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**Title:** Predictors of outcome for patients with severe hypercapnic respiratory failure requiring NIV

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**Body:** Background. NIV has been successfully applied in patients with COPD and acute hypercapnic respiratory failure (ARF), with a lower rate of complications compared to IMV. Not to identify patients who are likely to fail NIV can cause inappropriate delay in intubation, with increased morbidity and mortality. Aims and objectives. This study aims to determine predictors of NIV failure in this subtype of patients. Methods. We retrospectively evaluated COPD patients with ARF, undergoing NIV for at least 12h. To analyze the effect on the outcome (NIV failure leading to IMV or death), univariable and multivariable analyses were performed on the following parameters: age, gender, APACHE II and GCS scores, gas exchange at admission, during NIV and at discharge/death, length of stay. ROC curves for pH START and APACHE II were also performed. Results. 201 individuals were enrolled; NIV failure was observed in 50 patients. At the univariate analysis NIV was successful in patients with: lower APACHE II score ( $20.02 \pm 4.81$  vs  $24.84 \pm 6.35$ ,  $p < 0.001$ ) and PaCO<sub>2</sub> at admission ( $93.10 \pm 15.08$  vs  $98.45 \pm 16.09$ ,  $p = 0.029$ ) and after 2-4 hours of NIV ( $77.62 \pm 13.62$  vs  $82.12 \pm 15.24$ ,  $p = 0.044$ ), and higher pH at admission ( $7.26 \pm 0.06$  vs  $7.23 \pm 0.08$ ,  $p = 0.033$ ), and GCS score ( $12.94 \pm 2.44$  vs  $11.24 \pm 3.32$ ,  $p = 0.001$ ). In the logistic regression model only APACHE II was found to be an independent predictor of the outcome ( $p < 0.0001$ , OR 1.179, 95%CI 1.101-1.263 as quantitative variable;  $p < 0.0001$ , OR 3.753, 95%CI 1.798-7.835, as qualitative variable,  $> 20.5$ ). Conclusions. Our findings confirmed NIV effectiveness in COPD patients ARF; moreover APACHE II score, besides arterial pH, may be a useful parameter in predicting NIV failure.