Below What FEV$_1$ Should Arterial Blood be Routinely Taken to Detect Chronic Respiratory Failure in COPD?

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**Abstract**

*Introducción:* La gasometría arterial es la medición de elección para el diagnóstico de insuficiencia respiratoria crónica en la enfermedad pulmonar obstructiva crónica (EPOC). Se ha sugerido que el FEV$_1$ se sitúe entre el 30 y el 50% del valor teórico para su indicación, pero estas cifras nunca han sido validadas.

*Objetivo:* Identificar el post-broncodilatador (BD) FEV$_1$ y la saturación arterial de oxígeno (SaO$_2$) valores que proporcionen la mejor sensibilidad, especificidad y coeficientes de probabilidad (CP) para el diagnostico de insuficiencia respiratoria hipoxémica y/o hipercápnica en la EPOC estable.

*Métodos:* Se incluyeron 150 pacientes (39 con PaO$_2$ < 60 mm Hg [8 kPa], 14 de ellos con una PaCO$_2$ ≥ 50 mm Hg [6.7 kPa]). Los mejores puntos de corte para predecir la insuficiencia respiratoria crónica empleando los CP y las curvas Receiver Operating Characteristic.

*Resultados:* Un FEV$_1$ post-BD igual al 36% y una SaO$_2$ de 90% fueron los mejores valores predictivos de insuficiencia respiratoria hipoxémica y un FEV$_1$ post-BD igual al 33% para la variante hipercápnica. Un FEV$_1$ ≥ 45% descartó la insuficiencia respiratoria hipoxémica.

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**¿Cuál es el mejor FEV$_1$ para detectar insuficiencia respiratoria crónica en la EPOC estable?**

**Resumen**

Introducción: La gasometría arterial es el método estándar para el diagnóstico de insuficiencia respiratoria crónica en la enfermedad pulmonar obstructiva crónica (EPOC). Aunque se ha sugerido que el FEV$_1$ se sitúa entre el 30 y el 50% del valor teórico para su indicación, estos valores no han sido validados.

Objetivo: Identificar los valores de FEV$_1$ post-broncodilatador (BD) y la saturación arterial de oxígeno (SaO$_2$) que provengan de la mejor sensibilidad, especificidad y coeficientes de probabilidad (CP) para el diagnóstico de insuficiencia respiratoria crónica hipoxémica y/o hipercápnica en la EPOC estable.

Métodos: Se incluyeron 150 pacientes (39 con PaO$_2$ < 60 mm Hg [8 kPa], 14 de ellos con una PaCO$_2$ ≥ 50 mm Hg [6.7 kPa]). Se seleccionaron los mejores puntos de corte para FEV$_1$ post-BD y SaO$_2$ para predecir la insuficiencia respiratoria crónica empleando los CP y las curvas Receiver Operating Characteristic.

Resultados: Un FEV$_1$ post-BD igual al 36% y una SaO$_2$ del 90% fueron los mejores valores predictivos de insuficiencia respiratoria hipoxémica y un FEV$_1$ post-BD igual al 33% para la variante hipercápnica. Un FEV$_1$ ≥ 45% descartó la insuficiencia respiratoria hipoxémica.

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Introduction

Arterial blood gas (ABG) test is the usual clinical procedure for the diagnosis and treatment of chronic respiratory failure in chronic obstructive pulmonary disease (COPD).\(^2\) ABG by means of either radial artery puncture or puncture of another peripheral artery is the most recommended practice. Puncture of the ear lobe only reflects the arterial pressure of carbon dioxide (PaCO\(_2\)) and pulse-oximetry, which is the best non-harmful alternative, and is only useful for evaluating the evolution of respiratory insufficiency and/or adjusting oxygen therapy needs.\(^5\)

Chronic respiratory failure is defined as a state or situation in which the values of PaO\(_2\) are less than 60 mm Hg (8 kPa), with or without associated hypercapnia (PaCO\(_2\) ≥ 50 mm Hg [6.7 kPa]), breathing room air (in standard conditions).\(^5\) However, not all the patients with COPD, especially those with advanced stage, present hypoxicemic or hypercapnic respiratory failure.\(^7,8\) As ABG is a harmful diagnostic method and not always indicated in clinical practice, it would be useful if other functional variables that are much less harmful, such as FEV\(_1\), and SaO\(_2\), could indicate ABG with the best possible precision for the diagnosis of said respiratory failure.

