A 3-year prognostic score for adults with cystic fibrosis

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Original Article

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Abstract

Background: Therapeutic progress in patients with cystic fibrosis (CF) has resulted in improved prognosis over the past decades. We aim to reevaluate prognostic factors of CF and provide a prognostic score to predict the risk of death or lung transplantation (LT) within a 3-year period in adult patients.
Methods: We developed a logistic model using data from the French CF Registry and combined the coefficients into a prognostic score. The discriminative abilities of the model and the prognostic score were assessed by c-statistic. The prognostic score was validated using a 10-fold cross-validation.
Results: The risk of death or LT within 3 years was related to eight characteristics. The development and the validation provided excellent results for the prognostic score; the c-statistic was 0.91 and 0.90 respectively.
Conclusion: The score developed to predict 3-year death or LT in adults with CF might be useful for clinicians to identify patients requiring specialized evaluation for LT.

Keywords: Cystic fibrosis; Prognostic factors; Registry data; Logistic model; Prognostic score

1. Introduction

Cystic fibrosis (CF) is a multiorgan disease that affects primarily the lungs, causing diffuse bronchiectasis which often leads to progressive respiratory insufficiency and premature death [9]. Lung transplantation (LT) is proposed to CF patients with terminal respiratory failure with the aim of improving life expectancy and quality of life [25]. Although criteria for referring patients for LT have been proposed [14], the optimal timing for referring CF patients for transplantation remains difficult to establish in an individual patient. A recent study in France has shown that respiratory death in CF patients often occurs due to late or no referral for LT [19], suggesting the need to develop novel strategies for referring patients at high risk of death for transplant evaluation.

In the past 25 years, several statistical models have been developed to identify prognostic factors in CF patients. In their seminal study, Kerem et al. identified forced expiratory volume in 1 s (FEV_1) as the main prognostic factor and suggested that patients with an FEV_1 value less than 30% should be considered for LT [16]. Subsequent studies identified multiple other factors related to death in patients with CF including older age [17,21],

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female gender [16,17], lower body mass index (BMI) [21], pancreatic insufficiency [1,17], diabetes [1,17], *Pseudomonas aeruginosa* colonization [1,6], *Burkholderia cepacia* colonization [4,6,17], *Staphylococcus aureus* colonization [7], massive hemoptysis [11], pneumothorax [10] and high number of pulmonary exacerbations [4,17,21]. Although several attempts at developing prognostic scores have been performed in CF patients [1,4,13,17,20,21], it has proven difficult to develop a score that better predicts death than $FEV_1 < 30\%$ predicted [20]. Further, prognosis has dramatically improved over the past decades due to advance in integrated care provided by multidisciplinary teams in CF centers [2,8,12,18,23]. As a result, prognostic factors have changed over time and studies performed using data obtained in previous decades may not be appropriate for current evaluation of CF patients. For example, George et al. showed an important improvement in the survival of patients whose FEV_1 has fallen below 30% of predicted value. Consequently, they suggested that the threshold of 30% predicted for FEV_1 should no longer be considered in isolation as an indication for LT [12]. Moreover, pediatric mortality in patients with CF has almost disappeared in developed countries due to improvement in patients care by multidisciplinary teams [26].

The aim of the present study was to develop a 3-year predictive model that provides a prognostic score to better predict the risk of death or LT in adult patients with CF.

2. Materials and methods

2.1. The French Cystic Fibrosis Registry

We used data from the French Cystic Fibrosis Registry (French CF Registry). This registry contains longitudinal data on more than 8000 patients since 1992, which represents approximately 90% of all CF patients in France [3]. Each patient is assigned to a center specialized in CF, where his/her health status is regularly monitored. A numeric code is assigned to each patient to link information between specialized centers and the French CF Registry. This registry records annual health-check data for each subject including vital status, therapeutic management, anthropometry, spirometry, morbidity factors, consultations and hospitalizations, arterial blood gas, microbiological tests, pregnancy and paternity, and transplantations and sociodemographic data [3].

