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ORIGINAL ARTICLE

Association of body mass index with disease severity, phenotypes, and clinical presentation in patients with bronchiectasis

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Summary

Introduction/Aim: Bronchiectasis is a chronic respiratory condition characterized by permanent dilatation of the bronchi with chronic respiratory symptoms. Some studies have found association between malnutrition and bronchiectasis. However, research on obesity remains insufficient and further studies are needed. The aim was to evaluate the association between BMI (body mass index) and phenotypes, endotypes, clinico-radiological presentation and severity.

Methods: A retrospective study included 120 patients with bronchiectasis. The socio-epidemiological, clinical, radiographic and laboratory characteristics were compared using statistical analyzes, depending on BMI.

Results: The mean age was 61.3 ± 7.6 years. Underweight, normal, overweight, and obese accounted for 6.7%, 48.3%, 27.5%, and 17.5% of all patients. There were statistically significant differences in BACI score ($p = 0.01$), normal sputum finding ($p = 0.03$), lower hemoglobin level ($p = 0.02$) in the underweight group and eosinophil endotype in all groups except underweight ($p = 0.04$). The mean BACI (Bronchiectasis Aetiology and Co-morbidity Index) score had a rising trend from overweight and obese patients to normal weight the followed by the underweight category. Chronical colonization of Haemophilus was dominant in the underweight whereas Pseudomonas predominated in the overweight and obese. Asthma was most common in overweight and obese patients. We did not find differences between the groups in spirometry findings (but, the majority of all study patients with restriction belonged to the underweight group), Reiff score and radiological phenotype.

Conclusion: Underweight patients were females and they were younger than overweight patients, they had lower diffusion capacity, systemic inflammation and higher BACI score, post-infective phenotype and predominantly normal sputum bacterial analysis for colonization screening. On the other hand, overweight and obese patients had chronic colonization by P. aeruginosa, asthma comorbidity, and eosinophil endotype. Those differences are very important for future specific treatment.

Keywords: bronchiectasis, BMI, lung function, phenotype, endotype

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INTRODUCTION

Bronchiectasis is a chronic respiratory condition characterized by permanent dilatation of the bronchi and bronchioles caused by repeated inflammation and infections (1). This facilitates the collection of purulent secretions in airways, which further deteriorates symptoms and bacterial colonization (2). The most frequent symptoms are coughing, which can persist for a long time, expectoration of colored purulent sputum sometimes with hemoptysis, fever, weight loss, dyspnea and fatigue (3). Bronchiectasis can overlap with other chronic respiratory conditions such as asthma, chronic obstructive pulmonary disease (COPD), tuberculosis, pneumonia, cystic fibrosis and primary ciliary dyskinesia (4,5). For many years, bronchiectasis was an underrecognized disease, largely due to the lack of advanced diagnostic methods like computed tomography (CT) and its non-specific symptoms (5). Its symptoms are hidden under the already mentioned other diagnoses and conditions and they were just an incidental radiographic finding. In the past decade, there has been a significant increase in literature on bronchiectasis.

Some studies have found association between malnutrition and bronchiectasis. Patients with bronchiectasis had a lower body mass index (BMI) compared to the population without bronchiectasis (6). Also, because of mechanisms underlying the pathology of cystic fibrosis (CF) and its implications on nutrient absorption, weight loss is the dominant symptom in patients with CF bronchiectasis, which manifests as underweight (7). A poor nutritional status was related to mortality, skeletal muscle dysfunction with poor activity, decreased pulmonary function and it had a significant impact on patients' quality of life (8,9). On the contrary, a gain in weight can improve pulmonary function, mostly in CF bronchiectasis patients (7). There is lack of studies investigating obesity and bronchiectasis. A Turkish study by Onen and colleges suggested that a higher BMI had benefits in survival in patients with bronchiectasis (10). More studies are needed that examine the association of BMI with the phenotypes and characteristics of bronchiectasis.

The aim of this study was to evaluate the association between BMI and phenotypes, endotypes, clinico-radiological presentation, and severity of bronchiectasis.

MATERIAL AND METHODS

This is a retrospective study conducted at the Clinic for Pulmonology, University Clinical Center of Serbia. This study is in accordance with the Helsinki Declaration, and it has been approved by the Institutional Committee (841/2).

