Chronic obstructive pulmonary disease prognostic score: A new index

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Background. The evaluation of chronic obstructive pulmonary disease (COPD) has been shifting from spirometry to focus on the patients' overall health. Despite the existence of many COPD prognostic scales, there remains a large gap for improvement, in particular a scale that incorporates the current focus on overall health.
Methods. We proposed a new prognostic scale (the COPD Prognostic Score) through discussion among the authors based on published studies. Validation was retrospective, using data from the National Emphysema Treatment Trial.
Results. The scores ranged from 0-16, where 16 indicated the poorest prognosis. We assigned 4 points each for forced expiratory volume in one second (%predicted), the modified Medical Research Council dyspnea scale, and age; 2 points for the hemoglobin level; and one point each for decreased activity and respiratory emergency admission in the last two years. The validation cohort included 607 patients and consisted of 388 men (73.9%) and 219 women (36.1%), mean age 67 ± 6 years and an average forced expiratory volume in one second (% predicted) of 27 ± 7%. A one-point increase in the score was associated with increased all-cause death, with a hazard ratio of 1.28 (95%CI: 1.21-1.36. $P < 0.001$). The areas under the receiver operating characteristic curves for two-year and five-year all-cause death for the new scale were 0.72 and 0.66, respectively. These values were higher than those given by the body mass index, airflow obstruction, dyspnea, and exercise capacity (BODE) index and age, dyspnea, airway obstruction (ADO) index.
Conclusion. The preliminary validation for a new COPD prognostic scale: the COPD Prognostic Score was developed with promising results thus far. Above mentioned 16-point score accurately predicted 2-year and 5-year all-cause mortality among subjects who suffered from severe and very severe COPD.

Key words: COPD, prognosis, dyspnea, age, spirometry, hemoglobin

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD), which is characterized by non-fully reversible airflow limitation, systemic inflammation, and multiple comorbidities, is currently the fourth leading cause of death worldwide and predicted to be the third leading cause of death by 2030 (ref.[1,2]). COPD is now a concern not only for pulmonologists but also for physicians of all specialties including general practitioners. In the last century, the severity of COPD was evaluated primarily using the forced expiratory volume in one second (FEV_1) (% predicted) (ref.[3]). There has been a slow shift from spirometry to a focus on the patient's general health[1]. This change has occurred because recent studies have revealed the importance of systemic inflammation and systematic comorbidities of COPD.

To date, a number of validated prognostic scales are used. These scales are based on the following measurements: body mass index (BMI), airflow obstruction, dyspnea, and exercise capacity index (BODE index); age, dyspnea and the airway obstruction index (ADO index); the health, activity, dyspnea, and obstruction score; the Briggs prognostic index; a classification and regression tree; and the incremental shuttle walking test, BMI, airflow obstruction, dyspnea, and exercise capacity index[4-11]. These scales allow us to evaluate the systemic presentation of COPD. Nonetheless, the possibility for improvement remains.

In this article, we introduce our efforts to develop and validate a new COPD prognostic scale (the COPD Prognostic Score).

METHODS

Development of the COPD Prognostic Score

The following principles were used in the development of the COPD Prognostic Score: The components of previously validated prognostic scales were regarded as candidates for factors of the new prognostic score. New findings from a variety of published studies were incorporated during the development of the COPD prognostic score[3-37]. Hemoglobin levels were also regarded as a candidate component as studies have reported hemoglobin levels have considerable impact on the mortality of COPD

patients[34-37]. In a conscious effort to simplify the use of this prognostic score, factors needing specialized facilities such as exercise tolerance tests or tests that are not easily duplicated, were excluded. We predicted that a one-point increase in the total score was equivalent to a 1.3-fold increase in all-cause of death in the hazard ratio (HR), as reported for the BODE index[4]. The new prognostic scale was intended to be useful for evaluating non-advanced cases, as well as severe and very severe forms of COPD.

