the moderate group (score: 2–3) accounting for 56.9% ($n = 233$) and the severe group (score: 4–5) for 14.7% ($n = 60$).

BACES severity and HRQOL

Table 2 compares HRQOL and associated factors according to BACES severity in participants with NTM-PD. As BACES severity increased, symptoms of cough, dyspnea, and weight loss became more common. The Quality of Life–Bronchiectasis (QOL-B) score was lower in the physical functioning, role functioning, vitality, health perception, and respiratory symptom domains, while malnourishment, as defined using the Mini Nutritional Assessment–Short Form (MNA-SF) score and Prognostic Nutritional Index (PNI), was higher, in addition to a shorter 6-min walking distance (6MWD) (all $P < 0.05$). The size of these gaps was clinically meaningful for QOL-B domains, with differences between the mild and severe BACES groups far exceeding the minimal clinically important differences (MCIDs): physical functioning (8), role functioning (8), vitality (10), and health perception (8)[16]. The 6MWD also differed by ~ 60 m, well above MCID values reported for bronchiectasis (22–25 m)[17] and chronic obstructive pulmonary disease (30 m)[18].

After comparing spirometry measurements, body composition, and handgrip strength, we subdivided the study population according to sex in order to account for known sex-based differences in these parameters and the diagnostic cutoffs for sarcopenia and adipopenia (Table 3)[19,20]. As BACES severity increased, forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) were lower in both sexes, while the diffusing capacity of carbon monoxide (DL_{CO}) was lower in men (all $P < 0.05$). Body composition differed according to BACES severity, and the proportions of patients with adipopenia, possible sarcopenia, and sarcopenia were higher as BACES severity increased (all $P < 0.05$).

Regression analyses

We performed univariate and multivariate regression analyses to investigate relationships between the BACES score, and HRQOL and associated factors. After adjusting for confounding variables, the BACES score was

	Total ($n=409$)	Mild ($n=116$)	Moderate ($n=233$)	Severe ($n=60$)	P-value[a]
Age, years	64.0 [58.0; 71.0]	59.0 [54.0; 63.0]	65.0 [59.0; 71.0]	72.0 [66.5; 76.5]	< 0.001[b,c,d]
Men	113 (27.6)	5 (4.3)	64 (27.5)	44 (73.3)	< 0.001
BMI, kg/m^2	20.5 [18.7; 22.0]	21.1 [19.9; 22.2]	20.8 [18.9; 22.1]	17.6 [15.8; 19.8]	< 0.001[c,d]
Never smoker	320 (78.2)	109 (94.0)	183 (78.5)	28 (46.7)	< 0.001
Previous treatment history of tuberculosis	119 (28.6)	26 (22.4)	66 (28.3)	26 (43.3)	0.005
Previous treatment history of NTM	141 (34.5)	43 (37.1)	73 (31.3)	25 (41.7)	0.832
Respiratory comorbidities	264 (64.5)	84 (72.4)	145 (62.2)	35 (58.3)	0.038
Bronchiectasis	234 (57.2)	80 (69.0)	129 (55.4)	25 (41.7)	< 0.001
COPD	18 (4.4)	4 (3.4)	8 (3.4)	6 (10.0)	0.093
Asthma	12 (2.9)	4 (3.4)	7 (3.0)	1 (1.7)	0.535
Interstitial lung disease	8 (2.0)	1 (0.9)	6 (2.6)	1 (1.7)	0.542
Chronic pulmonary aspergillosis	8 (2.0)	0 (0.0)	3 (1.3)	5 (8.3)	< 0.001
Lung cancer	15 (3.7)	4 (3.4)	8 (3.4)	3 (5.0)	0.666
Mycobacterium species					0.064[e]
M. avium	137 (33.5)	39 (33.6)	85 (36.5)	13 (21.7)	
M. intracellulare	190 (46.5)	48 (41.4)	109 (46.8)	33 (55.0)	
M. abscessus subsp. *abscessus*	45 (11.0)	16 (13.8)	24 (10.3)	5 (8.3)	
M. abscessus subsp. *massiliense*	33 (8.1)	13 (11.2)	13 (5.6)	7 (11.7)	
M. kansasii	4 (1.0)	0 (0.0)	2 (0.9)	2 (3.3)	
AFB smear positive	163 (39.9)	39 (33.6)	90 (38.6)	34 (56.7)	0.006
Presence of cavity	247 (59.8)	29 (25.0)	158 (67.8)	57 (95.0)	< 0.001
Radiologic type ($n=408$)					< 0.001[e]
Fibrocavitary	66 (16.2)	2 (1.7)	30 (12.9)	34 (57.6)	
Nodular bronchiectatic	306 (75.0)	106 (91.4)	182 (78.1)	18 (30.5)	
Unclassified	36 (8.8)	8 (6.9)	21 (9.0)	7 (11.9)	

