In bronchiectasis, poor physical capacity correlates with poor quality of life

Jarkko Mäntylä, Witold Mazur, Tanja Törölä, Paula Bergman and Paula Kauppi

ABSTRACT
Purpose: Patients with bronchiectasis (BE) who suffer frequent exacerbations are likely to experience negative effects on quality of life (QoL) and require more healthcare utilization. We aimed to discover, in a cohort of Finnish BE patients, those risk factors that influence QoL.
Methods: Non-cystic fibrosis BE patients of a Helsinki University Hospital cohort were examined with high-resolution computed tomography (HRCT) of the chest. They completed a disease-specific quality of life-bronchiectasis (QoL-B) questionnaire in Finnish translation. We considered scores in the lowest quarter (25%) of that QoL-B scale to indicate poor QoL. The bronchiectasis severity index (BSI), FACED score, and modified Medical Research Council (mMRC) dyspnoea scale were used.
Results: Overall, of 95 adult BE patients, mean age was 69 (SD ± 13) and 79% were women. From the cohort, 82% presented with chronic sputum production and exacerbations, at a median rate of 1.7 (SD ± 1.6). The number of exacerbations (OR 1.7), frequent exacerbations (≥3 per year) (OR 4.9), high BSI score (OR 1.3), and extensive disease (≥3 lobes) (OR 3.7) were all predictive of poor QoL. Frequent exacerbations were associated with bronchial bacterial colonisation, low forced expiratory volume in 1 s (FEV1), and radiological disease severity. Based on the BSI, 34.1% of our cohort had severe disease, with 11.6% classified as severe according to their FACED score. The mMRC dyspnoea score (r = −0.57) and BSI (r = −0.60) correlated, in the QoL-B questionnaire, negatively with physical domain.
Conclusion: The strongest determinants of poor QoL in the cohort of Finnish BE patients were frequent exacerbations, radiological disease severity, and high BSI score. Neither comorbidities nor BE aetiology appeared to affect QoL. Reduced physical capacity correlated with dyspnoea and severe disease.
Study registration: University of Helsinki, Faculty of Medicine, 148/16.08.2017.

Introduction
Bronchiectasis is often difficult to cure completely (except in those cases having local bronchiectasis and being eligible for surgical treatment), so current treatment options aim to limit disease progression and to prevent exacerbations [1]. Because assessment of those subgroups that are likely to gain the most benefit from a specific intervention is important, measures such as respiratory questionnaires, symptom scores, or QoL measures indicating the benefit of interventions and analyzing their benefits are essential.

For example, spirometry provides a good assessment of lung function but does not assess specific health status or may not be sufficient to assess disease severity [2]. Similarly, radiographic examinations such as high-resolution computed tomography (HRCT) scans have revealed BE severity, but such findings do not correlate well with the clinical features of the disease [3]. Tests to estimate dyspnoea and physical capability (e.g. a six-minute walking test) are useful and standardised in routine praxis. One study, however, demonstrated that this walking test (6MWT) was not appropriate to describe BE severity [2].

Respiratory questionnaires developed for patients suffering from respiratory diseases can serve for study of symptom severity and development of symptoms both alongside disease progression and as a response to treatment. The St George’s Respiratory Questionnaire (SGRQ) and Leicester Cough Questionnaire were the first of these, and both assess respiratory symptoms and cough associated with respiratory diseases [4,5].

Other clinical assessment tools specific to BE include the bronchiectasis severity index (BSI) and FACED score. BSI was validated in 2014 [6], and the...
FACED score was established in the same year [7]. BSI includes e.g. hospitalizations and exacerbations; FACED includes the radiological extent of the disease, and dyspnoea in addition to lung function. Validated in 2014 as well, the QoL-B version 3.0 [8] was developed to qualify patient-reported outcomes (PRO) and to cover symptoms, physical and emotional functioning, and treatment burden and also to provide a disease-specific questionnaire.

Of interest is that, in an earlier study, neither lung function measured as FEV1% (ratio of forced expiratory volume in 1 s to forced volume capacity) nor disease severity correlated with sedentary behaviour or physical capacity, but exercise capacity did [9]. In addition, physical capacity correlated with the QoL social-functioning and respiratory symptom domains [9].