Preliminary validation

We used data from the National Emphysema Treatment Trial[12]. The following major entry criteria were used for the study: radiographic evidence of bilateral emphysema, FEV_1 (% predicted) ≤ 45%, arterial oxygen pressure ≥ 45 mmHg, arterial carbon dioxide pressure ≤ 60 mmHg, 6-minute walking distance (6MWD) ≥ 140 m, participation in pulmonary rehabilitation, not at high risk for perioperative morbidity or mortality, suitable for lung volume reduction surgery, and likely to complete the trial. At 17 clinical centers, 3,777 patients were evaluated from January 1998 to July 2002. Of the 1,218 patients who were eligible for enrollment, 608 patients and 610 patients were randomly assigned to the surgical and medical cohorts, respectively. Patient data in medical cohort of the study were utilized. Among the 610 patients, those who lacked data for the University of California Shortness of Breath Questionnaire (SOBQ) (N = 2) or hemoglobin (N = 1) were excluded, making the total number of patients included in the analysis N = 607 (ref.[12]).

Data related to some of the components of our prognostic scale were not provided directly in the dataset.. These components were estimated from other values. The Modified Medical Research Council dyspnea scale (mMRC) was estimated from the SOBQ as follows: SOBQ < 37, mMRC = 0; 37 ≤ SOBQ < 51, mMRC = 1; 51 ≤ SOBQ < 65, mMRC = 2; 65 ≤ SOBQ < 79, mMRC = 3; and 79 ≤ SOBQ, mMRC = 4. This correlation was based on a previous cross-sectional observation[13]. In the original dataset, nine patients aged ≤ 51 years and six patients aged ≥ 80 years were recorded as "age ≤ 51" and "age ≥ 80." We regarded the ages of these patients as 51 and 80 years, respectively. Decreased activity was recorded if a patient answered "yes" to the question, "I cannot go out for entertainment or recreation." Emergency Respiratory Admission was recorded for three months prior to evaluation.

The Wilcoxon rank sum test was used to compare the 2-year and 5-year mortality rates of patients in specific score ranges. The Cox hazard model was used to estimate the impact of a one-point increase in the total score on all-cause mortality in the HR. For a sensitivity analysis, the HR for all-cause death was also estimated in subgroups. The area under the receiver operating characteristic curve (AUC) was used to compare the prognostic abilities of the COPD Prognostic Score, the BODE index, and the ADO index. Kaplan-Meier curve with log-rank test was also drawn.

RESULTS

Development

We identified six major validated COPD prognostic scales. We classified the components used in these scales into 11 categories (Table 1). Of note, the FEV_1 (% predicted) and mMRC were used for all scales. The BMI and age were used for three scales. The exercise tolerance test, activity, and exacerbation were used for two scales (Table 1).

The COPD Prognostic Score was developed by combining the FEV_1 (% predicted), the mMRC, age, the hemoglobin level, exacerbation and/or respiratory infection requiring admission, and activity (Table 2). The score

Table 1. Components of major validated COPD prognostic scales.

	BODE index	ADO index	HADO-score	Scale by Briggs	i-BODE index	CART
Forced expiratory volume in one second (% predicted)	*	*	*	*	*	*
Modified Medical Research Council dyspnea scale	*	*	*	*	*	*
Body mass index	*			*	*	
Exercise tolerance test	*				*	
Age		*		*		*
General health condition			*			
Activity			*			*
Health related quality of life,				*		
Sex difference				*		
Exacerbation				*		*
Cardiovascular disease				*		

*: a component indicated in the left column is included in the prognostic scale in the top row.
BODE index: the body-mass index, airflow obstruction, dyspnea, and exercise capacity index
ADO index: the age, dyspnea, airway obstruction index
HADO-score: the health, activity, dyspnea, and obstruction score
i-BODE index: incremental shuttle walking test, body-mass index, airflow obstruction, dyspnea, and exercise capacity index
CART: a classification and regression tree

Table 2. The COPD Prognostic Score.