Table 1. Baseline characteristics at treatment initiation according to BACES severity in patients with NTM-PD. Data are presented as numbers (percentages) or medians [interquartile ranges]. AFB, acid-fast bacilli; BMI, body mass index; COPD, chronic obstructive pulmonary disease; NTM, nontuberculous mycobacteria; PD, pulmonary disease. [a]*P* for trend from the Cochran–Armitage trend test in categorical variables and *P*-values from the Kruskal–Wallis test in continuous variables, unless otherwise indicated. Statistically significant difference between [b]mild and moderate groups, [c]mild and severe groups, and [d]moderate and severe groups in post-hoc multiple comparison analysis. [e]*P*-values calculated using Fisher's exact test.

positively associated (adjusted odds ratio [95% confidence interval]) with cough (1.24 [1.04–1.48]), dyspnea (1.69 [1.28–2.27]), and weight loss (1.78 [1.36–2.36]) (Fig. 1). In the QOL-B questionnaire, the domains of physical functioning (estimate: −4.670, $P<0.001$), role functioning (estimate: −4.031, $P<0.001$), vitality (estimate: −2.564, $P=0.005$), health perception (estimate: −1.945, $P=0.044$), and respiratory symptoms (estimate: −2.259, $P=0.002$) were negatively associated with the BACES score (Table 4). The odds of malnutrition, as defined by the MNA-SF score (1.71 [1.21–2.45]) and PNI (2.14 [1.66–2.81]), also increased. The 6MWD was negatively associated (estimate: −18.015, $P<0.001$), although physical activity, measured using IPAQ-SF, did not correlate with the BACES score.

In men, the BACES score was negatively associated with FVC (estimate: −0.381, $P<0.001$), predicted percentage of FVC (estimate: −7.348, $P<0.001$), FEV_1 (estimate: −0.256, $P<0.001$), predicted percentage of FEV_1 (estimate: −5.534, $P=0.005$), and predicted percentage of DL_{CO} (estimate: −6.871, $P=0.004$) (Table 5). The BACES score was associated with adipopenia (1.15 [1.05–1.26]), but the odds of possible sarcopenia and sarcopenia were not significant.

In women, the BACES score was negatively associated with FVC (estimate: −0.174), predicted percentage of FVC (estimate: −3.598), and FEV_1 (estimate: −0.140) (all $P<0.001$). Adipopenia (1.08 [1.03–1.13]), reduced appendicular skeletal muscle index (ASMI; 1.52 [1.18–1.99]), handgrip strength (estimate: −1.145, $P<0.001$), possible sarcopenia (1.80 [1.35–2.45]), and sarcopenia (2.09 [1.48–3.03]) also correlated with the BACES score.

Discussion

In this study, the BACES score was related to HRQOL and associated clinical factors in patients with NTM-PD who initiated antibiotic treatment. The scoring system correlated with patients' symptoms, perceived well-being, malnutrition, body composition, lung function, 6MWD, and handgrip strength. The odds of adipopenia increased according to the BACES score in men and the odds of adipopenia and sarcopenia also increased according to the BACES score in women. Therefore, the BACES score can be used as a predictor for HRQOL and associated factors in patients with NTM-PD at the start of antibiotic treatment.

	Mild ($n=116$)	Moderate ($n=233$)	Severe ($n=60$)	P-value[a]
Initial symptom ($n=409$)				
Cough	61 (52.6)	142 (60.9)	44 (73.3)	0.008
Sputum	80 (69.0)	154 (66.1)	46 (76.7)	0.472
Hemoptysis	25 (21.6)	48 (20.6)	11 (18.3)	0.634
Dyspnea, mMRC ≥ 2	8 (6.9)	21 (9.0)	19 (31.7)	< 0.001
Weight loss, > 10% in 1 year	5 (4.3)	32 (13.7)	17 (28.3)	< 0.001
QOL-B ($n=406$)				
Physical functioning	73.3 [53.3; 86.7]	66.7 [53.3; 80.0]	50.0 [26.7; 73.3]	< 0.001[c,d]
Role functioning	86.7 [73.3; 93.3]	80.0 [60.0; 93.3]	66.7 [46.7; 80.0]	< 0.001[b,c,d]
Vitality	55.6 [44.4; 66.7]	55.6 [44.4; 66.7]	44.4 [33.3; 55.6]	0.006[c,d]
Emotional functioning	75.0 [62.5; 91.7]	83.3 [66.7; 100.0]	79.2 [66.7; 100.0]	0.321
Social functioning	75.0 [58.3; 91.7]	75.0 [55.6; 91.7]	70.8 [50.0; 95.8]	0.500
Treatment burden ($n=286$)	66.7 [50.0; 88.9]	66.7 [55.6; 88.9]	55.6 [33.3; 77.8]	0.063
Health perception	37.5 [25.0; 58.3]	33.3 [25.0; 50.0]	25.0 [16.7; 41.7]	0.017[c,d]
Respiratory symptoms	81.5 [74.1; 92.6]	81.5 [70.4; 92.6]	74.1 [63.0; 85.2]	0.001[c,d]
Nutritional status				
MNA-SF total score ($n=406$)	12.0 [10.5; 13.0]	11.0 [10.0; 12.0]	10.0 [8.5; 11.0]	< 0.001[b,c,d]
MNA-SF categories				0.007[e]
Normal nutritional status (12–14 points)	64 (55.2)	97 (42.2)	8 (13.3)	
At risk of malnutrition (8–11 points)	46 (39.7)	122 (53.0)	41 (68.3)	
Malnourished (≤ 7 points)	6 (5.2)	11 (4.8)	11 (18.3)	
PNI total score ($n=402$)	50.8 [47.3; 53.6]	50.3 [47.3;53.8]	44.1 [39.4;48.7]	< 0.001[c,d]
Malnutrition (PNI < 45)	12 (10.4)	28 (12.3)	34 (57.6)	< 0.001
Physical activity ($n=384$)				
IPAQ-SF MET-min/week	1268.5 [615.0; 1668.0]	1386.0 [594.0; 2244.0]	924.0 [297.0; 1746.0]	0.235
IPAQ-SF activity categories				0.156[f]
High	18 (16.7)	45 (20.6)	7 (12.1)	
Moderate	63 (58.3)	113 (51.8)	30 (51.7)	
Low	27 (25.0)	60 (27.5)	21 (36.2)	
6-min walking distance, m ($n=371$)	510.0 [450.0; 564.5]	504.5 [421.0; 550.0]	448.0 [405.0; 506.5]	< 0.001[c,d]