Study group and data collection

The study enrolled 120 patients diagnosed with bronchiectasis. The diagnosis of bronchiectasis was determined by chest CT scan and respiratory symptoms according to the European Respiratory Society guidelines (11). The data included the following: basic demographics data, clinical presentation and symptoms, radiological phenotypes, endotypes according to cell predominance in blood sample, sputum sample for bacteriological examination, BMI, hematological results of blood analysis, bronchiectasis etiology co-morbidity index (BACI), Reiff score, and pulmonary tests.

The modified Reiff scores indicating radiological severity of bronchiectasis were score calculated number of lobe involvement and dilatation degree (12). For quantitative assessment of comorbidities, BACI has been calculated. The BACI calculator is available online at http://www. ronchiectasisseverity.com. The spirometry function was classified according to the American Thoracic Society guidelines (13). Patients were categorized into four groups according to the World Health Organization expert consultation on BMI criteria: underweight (BMI<18.5 kg/m2), normal weight (18.5 ≤BMI<25.0 kg/m2), overweight (25.0 ≤BMI<30.0 kg/m2), and obese (BMI≥30.0 kg/m2) (14).

Endotypes of bronchiectasis were defined according to the types of inflammation (blood sample) and they were divided in three main groups - the first one with type 2 inflammation- eosinophilic endotype, the second one with neutrophilic inflammation and the third one with systemic inflammation.

Statistical analysis

Complete statistical analysis was performed with the SPSS software version 23 (Chicago). Numerical variables are presented as mean values with standard deviation, attribute variable as the frequency for continuous variables and were compared using the ANOVA. Chi-squared test was used to compare categorical variables, and data were presented as numbers with percentage. All analyses were assessed with the $p<0.05$ level of statistical significance. Results are presented as graphics and tables.

RESULTS

A total of 120 patients with bronchiectasis treated at the Clinic for Pulmonology from 2020 to 2022 were included. The mean age was 61.3 ± 7.6 years, and there were not statistically significant differences in age between the groups. Over 78% of the population group were smokers, with a statistically significant higher prevalence among patients with a BMI over 25 kg/m^2 ($p <0.03$).

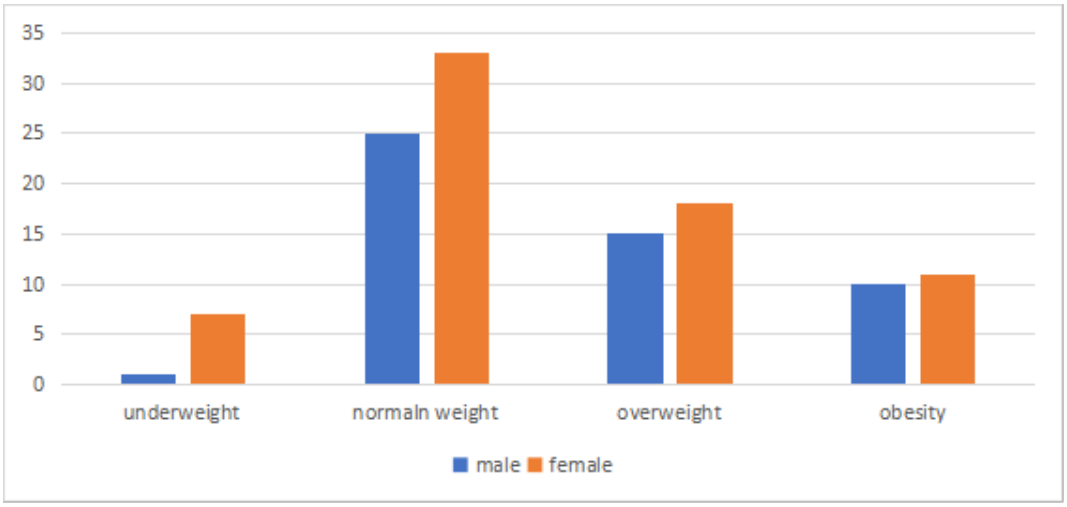

Figure 1. The frequency of patients with bronchiectasis according to gender in four groups

The mean BMI score of patients with bronchiectasis was 24.3 ± 2.9 kg/m2. Underweight, normal, overweight, and obese accounted for 6.7%, 48.3%, 27.5%, and 17.5% of all patients, respectively.

More than half of all patients (57.5%) were female, but there were no statistically significant frequency differences between groups. The frequency of patients according to gender in four groups is presented in **Figure 1**.

