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Original Article

Severity assessment of non-cystic fibrosis bronchiectasis by the FACED score

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ABSTRACT

Objectives: Bronchiectasis (BE) is a major health problem associated with a high morbidity and mortality. This study aimed to determine the relation of the FACED score (a multidimensional score contributing to stratify patients into risk categories) with the severity of non-cystic fibrosis bronchiectasis (NCFB) among our population.

Materials and Methods: This is a retrospective single center study of 105 consecutive patients with NCFB hospitalized for acute exacerbations (AE) at the Department of Respiratory Medicine of Fattouma Bourguiba Teaching Hospital in Monastir (Tunisia) between January 2005 and December 2017. Patients were divided into two groups (G): G1: FACED Score ≤ 2 and G2: FACED score ≥3. We compared different severity parameters of BE between the two groups.

Results: The study included 105 patients with NCFB. Patients of G2 had more comorbidities ($P = 0.028$), an altered respiratory function with a lower forced vital capacity (G1:2.73, G2:1.33 L; $P < 0.001$), a decreased PaO2 (88 vs. 68 mmHg; $P < 0.001$), a high CO2 level ($P < 0.001$), and a higher number of AE/year (0.96, 2.12 AE/year; $P < 0.001$). Hospitalizations for AE of G2 were characterized by a lower PaO2, a higher PaCO2 ($P < 0.001$), a longer course of antibiotic ($P < 0.001$) with an extended hospitalization ($P = 0.007$). An ultimate evolution toward chronic respiratory failure was more common in G2 ($P < 0.001$).

Conclusion: A high FACED score is associated with more symptoms, an altered respiratory function, a higher number and more severe AE, more health-care utilization with worse outcomes. Further studies are necessary to evaluate the impact of such scales in clinical practice.

Keywords: Bronchiectasis, Patient outcomes assessment, Respiratory function tests, Disease exacerbation, Hospitalization.

INTRODUCTION

Bronchiectasis (BE) is a major health problem associated with a high morbidity and mortality.[1,2] It is a chronic respiratory disease. characterized by abnormal and irreversible dilatation of the airways and symptoms such as chronic cough, purulent sputum production, hemoptysis, dyspnea and other distressing symptoms.[1] It is related to a vicious cycle of compromised host defenses, inflammation, impaired mucociliary clearance, chronic colonization with bacteria, and recurrent infection leading to destruction and remodeling of the bronchial wall.[2] Radiologically, there is abnormal and permanent dilatation of the bronchi.[2]

In recent years, BE has become a major health concern for several reasons. In fact, the clinical course of the disease is characterized by the occurrence of acute exacerbations (AE)

which progressively worsens dyspnea, lung function and deterioration in quality of life.[2,3] Thus, BE is associated with repeated hospitalizations and high morbidity and mortality, causing a significant economic burden.[4]

BE is classified as cystic fibrosis related BE and non-cystic fibrosis bronchiectasis (NCFB).[5] NCFB affects a heterogeneous population of patients with diverse etiologies. It is a multidimensional disease. It may result from various hereditary or acquired, local, or systemic diseases.[6]

Despite the limited number of effective treatment approaches and evidence-based management guidelines, it is necessary to evaluate disease severity meticulously to ensure better therapeutic approach.[7]

Several single variables such as the decline in lung function, different clinical parameters, radiological findings, and the presence of chronic colonization have been used to assess the severity of NCFB and to predict key outcomes of the disease.[8] However, the severity and prognosis of NCFB cannot be adequately assessed through a single variable analysis.[9]

Accordingly, few multidimensional scales have been published in recent years, using several different variables that are easily obtained and have a proven capacity for an accurate appreciation of the severity and the prognosis of the disease.[10,11] In this regard, two multidimensional validated scores are currently used to assess the severity of NCFB: The FACED score and the Bronchiectasis Severity Index (BSI).[10,11]

Martinez-Garcia *et al*. recently developed the FACED score, which comprises five variables: Functional (percentage of predicted forced expiratory volume in 1 s [FEV1% predicted]), physiological (age), microbiological (chronic colonization by *Pseudomonas aeruginosa*), radiological (number of lobes affected), and clinical parameter (degree of dyspnea, evaluated by the Medical Research Council [MRC] scale).[10] The FACED score is a scale contributing to stratify patients into risk categories.