Table 2. Health-related quality of life and associated factors at treatment initiation according to BACES severity. Data are presented as numbers (percentages) or medians [interquartile ranges]. [a]*P* for trend from the Cochran–Armitage trend test in categorical variables and *P*-values from the Kruskal–Wallis test in continuous variables, unless otherwise indicated. Statistically significant difference between [b]mild and moderate groups, [c]mild and severe groups, and [d]moderate and severe groups in post-hoc multiple comparison analysis. [e]Cochran–Armitage trend test with the response variable categorized as 'normal nutritional status' and 'other'. [f]Cochran–Armitage trend test with the response variable categorized as 'Low' and 'other'. Abbreviations: IPAQ-SF, International Physical Activity Questionnaire–Short Form; MET, metabolic equivalent of task; mMRC, modified Medical Research Council scale; MNA-SF, Mini Nutritional Assessment–Short Form; PNI, Prognostic Nutritional Index; QOL-B, Quality of Life Questionnaire–Bronchiectasis.

HRQOL is a multifaceted concept in which biological and physiological variables, symptoms, functional status, and general health perceptions are closely integrated with individual and environmental characteristics[21]. As diverse clinical conditions can affect HRQOL along with sociodemographic factors[22,23], a holistic approach is required to measure HRQOL. The NTM-KOREA study comprehensively evaluated HRQOL and associated factors by incorporating symptom assessment, questionnaires, laboratory tests, and physical measurements.

Various generic or disease-specific tools have been developed to measure HRQOL[24]. For instance, St George's Respiratory Questionnaire, the Leicester Cough Questionnaire, and the QOL-B are widely used in bronchiectasis with good validity, internal reliability, and repeatability[25]. However, no standard instruments have been developed for NTM-PD. Recent studies have used the QOL-B, NTM Module, and Patient-Reported Outcomes Measurement Information System Fatigue 7a to measure HRQOL in patients with NTM-PD[26–28]. In this study, we used the QOL-B questionnaire to measure HRQOL in patients with NTM-PD. As the BACES score increased, HRQOL measured using the QOL-B was poorer in many domains including respiratory symptoms. Regarding HRQOL, malnutrition and sarcopenia are two important health conditions. Nutritional status plays a pivotal role in preserving and improving HRQOL in the aged population[29]. Nutritional status is known to affect the development and progression of NTM-PD[30]. We found a high proportion of patients being at risk of malnutrition even in the BACES mild group (score: 0–1), and the odds of malnutrition increased along with BACES score. Sarcopenia, i.e., decline in muscle mass and function, results in increased levels of dependency