Table 1. Most frequent comorbidities in study group

COMORBIDITY	N (%)
Arterial hypertension	22 (18.3)
COPD	13 (10.8)
Asthma	11 (9.2)
Immunodeficiency	10 (8.3)
Hypothyroidism	4 (3.3)
Diabetes mellitus	3 (2.5)

Among all study subjects, the major comorbidities were arterial hypertension (18.6%), COPD (10.2%) asthma (9.4%), immunodeficiency (8.9%), hypothyroidism (3.7%) and diabetes mellitus (2.6%) **(Table 1)**. Regarding comorbidities, the overweight and obese group had the highest proportion of arterial hypertension, COPD and asthma, and the lowest proportion of DM and hypothyroidism compared with the other two BMI groups. A BACI score of over 6 was observed in 17 patients (14.1%).

According to spirometry tests, obstructive finding was the most common dysfunction in 61 (50.8%) patients, followed by normal in 43 (35.8%) and restrictive findings in 16 (13.4%) patients. In 99 (82.5%) patients, cylindrical type was diagnosed, varicose type was found in 8 (6.7%) and cystic type in 13 (10.8%). According to modified Reiff score, mild bronchiectasis was observed in 105 patients (87.5%), moderate was found in 9 patients (7.5%) and severe in 6 patients (5%).

All patients underwent sputum sample collection and analysis. In the study group, 78 patients' sputum specimens tested positive (65%). The most common isolated pathogen was P. aeruginosa, Haemophilus influenzae, Escherichia coli, Staphylococcus haemolyticus, and Aspergillus species.

Differences between groups are presented in **Table 2** and **Table 3**. There were statistically significant differences in BACI score (p = 0.01), normal sputum finding (p = 0.03), anemia and lower hemoglobin level (p = 0.02) in the underweight group and eosinophil endotype in all groups except for the underweight (p = 0.04). The

Table 2. Comparison of data and clinical variables among the four groups

BMI	Underweight	Normal weight	Overweight	Obesity	p
N (%)	8 (6.7)	58 (48.3)	33 (27.5)	21 (17.5)	
Male N (%) Female N (%)	1 (12.5) 7 (87.5)	25 (43.1) 33 (56.9)	15 (45.5) 18 (54.5)	10 (47.7) 11 (52.3)	0.25
Age years	59.5	60.2	65.7	59.8	0.406
BACI ≥6 N (%)	4 (50)	13 (22.4)	3 (9.1)	2 (9.5)	0.044
Sputum N (%) -normal -pathological	 7 (87.5) 1 (12.5)	 12 (20.7) 46 (79.3)	 11 (33.3) 22 (66.7)	 7 (33.3) 14 (66.7)	0.003
Microbiology	Haemophilus	Staphylococcus	Pseudomonas	Pseudomonas	
Clinical phenotype	Post-infectious	Post-infectious immunodeficiency	Asthma	Asthma COPD	
Endotype	systemic inflammation	eosinophilic	eosinophilic	eosinophilic	0.04
Thrombocytes 10^9/ml Hemoglobin 10^9/ml	256 117	224 132	226 134	243 133	0.583 0.002

Table 3. Comparison of data and radiological and functional findings among the four groups

BMI	Underweight	Normal weight	Overweight	Obesity	p
N (%)	8 (6.7)	58 (48.3)	33 (27.5)	21 (17.5)	
Radiological phenotype					
-cystic	1 (12.5)	4 (6.9)	3 (9.1)	2 (9.5)	0.287
-cylindrical	7 (87.5)	52 (89.6)	28 (84.8)	17 (81)	
-varicose	0	2 (3.5)	2 (6.1)	2 (9.5)	
Reiff score N (%)					
-mild	5 (62.5)	52 (89.6)	29 (87.9)	19 (90.6)	0.124
-moderate	3 (37.5)	4 (6.9)	1 (3)	1 (4.7)	
-severe	0	2 (3.5)	3 (9.1)	1 (4.7)	
Spirometry N (%)					
-normal	2 (25)	22 (37.9)	12 (36.4)	7 (33.3)	0.77
-obstruction	4 (50)	29 (50)	17 (51.5)	11 (52.4)	
-restriction	2 (25)	7 (12.1)	4 (12.1)	3 (14.3)	
Decreased diffusion capacity N (%)	5 (62.5)	21 (36.2)	20 (60.6)	15 (71.4)	0.81