Post-bronchodilator forced expiratory volume in one second ($FEV_{1)}$) (% predicted)					/4
0	75 ≤	FEV_1 (%predicted)			
1	55 ≤	FEV_1 (%predicted)	< 75		
2	40 ≤	FEV_1 (%predicted)	< 55		
3	30 ≤	FEV_1 (%predicted)	< 40		
4		FEV_1 (%predicted)	< 30		
Age					/4
0		Age	< 63		
1	63 ≤	Age	< 70		
2	70 ≤	Age	< 77		
3	77 ≤	Age	< 84		
4	84 ≤	Age			
Modified Medical Research Council dyspnea scale					/4
0	Not troubled with breathlessness except with strenuous exercise				
1	Troubled by shortness of breath when hurrying on the level or walking up a slight hill				
2	Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level				
3	Stops for breath after walking about 100 meters or after a few minutes on the level				
4	Too breathless to leave the house or breathless when dressing or undressing				
Hemoglobin level (g/L)					/2
0	Man	≥ 140	Woman	≥ 130	
1		120–139		110–129	
2		< 120		< 110	
Activity (Daily Activity Scale)					/1
0	(0: average middle age) Walking outside 1 hour/day on average. Practicing active sports (jogging, hiking, swimming) once a month.				
0	(I: average pre-elderly) Walking outside 30 min/day on average. Practicing sports a few times a year.				
0	(II: average elderly) Walking outside 10 min/day on average. Not practicing any sport.				
1	(III: inactive) Walking out few days a week. Rarely walking more than 10 min on one occasion.				
1	(IV: sedentary) Walking out less than once a week. Life is almost limited in the house.				
Respiratory emergency admission					/1
Have you had (an) emergency admission(s) for any respiratory disease during the last 24 months?					
0	No				
1	Yes				
Total score					/16

Prognosis criteria: 0-2 Good, 3-5 Fair, 6-8 Poor, 9-11 Severe, 12-16 Critical.

range was 0 to 16. The higher the calculated score, the poorer the patient prognosis.

See the discussion section of this article for arguments regarding the individual components of the COPD prognostic score.

Preliminary validation

The background characteristics of the 607 patients in the validation cohort are summarized in Table 3. In this cohort, 388 men (73.9%) and 219 women (36.1%) with a mean age of 67 ± 6 years had an average post-bronchodilator FEV_1 (% predicted) of 27 ± 7% (Table 3). The total scores ranged from three to thirteen and had a normal distribution, with an average of 8 ± 2 and a median of 8. In this cohort, 102 patients (16.8%) and 287 patients (47.3%) died during the first two and five years, respectively. There were no censored cases during the first five years.

The impact of a one-point increase in each component on two-year mortality is provided in Table 4.

The two-year mortality rates were 1/23 (4%), 8/102 (8%), 26/251 (10%), 48/185 (26%), and 19/46 (41%) for score ranges of 3/4, 5/6, 7/8, 9/10, and 11/12/13, respectively ($P < 0.001$). The five-year mortality rates were 4/23 (17%), 34/102 (33%), 106/251 (42%), 109/185 (59%), and 34/46 (74%) for score ranges of 3/4, 5/6, 7/8, 9/10, and 11/12/13, respectively ($P < 0.001$). The Kaplan-Meier curve is also shown (Fig. 1, Log-rank test $P < 0.001$)

A one-point increase in the score was associated with an increase in all-cause death, with a HR of 1.28 (95%CI: 1.21-1.36. $P < 0.001$) (Table 5). For the sensitivity analysis, we estimated the HR in some subgroups. The HRs in these subgroups were similar to the HR estimated for the whole cohort (Table 5).

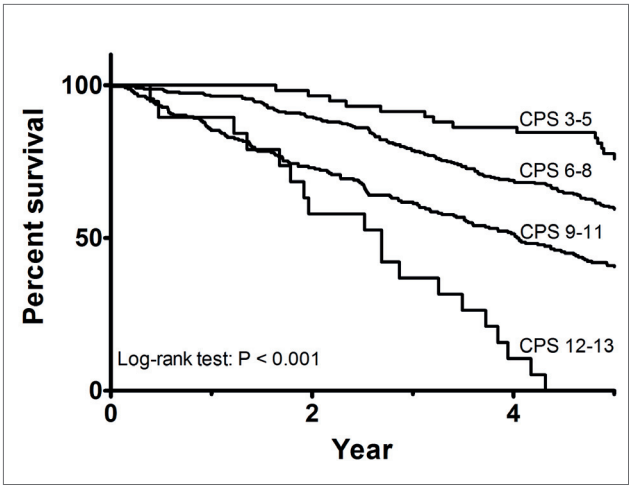

Fig. 1. Kaplan-Meier curve for all-cause death.
CPS: COPD prognostic score
No patient had a score 0, 1, 2, 14, 15, 16