2.2. Patients and data collection

The period of the study was 2010–2013. Patients alive and aged 18 years or older on 31st December 2010 and for whom vital status was known on 31st December 2013 were included in the study. Patients who received a lung transplant before 2010 and patients lost to follow-up between 2011 and 2013 were excluded from the study. Forty-two covariates (listed in Table 1 and Supplementary Table 1) considered as potential predictors and records of the year 2010 were extracted to predict the outcome, defined as death or LT before the end of 2013. Fig. 1 presents the selection scheme of patients who were included in the study.

2.3. Missing data imputation

In 2010, only 12% of patients had complete information for all the 42 potential predictors. However, the percentage of missing data represented only 4%, as illustrated in Table 1. To deal with missing data in the covariates, a multiple imputation by chained equations was used [27]. We assumed that data were missing at random that is, the probability of missingness depends on the values of the observed covariates.

2.4. Model development

The characteristics of patients according to the outcome were compared using chi-square test or Fisher's exact test for categorical variables, and the Mann–Whitney test for continuous variables. We developed a multivariable logistic regression model to predict the outcome of interest, defined as death or LT by the end of 2013. Covariates that were significantly associated to the outcome in 2013 (p value <0.25) with univariate analysis were considered for the multivariable logistic regression model. A forward stepwise selection process was used to select the subset of variables independently associated with the outcome. The predictors retained in the final model were combined into a prognostic score to easily estimate the individual risk of death or LT within 3 years. To this end, continuous predictors were transformed into categorical variables according to clinically relevant thresholds. The contribution of each predictor to the prognostic score was proportional to its regression coefficient. To help the clinician to easily obtain the prognostic score and the risk of death or LT in a 3-year period using the patient characteristics, a nomogram was provided.

2.5. Model performances

Performances of the developed model and the prognostic score were investigated in terms of discrimination and calibration. Discrimination assesses how well the model can distinguish patients with the outcome of interest and patients without. This was evaluated using the c-statistic, also known as the area under the receiver operating characteristic curve [5]. The calibration compares the observed proportion of events against the predicted probabilities. It was evaluated using the Hosmer-Lemeshow test [15]. These performances were tested for both the developed model and the prognostic score, on each imputed dataset.

2.6. Model internal validation

To avoid overestimation of the model performances, we performed an internal validation using a 10-fold cross-validation. Overestimation happens when the model performs well on the data used for development but not on test data. Cross-validation can help detect overestimate models and helps to assess how well the model fits new observations. We randomly partitioned the initial dataset into 10 subsamples, fitted the model on nine of the subsamples and evaluated its performances on the other. We repeated this ten times, leaving out each subsample once. The performance of the prognostic score was evaluated using the

Table 1
Characteristics of 2096 adult CF patients in 2010 according to vital status on December 31st 2013.