Because QoL in BE is far more complex than merely clinically assessed disease severity, here we studied the risk factors for poor QoL in a Finnish BE cohort by using clinical assessment tools.

Materials and methods

Participants

A total of 103 adult non-cystic fibrosis BE patients who had a doctor–patient relationship at Helsinki University Hospital (HUH) were willing to take part, and 95 did take part in this cross-sectional study. Patient recruitment was by a letter sent between August 2016 and March 2018 from the HUH district in Helsinki and in Espoo. Their BE diagnosis had been done by HRCT (high-resolution computed tomography) assessed by a radiologist. We excluded eight patients not fulfilling the diagnostic criteria for non-cystic BE confirmed by HRCT [10].

Quality of life (QoL) in bronchiectasis questionnaire

The QoL-B (version 3.0) is a multidimensional disease-specific questionnaire for patients with BE. Patients self-report their current condition by answering 37 questions categorised into eight different domains (respiratory symptoms, physical activity, role, emotional and social functioning, vitality, health perceptions, and treatment burden). The score for each domain ranges from 0 to 100, with higher scores representing fewer symptoms or better functioning. The QoL-B provides reliable and consistent results if re-tested and has high convergent validity [8,11]. The QoL-B has been translated into Finnish, which version was then applied in the current study.

Modified Medical Research Council scale (mMRC)

In patients with respiratory diseases, the mMRC dyspnoea scale is a reliable tool to assess functional disability due to dyspnoea. Dyspnoea occurring only upon strenuous exercise on level ground is graded as 0 points, shortness of breath when hurrying on level ground or walking up a slight hill receives 1 point, walking slower than people of the same age on level ground at one’s own pace, due to breathlessness or to a need to stop to catch a breath is 2 points, stopping for breath after walking 100 m or after a few minutes on level ground is 3 points, and breathlessness when dressing is graded as 4 points.

Bronchiectasis severity index (BSI)

BSI is a composite disease-specific prognostic index developed to aid in clinical decision-making related to BE. Specifically, the BSI was developed to predict mortality, severe exacerbations, frequency of exacerbations, and QoL [6]. The BSI combines the clinical, radiological, and microbiological features of BE, and includes the following parameters: body mass index (BMI), FEV1%, previous hospital admissions, number of exacerbations in the previous year, mMRC breathlessness score, pseudomonas species or species with other microorganisms, and radiological severity. The grading system of the BSI is mild (0–4 points), moderate (5–8 points), and severe (9 or more points) [6]. Extensive disease is determined as four or more lobes affected by bronchiectasis findings. The lingula was considered to be an independent lobe.

FACED score

The FACED score is another disease-specific prognostic index that aims to assess the probability of all-cause mortality over 5 or 15 years of follow-up [6,7,12]. FACED assesses various factors related to BE including lung function (FEV1) (F), age (A), pulmonary bacterial colonisation (C), number of lobes affected by BE (E), and dyspnoea (D). FACED scoring is graded as mild (0–2 points), moderate (3–4 points), or severe (5–7 points).

Patient and public involvement

This is part of the EMBARC study, with its data collected anonymously into the EMBARC database. Neither the patients nor the public was involved in the design, conduct, or reporting of our research. Dissemination of our research findings will be through
the Organisation for Respiratory Health in Finland and through the Finnish Allergy, Skin and Asthma Federation.

**Statistical analyses**

The independent-samples *t*-test and the Mann–Whitney *U* test served, respectively, to compare means and mean ranks. We compared the proportions by χ²-test and Fisher’s exact test. We considered scores in the lowest quarter (25%) of the scale to indicate poor QoL. We calculated Pearson’s correlation coefficient for various symptom domains of QoL and mMRC dyspnoea score and BSI index. Risk factors for poor QoL in BE we analysed by logistic regression analysis, with age, BMI, FEV1%, and FVC% considered as continuous variables. Statistical analyses were done with the Statistical for Social Sciences (SPSS) program, version 22 (IBM corporation, Armonk NY, USA).

**Ethical approval**

The ethics committee of HUH approved the study (registration number 214/13/03/01/2016).