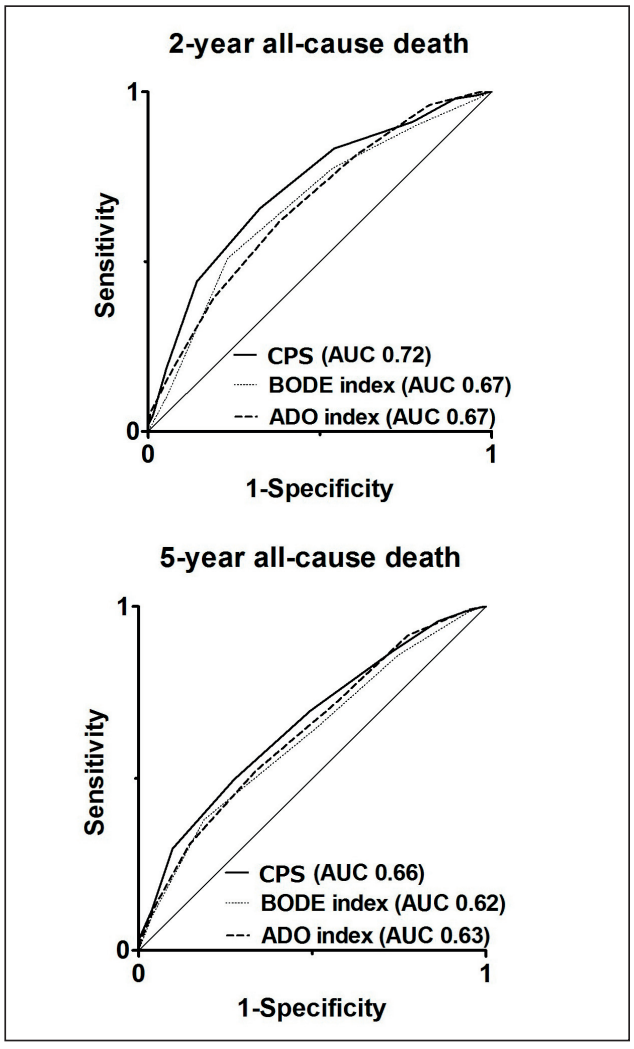

Fig. 2. Receiver operating characteristic curve for two-year and five-year all-cause death.
AUC: area under the receiver operating characteristic curve
CPS: the COPD Prognostic Score
BODE index: the body-mass index, airflow obstruction, dyspnea, and exercise capacity index
ADO index: the age, dyspnea, airway obstruction index

The AUC values for two-year and five-year all-cause death for the COPD Prognostic Score were 0.72 and 0.66 respectively.

DISCUSSION

A novel COPD prognostic scale (the COPD Prognostic Score), with a range of 0-16 was proposed by our group. This scale had higher AUC values for two- and five-year all-cause death than the BODE index and the ADO index when applied to severe to very severe forms of COPD. The novel features of our scale are as follows: we allocated two points for the hemoglobin level to improve prognostic ability, we introduced cutoffs between mMRC values of 0/1 and at an FEV_1 (% predicted) value of 75% to improve adaptability for mild cases[14]. We excluded BMI to improve prognostic ability for non-advanced cases, and we excluded 6MWD to improve feasibility in non-specialized facilities. The BODE index is a prognostic scale that is typically used for research purposes[4]. However, the requirements for 6MWD greatly limit the use of this index[5]. The ADO index is a simple established prognostic scale that has a similar concept as the BODE index[5,15]. Two large-scale prospective studies showed that the ADO index had a slightly better AUC values for all-cause death than the BODE index[5,9]. In addition to the three ADO index components (age, mMRC, and FEV_1 (% predicted)), the COPD Prognostic Score also included hemoglobin, emergency admission, and activity (Table 2). Given the recently emphasized significance of anemia, exacerbations, and activity for evaluation of COPD cases[1], the COPD Prognostic Score had a better prognostic ability than the ADO index as we expected. Discussion on each of the components and candidate factors are given below.