	Men				Women			
	Mild ($n=5$)	Moderate ($n=64$)	Severe ($n=44$)	P-value[a]	Mild ($n=111$)	Moderate ($n=169$)	Severe ($n=16$)	P-value[a]
Spirometry ($n=367$)								
FVC, L	4.4 [3.8; 4.5]	3.5 [2.8; 4.1]	2.7 [2.2; 3.2]	<0.001[c, d]	2.8 [2.4; 3.1]	2.4 [2.1; 2.8]	1.9 [1.4; 2.3]	<0.001[b, c,d]
FVC, % predicted	89.0 [86.0; 94.0]	81.5 [70.0; 91.5]	68.0 [57.0; 82.0]	0.001[c, d]	90.0 [82.0; 97.0]	83.0 [74.0; 94.0]	73.0 [53.0; 86.0]	<0.001[b, c]
FEV_1, L	3.2 [2.8; 3.4]	2.7 [2.3; 3.1]	2.3 [1.7; 2.5]	<0.001[c, d]	2.1 [1.8; 2.4]	1.9 [1.5; 2.2]	1.7 [1.2; 1.7]	<0.001[b, c,d]
FEV_1, % predicted	87.0 [86.0; 89.0]	88.0 [77.5; 96.5]	82.0 [55.0; 94.0]	0.181	86.0 [78.0; 100.0]	84.0 [72.5; 97.5]	83.0 [61.0; 88.0]	0.131
FEV_1/FVC	73.0 [72.0; 74.0]	77.5 [72.5; 85.5]	79.0 [72.0; 87.0]	0.318	76.0 [71.0; 80.0]	77.0 [72.0; 80.5]	84.0 [74.0; 90.0]	0.024[c]
DL_{CO} ($n=317$)	93.5 [86.0; 111.0]	90.0 [77.5; 98.0]	73.0 [56.0;93.0]	0.015[c]	84.0 [73.0; 93.0]	83.0 [70.0; 93.0]	73.0 [55.0; 88.0]	0.507
BIA ($n=379$)								
Body fat, %	19.4 [18.7; 20.0]	21.0 [18.0; 25.9]	16.0 [10.9; 20.8]	0.001[d]	28.1 [24.4; 32.8]	27.3 [20.9; 32.1]	19.5 [10.7; 23.4]	<0.001[c, d]
Abdominal fat, %	0.9 [0.9; 0.9]	0.9 [0.8; 0.9]	0.8 [0.8; 0.8]	<0.001[d]	0.9 [0.8; 0.9]	0.8 [0.8; 0.9]	0.8 [0.8; 0.8]	0.001[b, c]
FMI, kg/m^2	4.6 [4.4; 4.9]	4.4 [3.7; 5.8]	2.7 [1.8; 4.5]	<0.001[d]	6.1 [5.1; 7.1]	5.7 [4.1; 7.2]	3.1 [2.1; 3.6]	<0.001[c, d]
Adipopenia	0 (0.0)	9 (14.5)	22 (61.1)	<0.001	24 (22.6)	57 (36.3)	13 (100.0)	<0.001
FFMI, kg/m^2	18.3 [18.2; 18.6]	16.8 [15.9; 17.5]	15.4 [14.1; 16.8]	0.001[c, d]	14.9 [14.2; 15.5]	14.5 [13.7; 15.2]	12.3 [11.3; 13.4]	<0.001[c, d]
Lean-to-fat ratio	0.2 [0.2; 0.3]	0.3 [0.2; 0.4]	0.2 [0.1; 0.3]	<0.001[d]	0.4 [0.3; 0.5]	0.4 [0.3; 0.5]	0.2 [0.2; 0.3]	<0.001[c, d]
SMI, kg/m^2	10.3 [10.2; 10.7]	9.2 [8.7; 9.7]	8.3 [7.5; 9.0]	<0.001[c, d]	7.9 [7.5; 8.3]	7.7 [7.2; 8.1]	6.4 [5.8; 6.7]	<0.001[b, c,d]
ASMI, kg/m^2	8.1 [8.0; 8.1]	7.2 [6.8; 7.7]	6.6 [5.9; 7.2]	0.001[c, d]	5.9 [5.5; 6.3]	5.7 [5.3; 6.1]	4.6 [4.4; 4.9]	<0.001[b, c,d]
Reduced ASMI	1 (20.0)	23 (37.1)	25 (69.4)	0.001	36 (34.3)	79 (50.3)	12 (85.7)	<0.001
Handgrip, kg ($n=403$)	45.0 [37.8; 46.0]	35.5 [30.0; 42.3]	30.0 [24.9; 36.0]	0.003[c, d]	23.1 [20.4; 26.0]	20.4 [17.6; 24.9]	16.6 [14.0; 20.2]	<0.001[b, c,d]
Possible sarcopenia	0 (0.0)	11 (17.7)	16 (39.0)	0.005	15 (13.6)	42 (25.8)	11 (68.8)	<0.001
Sarcopenia ($n=381$)	0 (0.0)	7 (11.3)	10 (27.8)	0.019	8 (7.6)	33 (21.3)	9 (64.3)	<0.001

Table 3. Pulmonary function, body composition, and handgrip strength at treatment initiation according to BACES severity. Data are presented as numbers (percentages) or medians [interquartile ranges]. Anthropometric data are calculated using the following definitions: lean-to-fat ratio, fat-free mass divided by fat mass; appendicular skeletal muscle index (ASMI), sum of skeletal muscle mass in the arms and legs divided by the square of height; fat mass index (FMI), total body fat mass divided by the square of height; fat-free mass index (FFMI), fat-free mass divided by the square of height; and skeletal muscle mass index (SMI), total body muscle mass divided by the square of height. BIA, bioelectrical impedance analysis; DL_{CO}, diffusing capacity for carbon monoxide; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity. [a]*P* for trend from the Cochran–Armitage trend test in categorical variables and *P*-values from the Kruskal–Wallis test in continuous variables, unless otherwise indicated. Statistically significant difference between [b]mild and moderate groups, [c]mild and severe groups, and [d]moderate and severe groups in post-hoc multiple comparison analysis after Kruskal–Wallis test.

and disability. Consequently, HRQOL in individuals with sarcopenia is markedly impaired compared with that in individuals without sarcopenia[31]. Sarcopenia can lead to several harmful health consequences including falls, fractures, hospitalization, and death. We found a considerable proportion of possible sarcopenia and sarcopenia cases in the BACES moderate (score: 2–3) and severe (score: 4–5) groups. Moreover, the odds of sarcopenia were positively associated with the BACES score in women. Taken together, our results suggest that the BACES score reflects HRQOL and associated clinical factors in patients with NTM-PD.

