Early View

Correspondence

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

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Authors' contribution

Dr. Garcia made substantial contributions to the conception, design, acquisition, analysis, and interpretation of the work, and drafted the work and approved the version to be published.

Dr. Souza made substantial contributions to the conception of the work, analysis and interpretation of data, revised for critically important intellectual content, and approved the final version to be published.

Dr. Caruso made substantial contributions to the conception, design, analysis, and interpretation of the work, revised it for critically important intellectual content, and approved the version to be published.

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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 United Kingdom 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 multicenter 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 ICU admission, only medical admissions were included. There was 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 (SOFA) 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 OPALS score in our cohort according to the TRIPOD checklist for transparent reporting of a multivariable prediction model for individual prognosis [5].

OPALS score goes from zero to five points, based in variables related to the severity of acute illness at admission: oxygen ($\text{SpO}_2/\text{FiO}_2$) ≤ 185 (1 point); platelets $\leq 196 \times 10^9 \cdot \text{L}^{-1}$ (1 point); age ≥ 37.5 years (1 point); lactate $\geq 2.45 \text{ mmol} \cdot \text{L}^{-1}$ (1 point); sodium $\leq 130.5 \text{ mmol} \cdot \text{L}^{-1}$ (1 point). Higher scores were associated with higher mortality in the original study.

To test the hypothesis that 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. Armonk, NY: IBM). P-values ≤ 0.05 were considered significant.

Our cohort have less patients (n=73 medical patients) than the original OPALS cohort (n=242 total patients, n=147 medical patients) although has similarity regarding demographics, PH severity and in-hospital mortality. Compared to OPALS cohort our patients were of similar age (median age 48 years vs. 52 years), gender (females 75% vs. 68.2%), type of PH (group 1 PH 64% vs. 67%). Severity of PH based on number of patients on NYHC-Functional class III-IV was similar (76.3% vs. 83.5%). Variables used in OPALS score as sodium and platelets were also similar between both cohorts (median sodium in mEq/L 136 vs. 135 and median platelets $\times 10^9 \cdot \text{L}^{-1}$ 179 vs 194). In our cohort, lactate and $\text{SpO}_2/\text{FiO}_2$ ratio were higher than in the OPALS cohort (lactate 2.0 vs. 1.2 $\text{mmol} \cdot \text{L}^{-1}$ and $\text{SpO}_2/\text{FiO}_2$ ratio 267 vs. 168). In-

hospital mortality in our cohort was quite similar (41.1% in our cohort vs. 40.7% in medical patients of the OPALS cohort).

OPALS score model calibration plot and discrimination ROC curve are shown in Figure 1. The intercept was -0.07 (95% CI -0.17 to -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 of 0.77 (95% CI $0.66-0.88$) to predict in-hospital mortality, similar to the AUC-ROC described in the original study (AUC 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 cutoff of $OPALS \geq 2.5$ as proposed in the original cohort to predict in-hospital mortality, the unadjusted OR 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 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 still remains a challenging complication of advanced PH. Multicenter collaboration is necessary to develop robust clinical models that can support clinical decisions.

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Figure Legends

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