Patient characteristics	Missing data (%)	Total n = 2096 (%)	Alive without LT n = 1828 (%)	Death or LT n = 268 (%)	p value
Gender, Male	0	1101 (52.5)	960 (52.5)	141 (52.6)	1
CFTR genotype	0				<0.001
Classes 1–3		1373 (65.5)	1165 (63.7)	208 (77.6)	
Classes 4/5		254 (12.1)	238 (13.0)	16 (6.0)	
Classes unknown		469 (22.4)	425 (23.3)	44 (16.4)	
Airway colonization	0	2013 (96.0)	1747 (95.6)	266 (99.3)	
Achromobacter xylosoxidans	0	133 (6.6)	98 (5.6)	35 (13.2)	<0.001
Aspergillus fumigatus	0	641 (31.8)	556 (31.8)	85 (32.0)	0.02
Burkholderia cepacia	0	69 (3.4)	51 (2.9)	18 (6.8)	<0.001
Non-tuberculous mycobacteria	0	95 (4.7)	79 (4.5)	16 (6.0)	0.009
Pseudomonas aeruginosa	0	1319 (65.5)	1102 (63.1)	217 (81.6)	<0.001
Staphylococcus aureus	0	1290 (64.1)	1136 (65.0)	154 (57.9)	0.001
Stenotrophomonas maltophilia	0	203 (10.1)	166 (9.5)	37 (13.9)	0.001
Comorbidities	0	2007 (95.8)	1741 (95.2)	266 (99.3)	0.004
Cirrhosis	0	98 (4.9)	77 (4.4)	21 (7.9)	<0.001
Insulin-treated diabetes	0	343 (17.1)	256 (14.7)	87 (32.7)	<0.001
Pancreatic insufficiency	0	1758 (87.6)	1504 (86.4)	254 (95.5)	<0.001
Allergic bronchopulmonary aspergillosis	12 (0.6)	378 (18.9)	302 (17.5)	76 (28.7)	<0.001
Hemoptysis	9 (0.4)	204 (10.2)	152 (8.8)	52 (19.5)	<0.001
Pneumothorax	9 (0.4)	29 (1.5)	19 (1.1)	10 (3.8)	<0.001
Depression	30 (1.4)	147 (7.3)	114 (6.6)	33 (12.6)	<0.001
FEV_1, % predicted [a]	144 (6.9)	58.3 (39.4–79.8)	63.3 (44.9–82.3)	29.1 (22.2–36.3)	<0.001
FVC, % predicted [a]	150 (7.2)	79.0 (62.2–95.2)	82.4 (67.0–97.7)	50.3 (38.6–60.6)	<0.001
Age (years) [a]	0	25.5 (21–32.3)	25 (21–32)	26.5 (22–33)	0.02
Height (cm^2) [a]	84 (4.0)	167 (160–173)	167 (160–173)	165.9 (160–172)	0.26
Weight (kg) [a]	63 (3.0)	56 (50–63)	57 (51–64)	51 (46–57)	<0.001
BMI (kg/m^2) [a]	92 (4.4)	20.2 (18.5–22.1)	20.4 (18.9–22.3)	18.4 (17.3–20.0)	<0.001
Number of IV antibiotics courses/year [a]	22 (1.0)	1 (0–2)	1 (0–2)	3 (2–5)	<0.001
Number of IV antibiotics days/year [a]	76 (3.6)	14 (0–30)	0 (0–28)	45 (21–75)	<0.001
Number of days of hospitalization/year [a]	327 (15.6)	0 (0–23)	0 (0–1)	2 (1–3)	<0.001
Azithromycin	10 (0.5)	1254 (59.8)	1056 (58.1)	198 (74.2)	<0.001
Non-invasive ventilation	11 (0.5)	127 (6.1)	51 (2.8)	76 (28.5)	<0.001
Long-term oxygen therapy	11 (0.5)	230 (11.0)	97 (5.3)	133 (49.8)	<0.001
Oral corticosteroids	13 (0.6)	171 (8.2)	125 (6.9)	46 (17.3)	<0.001
Inhaled therapies	0	1873 (89.4)	1618 (88.5)	255 (95.1)	0.001
Inhaled antibiotics	0	1122 (59.9)	928 (57.4)	194 (76.1)	<0.001
Inhaled corticosteroids	0	1012 (54.0)	868 (53.6)	144 (56.5)	0.003

FEV_1%: forced expiratory volume in 1 s as percentage of predicted values.
FVC %: forced vital capacity as percentage of predicted values.
BMI: body mass index.
IV: intravenous.
CFTR: cystic fibrosis transmembrane conductance regulator.
LT: lung transplantation.
[a] Continuous variables, median (interquartile range).

c-statistic. The process above was repeated 10 times on each imputed datasets and we averaged all the values of c-statistic to produce a single estimation of it.

2.7. Sensitivity analysis

A total of 184 patients lost to follow-up have been excluded from the analysis. In order to provide the lack of impact of this exclusion on the model, we reanalyzed the data including these patients after imputation of their outcome.

The two outcomes (death without LT and occurrence of LT) may be predicted by different covariates. We further investigated if the use of the separate outcomes altered the interpretation, by reanalyzing our data using each individual component.

All statistical analyses were performed using R software version 3.3.1.