However, the BACES score alone may be limited in fully capturing HRQOL and associated factors. While our study found that HRQOL was lower among patients with higher BACES scores, it is important to note that even some patients with lower BACES scores experienced compromised HRQOL. Therefore, clinicians should be aware that patients with NTM-PD may experience substantial impacts on their HRQOL, warranting HRQOL assessment regardless of disease severity. Further research is needed on the development of more sophisticated assessment tools to better evaluate HRQOL in patients with NTM-PD. In addition, multidisciplinary strategies for improving HRQOL through both pharmacologic and non-pharmacologic interventions are necessary.

According to a recent study, physical inactivity was more prevalent in individuals with NTM-PD than in the general population. Moreover, physical inactivity was associated with disease severity, as evidenced by the presence of cavities, disease extent, and treatment requirement[32]. However, our results did not reveal a relationship between physical activity and the BACES score. The reasons for this disparity could lie in the study population and assessment tool. Our study was restricted to participants who were initiating antibiotic treatment, and the measurement tool, IPAQ-SF, has not been validated for patients with NTM-PD. Further research would be required using a fitness tracker in various stages of NTM-PD.

Current guidelines recommend a 'watchful waiting' approach rather than immediate treatment following the diagnosis of NTM-PD in selected cases[4]. However, clear guidance and detailed methods for managing this observation period remain lacking. A recent study has shown that HRQOL improved with NTM treatment, especially in patients with poor baseline HRQOL[33]. Additionally, higher BACES severity is associated with a lower spontaneous culture conversion rate[15]. Considering these findings and our results, the BACES score may serve as an indirect yet convenient tool for determining treatment strategies for NTM-PD, addressing not

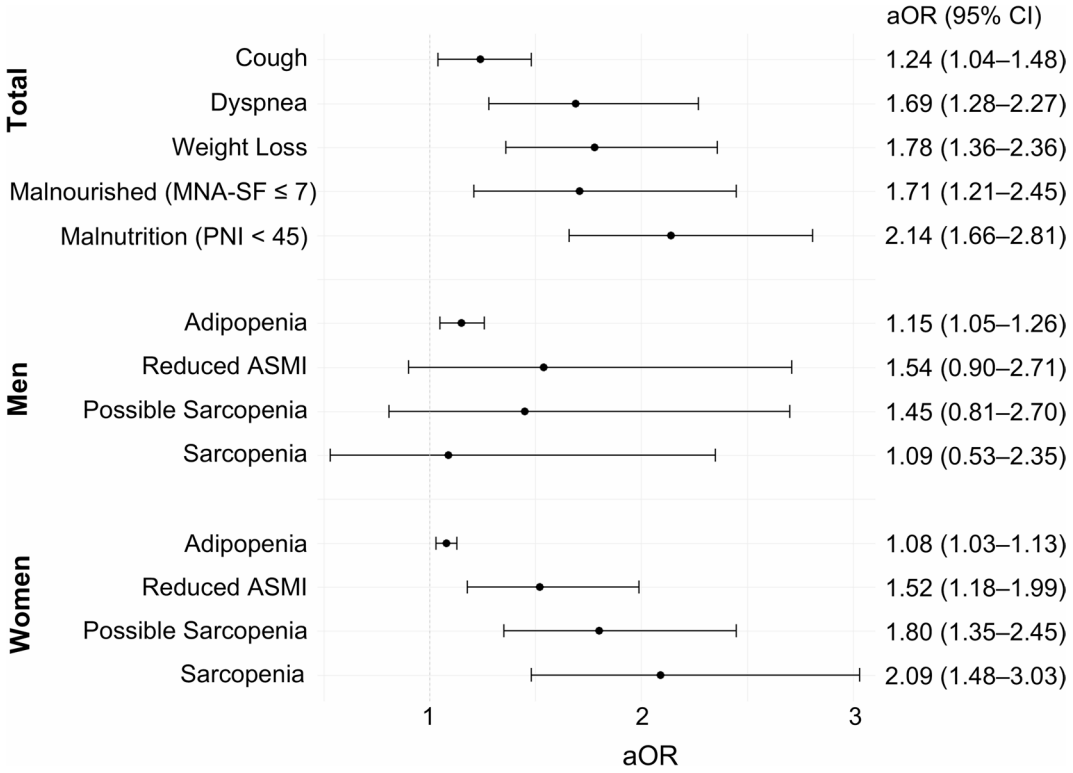

Fig. 1. Forest plot of adjusted odds ratios for the BACES score associated with HRQOL-related factors. The BACES score was treated as a continuous variable, ranging from 0 to 5.

only microbiologic outcomes but also patient-centered aspects. Specifically, early treatment initiation might be considered in patients with higher BACES scores. However, the BACES score is limited in evaluating changes in HRQOL due to treatment. The erythrocyte sedimentation rate, BMI, and cavity presence are the only variables that could be changed from all components that comprise the BACES score. Further research will be needed as more data from the NTM-KOREA cohort becomes available.

