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Should pulse oximeter saturations be included in the risk stratification for chronic obstructive pulmonary disease proposed by GesEPOC?*



¿Debe incluirse la Saturación basal de oxígeno en la estratificación de riesgo de la enfermedad pulmonar obstructiva crónica propuesta por GesEPOC?

To the Editor:

The 2017 edition of the Spanish Chronic Obstructive Pulmonary Disease Guidelines (GesEPOC) establishes a treatment algorithm based on the stratification of patient risk at 2 levels, low risk and high risk, according to three criteria: lung function, dyspnea grade, and history of exacerbations¹. This stratification was initially based on a theoretical framework designed to determine the probability of the patient presenting an unfavorable clinical course. Since the publication of the algorithm, several studies have evaluated its prognostic capacity and endorsed its usefulness in this respect^{2,3}.

Chronic respiratory failure is associated with a higher mortality rate in patients with chronic obstructive pulmonary disease (COPD)⁴. Peripheral oxygen saturation (SpO₂) is easy to determine by pulse oximetry, and values <92% correlate with the presence of severe hypoxemia^{5,6}. On this premise, we conducted a retrospective study of patients with stable COPD monitored in a pulmonology clinic to analyze whether including the SpO₂ measurement in the conventional GesEPOC risk criteria would improve the prognostic capacity of the algorithm. Consecutive patients with a diagnosis of COPD⁷ and a history of smoking (cumulative consumption >10 pack-years) were included. The following variables obtained at the first visit were recorded: lung function, body mass index (BMI), mMRC dyspnea grade, resting SpO₂ (determined by the physician in clinically stable patients, breathing room air, at rest, and prior to physical examination), and history of exacerbations prior to inclusion, taking into account both moderate (requiring outpatient treatment with antibiotics and/or steroids) and severe (requiring emergency or hospital admission) exacerbations. Patients were classified as high risk and low risk according to the current GesEPOC criteria¹ (in the presence of any of the following criteria the patient would be categorized as high risk: FEV1% <50%, dyspnea ≥2 if treated, 2 or more moderate exacerbations or ≥1 severe exacerbations the previous year), and this was compared with a classification in which high-risk patients were categorized as SpO₂ <92% (high risk-SpO₂ <92%) and SpO₂ ≥92% (high risk-SpO₂ ≥92%). A Cox regression survival analysis was performed to compare the two classifications: model 1 was obtained with the conventional GesEPOC classification; and model 2 included the variable SpO₂ in the classification. The models were adjusted for age and comorbidity measured with the unadjusted Charlson index. The Akaike information criterion (AIC) was obtained for model com-

parison. Adjusted survival curves were obtained. Data collection was approved by the Santiago-Lugo Research Ethics Committee.

Overall, 710 patients were included, of whom 632 were men (89%), with a mean age of 68.3 ± 9.6 years, post-bronchodilator FEV1% 50.5 ± 17.2, and BMI 28.3 ± 5.2 kg/m². One quarter (25.9%) were active smokers and the pack-year index was 59.3 ± 30.7. The Charlson comorbidities index was 1.98 ± 1.41. In total, 522 patients were classified as high risk (73.5%) and 188 (26.5%) as low risk. The mean SpO₂ was 93.1 ± 4.6%. One hundred and sixty-four (23.1%) had SpO₂ <92%, of which 155 were high risk. Mean follow-up time was 53.9 ± 26.7 months.

Overall mortality during follow-up was 25.8%, with significant differences between the low-risk group and the high risk group (10.1% vs 31.5%; *P* < .0001, respectively). The high risk-SpO₂ group <92% had a mortality rate of 54.2%, compared with 21.9% in the high risk-SpO₂ group ≥92% (*P* < .0001). In the Cox regression analysis, compared to the low-risk group, high-risk patients with SpO₂ <92% have a greater risk of mortality (HR: 4.79; 95% CI: 2.90–7.91; *P* < .001) than high-risk patients with SpO₂ ≥92% (HR: 1.7; 95% CI: 1.02–2.80; *P* < .001) (Table 1; model 2) (Fig. 1).

In our study, the addition of the SpO₂ variable to the conventional GesEPOC criteria improves its prognostic capacity and classifies patients more precisely in terms of their mortality risk.

Factors, such as impaired ventilation-perfusion, dysregulation of respiratory center drive, or inspiratory muscle dysfunction due to pulmonary hyperinflation, contribute to the development of hypoxemia in COPD patients, impacting negatively on their life expectancy^{8–11}. A cut-off point of SpO₂ ≥92% is highly sensitive for ruling out respiratory failure, while SpO₂ ≤88% is highly specific for confirming it^{5,6}. Taking a pragmatic approach, and to avoid excluding any patient with respiratory failure, we selected a value of SpO₂ <92%⁵. Thus, not all patients would meet the criteria for initiating long-term oxygen therapy (LTOT), so an intense bronchodilator therapy, sustained smoking abstinence, and early onset of respiratory rehabilitation would hypothetically improve baseline SpO₂ values^{12–15} and consequently, life expectancy. In line with the concept of personalized treatment proposed by GesEPOC, our approach may of particular interest in high-risk individuals with SpO₂ <92% in whom the recommended initiation therapy would be a long-acting β₂-agonist inhaled corticosteroid, as would correspond to the COPD-asthma phenotype. These subjects may benefit from early initiation of dual bronchodilation, despite the clinical impact that could be achieved with an inhaled corticosteroid. Furthermore, although this was not an objective of the study, we must point out that 9 patients in the low-risk group had SpO₂ <92%. While this accounted for a very low percentage of patients, we believe that further studies that characterize these individuals in more depth may be needed to assess the clinical relevance of this finding.