3. Results

3.1. Data description

There were 2096 patients in the French CF Registry who satisfied the study criteria. A total of 268 (13%) died or received LT within the 3-year follow-up period, including 55 deaths without LT and 213 transplantations. Patient characteristics according to death or LT at 3 years are provided in Table 1. Significant differences in baseline characteristics were observed between patients who died or received LT during the 3-year follow-up period and those who

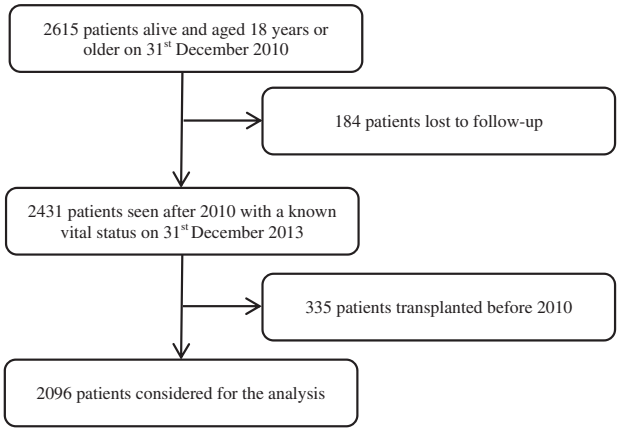

Fig. 1. Patients selection in the French CF Registry on 31st December 2010.

remained alive without LT. The median (interquartile range) age of patients at death or LT was 26.5 (22–33) years. Patients who died or received LT had lower BMI, FEV_1 and forced vital capacity (FVC), and had higher rates of airway microbial colonization than patients who remained alive without LT.

Patients who died or received LT were more likely to have been diagnosed with ABPA, hemoptysis, pneumothorax, insulin-treated diabetes, liver cirrhosis and depression. Treatment burden was also higher in these patients with higher rates of long-term oxygen therapy, non-invasive ventilation, oral corticosteroids, azithromycin and higher number of days with intravenous (IV) antibiotics and hospitalization.

3.2. Model development

The results of the multivariable logistic regression obtained after forward selection for variables associated with death or LT are shown in Table 2. The predictive model included 3 predictors directly related to the patient clinical characteristics in particular: FEV_1, BMI and *Burkholderia cepacia* colonization. It also identified 5 therapeutic variables, namely oral corticosteroids, long-term oxygen therapy, non-invasive ventilation, number of IV antibiotics courses per year and number of days of hospitalization per year. The risk of death or LT was higher for patients with lower values of FEV_1, BMI or with *Burkholderia cepacia* colonization.

Table 2
Logistic regression model for prediction of within 3-year death or lung transplantation in adults with CF.

	Odds ratio (95% CI)	p value
FEV_1, % predicted	0.94 (0.92–0.95)	<0.001
BMI (kg/m^2)	0.87 (0.81–0.93)	<0.001
Burkholderia cepacia colonization		0.007
Test negative	1	
Test positive	3.15 (1.55–6.41)	
No test	1.17 (0.23–5.93)	
Number of intravenous antibiotics courses/year	1.16 (1.07–1.26)	<0.001
Number of days of hospitalization/year	1.17 (1.06–1.28)	0.001
Oral corticosteroids	2.05 (1.25–3.35)	0.004
Long-term oxygen therapy	2.81 (1.83–4.32)	<0.001
Non-invasive ventilation	1.74 (1.01–3.00)	0.04

Furthermore, the risk of death or LT within 3 years increased with number of days of hospitalization per year, number of IV antibiotics courses per year, the use of oral corticosteroids, long-term oxygen therapy and non-invasive ventilation. The Hosmer–Lemeshow test for this model showed good agreement between the predicted and observed values on 95% of the imputed datasets. The average c-statistic of the model across the imputed datasets was 0.91 (95% CI: 0.89–0.93). The model was correctly specified and had an excellent ability to distinguish individuals who experienced the outcome, and those who did not.

Furthermore, we considered the rate of decline in FEV_1 before 2010 as a potential predictor. For each subject, this was estimated by using a linear mixed model with a random intercept and linear slope. The rate of decline of FEV_1 before study entry was not a better predictor than the value of FEV_1 at the study entry. Thus, it was not considered further.

3.3. Prognostic score

We developed a prognostic score, which was a weighted score calculated from the 8 predictors (Table 2). The parameters of the model were reestimated after transforming continuous variables into categorical variables according to clinically relevant thresholds. A value proportional to each estimated parameter was added to the score (Table 3).