The first report of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommended carrying out ABG under standard conditions in stable COPD patients when post-bronchodilator FEV\(_1\) (BD) was less than 40% of the predicted value as the best cut-point.\(^9\) However, its most recent update recommended a value less than 50%, consistent with a severe spirometric classification (stage 3) of the disease.\(^10\) It should be mentioned that the National Institute for Clinical Excellence (NICE) guideline proposes carrying out ABG when the pre-BD FEV\(_1\) is less than 30% predicted and also recommends it in less severe patients when pre-BD FEV\(_1\) is between 30% and 49% predicted or SaO\(_2\) is equal or less than 92%.\(^5\) However, none of these cut-points has been validated to date.

It should be mentioned that there has been one retrospective study that has proposed a threshold of less than 40% the predicted value as the best FEV\(_1\) cut-point for ABG.\(^11\) It is obvious that if the cut-point is very high, all the patients with hypoxicemic or hypercapnic respiratory insufficiency will be diagnosed, although many others, whose levels do not reach said level, could unnecessarily undergo ABG, with its risks and usual costs.\(^12\) However, if the FEV\(_1\) cut-point is lower, some patients with respiratory failure will go undiagnosed, which can entail the appearance of complications of the underlying respiratory failure.

The hypothesis that we contemplated was that adequate post-BD FEV\(_1\) and SaO\(_2\) values should be identified to rule out the presence of chronic respiratory failure, which would help to better direct the indication of ABG in patients with advanced stable COPD. The objective of our study was, therefore, to research the most adequate cut-points for post-BD FEV\(_1\) and SaO\(_2\), evaluating the interrelations between FEV\(_1\) (expressed as percentage of the predicted value) and SaO\(_2\) (as percentage) on one hand, and the PaO\(_2\) and PaCO\(_2\) (in mmHg) values on the other, in 150 patients with stable COPD representing the complete spectrum of the disease.
and NPV.\textsuperscript{15} The estimations of the sensitivity are necessary for the calculation of the likelihood ratios (LR), which are defined as the probability of a certain value in a patient affected by clinical symptoms in comparison with the probability in another patient that does not have said clinical condition. A positive LR (+), calculated by the sensitivity/(1-specificity) ratio, above 10 is necessary for the diagnostic test to be considered as having powerful confirmatory evidence of the clinical symptoms, while a negative LR (−), calculated with the ratio (1-sensitivity)/specificity lower than 0.10, is considered sufficient to rule out the condition. The LR are not modified by the prevalence of the underlying clinical profile, therefore they are robust tools for evaluating disease biomarkers.

In this sense, the LR were used to evaluate the best post-BD FEV\textsubscript{1} (as percentage of predicted) and SaO\textsubscript{2} (in percentage) predictive values using PaO\textsubscript{2} < 60 mm Hg as a primary objective,\textsuperscript{18} with or without associated hypercapnia (PaCO\textsubscript{2} ≥ 50 mm Hg). The calculations were done with SPSS/PC (version 15.0, SPSS Inc., Chicago, IL, USA) and MedCalc (version 9.3.9.0; MedCalc, Mariakerke, Belgium).

Results

Table 1 shows the main characteristics of our study population. A total of 39 patients with COPD (26%) presented chronic respiratory failure: 25 had isolated severe arterial hypoxemia (PaO\textsubscript{2} < 60 mm Hg) and 14 had associated hypercapnia (PaCO\textsubscript{2} ≥ 50 mm Hg). Both the obese patients (body mass index, 32 ± 2 kg/m\textsuperscript{2}; n = 18; 12%) as well as the non-obese ones (24 ± 3 kg/m\textsuperscript{2}; n = 132; 88%) showed similar PaCO\textsubscript{2} values (42 ± 6 and 41 ± 6 mm Hg) and pH (7.39 ± 0.90 and 7.40 ± 0.10), respectively. The PaO\textsubscript{2} in patients with hypoxic respiratory failure (54 ± 5 mm Hg) and in those with hypercapnic respiratory insufficiency (52 ± 5 mm Hg) was not different (P = .11); in contrast, PaCO\textsubscript{2} was significantly higher in the group of hypercapnic respiratory failure (55 ± 5 mm Hg) compared with those that only had the hypoxic variety (44 ± 4 mm Hg) (P < .05).

Fig. 1 includes the two ROC curves with the best post-BD FEV\textsubscript{1} cut-points for the evaluation of hypoxic (Fig. 1a) and hypercapnic respiratory failure (Fig. 1b), including the respective AUC, all of which were significant (interval 0.81–0.82; P < .01 in each).