Our study has limitations and essentially serves to generate debate. It is a retrospective study, conducted in a single center. The number of low-risk patients was very low, as SpO₂ could not be used as a variable in these subjects. We cannot rule out that many of these patients were prescribed LTOT during follow-up, which could have influenced the reported mortality figures. Patients could not be stratified according to SpO₂ ranges to avoid reducing statistical power. Despite these limitations, we believe that our results could be a stim-

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Table 1
Results of logistic regression analysis based on the conventional GesEPOC classification (model 1) or with the inclusion of peripheral oxygen saturation (model 2).

	Model 1		Model 2	
	HR (95% CI)	P	HR (95% CI)	P
<i>Classification according to conventional GesEPOC criteria</i>				
Low risk (reference)				
High risk	2.53 (1.57–4.08)	<.001		
<i>Classification according to conventional GesEPOC criteria + SpO2</i>				
Low risk (reference)				
High risk + SpO2 ≥92%			1.7 (1.02–2.80)	<.001
High risk + SpO2 <92%			4.79 (2.90–7.91)	<.001
Charlson comorbidity index	1.31 (1.21–1.42)	<.001	1.31 (1.21–1.43)	<.001
Age	1.04 (1.2–1.06)	<.001	1.04 (1.02–1.06)	<.001

95% CI: 95% confidence interval; SpO2: peripheral oxygen saturation determined by pulse oximetry. Model 1 was analyzed using the conventional GesEPOC classification of high and low risk. In model 2, high-risk patients were classified according to their SpO2 value. Both models were adjusted for age and Charlson comorbidity index. The AIC for model 1 is 2,194.44 and for model 2, it is 2,063.95.