**Results**

Of the 95 patients, 23 reported poor QoL, and 69 did not, and three patients failed to complete the questionnaire (Table 1). A score in the lowest quarter of the scale, less than 25%, represented poor QoL. Those BE patients with poor QoL had significantly reduced values in every symptom domain that we more closely analysed, but mostly in the physical, role, health, and social domains (Table 2).

Further, patients with poor QoL had more severe dyspnoea (mMRC mean scores of 2.4 vs. 1.5) and more severe BE disease (BSI of 10.5 vs. 6.9), more frequent exacerbations (four vs. two over the past 12 months), more extensive disease, and more frequent bacterial colonisation and cystic changes.

The mMRC dyspnoea score showed a moderate negative correlation with physical domain (*r* = −5.72, *p* < 0.01) in the QoL questionnaire (Supplementary Table 3). Similarly, BSI showed a moderate negative correlation with physical domain (*r* = −5.96, *p* < 0.01) (Supplementary Table 3).

Our analysis of risk factors for poor QoL showed that numbers of exacerbations, BSI, mMRC, extensive disease, and frequent exacerbations were important. With the analysis adjusted for age and gender, numbers of exacerbations (OR 1.7), higher score of BSI (OR 1.3), higher score of mMRC (OR 3.3), extensive disease (OR 3.7), and frequent exacerbations (OR 4.9) elevated the risk for a poor QoL (Table 4). Neither comorbidities nor BE aetiology appeared to affect the QoL (Table 4).

| **Table 1.** Clinical characteristics of bronchiectasis patients with and without poor quality of life. |
|---|---|---|---|---|---|---|---|---|---|
| **N** = 92, Missing **n** = 3 | **Poor QoL (n = 23)** | **Others (n = 69)** | **p-Value** |
| Age, median | 72 | 71 | 0.18 |
| Gender, female | 95.7 | 75.4 | 0.03 |
| Ever-smokers (%) | 21.7 | 36.2 | 0.2 |
| BMI, mean (±SD) | 26.8 (5.2) | 25.7 (5.5) | 0.37 |
| FEV1%, mean (±SD) | 84.3 (3.4) | 88.9 (2.4) | 0.22 |
| mMRC, mean (±SD) | 2.43 (0.896) | 1.49 (1.093) | < 0.01 |
| BSI (±SD) | 10.5 (3.8) | 6.9 (4.0) | < 0.01 |
| FACED, mean (±SD) | 3.1 (1.3) | 2.5 (1.5) | 0.05 |
| Exacerbations (median) | 4 | 2 | < 0.01 |
| Extensive disease (%) | 87 | 62.3 | 0.03 |
| Ever had bacterial colonisation (%) | 43.5 | 30.4 | 0.25 |
| Cystic changes (%) | 13 | 5.8 | 0.26 |
| Aetiology (%) | | | | | |
| Idiopathic | 21.7 | 47.8 | 0.03 |
| Asthma | 39.1 | 23.2 | 0.14 |
| Postinfected | 8.7 | 11.6 | 0.7 |
| Other | 30.4 | 17.4 | 0.18 |

**BMf:** body mass index (kg/m²); FEV1%: FEV1/FVC: forced expiratory volume in 1 s/forced vital capacity; QoL: quality of life; mMRC: modified Medical Research Council; BSI: bronchiectasis severity index.

| **Table 2.** QoL symptom domains and the interquartile ranges for all patients, patients with poor quality of life and the others. |
|---|---|---|---|---|---|---|---|---|
| QoL domain | Median | IQR | Q1 (0–25%) | Q2 (25–50%) | Q3 (50–75%) | Q4 (75–100%) | Median | IQR |
| All (N = 92) |  |
| Physical | 60 | 60 | 19.7 | 34.2 | 70.1 | 88.7 | 13.3 | 27 |
| Role | 60 | 46.7 | 29.6 | 49.9 | 75.1 | 93.9 | 33.3 | 26.7 | 80 | 40 | < 0.01 |
| Vitality | 50 | 33.4 | 31.4 | 44.9 | 54.6 | 72.9 | 33.3 | 22.2 | 55.6 | 22.3 | < 0.01 |
| Emotion | 75 | 25 | 51.1 | 68.8 | 87.3 | 92.8 | 50 | 25 | 83.3 | 25 | < 0.01 |
| Social | 58.3 | 41.7 | 34.1 | 49.6 | 65.1 | 77.1 | 33.3 | 33.3 | 66.7 | 27.8 | < 0.01 |
| Treatment burden | 77.8 | 44.4 | 51.9 | 69.6 | 78.8 | 88.4 | 44.4 | 33.4 | 77.8 | 33.3 | < 0.01 |
| Health | 41.7 | 33.3 | 26.2 | 31.9 | 48.2 | 69.2 | 25 | 16.6 | 50 | 33.4 | < 0.01 |
| Respiration | 57.45 | 30 | 35.4 | 50.8 | 62.3 | 74.9 | 37 | 15 | 63 | 28 | < 0.01 |
| Summary | 450 | 260.5 | 261.9 | 392.8 | 524.1 | 644.9 | 270.8 | 82.8 | 529.6 | 117.3 | < 0.01 |