Components of COPD Prognostic Score

FEV_1 (% predicted): The FEV_1 (% predicted) is an inevitable parameter for evaluating COPD, as the definition of the disease clearly indicates. All existing prognostic scales assign multiple points for FEV_1 (% predicted). The limitation of FEV_1 (% predicted) is that among the key COPD parameters, only the FEV_1 (% predicted) is adjusted for age, which causes a paradox. For example, when comparing an 80-year-old man who has an FEV_1 of 1.5 L and an FEV_1 (% predicted) of 60% with a 40-year-old man who has an FEV_1 of 2.0 L and a FEV_1 (% predicted) of 50%, the 40-year-old man is younger and has a larger FEV_1 (mL). However, the FEV_1 (% predicted) suggests that the 80-year-old man is healthier. When we interpret the FEV_1 (% predicted), we must take the patient's age into consideration. Post-bronchodilator FEV_1 (% predicted) values are preferred over pre-bronchodilator FEV_1 (% predicted) values.

Age: Age is a major risk factor for death in any situation. Some scoring systems adopt an age component to determine the prognosis of patients with COPD (ref.[5,8,9]). However, some argue that allocating an overly large score for the age component in the COPD prognostic scale may reduce COPD specificity[15].

Table 3. Background patient characteristics.

N	607
Age (year)	67 ± 6
Sex (woman)	219 (36.1%)
forced expiratory volume in one second (% predicted)	27 ± 7
Estimated mMRC dyspnea scale	
0	48 (7.9%)
1	66 (10.9%)
2	147 (24.2%)
3	186 (30.6%)
4	157 (25.9%)
Six-minute walking distance (m)	369 ± 96
Body mass index (kg/m^2)	24.7 ± 3.5
Hemoglobin (g/L)	147 ± 12
Recent emergency admission	89 (28.2%)
Decreased activity	112 (18.5%)
St. George Respiratory Questionnaire (total score)	54 ± 13
Use of long-term oxygen therapy	331 (54.5%)
the body-mass index, airflow obstruction, dyspnea, and exercise capacity index (0-10)	5 ± 2
the age, dyspnea, airway obstruction index (0-10)	6 ± 1
the COPD Prognostic Score (0-16)	8 ± 2

±: standard deviation
COPD – chronic obstructive pulmonary disease, mMRC – modified Medical Research Council

Table 4. Impact of each component score on two-year mortality.

Component	Odds ratio (95% confidence interval)	*P*
FEV_1 (% predicted)	2.38 (1.46-3.89)	<0.001
Age	1.53 (1.16-2.03)	<0.001
Modified Medical Research Council	1.40 (1.15-1.70)	<0.001
Hemoglobin level	2.07 (1.39-3.08)	<0.001
Activity	1.78 (1.15-2.77)	0.010
Respiratory emergency admission	2.94 (1.77-4.90)	<0.001

These odds ratio were estimated from single-variable logistic regression using 2-year death as objective variable.

Table 5. Hazard ratio (HR) for all-cause death by one point increase of the COPD Prognostic Score.

		N	HR (95%CI)
Whole cohort		607	1.28 (1.21-1.36)
Subgroup analysis			
Age	< 67	286	1.30 (1.19-1.42)
	≥ 67	321	1.25 (1.16-1.34)
Forced expiratory volume in one second(%predicted)	< 27	320	1.30 (1.19-1.41)
	≥ 27	287	1.23 (1.13-1.33)
Modified Medical Research Council dyspnea scale	0, 1, 2	260	1.26 (1.15-1.39)
	3, 4	347	1.40 (1.28-1.53)
the COPD Prognostic Score	< 9	376	1.24 (1.10-1.39)
	≥ 9	231	1.34 (1.15-1.57)

P value was < 0.001 for all HR.
CI – confidence interval, COPD – chronic obstructive pulmonary disease, HR – hazard ratio

Dyspnea: Dyspnea is a subjective feeling of breathing discomfort. The impact of dyspnea on the prognosis of COPD cases has been emphasized in the last decade[4,16,17]. Some have reported that the impact of dyspnea on mortality is even stronger than that of the FEV_1 (% predicted) (ref.[5,16]). Among many dyspnea scales, the mMRC is commonly used for COPD prognostic scales and for daily practice[4-11]. The advantage of the mMRC over other dyspnea scales is its simplicity and the use of solid intervals between scores[18]. Another established scale for dyspnea is the SOBQ (ref.[19,20]), primarily used for research purposes due to its relative complexity. In some prognostic scales,

mMRC values of 0 and 1 were grouped into the same category[4,5], probably as patients with mMRC values of 0 and 1 have a similar positive survival prognosis. However, the clinical presentation, especially Quality of life (QOL), differs significantly between patients with mMRC values of 0 and 1.