This scale has been validated in several countries.[12,13] Nonetheless, there is little information regarding NCFB in African countries. Furthermore, to the best of our knowledge, there are no published data related to the study of the FACED score in the latter countries.

The aim of this study is to determine the relation of the FACED score with the severity of NCFB among our North-African based population.

MATERIALS AND METHODS

Study design and subjects

This is a retrospective single center study of 105 consecutive patients with NCFB hospitalized for AE in the Department of Respiratory Medicine of Fattouma Bourguiba Teaching Hospital in Monastir (Tunisia) between January 2005 and December 2017.

All the patients had a diagnosis of BE according to the current recommendations. It was diagnosed by high-resolution computed tomography (HRCT) scan of the chest in patients with a compatible clinical presentation.[14]

Inclusion criteria were: Age of 18 years or greater, proven BE on HRCT, and follow-up period of at least 1-year.

Potential participants were not included based on the following criteria: Patient with cystic fibrosis related BE, presence of active malignancy, primary diagnosis of pulmonary interstitial disease or fibrosis, chronic obstructive pulmonary disease (COPD), or asthma as a primary respiratory diagnosis.

Patients were excluded if they lacked complete data to calculate the FACED score or other sufficient important data related to: Respiratory functional tests, AE or hospital admissions, treatments, and evolution.

Data collection

Data on demographic variables (gender, age, body mass index), smoking habit, presence of comorbidities, and clinical features such as baseline dyspnea grade as defined by modified MRC, radiological variables (number and location of involved lobes, and type of BE), etiology of BE, number of hospitalization for AE-NCFB during the follow-up period, number of AE-NCFB/year, pulmonary function tests, microbiological findings (colonization by potentially pathogenic microorganisms), and use of long-term oxygen therapy and medications were collected from medical records. Spirometry and blood gases were performed in the stable period.

We used the consensus-based definition for BE exacerbation: A person with BE with deterioration in three or more of the following key symptoms for at least 48 h: Cough; sputum volume and/or consistency; sputum purulence; breathlessness and/or exercise tolerance; fatigue and/or malaise; and hemoptysis AND a clinician determines that a change in BE treatment is required.[15] We defined severe exacerbation as an exacerbation requiring hospital admission. The latter was defined as a medical ward stay of greater than 24 h.

The mean number of AEs per year was calculated based on the available data in medical records, including hospitalizations for AE in our department or in other hospitals reported by patients, visits to emergency department for AE, and all reported AE during different consultations.

We collected also details related to hospitalizations for AE-NCFB (blood gases results, length of hospitals stay and

antibiotic treatment, C-reactive protein [CRP], and white blood cells [WBC] count). We calculated the mean number of each variable related to the different hospitalizations.

Data on prognosis (cumulative number of deaths for all-causes) were collected from hospital medical records or through the telephone.

Severity of disease

The disease severity was calculated using the FACED score [Table 1]. The latter predicts the probability of all-cause mortality after 5 years of follow-up.[16] It is also a tool to assess clinically relevant outcomes.

This score incorporates five dichotomic variables: Percentage of predicted FEV1 in %, age, presence of chronic colonization by *P. aeruginosa*, radiographic extension, and dyspnea. The severity of dyspnea was assessed according to the MRC breathlessness scale. All patients underwent spirometry. Spirometry results were expressed as percentage (%) of the predicted value. Sputum cultures were analyzed according to the standard methods to assess the presence of pathogens.[17] Chronic colonization was defined by the isolation of potentially predominant pathogenic bacteria in a sputum culture on two or more occasions, at least 3 months apart in a 1-year period.[14] The radiological evaluation represents the extent of BE according to the number of lung lobes involved (the lingula was considered as independent lobe).[9,18]

The total score is calculated by summing the scores for each variable and can range from 0 to 7 points. This score classifies BE into three severity classes: Mild BE (overall score 0–2 points), moderate BE (overall score 3–4 points), and severe BE (overall score 5–7 points).