Fig. 2 illustrates a nomogram which facilitates the use of the predictive model and the calculation of the prognostic score for each CF patient, given his or her characteristics. The nomogram provides a score value according to the scale given at the top of the figure. All the scores calculated for the eight predictors are then summed to obtain the prognostic score of the patient. The risk of death or LT corresponding to the prognostic score is given by the scale at the bottom of the figure.

A logistic regression using only the prognostic score as predictor of death or LT provided an odds ratio of 2.75 (95%CI 2.47–3.06, p value $<10^{-3}$). The risk of death or LT was greater for higher scores. The fitting of the prognostic score provided an average discriminant ability of 0.91 (95% CI: 0.89–0.92) which indicated good discriminative ability, and thus supports the use of this score to predict death or LT in a 3-year period. The Hosmer–Lemeshow test indicated that there were no significant differences between the prognostic score's predictions and the observed values on all the imputed datasets. These results were confirmed with the cross-validation of the prognostic score, which provided a c-statistic of 0.90 (95% CI: 0.88–0.93).

3.4. Classes of score

Based on risk of death or LT, we classified patients into three groups with low, intermediate and high risk (see Supplementary Fig. 1 for detailed risk of death or LT at each level of the score). From the score 0 to 1.5, the percentages of death or LT were lower than 2%. From the score 2 to 3.5, the percentages of death or LT were ranged between 7% and 15%. Finally, for the scores higher or equal to 4, the percentages of death or LT were ranged between 33% and 100%. Using the above distribution of death or LT in each value of the score, we created three risk groups. In the

Table 3
Risk score for prediction of within 3-year death or lung transplantation in adults with CF.

	Coefficient	Odds ratio (95% CI)	p-value	Score
FEV_1, % predicted			$<10^{-3}$	
> = 60	0	1		0
[30–60]	1.60	4.97 (2.53–9.74)		1.5
<30	2.99	19.91 (9.79–40.49)		3
BMI (kg/m^2)			$<10^{-3}$	
> = 18.5	0	1		0
[16–18.5]	0.70	2.01 (1.41–2.86)		0.5
<16	1.21	3.36 (1.62–6.97)		1
Burkholderia cepacia colonization			0.01	
Test negative	0	1		0
Test positive	1.08	2.96 (1.45–6.03)		1
No test	-0.10	0.90 (0.19–4.35)		0
Number of intravenous antibiotics courses/year			$<10^{-3}$	
0	0	1		0
[1-2]	0.61	1.84 (1.07–3.18)		0.5
>2	1.37	3.92 (2.29–6.72)		1
Hospitalization (yes vs no)	0.33	1.39 (0.95–2.03)	0.09	0.5
Oral corticosteroids (yes vs no)	0.80	2.20 (1.35–3.58)	10^{-3}	1
Long-term oxygen therapy (yes vs no)	1.12	3.08 (2–4.73)	$<10^{-3}$	1
Non-invasive ventilation (yes vs no)	0.69	1.99 (1.16–3.42)	0.01	1

first group (score ≤ 1.5), the score identified a group at very low risk of death or LT (1%) at 3 years. The second group (score [2–3.5]) corresponded to patients at moderate risk of death or LT (10%) at 3 years. Lastly, the highest group (score ≥ 4) identified patients with a very high risk of death or LT (55%) at 3 years (Fig. 3).

3.5. Comparison between the prognostic score and its components

We compared the diagnostic accuracy of the prognostic score with the one provided by each of its components. The discriminant ability of the prognostic score (c-statistic 0.91, 95% CI: 0.89–0.92) was significantly higher than the one provided by each of its components. In particular, it was significantly higher than the discriminant ability obtained with the criterion of FEV_1 < 30% for LT eligibility (c-statistic 0.74, 95% CI: 0.71–0.77) (see Supplementary Table 2 for details).

