External validation of the OPALS prediction model for in-hospital mortality in patients with acute decompensated pulmonary hypertension

To the Editor:

We were very pleased to read the article "Critical care outcomes in patients with pre-existing pulmonary hypertension: insights from the ASPIRE registry", recently published in *ERJ Open Research* [1].

In that paper, the authors conducted a retrospective cohort study in the UK and described an exploratory score named OPALS, which was associated with in-hospital mortality in critical patients admitted due to acute decompensated pulmonary hypertension (PH).

We recently published the results of our multicentre retrospective cohort study, based on electronic healthcare records from January 2014 to December 2019 in two university-based hospitals in Sao Paulo, Brazil [2]. We included 73 patients with acute decompensated PH groups 1 and 4 after an unplanned intensive care unit admission (ICU); only medical admissions were included. There were no missing data for any of the variables of interest. We developed and internally validated a machine learning derived decision tree model to predict in-hospital mortality of patients admitted due to acute decompensated PH. In our study, the European Respiratory Society/European Society of Cardiology PH risk assessment and Sequential Organ Failure Assessment Score were predictors of in-hospital mortality.

Predicting outcomes early at ICU admission may be useful for decision-making in terms of interventions and to understand the clinical course of acute decompensated PH [3, 4]. We aimed to test and externally validate the OPALS score in our cohort according to the TRIPOD checklist for transparent reporting of a multivariable prediction model for individual prognosis [5].

The OPALS scale runs from 0 to 5 points, based in variables related to the severity of acute illness at admission: oxygen (oxygen saturation measured by pulse oximetry/inspiratory oxygen fraction (S_{pO_2}/F_{IO_2}) ratio $\leqslant$185) (1 point); platelets $\leqslant$196×10^9 L^{-1} (1 point); age $\geqslant$37.5 years (1 point); lactate $\geqslant$2.45 mmol·L^{-1} (1 point); and sodium $\leqslant$130.5 mmol·L^{-1} (1 point). Higher scores were associated with higher mortality in the original study.

To test the hypothesis that the OPALS score was associated with in-hospital mortality in our cohort, we employed multivariate logistic regression. We evaluated the predictive performance of the OPALS score, examining the calibration and discrimination of the regression model. Calibration was evaluated by plotting observed proportions *versus* predicted probabilities, and by calculating the calibration slope and intercept. Discrimination was assessed with the area under the receiver operating characteristic curve (AUC-ROC). Statistical analyses were performed using SPSS software (version 23.0: IBM, Armonk, NY, USA). A p-value $\leqslant$0.05 was considered significant.

Our cohort had fewer patients (73 medical patients) than the original OPALS cohort (242 total patients, 147 medical patients) but was similar regarding demographics, PH severity and in-hospital mortality. Compared to the OPALS cohort, our patients were of similar age (median age 48 *versus* 52 years), sex (females 75% *versus* 68.2%), type of PH (group 1 64% *versus* 67%). Severity of PH based on the number of patients in New York Heart Association functional class III–IV was similar (76.3% *versus* 83.5%).
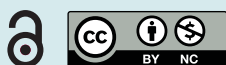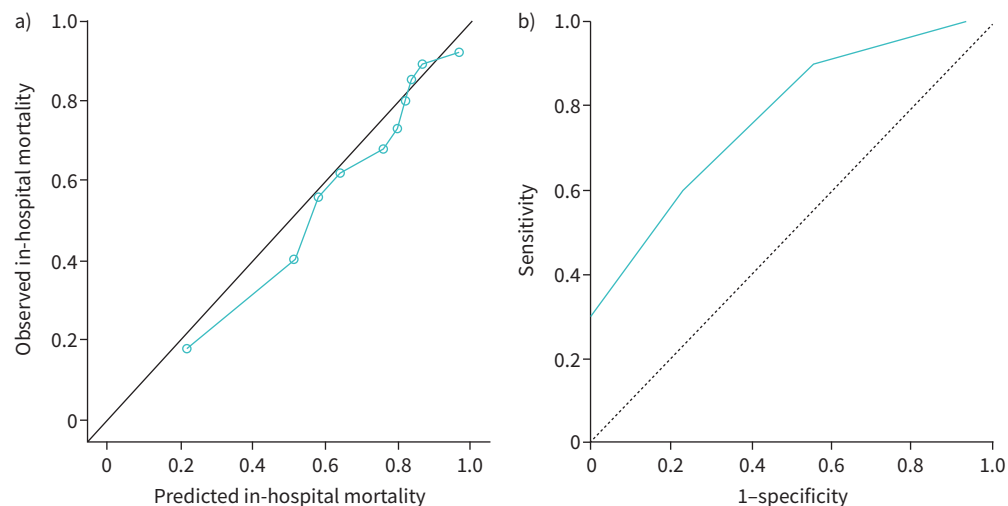
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In this external validation of the OPALS prediction model for in-hospital mortality in patients with acute decompensated pulmonary hypertension admitted to the intensive care unit, discrimination was very good and similar to the derivation cohort https://bit.ly/3sa8oQy

FIGURE 1 a) Calibration plot showing deciles of observed and predicted probabilities: $R^2=0.97$ and the intercept was −0.07 (95% CI −0.17−−0.03) with a slope of 1.05 (95% CI 0.90–1.19). b) The receiver operating characteristic curve of the OPALS score for predicting in-hospital mortality among patients admitted due to acute decompensated pulmonary hypertension in out cohort.

Variables used in the OPALS score, such as sodium and platelets, were also similar between both cohorts (median sodium 136 *versus* 135 mEq·L^{-1} and median platelets 179 *versus* 194×10^9 L^{-1}). In our cohort, lactate and S_{pO_2}/F_{IO_2} ratio were higher than in the OPALS cohort (lactate 2.0 *versus* 1.2 mmol·L^{-1} and S_{pO_2}/F_{IO_2} 267 *versus* 168). In-hospital mortality in our cohort was quite similar (41.1% in our cohort *versus* 40.7% in medical patients of the OPALS cohort).

The OPALS score model calibration plot and discrimination receiver operating characteristic curve are shown in figure 1. The intercept was −0.07 (95% CI −0.17−−0.03) with a slope of 1.05 (95% CI 0.90–1.19). R^2 was 0.97, indicating a high calibration between model performance and actual outcome. The OPALS score had an AUC-ROC of 0.77 (95% CI 0.66–0.88) to predict in-hospital mortality, similar to the AUC-ROC described in the original study (0.78). On our cohort, OPALS showed sensitivity of 0.60 (95% CI 0.40–0.77%), specificity of 0.76 (95% CI 0.61–0.88%), positive predictive value of 0.64 (95% CI 0.49–0.76%) and negative predictive value of 0.73 (95% CI 0.63–0.81%). Using the cut-off of OPALS ⩾2.5, as proposed in the original cohort, to predict in-hospital mortality, the unadjusted odds ratio for in-hospital mortality was 3.19 (95% CI 1.54–6.70).

In conclusion, the performance of the OPALS score in our cohort was similar to that in the derivation cohort, with very good calibration and similar discrimination. The main limitations in the present study are the small sample and the retrospective design. However, the lack of missing data and the robust methodological approach used for this external validation adds important information for physicians involved in the care of critical patients with PH.

Further studies are needed to evaluate the OPALS model in larger cohorts. Acute decompensation of PH remains a challenging complication of advanced PH. Multicentre collaboration is necessary to develop robust clinical models that can support clinical decisions.

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