Q1–Q4 quarters are introduced as mean values.
Table 3. Correlation of mMRC score and BSI with various symptom domains.

| Domain                  | mMRC (N = 92) | BSI (N = 88) | p-Value | p-Value |
|-------------------------|---------------|--------------|---------|---------|
| Physical                | −0.57         | −0.59        | 0.00    | 0.00    |
| Role                    | −0.46         | −0.47        | 0.00    | 0.00    |
| Vitality                | −0.34         | −0.34        | 0.01    | 0.01    |
| Emotion                 | −0.25         | −0.34        | 0.01    | 0.01    |
| Social                  | −0.23         | −0.23        | 0.02    | 0.02    |
| Treatment burden        | −0.21         | −0.41        | 0.00    | 0.00    |
| Health                  | −0.32         | −0.44        | 0.00    | 0.00    |
| Respiration             | −0.29         | −0.39        | 0.00    | 0.00    |

mMRC: modified Medical Research Council; BSI: bronchiectasis severity index.

Table 4. Risk factors for poor quality of life in bronchiectasis.

| Adjusted age and gender | p-Value | Ext(B) | 95% CI for EXP(B) |
|-------------------------|---------|--------|-------------------|
| Gender (women)          | 0.06    |        |                   |
| Age                     | 0.21    |        |                   |
| Cardiovascular disease  | 0.44    | 1.571  | 0.5               |
| Psychiatric disease     | 0.07    | 0.224  | 0.05              |
| Connective tissue       | 0.21    | 0.974  | 0.93              |
| BMI                     | 0.3     | 0.951  | 0.87              |
| FEV1%                   | 0.27    | 1.013  | 0.99              |
| Asthma diagnosis        | 0.28    | 0.532  | 0.17              |
| Asthma aetiology        | 0.18    | 0.979  | 0.94              |
| Exacerbations           | 0.00    | 1.718  | 1.29              |
| Faced                 | 0.16    | 1.354  | 0.89              |
| BSI                    | <0.01   | 1.258  | 1.09              |
| mMRC                   | <0.01   | 0.427  | 0.25              |
| Extensive disease       | 0.05    | 3.687  | 0.97              |
| Have ever bacterial     | 0.21    | 0.518  | 0.19              |
| Exacerbator 3/year      | <0.01   | 4.946  | 1.69              |

BMI: body mass index (kg/m²); FEV1%: FEV1/FVC: forced expiratory volume in one second/forced vital capacity; QoL: quality of life; BSI: bronchiectasis severity index; mMRC: modified Medical Research Council.

Table 5. Characteristics of two sub-group, BE patients with 0–2 exacerbations annually and BE patients with ≥3 exacerbations annually.