Grouping

We determined for each patient the FACED score. Patients were divided into two groups (G): G1: FACED score ≤2 (mild BE) and G2: FACED score ≥3 (moderate and severe BE). We compared different severity parameters of BE between the two groups at baseline status and during AE.

Table 1: The FACED score.

Variables		Values	Points
F	FEV1	≥50%	0
		<50%	2
A	Age	<70 years	0
		≥70 years	2
C	Chronic colonization	No pseudomonas	0
		Presence of *Pseudomonas*	1
E	Extension	1–2 lobe	0
		>2 lobes	1
D	Dyspnea	0–2 MRC	0
		≥3 on MRC scale	1

Mild bronchiectasis: 0–2 points, moderate: 3–4 points, severe: 5–7 points. FEV1: Forced expiratory volume in one second, MRC: Medical Research Council dyspnea scale

Ethics

This research is a retrospective study utilizing the NCFB database of our department and no specific patient identifiable information was used. Patient confidentiality was maintained by de-identification of all data. The Institutional Ethics Committee was contacted and we were exempted from a formal ethical approval. In fact, this kind of retrospective data study can be exempted from an official ethical permission and all the steps were taken to ensure the anonymity and confidentiality of the data.

Statistical analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences V. 20 for Windows. Categorical variables were expressed in absolute values and proportions. Continuous variables were expressed as mean ± SD. Means were compared using the Student's *t*-test for independent samples. Proportions between groups were compared using the Chi-square test. $P < 0.05$ was considered significant.

RESULTS

Baseline characteristics of patients with NCFB

A total of 105 patients fulfilled the eligibility criteria and were included in the study. The baseline characteristics of the patients included are described in [Table 2]. The mean age of the total sample was 56 ± 18 years, with 53% males, and 7% current or former smokers. The mean FEV1 was 1.44 ± 1 (51 ± 24% of predicted). The mean number of BE AEs per year was 1.6 ± 1.3. The mean FACED score was 2.7 ± 2. Patients were followed for a mean period of 56 months. Forty-two patients (40%) were treated by long-acting beta-2 agonist. No patient had a long-term antibiotic treatment.

According to the FACED score, 44% of the patients had mild BE (46 cases): Group 1; 33% moderate BE (35 cases) and 23% severe BE (24 cases): Group 2 [Figure 1].

Concerning the etiology of NCFB, data analysis revealed that 58 patients (55%) had idiopathic NCFB. The most common cause being post-infectious (non-tuberculosis) and accounting for 22 (21%). Different other causes were identified: Post-tuberculosis (13 patients – 12%), primary ciliary dyskinesia (5 patients – 5%), primary immunodeficiencies (4 patients – 4%), and foreign body airway obstruction (3 patients – 3%).

Table 2: Baseline characteristics of NCFB patients.

	Number/ mean	Frequency (%)
N patients	105	
Age	56±18	
Gender (male)	55	53
Smoking (current/former)	8	7
Pack years	39±26	
N of attained lobes	3.3±1.7	
N of comorbidities ≥1	67	64
mMRC ≥2	75	71
FEV_1 (L)	1.44±1	
FEV_1(%)	51±24	
FVC (L)	1.94±1	
FVC (%)	57±21	
FEV_1/FVC (%)	71±15	
FEV_1<50%	64	61
PaO2 (mmHg)	76±17	
PaCO2 (mmHg)	40±6	
N acute exacerbations/year	1.6±1.3	
Frequent exacerbators (N AE≥2/y)	37	35
N H pulmonary department/year	0.8±0.5	
H in ICU	14	13
Chronic respiratory failure	36	34
Home Oxygen	22	21
Follow-up (month)	56	