mean BACI score had a rising trend from overweight and obese patients to normal weight followed by the underweight category, but the majority were in the group with a low to intermediate risk for mortality. The chronical colonization of Haemophilus was dominant in the underweight and Pseudomonas in overweight and obese group. Underlying causes were identified and the most frequent was post-infection in all groups except for the obese, but those associated with asthma were most common in overweight and obese patients. We did not find statistically significant differences between groups in spirometry findings, Reiff score and radiological phenotype. About half of all four groups had obstructive spirometry finding, as expected. Diffusion capacity was decreased in all groups except in groups with normal BMI, in more than half of patients. **Tables 2 and 3** revealed that underweight individuals were the youngest, predominantly female, and had the highest number of patients with a BACI score over 6, as well as the highest incidence of decreased diffusion capacity and anemia.

DISCUSSION

The purpose of this bronchiectasis population study was to determine whether any subtype (endotype, clinical phenotype, radiological phenotype), pulmonary test findings or severity scores of bronchiectasis were correlated with the patients' BMI. To the best of our knowledge, this is the first study in our country to evaluate factors associated with bronchiectasis.

Numerous studies have highlighted that non-CF bronchiectasis predominantly affects older adults, while CF bronchiectasis is more common in younger individuals. Most patients are over 65 years old, and that predomination has a correlation with comorbidities (15). In several bronchiectasis studies, patients with bronchiectasis were predominantly elderly, with a higher prevalence in females than males (16, 17). Our results are in accordance with these data. The average age was 60 years and females were predominant in all four groups unrelated to BMI. As previously mentioned, the elderly had more comorbidities, with cardiovascular conditions being the most prevalent, consistent with our findings. The association of bronchiectasis with asthma and COPD has been clearly demonstrated in previous studies. There are two main ways in which COPD and bronchiectasis can be associated: COPD can lead to the development of bronchiectasis through persistent airway inflammation and repeated infections; bronchiectasis resulting from other causes in non-smokers can lead to irreversible airway obstruction and subsequent COPD (18, 19). Following arterial hypertension, asthma and COPD presented the most dominant comorbidity in the study population. The higher frequency of COPD in obese individuals may be attributed to associations with metabolic syndrome and the use of corticosteroid therapy (20).

Basically, bronchiectasis is a neutrophilic disorder in about more than 50% of cases according to literature data (21). Contrary to this data, our bronchiectasis participants demonstrated a higher blood eosinophil count and eosinophilic endotype. The reason is the predominance of asthma and COPD underlying disease in overweight and obese patients with this clinical phenotype. Asthma is dominantly eosinophilic disease and COPD has an association with eosinophils in some phenotypes (22). This is important because patients with the eosinophilic endotype benefit from inhaled corticosteroids, while those with the neutrophilic endotype respond better to antibiotics (21,22). Malnutrition is a frequent finding in chronic inflammatory respiratory diseases, so patients have increased mortality risk, exacerbations, chronic colonization of P. aeruginosa and systemic inflammatory amplification (1, 23). This is partly in accordance with our results for underweight patients, systemic inflammation is the dominant endotype and post-infectious is the dominant clinical\etiology phenotype. However, P. aeruginosa was the most frequent microbiology in other groups, not in the underweight. The reason are probably scarce results. Only one had positive sputum bacteriological finding.

BMI has no influence or correlation with structural radiological phenotype. There was no difference between groups in localization and frequency of the three types. The predomination was in the lower lobes and more than 60% of our entire study population had a post-infectious phenotype. That is in accordance with literature data and with etiology, because lower lobe distribution is most often seen in post-infectious bronchiectasis (24). One Chinese study from 2016 showed the absence of correlation between the extent of bronchiectasis and BMI and spirometry tests (25). In contrast, a Korean study found a negative correlation between the extent of bronchiectasis and BMI in moderate to severe disease (26). We did not find this correlation with Reiff 's score for severity.

We hypothesized that being underweight would be associated with worse lung function. Our results confirmed that 75% of them had abnormal spirometry findings. A high percentage of obstruction was in all four BMI groups. The majority of all study patients with restrictions were in the underweight group. The reason for the restriction finding in low BMI group is probably a loss of muscle mass, low physical activity and strength in those patients (27, 28). In a large multicenter study, BMI was found to be positively associated with the forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) in patients who had bronchiectasis and were on mechanical ventilation (28, 29). Additionally, numerous studies on COPD and bronchiectasis patients have examined the relationship between BMI and pulmonary function tests, demonstrating a positive correlation between lower BMI and decreased values in FVC, FEV1, and diffusion capacity (29). The results of our study are in line with those previous studies, except for diffusion capacity where there were no differences between groups. Long-term studies are needed to better identify the effect of a low BMI on the reduction of pulmonary function and diffusion capacity.