|                      | Exacerbation | Exacerbation ≥3/year | N | 0–2/year | 3/year | p-Value |
|----------------------|--------------|----------------------|---|----------|--------|---------|
| Gender, female, N (%)| 95           | 45 (80.4)            |   | 30 (76.9) | 0.69   |         |
| Age, median (IQR)    | 95           | 71 (65.5–76)        |   | 72 (58–78) | 0.79   |         |
| BMI, mean (±SD)      | 92           | 25.6 (5.7)          |   | 26.6 (4.9) | 0.40   |         |
| Ever-smokers, N (%)  | 95           | 20 (35.7)           |   | 12 (30.8)  | 0.62   |         |
| FEV1%, mean (±SD)    | 90           | 93.2 (23.8)         |   | 79.1 (22.6) | <0.01 |         |
| Exacerbations, median (IQR) | 95 | 1 (0–2) | 4 (3–5) | <0.01 |
| Extensive disease, N (%) | 95 | 34 (60.7) | 3 (79.5) | 0.05 |
| Ever had bacterial colonisation, N (%) | 95 | 11 (19.6) | 21 (53.8) | <0.01 |
| Cystic changes, N (%) | 95 | 4 (7.1) | 5 (12.8) | 0.48 |
| Poor QoL, N (%)      | 95           | 8 (14.8)            |   | 15 (39.5)  | <0.01 |         |
| mMRC, median (IQR)   | 95           | 1 (1–2)             |   | 2 (1–3)    | <0.01 |         |
| BSI, mean (±SD)      | 95           | 5.9 (3.2)           |   | 10.5 (3.9) | <0.01 |         |
| FACED, mean (±SD)    | 95           | 2.4 (1.5)           |   | 2.9 (1.5)  | 0.12  |         |
| Aetiology            | 95           | 95 (100)            |   | 100 (100)  |       |         |
| Idiopathic, N (%)    | 95           | 26 (46.4)           |   | 15 (38.5)  | 0.44  |         |
| Asthma, N (%)        | 95           | 13 (23.2)           |   | 12 (30.8)  | 0.41  |         |
| Postinfected, N (%)  | 95           | 7 (12.5)            |   | 3 (7.7)    | 0.52  |         |
| Other, N (%)         | 95           | 10 (17.9)           |   | 9 (23.1)   | 0.53  |         |

BMI: body mass index (kg/m²); FEV1%: FEV1/FVC: forced expiratory volume in one second/forced vital capacity; QoL: quality of life; mMRC: modified Medical Research Council; BSI: bronchiectasis severity index.

Table 6. Quality of life domains of all and of those with at least three annual exacerbations compared to the others.

|                      | Mean (SD) | Mean (SD) | p-Value |
|----------------------|-----------|-----------|---------|
| Domain               | All (N = 92) | Frequent exacerbators (N = 38) | Others (N = 54) |
| Physical             | 60 (31.9) | 42.1 (30) | 65.4 (32) | 0.01 |
| Role                 | 60 (27.9) | 50.2 (26) | 70.5 (27) | <0.01 |
| Vitality             | 50 (20.7) | 47.9 (19) | 53.1 (21) | 0.24 |
| Emotion              | 75 (22.2) | 70.2 (24) | 78.4 (20) | 0.11 |
| Social               | 58 (24.4) | 51.1 (26) | 60.2 (23) | 0.14 |
| Treatment burden     | 77.8 (24.8) | 59.5 (25) | 81.1 (20) | <0.01 |
| Health               | 41.7 (21.1) | 35.6 (18) | 49.7 (22) | <0.01 |
| Respiration          | 57 (19.7) | 49.6 (20) | 60.3 (18) | 0.14 |
| Summary              | 450 (151.8) | 393.8 (147) | 496.5 (143) | <0.01 |

According to BSI results, of all the BE patients, 22% had mild disease, 44% moderate disease, and 34% severe disease. Overall, the BE cohort had a mean BSI value of 7.7 (±4.2) and median value of 7 (±2.0). When BE severity was estimated according to the FACED index, 42% of patients had mild BE, 46% moderate, and 12% severe. The mean FACED score was 2.6 (±1.5); the median was 3.0 (±1.5).

Patients with frequent exacerbations (≥3 per year) had significantly poorer lung function (FEV1 of 79% vs. 93%, p < 0.01), had poorer physical tolerance (mMRC of 1 vs. 2, p < 0.01), were more symptomatic with dyspnoea, had more severe disease (BSI of 6 ± 3.2 vs. 10 ± 3.9, p < 0.01), more frequent bacterial colonisation (19.6% vs. 53.8%, p < 0.01) and cystic BE changes, and more often had asthma as the aetiology for their BE (30% vs. 23%) than did those with frequent exacerbations (Table 5). In addition, more patients had poor QoL (38.5%) among the frequent exacerbation group than did those with zero or only a few exacerbations (14.3%, p < 0.01) (Table 5).