NCFB: Non cystic fibrosis bronchiectasis, N: Number, mMRC: Modified Medical Research Council, FEV1: Forced expiratory volume in one second, FVC: Forced vital capacity, PaO2: Oxygen arterial tension, PaCO2: Carbon dioxide arterial tension, AE: Acute exacerbation, y: Year, H: Hospitalization, ICU: Intensive care unit, L: Liter

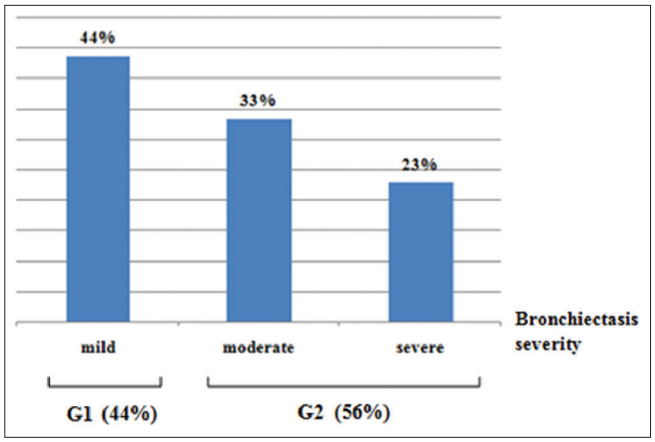

Figure 1: Patients grouping and risk stratification according to the FACED score.

During the period of follow-up, five patients from the G2 died, whereas we did not note any death in G1.

We compared different severity parameters of BE concerning the baseline status and AE between the two groups of patients: G1: FACED score ≤2 (46 patients, 44%) and G2: FACED Score ≥ 3 (59 patients, 56%) [Figure 1].

Comparison between the two groups at the baseline

Group 2 was characterized by a higher number of females with more associated comorbidities. Several other variables were significantly associated with a high FACED score. Patients of Group 2 had an altered respiratory function, a greater number of AE per year, with more hospitalizations and an ultimate evolution toward chronic respiratory failure [Table 3].

Comparison of severe AE-NCFB features between the two groups

There was no significant difference in mean CRP level between the two groups (P = 0.15). A high FACED score (G2) was associated with a decreased arterial oxygen tension (PaO2), an increased PaCO2, and an increased number of WBC. We observed a significant difference between the two groups in terms of hospital stay (P = 0.007) and antibiotic treatment durations (P < 0.001). Group 2 had a longer course of antibiotics with an extended hospitalization [Table 4].

DISCUSSION

NCFB is associated with a high morbidity and mortality.[1,2] Stratifying patients into severity classes is a major concern related to the disease to ensure the best care. In line with this target, the FACED score was conceived.[10] This study aimed to determine the relation of the FACED score with the severity of NCFB among our North-African based patients. The results suggest that a high FACED score is associated with more symptoms, an altered respiratory function, a higher number and more severe AE, and more health-care utilization with worse outcomes.

Some variables were used to assess and predict NCFB outcomes. In fact, FEV1 has been used to define the severity of BE in different reports.[3,10,19] The decline in lung function also correlates with clinical parameters, the risk of AE occurrence, and the presence of chronic colonization by *P. aeruginosa*.[3,8] Furthermore, CT findings provide important information about structural abnormalities in airway diseases and the extent of the lesions.[20] CT scores, such as the modified Reiff *et al*. score and Bhalla *et al*. score, have also been proposed as indicators of disease severity.[21,22] Other variables, such as age, airway chronic colonization, and quality of life, have proved usefulness in this respect by showing a correlation with mortality in BE.[8] However, these separate parameters did not correlate adequately with the severity of NCFB.[7-9] Indeed, just one of these factors on its own is certainly inadequate for predicting outcomes or helping in clinical decision-making.[7-9]A scoring system including different variables was then essential to a better assessment of BE severity. There are mainly two scales that can be used to assess the severity and the prognosis of the

Table 3: Comparison between the two groups at the baseline.