The principal strength of this study is its prospective design, which captured the actual experiences of patients with NTM-PD in a clinical setting. Patients from referral hospitals representative of all regions of South Korea were also included, which enhances the generalizability of our findings. Unlike previous studies that primarily evaluated the BACES score for predicting mortality or microbiological outcomes, our study expanded its application to patient-centered metrics such as HRQOL, nutritional status, and sarcopenia. This broadens the clinical relevance of the BACES score and makes our findings more applicable in real-world practice.

However, this study has some limitations. First, although we used data from a prospective cohort, the present analysis was cross-sectional. Second, all measurements were obtained within four weeks of the initiation of antimycobacterial therapy. Therefore, extrapolation to patients managed with watchful waiting should be performed with caution. Nonetheless, the combined evidence from our findings and previous reports—showing that higher BACES scores predict faster disease progression—indicates that the score may serve as a convenient predictor to support treatment decisions in the post-diagnosis phase[13]. Future studies that follow both treated and untreated cohorts will be essential for confirming this role. Lastly, as age and BMI are inherently included in the BACES score, we did not adjust for them separately in our analysis. Supplementary analyses showed that BMI (plus age) did not significantly outperform the BACES score in predicting outcomes, such as adipopenia, sarcopenia, and symptoms. This approach preserves the original structure and interpretability of the score, although the potential influence of age and BMI on the outcomes should still be considered.

In conclusion, the BACES score was related to HRQOL and associated factors in patients with NTM-PD requiring treatment. HRQOL and associated clinical conditions were significantly compromised, and the strong relationship between higher BACES scores and poor HRQOL persisted after adjusting for confounding variables. Therefore, the BACES score can be considered a supplementary tool to evaluate HRQOL and associated clinical factors at the start of treatment in patients with NTM-PD.

Methods

Participants

NTM-KOREA is an ongoing nationwide prospective cohort study that began on February 28, 2022 (ClinicalTrials.gov identifier: NCT03934034)[34]. Patients starting treatment for NTM-PD were enrolled from eight institutions across South Korea. The eligibility criteria were: (1) aged ≥ 19 years; (2) diagnosed with NTM-PD per current guidelines[4]; (3) having one of the following etiologic organisms: *Mycobacterium avium* complex, *Mycobacterium*

	Univariate analysis			Multivariate analysis		
	β	SE	*P*-value	β	SE	*P*-value
Symptom						
Cough	0.233	0.084	0.005	0.214	0.092	0.020
Sputum	0.040	0.086	0.641			
Hemoptysis	−0.028	0.099	0.777			
Dyspnea, mMRC ≥ 2	0.580	0.135	< 0.001	0.525	0.146	< 0.001
Weight loss, > 10% in 1 year	0.581	0.129	< 0.001	0.575	0.141	< 0.001
QOL-B[a]						
Physical functioning	−4.944	0.950	< 0.001	−4.670	1.021	< 0.001
Role functioning	−4.336	0.825	< 0.001	−4.031	0.896	< 0.001
Vitality	−2.139	0.852	0.013	−2.564	0.917	0.005
Emotional functioning	0.763	0.856	0.374			
Social functioning	−0.771	0.967	0.426			
Treatment burden	−0.926	1.236	0.454			
Health perception	−1.887	0.891	0.035	−1.945	0.962	0.044
Respiratory symptoms	−2.324	0.653	< 0.001	−2.259	0.710	0.002
MNA-SF score	−0.490	0.084	< 0.001	−0.614	0.090	< 0.001
Malnourished (MNA-SF ≤ 7)	0.459	0.164	0.005	0.535	0.179	0.003
PNI score	−1.428	0.207	< 0.001	−1.377	0.226	< 0.001
Malnutrition (PNI < 45)	0.795	0.126	< 0.001	0.760	0.134	< 0.001
IPAQ-SF, low activity	0.161	0.092	0.080			
6-min walking distance, m	−19.982	4.073	< 0.001	−18.015	4.374	< 0.001

Table 4. Regression analyses between the BACES score and health-related quality of life and associated factors. Adjusted for smoking status; history of tuberculosis; and respiratory comorbidities, including bronchiectasis, chronic obstructive pulmonary disease, asthma, interstitial lung disease, chronic pulmonary aspergillosis, and lung cancer, unless otherwise indicated. [a]Adjusted for smoking status, history of tuberculosis, and bronchiectasis. IPAQ-SF, International Physical Activity Questionnaire–Short Form; mMRC, modified Medical Research Council scale; MNA-SF, Mini Nutritional Assessment–Short Form; PNI, Prognostic Nutritional Index; QOL-B, Quality of Life Questionnaire–Bronchiectasis.

abscessus (subspecies *abscessus*, sub. *massiliense*), or *Mycobacterium kansasii*; and 4) ≤ 4 weeks of starting antibiotic treatment.

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

- 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).

All participants provided written informed consent, and all procedures were conducted in accordance with the approved protocol, the relevant guidelines and regulations, and the ethical principles of the Declaration of Helsinki. Participants in the NTM-KOREA cohort were included in our previous analysis[33].