Patients with frequent exacerbation not only had poorer QoL but also in the closer investigation domains: physical, vitality, health, and respiratory domains were significantly reduced (p < 0.01) (Supplementary Table 6).

Discussion

Exacerbations of BE, extensive disease, and poor physical tolerance led to a significantly increased risk for poor QoL. In particular, frequent exacerbations led to increased risk for poor QoL by five-fold. Here, both disease severity (BSI) and physical tolerance (assessed by mMRC) negatively correlated with the QoL questionnaire’s physical domain. Although BSI evidently can accurately predict the hospitalisations, exacerbations, and mortality of non-cystic fibrosis BE patients, BSI is more challenging to use in clinical practice. The
reason is that it includes information also on lung function parameters and radiological findings, all of which makes BSI better suited to scientific purposes [6,13]. The mMRC and QoL scores have served to demonstrate the effect of new treatment options for BE [13].

The domains with the poorest overall self-reported results in the QoL questionnaire were health, vitality, and respiration. These scores are found to be stable if measured during a stable phase of BE, and they can serve to differentiate between mild, moderate, and severe BE patients [7]. One 2-year follow-up study of 19 BE patients did find, however, that physical functioning, role functioning, and health perceptions improved with treatment at a specialized care centre [14].

Our logistic regression analysis showed lower mMRC to be protective (OR 0.43) for poor QoL. Our finding of significantly reduced vitality score and mMRC score as correlating with the physical domain (correlation −0.57, p < 0.01) is in accordance with others’ findings of BE patients’ reduced physical activity, when compared to the activity levels of gender- and age-matched individuals without BE [15]. Further, exercise capacity is an important hallmark, correlating with quality of life domains of social functioning and respiratory symptoms [9]. Respiratory symptoms were able to explain 38% of the variance in BE patients’ sedentary behavior (r² 0.384), and of such patients, 23% we estimated to be physically inactive and 16% low active [9]. In the same study, neither FEV1% nor BSI correlated with sedentary behavior nor physical activity [9].

The identification of patients at high risk for exacerbations may be valuable to guide clinical decision-making with regard to factors such as the frequency and intensity of follow-up and use of long-term antibiotic therapy. Our scoring systems to assess BE severity gave different results for severe disease because 34.1% of patients were estimated to have severe BE according to BSI scoring, whereas only 11.6% classified as having severe BE with FACED grading. Similar results came in 2019 from an Australian cohort, with 58% of their cohort having severe disease according to the BSI, whereas 17% had FACED-defined severe disease [16]. Our results are also in good agreement with the observations of a large multidimensional severity assessment in 2016 that reported, in predicting overall clinically important disease-related outcomes, that the BSI is superior to FACED [13]. The BSI includes parameters for previous hospital admissions and the number of exacerbations in the previous year, whereas FACED includes a parameter for age [6,7,12]. Earlier, BSI was considered a tool for scoring the severity of BE and FACED a tool for predicting mortality [17,18].

When phenotyping BE patients, BE caused by connective-tissue disease has been associated with a poor prognosis and rapid disease progression [19]. Immunodeficiency, COPD, and allergic bronchopulmonary aspergillosis (ABPA) have been associated with recurrent exacerbations [19].

Whereas BE patients with COPD reported significantly worse QoL [17], in the current study we found poor QoL regardless of background aetiology in BE patients with exacerbations, and especially in those with frequent exacerbations. For our patients, neither asthma nor comorbidities were statistically significant risk factors for poor QoL. However, the number of our BE patients with COPD was so small that we did not include it here as an independent variable.

Previous severe exacerbations (OR 2.6) or an exacerbation in the past 12 months can be predictive of future exacerbations [6]. We found that the number of exacerbations, frequent exacerbations (OR 4.9), or extensive disease raised the risk for poor QoL in the analysis adjusted for age and gender. The negative effect on the QoL of exacerbations is understandable because exacerbations of BE mean periods of symptomatic disease with the need for additional treatment and usually also emergency or other unscheduled health care visits. In 2015 came a report that the median duration of an exacerbation was 16 days, and 16% of patients had at least one exacerbation with a duration of more than 35 days [20]. Thus, the association of poor QoL with exacerbations is crucial. BE patients with frequent exacerbations are recommended to have follow-up in specialized care centers in order to reduce exacerbations but also to prevent lung function deterioration and to maintain good QoL [18]. The current guidelines focus on recommending special care for those with three or more yearly exacerbations and for those on long-term antimicrobial therapy [1,21].