	G1 (Mild)	G2 (Mod/Sev)	*P*-value
Gender (male, %)	68.9	40.7	0.004
BMI (kg/m^2)	23.3	23	0.83
N of comorbidities ≥1 (%)	52.2	72.9	0.028
FVC (L)	2.73	1.33	<0.001
FVC (%)	73	45	<0.001
FEV1/FVC (%)	78	66	<0.001
PaO2 (mmHg)	88	68	<0.001
PaCO2 (mmHg)	37.6	42.8	<0.001
N AE / year	0.96	2.12	<0.001
N H pulmonary department/year	0.51	1.1	<0.001
N H in ICU/year	0.01	0.16	0.016
NIV (%)	0	22	0.001
IMV (%)	0	15.3	0.013
Chronic respiratory failure (%)	6.5	56	<0.001
Home oxygen (%)	0	37.3	<0.001

G1: Group 1, G2: Group 2, Mod: Moderate, Sev: Severe, BMI: Body mass index, N: Number, FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second, PaO2: Oxygen arterial tension, PaCO2: Carbon dioxide arterial tension, AE: Acute exacerbation, H: Hospitalization, ICU: Intensive care unit, L: Liter, NIV: Non-invasive ventilation, IMV: Invasive mechanical ventilation, y: Year

Table 4: Comparison of AE-NCFB features between the two groups.

	G1 (Mild)	G2 (Mod/Sev)	*P*-value
PaO2 (mmHg)	81.55	62.3	<0.001
PaCO2 (mmHg)	38.2	45.2	<0.001
CRP (mg/L)	28	42	0.15
WBC (cells/mm^3)	9232	11393	0.014
Duration of antibiotic treatment (days)	9.8	14	<0.001
Duration of hospitalization (days)	9.9	13.3	0.007

AE: Acute exacerbation, NCFB: Non-cystic fibrosis bronchiectasis, G1: Group 1, G2: Group 2, Mod: Moderate, Sev: Severe, PaO2: Oxygen arterial tension, PaCO2: Carbon dioxide arterial tension, CRP: C-reactive protein, WBC: White blood cells

NCFB: The FACED and BSI scores. The FACED score is a multidimensional scale. It was conceived and validated for the 1st time by Martinez-Garcia *et al*.[10] The latter conducted an observational multicenter study including 819 patients diagnosed with NCFB using HRCT. The outcome was 5-year all-cause mortality after radiological diagnosis. Different parameters were studied to establish the score. The final seven-point score incorporated five variables. It stratifies patients into three severity risk categories to predict the likelihood of mortality.

The FACED score is an easy-to-use multidimensional tool that has demonstrated an excellent prognostic value for mortality in patients with BE.[10] One of the important advantages of the FACED score is its simplicity. The constituent variables of the score are very easy to memorize and the total score is easy to obtain, calculate, and interpret. In our research, it was not possible to study the prognosis value of the FACED score due to the low number of death in our population.

This score was conceptualized basically to predict the likelihood of 5-year mortality of NCFB of any etiology.[9] However, it was used to assess other severity parameters of BE in other studies. In fact, the FACED score was studied and validated in different populations.[9,12,13] In this context, a Latin America validation of the FACED score was performed. Athanazio *et al*. conducted a retrospective and multicenter study including 651 patients with BE. Even if the clinical features and etiologies were different from the original cohort of Martinez-Garcia *et al*., the FACED score maintained an excellent power to predict all-cause and respiratory mortality. The score maintained also an excellent discriminatory power by identifying a profile of increased severity in patients with BE that was similar to that seen in the original Spanish study. Furthermore, the authors demonstrated that the score has a good capacity to predict AE and hospitalizations.[12] These results are in agreement with our findings. In a recent study, an increasing disease severity as measured by FACED score was correlated with a lower quality of life.[5]

