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Original Article

Below What FEV_1 Should Arterial Blood be Routinely Taken to Detect Chronic Respiratory Failure in COPD?☆

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A R T I C L E   I N F O

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A B S T R A C T

Introduction: To diagnose and assess chronic respiratory failure in stable chronic obstructive pulmonary disease (COPD) the measurement of arterial blood gases (ABG) is required. It has been suggested that ABG could be determined for this purpose when FEV_1 ranges between 50% and 30% predicted, but these thresholds are not evidence-based.
Objective: To identify the post-bronchodilator (BD) FEV_1 and arterial oxygen saturation (SaO_2) values that provide the best sensitivity, specificity, and likelihood ratio (LR) for the diagnosis of hypoxaemic and/or hypercapnic chronic respiratory failures in stable COPD.
Methods: A total of 150 patients were included (39 with $PaO_2 < 60$ mm Hg [8 kPa], 14 of them with a $PaCO_2 \geq 50$ mm Hg [6.7 kPa]). The best post-BD FEV_1 and SaO_2 cut-off points to predict chronic respiratory failure were selected using the PC and the Receiver Operating Characteristics (ROC) curves.
Results: A post-BD FEV_1 equal to 36% and an SaO_2 of 90% were the best predictive values for hypoxaemic respiratory failure and a post-BD FEV_1 equal to 33% for the hypercapnic variant. An $FEV_1 \geq 45\%$ ruled out hypoxaemic respiratory failure.
Conclusion: A post-BD FEV_1 of 36% is the best cut-off point to adequately predict both hypoxaemic and hypercapnic respiratory failure in the patient with stable COPD. For its part, an SaO_2 of 90% is the best value for isolated hypoxaemic failure. These values could be considered for future clinical recommendations/guidelines for COPD.

¿Cuál es el mejor FEV_1 para detectar insuficiencia respiratoria crónica en la EPOC estable?

Palabras clave:
Limitación al flujo aéreo
Gasometría arterial
Insuficiencia respiratoria crónica
Intercambio pulmonar de gases

R E S U M E N

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 los valores de FEV_1 post-broncodilatador (BD) y saturación arterial de oxígeno (SaO_2) que proporcionen 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] y 14 de ellos con una $PaCO_2 \geq 50$ mm Hg [6.7 kPa]). Se seleccionaron los mejores puntos de corte de 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 $FEV_1 \geq 45\%$ descartó la insuficiencia respiratoria hipoxémica.

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Conclusión: Un FEV_1 post-BD igual al 36% se erige en el mejor punto de corte para predecir adecuadamente tanto la insuficiencia respiratoria hipoxémica como la hipercápnica en el paciente con EPOC estable. Por su parte, una SaO_2 del 90% ofrece el mejor valor para la insuficiencia hipoxémica aislada. Estos valores podrían ser considerados para futuras recomendaciones/guías clínicas de la EPOC.

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).[1,2] 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 ($PaCO_2$)[3,4] 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 ($PaCO_2 \geq 50$ mm Hg [6.7 kPa]), breathing room air (in standard conditions).[6] However, not all the patients with COPD, especially those with advanced stage, present hypoxemic 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 hypoxemic 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 $PaCO_2$ (en mmHg) values on the other, in 150 patients with stable COPD representing the complete spectrum of the disease.

Methods

Study Population and Measurements

The patients included ($n = 150$) corresponded with all those patients who were undergoing studies of the distributions of the ventilation–perfusion relationship in our center by means of the multiple inert gas elimination technique.[13] The origin of the patients was as follows: 21 had been hospitalized due to previous COPD exacerbation; 59 patients had undergone extirpation of a lung nodule ($n = 29$), lung volume reduction surgery ($n = 11$) or lung transplantation ($n = 19$); and the 70 remaining patients were recruited for several studies, of whom only 10 had mild COPD (GOLD stage 1). These measurements were done in specific experimental conditions throughout the period between 1987 and 2008, using three different blood gas analyzers (IZASA model ILBG 3, IZASA model IL1302 and Bayer 800) in 14 different studies whose results have been extensively published.[14] The measurements of ABG were taken under stable conditions, at least three months after the last exacerbation, in duplicate, breathing room air, in a sitting position and at sea level. The SaO_2 values were obtained from these blood gas samples.[14] We excluded patients with concomitant processes or comorbidities (heart failure, diabetes mellitus or other chronic respiratory diseases, such as sleep apnea syndrome).[14] All the patients were active smokers ($n = 30$) or ex-smokers ($n = 120$) and the majority were male ($n = 142$). The distribution by stages according to the GOLD report was: 15 patients (10%), stage 1; 40 (27%), stage 2; 32 (21%), stage 3; and 63 (42%), stage 4. All the patients accepted to participate and signed the respective informed consents after a detailed description of each study and they were approved by the ethics committee of the Hospital Clínic, Universitat de Barcelona.

Statistical Analysis

The results are expressed as mean ± standard deviation for the variables with normal distribution or as median and percentiles 5 and 95 (P_5–P_{95}) for the abnormal distribution. Using as target variables the universal values of PaO_2 and $PaCO_2$ defining respiratory failure,[6] *Receiver Operating Characteristic* (ROC) curves were calculated, dividing said variables dichotomically in isolated chronic respiratory failure ($PaO_2 < 60$ mm Hg [8 kPa] versus $PaO_2 \geq 60$ mm Hg) and/or hypercapnic ($PaO_2 < 60$ mm Hg and $PaCO_2 \geq 50$ mm Hg [6.7 kPa] versus $PaCO_2 < 50$ mm Hg) and constructing said curves to determine the best value of FEV_1 (expressed as percentage of predicted) and SaO_2 (in percentage) to predict both types of respiratory failure (hypoxemic and hypercapnic). Likewise, the area under the curve (AUC) was calculated for each ROC curve non-parametrically.[15,16]

The predictive values were also calculated, both positive (PPV) and negative (NPV), to evaluate the best positive and negative results of the procedure.[17] Afterwards, we explored the diagnostic capacity for prediction of post-BD FEV_1 in the interval of 30% and 50% of the predicted value, and SaO_2, between 90% and 94%, and respective cut-points were selected that included the best sensitivity and specificity. We also evaluated the means and 95% confidence intervals (95% CI) for the sensitivity, specificity, PPV