3.6. Sensitivity analyses

The model obtained after imputation of the outcome of patients lost to follow-up included the same predictors as the model excluding patients lost to follow-up. The characteristics at baseline of these lost to follow-up patients lead us to believe that they were patients with a low risk of death or LT (Supplementary Table 3). Using our prognostic score, we obtained their median

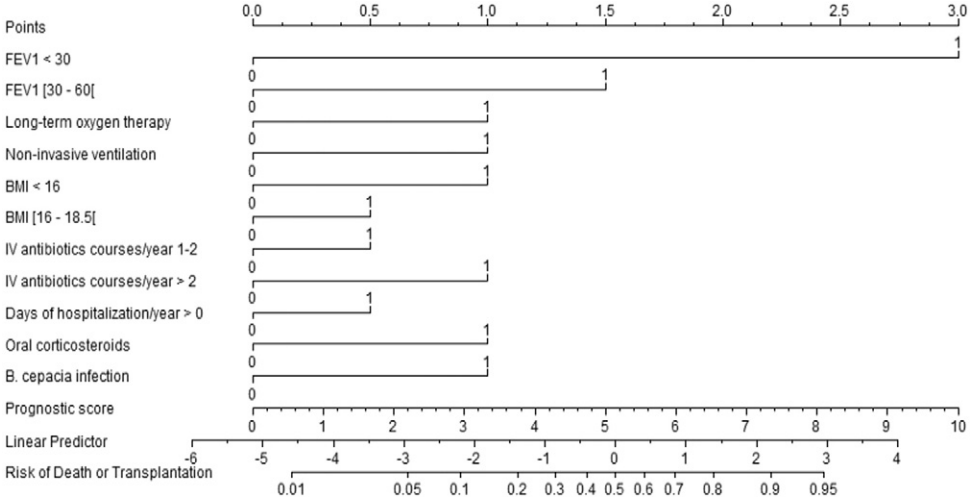

Fig. 2. Nomogram designed to estimate risk of death or lung transplantation. To display the application of the nomogram, we calculated the score and the corresponding risk of death or LT of a given patient. The patient is an 18 years old female gender with a FEV_1 at inclusion of 54% predicted (1.5 points) and a BMI at inclusion of 20.57 kg/m^2 (0 point). She had 2 IV antibiotics courses in the year 2010 (0.5 points). She had no oral corticosteroids (0 point), no long-term oxygen therapy (0 point), no non-invasive ventilation (0 point), no colonization with *Burkholderia cepacia* (0 point) and no days of hospitalization in the year 2010 (0 point). These clinical characteristics correspond to a total of 2 points and a risk of death or LT of 0.04. Thus, the expected risk of death or LT within the next 3 years is estimated at 4%.

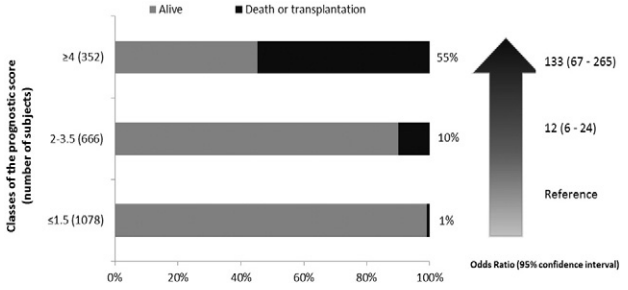

Fig. 3. Three-year risk of death or lung transplantation according to proportion of events in each score.

(interquartile range) score: 0.5 (0–1.5), indicating a low risk of death or LT at 3 years.

Next, we examined the impact of having chosen a composite outcome (occurrence of LT or death without LT) versus analyzing them as separate outcomes. The results of these analyses are presented in Tables 4 and 5 Supplementary materials respectively. Factors associated with LT were remarkably comparable with those obtained for the composite outcome. Factors associated with death without LT likely reflected some of the relative contraindications to transplant (for example cirrhosis, older age, *Burkholderia cepacia* colonization), but no treatment-associated variables.

4. Discussion

We used the most recent data from the French CF Registry to identify current prognostic factors in adults with CF. Eight risk factors were associated with death or LT within 3 years for adults: FEV_1, BMI, *Burkholderia cepacia* colonization, number of IV antibiotics courses per year, number of days of hospitalization per year, use of long-term oxygen therapy, non-invasive ventilation and use of oral corticosteroids. These factors were combined in a single prognostic score which showed good performance in terms of calibration and discrimination. This score allowed the identification of three groups of patients with markedly different risks of poor outcomes: from the lowest to the highest group, there was more than a 50-fold increase in the risk of death or LT. Importantly, the developed score was better at predicting the risk of death or LT than its individual components (especially $FEV_1 < 30\%$), confirming the multidimensional nature of disease severity in CF. These findings confirm data by George et al. who suggested that $FEV_1 < 30\%$ predicted is not by itself sufficient for the identification of patients at risk of poor outcome (i.e., LT or death without LT) in the modern era of CF care [12]. It extends these data by identifying important variables to poor outcomes in adults CF patients and by combining them in a clinically usable score.