Table 2 demonstrates the values for sensitivity, LR+, PPV, specificity, LR− and NPV for predicting the diagnosis of isolated hypoxic (PaO\textsubscript{2} < 60 mm Hg) or hypercapnic respiratory failure (PaO\textsubscript{2} < 60 mm Hg with PaCO\textsubscript{2} ≥ 50 mm Hg). Table 2A indicates that a post-BD FEV\textsubscript{1} equal to 36% is the threshold with greater capacity for predicting hypoxic respiratory failure (sensitivity: 0.87; LR+: 2.79; PPV: 0.49; specificity: 0.68; LR−: 0.19; NPV: 0.94). With the use of this cut-point, a lower number of false positives were found (n = 35; 23%) compared with a post-BD FEV\textsubscript{1} < 50%\textsuperscript{10} (n = 56; 37%). The latter included a lower number of false negative cases (n = 0) than the selected cut-point (n = 5; 3%). The analysis of the ROC curve for obese patients with COPD demonstrated that the best post-BD FEV\textsubscript{1} for predicting hypoxic respiratory failure is very close (34%) to that of the population studied in our paper.

Table 2B emphasizes a post-BD FEV\textsubscript{1} equal to 33% as the cut-point with greater discriminating capacity for hypercapnic respiratory failure, including the best levels of sensitivity (0.93), LR+ (2.65), PPV (0.21), specificity (0.65), LR− (0.10) and NPV (0.99). We observed 30 false-positive cases (22%) compared with the 56 (37%) when a post-BD FEV\textsubscript{1} < 50% was used,\textsuperscript{10} although there were no false negative cases with the latter value. It should be highlighted that a post-BD FEV\textsubscript{1} equal to 35% was an adequate value for ruling out hypercapnic respiratory failure (LR−: 0).

Last of all, Fig. 2 includes the ROC curve that identifies 90% as the best SaO\textsubscript{2} value for suspecting the diagnosis of hypoxic respiratory failure (sensitivity: 0.73; LR+: 24.33; PPV: 0.91; specificity: 0.97; LR−: 0.27; NPV: 0.91). Likewise, an SaO\textsubscript{2} ≥ 91% (LR+: 15.20) was sufficient for suspecting the diagnosis of hypoxic respiratory failure.
In addition, FEV\textsubscript{1} an FEV\textsubscript{1} were not measured. However, these limitations observed that 5,10,23,24 which 9 20 Our findings confirm that a post-BD FEV\textsubscript{1} or the NICE guidelines, investigated until a similar line to that of our study, Franciosi et al. report. siderably lower than that currently recommended by the GOLD chronic respiratory failure in stable COPD, a level which is con-1

Discussion

Our study suggests, as an evidence-based novelty that 36% post-BD FEV\textsubscript{1} is the best cut-point for the diagnosis and evaluation of chronic respiratory failure in stable COPD, a level which is considerably lower than that currently recommended by the GOLD report.\textsuperscript{10} In addition, FEV\textsubscript{1} ≥ 45% rules out chronic respiratory failure. Furthermore, for hypercapnic chronic respiratory failure, the best cut-point is even lower (33%) than the currently recommended values.\textsuperscript{5,10} As for SaO\textsubscript{2}, the values situated between 90% and 91% give the greatest capacity for predicting chronic hypoxemic respiratory failure.

There are no previous studies identifying the best FEV\textsubscript{1} to indicate ABG for the diagnosis and the evaluation of chronic respiratory failure in stable COPD patients. In a retrospective study with the objective of researching the utility of FEV\textsubscript{1} for determining the presence of severe arterial hypoxemia and developing the best strategy of continuous home oxygen therapy, Lim et al.\textsuperscript{15} concluded that FEV\textsubscript{1} was adequate for screening chronic hypoxemic respiratory failure, but without estimating the best FEV\textsubscript{1} to warrant ABG. Along a similar line to that of our study, Franciosi et al.\textsuperscript{20} investigated which could be the best clinical and functional markers of severity in the clinical practice in 145,000 patients affected by COPD. They concluded that PaO\textsubscript{2} was one of the most relevant markers for differentiating the different spirometric stages of the disease; nevertheless, the most adequate FEV\textsubscript{1} value for performing ABG in a patient with stable COPD was not determined. Using an analysis of the main components for evaluating the potential of multidimen-

![Fig. 2. ROC curves (continuous line) with respective 95% CI (dashed line) for different SaO\textsubscript{2} values (expressed as percentage) and the cut-points for the diagnosis for hypoxemic chronic respiratory failure. The cut-point in bold has diagnostic value. AUC: area under the curve.](image)