Similarly, diminished lung function expressed as FEV1 has been a reported risk factor for future exacerbations [6]. Although those patients with poor QoL had poorer lung function than did others, we did not identify lung function as a risk factor for future exacerbations. This may be due to our relatively small study population, together with our study population’s relatively well-preserved lung function.

Our findings were in agreement with those of a group who reported diminished physical activity of BE patients compared to that of healthy study individuals (measured by a pedometer) and that dyspnoea, pulmonary function, and long-term oxygen therapy were independently associated with physical activity
Physical training in different forms is advisable as part of BE patient therapy [1]. Further, high-intensity inspiratory muscle training leads to increased walk capacity and reduces fatigue in BE patients [23].

The limitations of the current study include its relatively small-sized cohort and the cross-sectional setting of its QoL analysis. The small sample size is a result of the small number of subjects recruited in the original study. The study strengths are the multifaceted perspective on symptoms resulting from comparison of the QoL questionnaire with mMRC, BSI, and FACED score results, and the fact that no data for QoL questions and mMRC scale results were missing.

Conclusions
Exacerbations in BE patients, especially frequent exacerbations, caused increased risk for poor QoL, but neither comorbidities nor BE aetiology appeared to affect QoL. In addition, more extensive disease or greater severity of BE elevated risk for poor QoL. Furthermore, the mMRC score for dyspnoea and BSI for severity of BE showed the strongest negative correlations with physical functioning in BE. When seeking strategies to improve QoL in BE, the focus should thus be upon preventing exacerbations and supporting physical fitness to reduce exercise-induced dyspnoea and to support patients’ ability both to cope with daily life activities and to cope with extensive disease.

Acknowledgments
The authors would like to acknowledge all the patients who participated in this study.

Disclosure statement
In relation to this study, the authors declare that there are no conflicts of interest.

Disclaimer
The funders of the study had no role in the study design, data collection, data analysis, data interpretation or writing of the report.

Contributorship statement
PK was responsible for the design, analysis, interpretation, drafting, and finalisation of the manuscript. WM was involved in the analysis, interpretation, drafting, and finalisation of the manuscript. JM was responsible for the data collection, analysis, interpretation, drafting, and finalisation of the manuscript. TT was involved in the data collection, drafting, and finalisation of the manuscript. PB provided statistical assistance and was involved in the finalisation of the manuscript.

Data-sharing statement
This is part of the EMBARC study, and data can be obtained from EMBARC register or from the authors by an approved application.

Funding
This study was supported by funding of the Foundation of the Finnish Anti-Tuberculosis Association, the Finnish Research Foundation of the Pulmonary Diseases, and the University of Helsinki and Helsinki University Hospital, Heart and Lung Center, Department of Respiratory Diseases, Helsinki, Finland. The Finnish Research Foundation of the Pulmonary Diseases.

Notes on contributors
Jarkko Mäntylä is a Chief Physician in Respiratory Medicine at Jorvi hospital, Espoo. His research focuses on bronchiectasis.

Witold Mazur is a Head of Pulmonary Department at Helsinki University Hospital and Adj. Professor. His research focuses on chronic obstructive pulmonary disease, asthma, and bronchiectasis.

Tanja Törölä is a Specialist in Respiratory Diseases and Allergology, at the Skin and Allergy Hospital, Helsinki. Her research focuses on asthma, chronic obstructive lung disease and bronchiectasis.

Paula Bergman is a teacher in the Faculty of Medicine in the University of Helsinki and Biostatistical consultant in Helsinki University Hospital.

Paula Kauppi is a Chief Physician of Respiratory Medicine of Helsinki University Hospital and Adj. Professor. Her research focuses on asthma, obstructive lung diseases, allergy, and bronchiectasis.