Data collection

This study was a cross-sectional analysis based on the baseline data from the NTM-KOREA cohort. All variables, including the BACES score, HRQOL, nutritional and physical assessments, as well as functional outcomes, were collected at the time of cohort enrollment, which was within four weeks of antibiotic treatment initiation. We gathered demographic and clinical data during enrolment from the registered databases of NTM-KOREA (iCreaT ver. 2.0 [https://www.icreat/nih.go.kr]). Baseline characteristics included age, sex, BMI, smoking history, and comorbidities. Microbiological data included etiological organisms and smear results. Local thoracic radiologists or experienced pulmonary physicians interpreted chest computed tomography scans and classified them as the nodular bronchiectatic or fibrocavitary type. Radiologic subtypes not belonging to these types, such as focal cavity, nodule, mass, or consolidation, were designated as unclassifiable[35].

	Univariate analysis			Multivariate analysis		
	β	SE	*P*-value	β	SE	*P*-value
Men						
Spirometry[a]						
FVC, L	−0.476	0.067	< 0.001	−0.381	0.062	< 0.001
FVC, % predicted	−7.713	1.503	< 0.001	−7.348	1.552	< 0.001
FEV_1, L	−0.313	0.054	< 0.001	−0.256	0.051	< 0.001
FEV_1, % predicted	−5.136	1.864	0.007	−5.534	1.913	0.005
FEV_1/FVC	1.762	1.023	0.088			
DL_{CO}, % predicted	−6.762	2.177	0.003	−6.871	2.301	0.004
BIA						
Body fat, %	−2.519	0.617	< 0.001	−0.957	0.716	0.185
Abdominal fat, %	−0.024	0.005	< 0.001	−0.012	0.006	0.042
FMI, kg/m^2	−0.809	0.179	< 0.001	−0.354	0.207	0.090
Adipopenia	0.234	0.038	< 0.001	0.140	0.044	0.002
FFMI, kg/m^2	−0.722	0.161	< 0.001	−0.457	0.183	0.014
Lean-to-fat ratio	−0.041	0.01	< 0.001	−0.017	0.012	0.168
SMI, kg/m^2	−0.499	0.098	< 0.001	−0.319	0.114	0.006
ASMI, kg/m^2	−0.297	0.090	0.001	−0.171	−0.107	0.114
Reduced ASMI	0.810	0.235	< 0.001	0.432	0.277	0.118
Handgrip, kg	−2.940	0.791	< 0.001	−1.922	0.973	0.051
Possible sarcopenia	0.571	0.239	0.017	0.369	0.303	0.221
Sarcopenia	0.669	0.287	0.020	0.083	0.375	0.824
Women						
Spirometry[a]						
FVC, L	−0.202	0.030	< 0.001	−0.174	0.026	< 0.001
FVC, % predicted	−3.680	0.886	< 0.001	−3.598	0.898	< 0.001
FEV_1, L	−0.160	0.027	< 0.001	−0.140	0.023	< 0.001
FEV_1, % predicted	−1.307	1.109	0.240			
FEV_1/FVC	1.035	0.475	0.030	0.997	0.467	0.034
DL_{CO}	−1.501	1.048	0.153			
BIA						
Body fat, %	−2.145	0.399	< 0.001	−1.429	0.401	< 0.001
Abdominal fat, %	−0.012	0.003	< 0.001	−0.010	0.003	< 0.001
FMI, kg/m^2	−0.566	0.100	< 0.001	−0.326	0.097	< 0.001
Adipopenia	0.135	0.025	< 0.001	0.075	0.025	0.003
FFMI, kg/m^2	−0.352	0.069	< 0.001	−0.261	0.072	< 0.001
Lean-to-fat ratio	−0.033	0.007	< 0.001	−0.019	0.007	0.005
SMI, kg/m^2	−0.251	0.041	< 0.001	−0.189	0.042	< 0.001
ASMI, kg/m^2	−0.210	0.033	< 0.001	−0.157	0.034	< 0.001
Reduced ASMI	0.550	0.123	< 0.001	0.421	0.133	0.002
Handgrip, kg	−1.306	0.275	< 0.001	−1.145	0.293	< 0.001
Possible sarcopenia	0.675	0.145	< 0.001	0.589	0.152	< 0.001
Sarcopenia	0.876	0.176	< 0.001	0.735	0.182	< 0.001

Table 5. Regression analyses between the BACES score and pulmonary function, body composition, and handgrip strength. Anthropometric data were calculated using the following definitions: lean-to-fat ratio, fat-free mass divided by fat mass; appendicular skeletal muscle index (ASMI), sum of skeletal muscle mass in the arms and legs divided by the square of height; fat mass index (FMI), total body fat mass divided by the square of height; fat-free mass index (FFMI), fat-free mass divided by the square of height; and skeletal muscle mass index (SMI), total body muscle mass divided by the square of height. BIA, bioelectrical impedance analysis; DL_{CO}, diffusing capacity for carbon monoxide; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity. Adjusted for smoking status, MNA-SF score, and PNI, unless otherwise indicated. [a]Adjusted for smoking status, height, tuberculosis history, and respiratory comorbidities.