Exercise tolerance test: Exercise tolerance tests, namely the 6MWD, the shuttle walk test, and maximal oxygen uptake, may be more important for COPD patients than results from respiratory function tests or dyspnea quantification[4,10,11,21]. In 2004, Celli et al. reported that the 6MWD is an independent prognostic factor, even after adjusting for the FEV_1 (% predicted) and the mMRC (ref.[4]). However, exercise capacity tests typically have limitations for daily practical use[15]. First, testing exercise capacity requires specialized facilities. These tests are not applicable to those who cannot walk (or ride a bicycle). The main COPD population is elderly with comorbidities such as orthopedic disorders which negatively affect movement. Furthermore exercise capacity tests are risky as they can cause hypoxia. Therefore, most of the recently devised COPD prognostic scales do not include an exercise capacity test[5-9].

QOL: QOL or health-related QOL is important to most people along with life prognosis. The QOL specific to patients with respiratory disease was first analyzed by Fine et al. using the St. George Respiratory Questionnaire (SGRQ), followed by the COPD-specific SGRQ and the COPD Assessment Test(ref.[22,23]). These questionnaires are used alone or as part of other prognostic scales[8]. Although we accept the usefulness of QOL questionnaires, we did not adopt a QOL questionnaire as a component of our prognostic scale because these questionnaires are lengthy.

Activity: Activity is a concept that is similar to QOL and is often regarded as part of QOL (ref.[22]). The activity component is the strongest predictor of death among the four scores of the SGRQ: Symptom, Activity, Impact, and Total score (ref.[24]). It is difficult to select the most accurate activity scoring system as they are not widely used in COPD. The activity component of the SGRQ is the best established scale but it is too complicated for daily use[22,23]. Schnohr's activity scale, which has four activity classes, is simple and strongly related to the mortality of COPD patients[25,26]. However, the scale was originally designed for healthy people and not for chronically ill. The Eastern Cooperative Oncology Group performance status is a commonly accepted scale that has five classes for individuals who are still alive[27]. However, this scale is for deteriorated malignancy cases and is not designed for evaluating relatively healthy people. Given the recent attention to evaluating the activity of patients with chronic respiratory diseases, it is anticipated that a simple four- or five-class activity scale that is easily applicable to a wide range of almost normal to severely affected patients, like the mMRC, will be developed (Table 2). The absence of the 6MWD may be partially replaced by a parameter of activity.

General health condition: General health condition is a component of the HADO score[6,7]. Although we agreed that the general health condition is an indicator of death, we did not include this factor in our scale because reconstruction has not been sufficiently demonstrated for this score.

BMI: The BMI is a simple measurement that is used to evaluate malnutrition in COPD patients[4,8]. However, the association between BMI and survival is only observed in severe and very severe COPD cases[28]. Another issue associated with the use of BMI for a COPD prognostic scale is that the average BMI is highly variable depending on the country. In the validation cohort of the BODE index, the mean BMI was 27.5 kg/m^2 in Spain and 23.4 kg/m^2 in Venezuela[4]. It is difficult to set a universal cutoff value that is acceptable for all.

Respiratory emergency admission: Exacerbation is a strong risk factor for death, follow up exacerbation, and future lung function deterioration[29,30]. As a patient suffers from more exacerbations, the prognosis becomes poorer. We used respiratory emergency admission rather than exacerbation for the current prognostic scale, primarily for two reasons. First, exacerbation without hospital admission is a weaker predictor of death than exacerbation with hospital admission. Second, the GOLD definition of exacerbation (subjective deterioration more than day-to-day change) depends on a subjective statement by the patient[1] and thus is not objective enough. Although the indication for emergency hospital admission can also differ due to differences in health care systems and the mentality of the COPD patients, we believe that the indication for admission is more reliable than the GOLD definition of exacerbation.