ORCID
Jarkko Mäntylä http://orcid.org/0000-0002-9640-4872
Paula Kauppi http://orcid.org/0000-0002-1065-330X

References
[1] Polverino E, Goeminne PC, McDonnell MJ, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J. 2017;50. DOI:10.1183/13993003.00629-2017.
[2] Lee AL, Button BM, Ellis S, et al. Clinical determinants of the 6-minute walk test in bronchiectasis. Respir Med. 2009;103(5):780–785.
[3] Eshed I, Minski I, Katz R, et al. Bronchiectasis: correlation of high-resolution CT findings with health-related quality of life. Clin Radiol. 2007;62(2):152–159.

[4] Wilson CB, Jones PW, O’leary CJ, et al. Validation of the St. George’s Respiratory Questionnaire in Bronchiectasis. Am J Respir Crit Care Med. 1997;156(2):536–541.

[5] Murray MP, Turnbull K, MacQuarrie S, et al. Validation of the Leicester Cough Questionnaire in non-cystic fibrosis bronchiectasis. Eur Respir J. 2009;34(1):125–131.

[6] Chalmers JD, Goeminne P, Aliberti S, et al. The bronchiectasis severity index: an international derivation and validation study. American Journal of Respiratory and Critical Care Medicine. 2014;189(5):576–585.

[7] Martínez-García MA, de Gracia J, Vendrell Relat M, et al. Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. Eur Respir J. 2014;43(5):1357–1367.

[8] Quittner AL, Marciel KK, Salathe MA, et al. A preliminary quality of life questionnaire-bronchiectasis. Chest. 2014;146(2):437–448.

[9] Bradley JM, Wilson JJ, Hayes K, et al. Sedentary behaviour and physical activity in bronchiectasis: a cross-sectional study. BMC Pulm Med. 2015;15(1):61.

[10] Mäntylä J, Mazur W, Törölä T, et al. Asthma as aetiology of bronchiectasis in Finland. Respir Med. 2019;152:105–111.

[11] Olveira C, Olveira G, Espíldora F, et al. Validation of a quality of life questionnaire for bronchiectasis: psychometric analyses of the Spanish QOL-B-V3.0. Qual Life Res. 2014;23(4):1279–1292.

[12] Ellis HC, Cowman S, Fernandes M, et al. Predicting mortality in bronchiectasis using bronchiectasis severity index and FACED scores: a 19-year cohort study. Eur Respir J. 2016;47(2):482–489.

[13] McDonnell MJ, Aliberti S, Goeminne PC, et al. Multidimensional severity assessment in bronchiectasis: an analysis of seven European cohorts. Thorax. 2016;71(12):1110–1118.

[14] Magge A, Ashraf S, Quittner AL, et al. Quality of life in patients with bronchiectasis: a 2-year longitudinal study. Ann Transl Med. 2019;7(14):334.

[15] Cakmak A, Inal-Ince D, Sonbahar-Ulu H, et al. Physical activity of patients with bronchiectasis compared with healthy counterparts: a cross-sectional study. Hear Lung. 2020;49(1):99–104.

[16] Visser SK, Bye PTP, Fox GJ, et al. Australian adults with bronchiectasis: the first report from the Australian Bronchiectasis Registry. Respir Med. 2019;155:97–103.

[17] Terpstra LC, Biesenbeek S, Altenburg J, et al. Aetiology and disease severity are among the determinants of quality of life in bronchiectasis. Clin Respir J. 2019;13(8):521–529.

[18] Mendes MA, Chalmers JD. Predicting outcomes in bronchiectasis. Pulmonology. 2018;24(3):146–148.

[19] Flume PA, Chalmers JD, Olivier KN. Advances in bronchiectasis: endotyping, genetics, microbiome, and disease heterogeneity. Lancet. 2018;392(10150):880–890.

[20] Brill SE, Patel ARC, Singh R, et al. Lung function, symptoms and inflammation during exacerbations of non-cystic fibrosis bronchiectasis: a prospective observational cohort study. Respir Res. 2015;16(1):16.

[21] Hill A T, Sullivan LA, Chalmers J D, et al. British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019;74(Suppl 1):1–69.

[22] José A, Ramos TM, de Castro RAS, et al. Reduced physical activity with bronchiectasis. Respir Care. 2018;63(12):1498–1505.

[23] Ozalp O, Inal-Ince D, Cakmak A, et al. High-intensity inspiratory muscle training in bronchiectasis: a randomized controlled trial. Respirology. 2019;24(3):246–253.