BACES score

The BACES score was calculated with BMI < 18.5 kg/m^2, age ≥ 65 years, presence of cavities, elevated erythrocyte sedimentation rate, and male sex each equating to 1 point[11]. Patients with a score of 0–1 were classified into the mild group; 2–3, moderate group; and 4–5, severe group[12–14].

HRQOL and associated factor measurement

HRQOL is associated with various clinical variables, including nutritional status, sarcopenia, and physical activity[29,31,36]. The following data were collected to measure HRQOL and associated health conditions: (1) respiratory or constitutional symptoms; (2) self-reported data using the QOL-B questionnaire, MNA-SF questionnaire, and IPAQ-SF; (3) laboratory-based data of PNI; and (4) measurement-based data, such as 6MWD, handgrip strength, body composition, and spirometry measurements (FEV_1, FVC, FEV_1/FVC, and DL_{CO}).

The HRQOL of patients with NTM-PD was measured using the QOL-B questionnaire, which comprises 37 items covering respiratory symptoms, physical functioning, vitality, role functioning, health perception, emotional functioning, social functioning, and treatment burden[16]. The score range for each domain is 0–100, with higher values indicating a better quality of life. 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[33].

Nutritional status was assessed using MNA-SF and PNI. The MNA questionnaire evaluates dietary intake, recent weight change, neuropsychological issues, and functional abilities[37]. It is a simple, effective questionnaire for assessing the nutritional status of older adults and patients with respiratory diseases[38,39]. MNA-SF can effectively identify malnutrition in patients with NTM-PD[40]. Participants with MNA-SF scores of 12–14 were classified as having a normal nutritional status; 8–11, as being at risk of malnutrition; and ≤ 7, as being malnourished[40]. The PNI was initially developed for the composite assessment of perioperative nutritional status in patients with malignancies, with its use later extended to various diseases[41–43]. The PNI score is calculated using the following formula: 10 × serum albumin value (g/dL) + 0.005 × total lymphocyte count in the peripheral blood (/mm^3). Participants with PNI < 45 were assigned to the malnutrition group[44].

Anthropometric data to identify participants with sarcopenia were collected using multi-frequency bioelectrical impedance analysis. Bioelectrical impedance analysis can produce reliable body composition estimates compatible with those measured using dual-energy X-ray absorptiometry[45]. The detailed models used are presented in Supplementary Table S1. Adipopenia is defined as a fat mass index (total body fat mass divided by the square of height) < 3.0 kg/m^2 for men and 5.0 kg/m^2 for women[19]. Handgrip was measured using a Jamar® hydraulic hand dynamometer (Model 5030J1; Sammons Preston, Bolingbrook, IL, USA). Possible sarcopenia was defined as reduced handgrip strength (< 28 kg for men and < 18 kg for women) according to the Asian Working Group for Sarcopenia (2019)[20]. Sarcopenia was diagnosed if patients also had reduced ASMI (sum of skeletal muscle mass in the arms and legs divided by the square of height: <7.0 kg/m^2 for men and 5.7 kg/m^2 for women)[20].

Physical activity was evaluated with the IPAQ-SF questionnaire that collects information on the time spent in sedentary activities, walking, as well as in moderate- and vigorous-intensity activities over the past 7 days. IPAQ-SF has demonstrated feasibility in national and regional prevalence studies[46].

All questionnaires and assessment tools used in this study were either used with appropriate permissions (QOL-B) or were publicly available for research purposes (MNA-SF, IPAQ-SF) and were implemented in accordance with their respective usage guidelines.

Statistical analysis

Data are presented as median with interquartile range for continuous variables and as proportion for categorical variables. The Kruskal–Wallis test was performed to compare continuous variables among multiple groups. Post-hoc comparisons were performed using Dunn's test. To control for the increased risk of type I errors due to multiple comparisons, the Bonferroni correction was applied. Fisher's exact test was performed to compare categorical variables. For the BACES mild, moderate, and severe groups, the Cochran–Armitage trend test was performed to assess trends across the ordered groups. Linear and logistic regression analyses were performed to identify factors associated with BACES scores as well as with HRQOL and related factors. Clinically relevant variables based on previous studies were included as covariates in the models (e.g., smoking status, tuberculosis history, respiratory comorbidities, MNA-SF, and PNI). Given that the BACES score already includes age, BMI, and sex as components, these variables were not included separately in the multivariable models to avoid collinearity. $P < 0.05$ indicated statistical significance. All statistical analyses were conducted using the R software (v.4.3.1; The R Foundation for Statistical Computing, Vienna, Austria).

Data availability

De-identified clinical data can be shared with qualified researchers. Proposals for data usage will undergo review 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).

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Author contributions

N.K., J-J.Y., Y.P., Y.A.K., H.S., J.W., G.I.L, and J.M. designed the study. Y.P., Y.A.K., H.H, J-Y.K., H-J.K., N.K., B.W.J., K-W.J., Y-S.K., J-J.Y., D.J., T.S.S., J.H.L., and J.M. acquired the data. Y.R.K., J.K. and N.H.P. managed the data. Y.P. and J.M. conducted the formal analysis. Y.P. drafted the manuscript, and all authors reviewed and approved the final version.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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