The association between BMI and anemia is controversial due to few studies reporting direct association with increasing BMI increases the chance of anemia, while others reported the opposite (30, 31). Inadequate daily iron or dietary nutrient intake is the reason for lower BMI and anemia and this can be the reason for the correlation between underweight and anemia. Lower values of hemoglobin are statistically significant in the underweight group of our study population, which is in line with literature data.

CONCLUSIONS

This study shows that the majority of patients with bronchiectasis in our study population have a normal BMI. Underweight patients were females and younger than overweight patients, they had lower lung function, amplified systemic inflammation, higher BACI score, post-infective phenotype and predominantly normal sputum bacterial analysis for colonization screening. On the other hand, overweight and obese had chronic colonization by P. aeruginosa, asthma comorbidity and eosinophil endotype. Those differences are very important for future decisions about a specific treatment. Improving nutritional status might help improve the disease outlook. Larger sample sizes are needed to measure nutritional status and body composition as an important role of nutrition in bronchiectasis.

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Author contributions: Conception and design JJ, data collection DV and ZB, writing the article JJ and ZB, statistical analysis AZ, critical revision of the article AZ and DV.

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POVEZANOST INDEKSA TELESNE MASE SA TEŽINOM BOLESTI, FENOTIPOVIMA I KLINIČKOM PREZENTACIJOM KOD BOLESNIKA SA BRONHIEKTAZIJAMA

Jelena Janković[1,2], Zlatan Bojić[1], Dragan Vukosavljević[1], Andrej Zečević[1]

Sažetak

Uvod/cilj: Bronhiektazije su hronično respiratorno stanje koje karakteriše trajna dilatacija bronhija se hroničnim respiratornim simptomima. Neke studije su otkrile povezanost između pothranjenosti i bronhiektazija ali je nedovoljno studija na temu gojaznosti. Cilj studije bio je da se proceni povezanost BMI (body mass index) sa fenotipom, endotipom, kliničko-radiološkom prezentacijom i težinom bolesti.

Metode: Retrospektivnom studijom obuhvaćeno je 120 pacijenata sa bronhiektazijama. Socio-epidemiološke, kliničke, radiografske i laboratorijske karakteristike upoređene su sa BMI.

Rezultati: Prosečna starost bila je 61,3 ± 7,6 godina. Pothranjenost, normalna težina, prekomerna težina i gojaznost činili su 6,7%, 48,3%, 27,5% i 17,5% svih pacijenata. Postojale su statistički značajne razlike u BACI (Bronchiectasis Aetiology and Co-morbidity Index) skoru (p = 0,01), normalnom nalazu sputuma (p = 0,03), nižem nivou hemoglobina (p = 0,02) u grupi pothranjenih i endotipu eozinofila u svim grupama osim u grupi pothranjenih (p = 0,04). BACI skor je imao trend rasta od pacijenata sa prekomernom težinom i gojaznih do normalne težine praćene kategorijom pothranjenih. Hronična kolonizacija Haemophilus vrstom bila je dominantna kod pothranjenih, a Pseudomonas je bio zastupljeniji kod onih sa prekomernom težinom i gojaznih. Astma je bila najčešća kod pacijenata sa prekomernom težinom i gojaznih. Nije bilo razlike u nalazu spirometrije (ali većina svih ispitanika sa restrikcijom bila je u grupi pothranjenih), Reiff skoru i radiološkom fenotipu.

Zaključak: Pothranjeni pacijenti bili su ženskog pola i mlađi od pacijenata sa prekomernom težinom (imali su niže vrednosti difuzijskog kapaciteta pluća), sistemsku inflamaciju, viši BACI skor, postinfektivni fenotip i pretežno normalnu analizu sputuma za skrining kolonizacije. Nasuprot tome, pacijenti sa prekomernom težinom i gojazni su imali hroničnu kolonizaciju P. aeruginosa, komorbiditet astme i eozinofilni endotip. Ove razlike su važne za odluku o specifičnom lečenju.

Ključne reči: bronhiektazije, BMI, plućna funkcija, fenotip, endotip

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