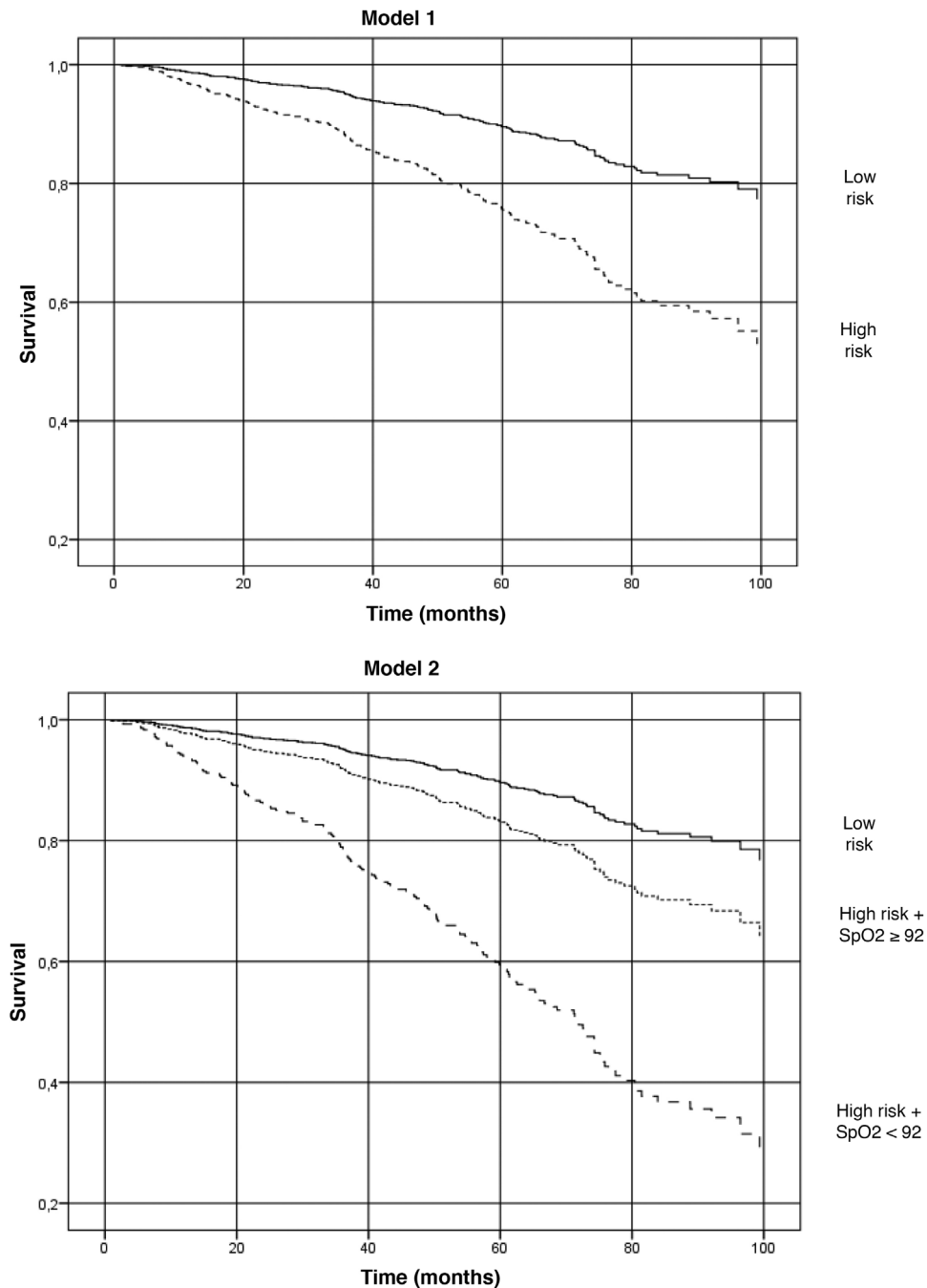


Fig. 1. Survival curves according to conventional risk criteria (model 1) or with the inclusion of peripheral oxygen saturation (model 2).

ulus for carefully designed studies that assess the inclusion of SpO₂ in the conventional criteria for high-risk patients.

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Conflict of interests

The authors declare that they have no conflict of interests directly or indirectly related with the contents of this manuscript.

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Sleep Duration and Cutaneous Melanoma Aggressiveness. A Prospective Observational Study in 443 Patients



Duración del sueño y agresividad del melanoma cutáneo. Un estudio observacional prospectivo con 443 pacientes

Dear Editor,

Both short and long sleep duration have been associated with an increased prevalence and incidence of cancer,^{1,2} but its relationship with cancer aggressiveness remains unknown. We have previously described an association between cutaneous melanoma and sleep-disordered breathing based on a prospective multicentric cohort.³ In the present paper, we describe the results of a post-hoc analysis aiming to evaluate the association between subjective sleep duration and objective parameters of melanoma aggressiveness.

This is an observational, cross-sectional, multicenter study that included 443 consecutive patients with a diagnosis of melanoma from 29 Spanish hospitals. Patients were excluded if they had in situ melanoma or had received previous treatment with continuous positive airway pressure. The study was approved by the ethics committees of all the hospitals, and all the patients gave their informed consent. Each patient completed a clinical questionnaire which included anthropometric measurements, relevant antecedents, medication, sleep apnea symptoms, presence of insomnia and somnolence (Epworth Sleepiness Scale).

Sleep duration was assessed by asking the patients the following question: How many hours of sleep (including naps) have you had on average in a 24-h period during the last year (year prior to the diagnosis of melanoma)? Participants estimated habitual sleep duration using full hour units. Snoring time was also quantified in the sleep study records.

All patients underwent a sleep study by means of a home respiratory polygraphy and a peripheral blood test. Patients were divided into three groups depending on their daily sleep duration: appropriate sleep duration (between 6 and 8 h), short sleepers (<6 h) and long sleep duration (>8 h). The independent relationship between melanoma aggressiveness factors and sleep duration was determined by introducing into a multivariate logistical regression analysis those variables which could, in the opinion of the researchers, also have clinical importance as confounders: age, sex, AHI, BMI and hypnotics intake. This relationship was evaluated by Hazard Ratio (CI95%), considering the group of patients with appropriate sleep duration as the control group. The degree of melanoma aggressiveness was measured by histological variables such as the Breslow thickness, the tumor mitotic rate (≥ 5 vs. < 5 mitoses per mm²), the histological presence of ulceration and regression and positive sentinel lymph node (SLN) involvement. The cut-off points for the Breslow thickness were established at 1, 2 and 4 mm, according to international guidelines.⁴

443 patients were finally included in the study. Mean age was 55.9 ± 15.3 years, and 50.6% were male. The mean BMI was 27.3 ± 4.5 kg/m² and the median Epworth score was 6 (IQR: 3–8). The median of the Breslow thickness was 0.85 mm (IQR: 0.49–1.80). A Breslow thickness above 1, 2 and 4 mm was found in, respectively, 44, 22.3 and 8.8% of the patients. Ulceration was present in 16%, regression in 23.3%, and SLN was positive in 10.6% of patients. The median AHI was 8.6 (IQR: 2.8–20.2). The mean sleep duration was 7.4 ± 1.27 h, with 4.7% sleeping <6 h, 77.9% between 6 and 8 h and 17.4% >8 h. 8.4% of the patients presented insomnia and 12% were taking hypnotic drugs. The sleep study time was 7.2 h (IQR: 6.6–8) and the snoring study time was 6.9 h (IQR: 6.5–7.7). The correlation between subjective sleep duration and snoring study time was $r = 0.86$, $p < 0.0001$.

There was a statistically significant correlation between sleep duration and the Breslow index (r : 0.26; $p = 0.001$). Those patients with more aggressive melanoma (Breslow ≥ 2 mm vs < 2 mm, and