Our goal was to examine prognostic factors associated with poor outcomes in adult CF patients, leading to the choice of a combined outcome defined as death without LT or occurrence of LT. Although older studies, which were performed at a time when LT was less developed, have focused on death without considering LT, the choice of studying a combined outcome of death without LT or occurrence of LT was also used in previous study [21]. As sensitivity analyses, we reanalyzed our data using the occurrence of LT and death without LT as separate outcomes. The findings obtained when considering the occurrence of LT as the primary outcome were quite close to those obtained when considering the composite outcome, largely reflecting the fact that 80% of the patients in the combined outcome underwent a LT. Focusing only on death without LT would have biased our analyses towards patients with relative contraindication to transplant and considerably reduced the usefulness of our score, which is intended to be used in all adult patients with CF. Thus, the use of the composite outcome of death without LT or the occurence of LT appeared appropriate in the present era when LT has become the standard of care in CF patients with refractory respiratory insufficiency.

The present study has several strengths. Analyses were performed using data from the French CF Registry that covers around 90% of French CF patients. Our model was developed using a large variety of covariates considered as potential predictors of poor outcome in patients with CF. The continuous variables included in the prognostic score were categorized using predetermined (based on clinical knowledge) cut-offs, which appeared easier for use in daily practice. The study focused on adults with CF because death from CF in children is now very rare in developed countries [26], and because over 95% of LT in France are performed in adults. Missing covariates data, a common issue in observational studies, were handled using the multiple imputation approach, which helped to minimize data loss, avoid biased estimates, and provide better estimations [24]. We also recognize limitations to the present study. Some covariates, such as professional status and marital status, available in the French CF Registry were not included in the models because of a high percentage of missing data. Additionally, variables not collected in the French CF Registry such as physical activity and exercise capacity, pulmonary hemodynamics [22,28] may also be important in assessing the prognosis of CF adults. On the other hand, these variables may not be routinely obtained in all CF patients, and thus may not be appropriate for inclusion in a score designed for referring patients for specialized evaluation for LT. Patients who received combined lung-liver transplantation during the follow-up were considered as having an outcome, whereas patients who received isolated liver transplantation during the follow-up were not considered as having a poor outcome. Because isolated liver transplantation was performed in a very small number of patients (as less than 5 patients per year received liver or lung/liver transplantation), this choice was unlikely to alter our conclusions. The 184 patients who were lost to follow-up (i.e., those with an unknown outcome at the end of the study) were excluded from the analyses. Analyses of the clinical characteristics of these patients suggested that, most patients lost to follow-up were those with milder disease and were at very low risk of death or LT. Additionally, sensitivity analyses suggested that the exclusion of these patients had only limited impact on our results. The vital status of patients corresponded to the one at the end of the year, and the use of annual data did not exclude the possibility that the prognosis could have changed considerably between the last visit and the end of the year. Lastly, the prognostic score included variables related to the patient's status (FEV_1, BMI, *Burkholderia*

cepacia) and also variables related to therapeutic interventions (hospitalization, IV antibiotics, oral corticosteroids, non-invasive ventilation, long-term oxygen therapy) that rely on physician choices. Future studies should aim address the validity of this score in other countries with different healthcare systems. Additionally, the value of assessing longitudinal changes (e.g., related to treatment modifications) in the score in individual patients should be evaluated in the future.

The prognostic score was built after reevaluation of prognostic factors in adult patients with CF, to predict the risk of death or LT in a 3-year period. This score showed good performance and was significantly better in terms of discrimination than its components, including the criterion of FEV_1 lower than 30% proposed for LT eligibility. If validated in other settings, this score could be a useful tool in the future for selecting patients requiring an evaluation for LT.

Conflicts of interest

None

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcf.2017.03.004.

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