The FACED score was also compared to the BSI in different populations. The BSI was introduced by Chalmers *et al*.[11] This score included HRCT score, FEV1, MRC dyspnea score, bacterial colonization (*P. aeruginosa* or other pathogenic bacteria), prior hospital admission, and exacerbations. They found that the BSI was a sensitive tool in predicting future risks of hospitalization and mortality.[11] McDonnell *et al*. evaluated both the FACED and BSI scores in a large population of 1612 patients including seven European cohorts. Both scores had a good discriminatory predictive value for mortality.[13] However, the BSI was superior to FACED score in predicting multiple clinically useful outcomes including respiratory symptoms, AE, hospital admissions, quality of life, exercise capacity, and lung function decline.[13] In other studies, the comparison between the two scores revealed that both scoring systems had similar predictive power for 5-year mortality with high specificity with a minor proportion of patients having discordant BSI and FACED scores.[16,23] Whilst both scores were able to predict 5-year mortality, the FACED score was superior.[16] Other conflicting results were found in a study including Aboriginal Australians. The latter were significantly younger and died at a significantly younger age than other groups. A milder assessed disease by FACED scores did not imply a better prognosis.[24] Hence, extrapolating prognostic scores based on specific cohorts to other populations must be done with caution.[24]

Patients with BE have frequent exacerbations that cause significant morbidity, mortality, and health-care costs.[14] AE of BE is associated with increased airways and systemic inflammation,[25] progressive lung damage,[2,26] poor quality of life, daily symptoms,[27] lung function decline,[28] and mortality.[11] The European registry data showed that approximately 50% of European BE patients have at least 2 AE per year and one-third require at least one hospitalization per year.[29] Although the FACED score has demonstrated a great prognostic capacity in BE and predicts future events like AE, it does not include the number or severity of exacerbations as a separate variable.[30] The E-FACED is a new scale including the number of severe exacerbations in 1 year. It was recently constructed and validated by Martinez-Garcia *et al.* to increase its capacity to predict future events (AE) and its prognostic value. The E-FACED score significantly increased the FACED capacity to predict future events (AE) while maintaining the score's simplicity and prognostic capacity.[30]

The economic burden of BE has been assessed by some studies. The costs are related to treatments, emergency visits, hospitalizations, and need for intensive care.[2,4,31] They increase significantly with the severity. A higher FACED score was associated with increased costs.[31]

To the best of our knowledge, this is the first study that has investigated the relation of the FACED score with the severity of NCFB in a North-African population. Among the strengths of the present study, is the availability of data to study several parameters related to the severity of the disease. Furthermore, the results represent the real-life situation in our hospital. Moreover, our NCFB population was not treated with long-term (≥3 months) anti-inflammatory or antibiotic medications and provides some insight on the natural history of the disease..

Nevertheless, the current study is not without limitations. First, given the retrospective character of this research, not all variables could be collected for every patient. For example, some AE may not be documented in the medical records leading to an under-appreciation of the real number of these events. On another hand, some investigations were not available for all patients and the impact of such missing data on selection bias should be considered. Second, it is a single-center study with a relatively small number of patients, which could have certain implications on the their interpretation. Furthermore, the mean period of follow-up was 56 months and they ere few death which precluded the predictive ability of the FACED score regarding mortality. In addition, the majority of the patients had either idiopathic or post-infective NCFB. Thus, the results may not be generalized to other NCFB populations having different etiology proportions. Finally, we considered HRCT reports in medical records to define cases of BE. The accurate assessment of BE may differ from one reporting radiologist to another.

CONCLUSION

Our results suggest that a high FACED score is associated with more symptoms, an altered respiratory function, a higher number and more severe AE, and more health-care utilization with worse outcomes. This scale provided a clinically relevant evaluation of disease severity. However, NCFB is characterized by its heterogeneity in terms of etiologies, clinical presentations, radiological findings, biological parameters, and bacterial features. The incorporation of other elements in the scoring system may be required. Further studies are needed to determine how such scales may have an impact on clinical practice, phenotyping process, and treatments choice in the scope of personalized medical care.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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