Table 2

<table>
<thead>
<tr>
<th>FEV\textsubscript{1}</th>
<th>Sensitivity</th>
<th>LR+</th>
<th>PPV</th>
<th>Specificity</th>
<th>LR−</th>
<th>NPV</th>
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<tbody>
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<td>(A)</td>
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<tr>
<td>30%</td>
<td>0.61 (0.45–0.76)</td>
<td>2.73 (1.79–4.18)</td>
<td>0.49 (0.35–0.63)</td>
<td>0.77 (0.68–0.85)</td>
<td>0.50 (0.33–0.70)</td>
<td>0.85 (0.76–0.91)</td>
</tr>
<tr>
<td>35%</td>
<td>0.85 (0.69–0.93)</td>
<td>2.68 (1.98–3.64)</td>
<td>0.48 (0.36–0.61)</td>
<td>0.68 (0.59–0.77)</td>
<td>0.22 (0.10–0.43)</td>
<td>0.93 (0.84–0.97)</td>
</tr>
<tr>
<td>36%</td>
<td>0.87 (0.72–0.95)</td>
<td>2.76 (2.05–3.73)</td>
<td>0.49 (0.37–0.61)</td>
<td>0.68 (0.59–0.77)</td>
<td>0.19 (0.09–0.39)</td>
<td>0.94 (0.85–0.98)</td>
</tr>
<tr>
<td>40%</td>
<td>0.90 (0.75–0.97)</td>
<td>2.50 (1.90–3.26)</td>
<td>0.47 (0.35–0.58)</td>
<td>0.64 (0.54–0.73)</td>
<td>0.15 (0.06–0.36)</td>
<td>0.95 (0.86–0.98)</td>
</tr>
<tr>
<td>45%</td>
<td>0.97 (0.84–1.00)</td>
<td>2.08 (1.69–2.55)</td>
<td>0.42 (0.32–0.53)</td>
<td>0.53 (0.43–0.63)</td>
<td>0.09 (0.02–0.32)</td>
<td>0.98 (0.90–1.00)</td>
</tr>
<tr>
<td>50%</td>
<td>1.00 (0.89–1.00)</td>
<td>2.00 (1.65–2.38)</td>
<td>0.41 (0.31–0.52)</td>
<td>0.49 (0.40–0.59)</td>
<td>0.05 (0.00–0.26)</td>
<td>1.00 (0.92–1.00)</td>
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<tr>
<td>(B)</td>
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<tr>
<td>30%</td>
<td>0.71 (0.42–0.90)</td>
<td>2.50 (1.63–3.81)</td>
<td>0.20 (0.11–0.35)</td>
<td>0.71 (0.63–0.78)</td>
<td>0.23 (0.06–0.63)</td>
<td>0.96 (0.89–1.00)</td>
</tr>
<tr>
<td>33%</td>
<td>0.93 (0.64–1.00)</td>
<td>2.63 (2.00–3.45)</td>
<td>0.21 (0.12–0.34)</td>
<td>0.65 (0.56–0.72)</td>
<td>0.00 (0.00–0.43)</td>
<td>0.99 (0.93–1.00)</td>
</tr>
<tr>
<td>35%</td>
<td>1.00 (0.73–1.00)</td>
<td>2.52 (2.05–3.10)</td>
<td>0.20 (0.12–0.32)</td>
<td>0.60 (0.51–0.68)</td>
<td>0.00 (0.00–0.47)</td>
<td>1.00 (0.94–1.00)</td>
</tr>
<tr>
<td>40%</td>
<td>1.00 (0.73–1.00)</td>
<td>2.23 (1.85–2.70)</td>
<td>0.19 (0.11–0.30)</td>
<td>0.55 (0.46–0.64)</td>
<td>0.00 (0.00–0.51)</td>
<td>1.00 (0.94–1.00)</td>
</tr>
<tr>
<td>45%</td>
<td>1.00 (0.73–1.00)</td>
<td>1.80 (1.54–2.08)</td>
<td>0.15 (0.10–0.25)</td>
<td>0.44 (0.36–0.53)</td>
<td>0.00 (0.00–0.65)</td>
<td>1.00 (0.92–1.00)</td>
</tr>
<tr>
<td>50%</td>
<td>1.00 (0.73–1.00)</td>
<td>1.68 (1.46–1.93)</td>
<td>0.15 (0.10–0.24)</td>
<td>0.40 (0.32–0.49)</td>
<td>0.00 (0.00–0.71)</td>
<td>1.00 (0.92–1.00)</td>
</tr>
</tbody>
</table>

The values in bold indicate the selected cut-points. LR+: positive likelihood ratio; LR−: negative likelihood ratio; NPV = negative predictive value; PPV: positive predictive value.
In short, future clinical guidelines or recommendations for COPD could consider the cut-points for FEV₁ and SaO₂ suggested by our study. This would avoid the practice of unnecessary arterial punctures, which may always result in side effects and patient discomfort as well as excessive costs for health-care systems.

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**Conflicts of Interests**

Roberto Rodríguez-Roisin presides on the GOLD Executive Committee. The remaining authors have no conflict of interests.

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**References**