Gender differences: These differences for COPD survival prognosis have been reported repeatedly but remain controversial[8,31-33]. Some have reported that women have better survival[8,31,32] , but others describe contradictory findings[33]. We hypothesize that it is difficult to adjust all coverable parameters in multiple-variable analysis when comparing both sexes because the two sexes have different FEV_1 predicting formulas and different reference values for exercise tolerance tests.

Cardiovascular disease is one of the most frequent and important comorbidity for COPD patients. We agree that comorbid cardiovascular diseases are an important prognostic factor for COPD cases[8]. Nonetheless, we decided not to include the cardiovascular diseases in this prognostic scale as the diagnosis is usually physician-dependent.

Hemoglobin levels: Hemoglobin levels are one of the most common blood tests. Anemia is observed in 10 - 15% of patients with COPD (ref.[34]). Anemic COPD patients have a higher risk of death, morbidities, and hospital admission in comparison to non-anemic COPD patients[34-36]. The link between anemia and mortality remains strong after adjusting for other commonly used COPD parameters[35]. Decreased hemoglobin impairs oxygen delivery to tissues and results in dyspnea, deteriorated exercise capacity, and extra cardiac effort[34]. Interestingly, hemoglobin levels have a different meaning for COPD and non-COPD individuals. Among the non-COPD cohort, hemoglobin has a J-shaped curve in relation to mortality, with worse outcomes among both anemic and polycythemic individuals[37]. However, in a cohort of COPD patients, patients with polycythemia have the best prognosis and patients

with anemia have the poorest prognosis[35]. This difference is probably due to the fact that polycythemia can compensate for poor oxygen delivery.

Limitations

We have to comment on some limitations of our study. The first limitation is the retrospective nature of the study. A prognostic scale should be validated in a prospective manner. Therefore, we are conducting a prospective study to validate this prognostic scale[38]. The orthodox method of building a prognostic scale consists of two steps: the development of a scale using an initial cohort, and the validation of the scale using another patient cohort[4-11]. As the impact of each component varied greatly across studies, probably due to background patient characteristics[4-11] depending on a single development cohort is potentially risky. Furthermore, we can access extensive knowledge about life prognostic factors for COPD from previous studies[3-37], which were discussed. It seems a reasonable strategy to develop a new prognostic scale without using a development cohort. The second limitation is that the validation cohort consisted of patients with FEV_1 (% predicted) values < 45%. Therefore, the adaptability of this scale for milder COPD cases has not yet been sufficiently proved but will be covered in the prospective study which will also include COPD patients with post-bronchodilator FEV_1 (≤ 60% predicted) (ref.[38]). Finally, several parameters were not evaluated directly and needed to be calculated based on other parameters.

CONCLUSION

In conclusion, we have developed a novel COPD prognostic scale: the COPD Prognostic Score. In addition to the three ADO index components of age, mMRC, and FEV_1 (% predicted), the COPD Prognostic Score also included hemoglobin, respiratory emergency admission, and activity. Our preliminary validation suggested that the new scale has a better prognostic ability than the BODE and the ADO indices. Another validation in a prospective study is anticipated.

ABBREVIATIONS

COPD, Chronic obstructive pulmonary disease; FEV_1, Forced expiratory volume in one second;

HR, hazard ratio; BODE index, The body mass index, airflow obstruction, dyspnea, and exercise capacity index; BMI, body mass index; ADO index,: the age, dyspnea, airway obstruction index;

6MWD, 6-minute walking distance; SOBQ, University of California Los Angeles Shortness of Breath Questionnaire; mMRC, modified Medical Research Council dyspnea scale; SGRQ, St. George Respiratory Questionnaire; QOL, quality of life.

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Author contributions: NH, VK: initially calculated the pilot version of the prognosis assessment tool that was used for the Czech data – Ciliary Study (ref.[39]); NH, TK: design, analyses, manuscript drafting; VK, BN, KH, MP: final version, implemented the COPD Prognosis Score for the Czech multicenter database of severe COPD (ref.[38]); MP: responsibility for the contemporary prospective validation of the COPD Prognosis Score.

Conflict of interest statement: The authors state that there are no conflicts of interest regarding the publication of this article.

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