



The 12th World Congress on CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

External Validation of a Firth-Penalized EASIX mortality Model Across Four Independent Latin American and One United States Hispanic-based Cohorts of patients with Multiple Myeloma

Gledy Jimenez Tornero, Viviana Olaya Colorado, Yanjia Zhang, Anshul Saxena, Susy Bazán Ruiz, Eduardo Bendezu, David Orcossupa Quispe, Romain Alvarez Puerta, Sommer Porras, Maria Alejandra Vera Vasquez, Rosa Vengoa Figueroa, Cesar Samanez, Alejandro Munoz, Michael Amarillo, Diana Martinez, Catalina Zapata, Leidy Valencia, Marco Ruiz

Hospital Nacional Alberto Sabogal Sologuren, Lima, Peru, Centro Oncológico de Antioquia, Medellín, Colombia, Miami Cancer Institute, Miami, FL, USA, Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru, Oncosalud – Auna, Lima, Perú

INTRODUCTION

Endothelial activation and damage are becoming established as relevant components in the prognosis of multiple myeloma. The Endothelial Activation and Stress Index (EASIX), calculated from lactate dehydrogenase, creatinine, and platelet count, as well as its variants, have shown potential associations with survival, treatment-related complications, and adverse events in different multiple myeloma populations.

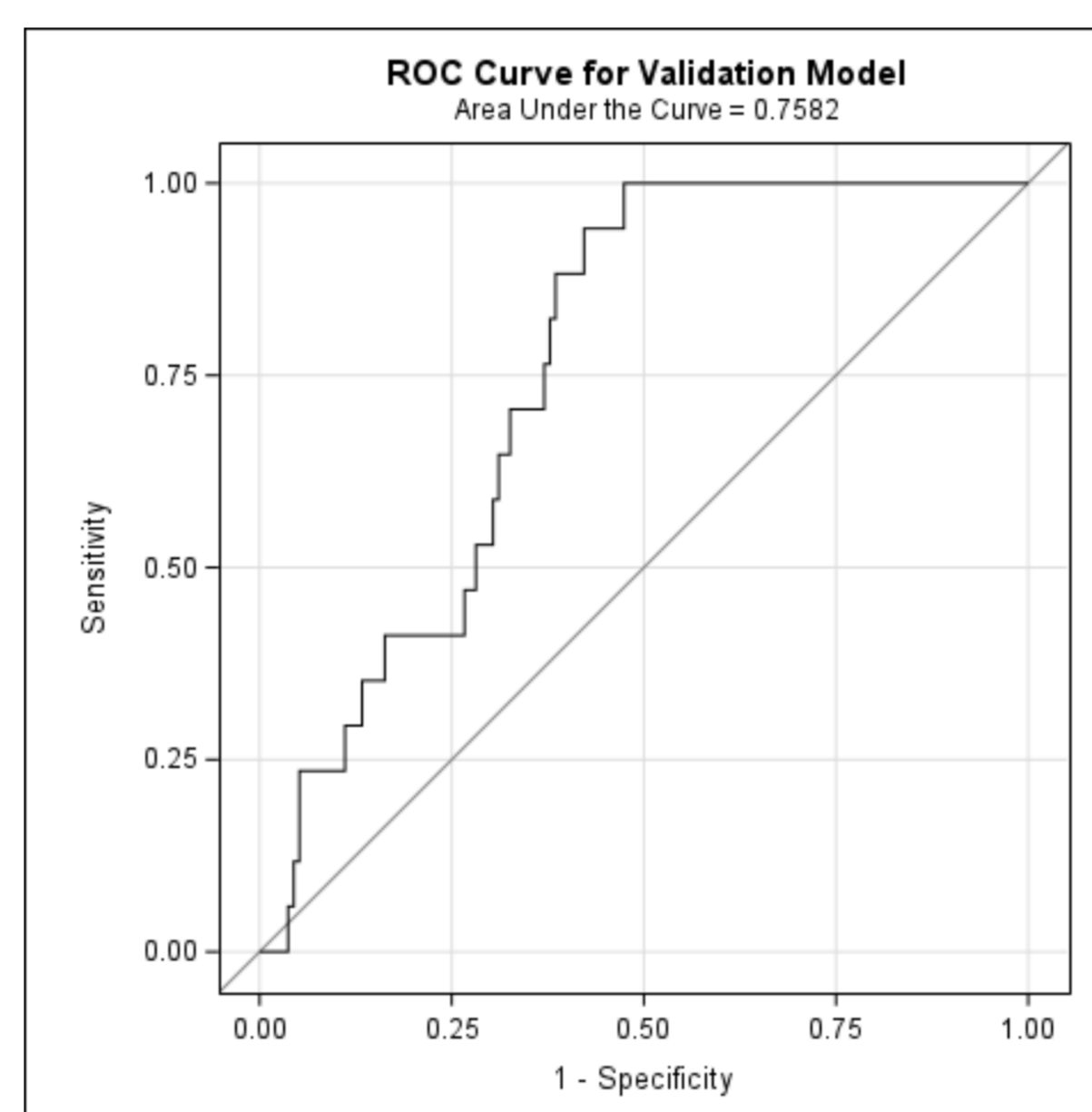
Recent data from Hispanic studies also suggest a relationship with mortality; however, the reproducibility and external validity of these models in independent Hispanic populations remain insufficiently evaluated. In this context, this study aims to evaluate the external validity and generalizability of a mortality prediction model based on EASIX with Firth penalization in an independent cohort of Hispanic patients.

METHODS

This retrospective cohort study included two Hispanic populations. The development cohort consisted of 167 patients from Latin America, with 24 deaths (14.4%), of whom 88 complete cases were used for multivariable modeling. The validation cohort included 155 patients from a US-based Hispanic population, with 20 deaths (12.9%). The dataset included demographic and clinical variables such as age, sex, body mass index (BMI), and baseline \log_2 (EASIX). Multivariable modeling was performed using Firth penalization. Model performance was evaluated using calibration slope, shrinkage factor, area under the curve (AUC), concordance, and predicted versus observed mortality by deciles.

RESULTS

In the validation cohort, the linear predictor (LP) from the development model remained a strong independent predictor of mortality ($\beta = 1.0069$, $SE = 0.3353$, $p = 0.0027$), corresponding to an odds ratio of 2.74 (95% CI 1.42–5.28). The calibration slope was approximately 1.0, indicating excellent calibration and minimal overfitting. Discriminative performance was robust, reflected by an AUC of 0.758 and a concordance of 75.8%, confirming the model's ability to accurately distinguish patients by mortality risk. The global likelihood ratio test was significant ($\chi^2 = 9.66$, $p = 0.0019$), confirming meaningful predictive signal of the development model in the external dataset.



CONCLUSION

Across two independent cohorts with similar event rates (~12–14%), the EASIX-derived mortality prediction model demonstrated strong reproducibility, with preserved effect size, excellent calibration, and stable discrimination. These findings support EASIX as a robust, generalizable biomarker of mortality risk, suitable for broader clinical application.

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CONTACT

Gledy Jimenez Tornero. MD
gledyjimeneztornero@gmail.com



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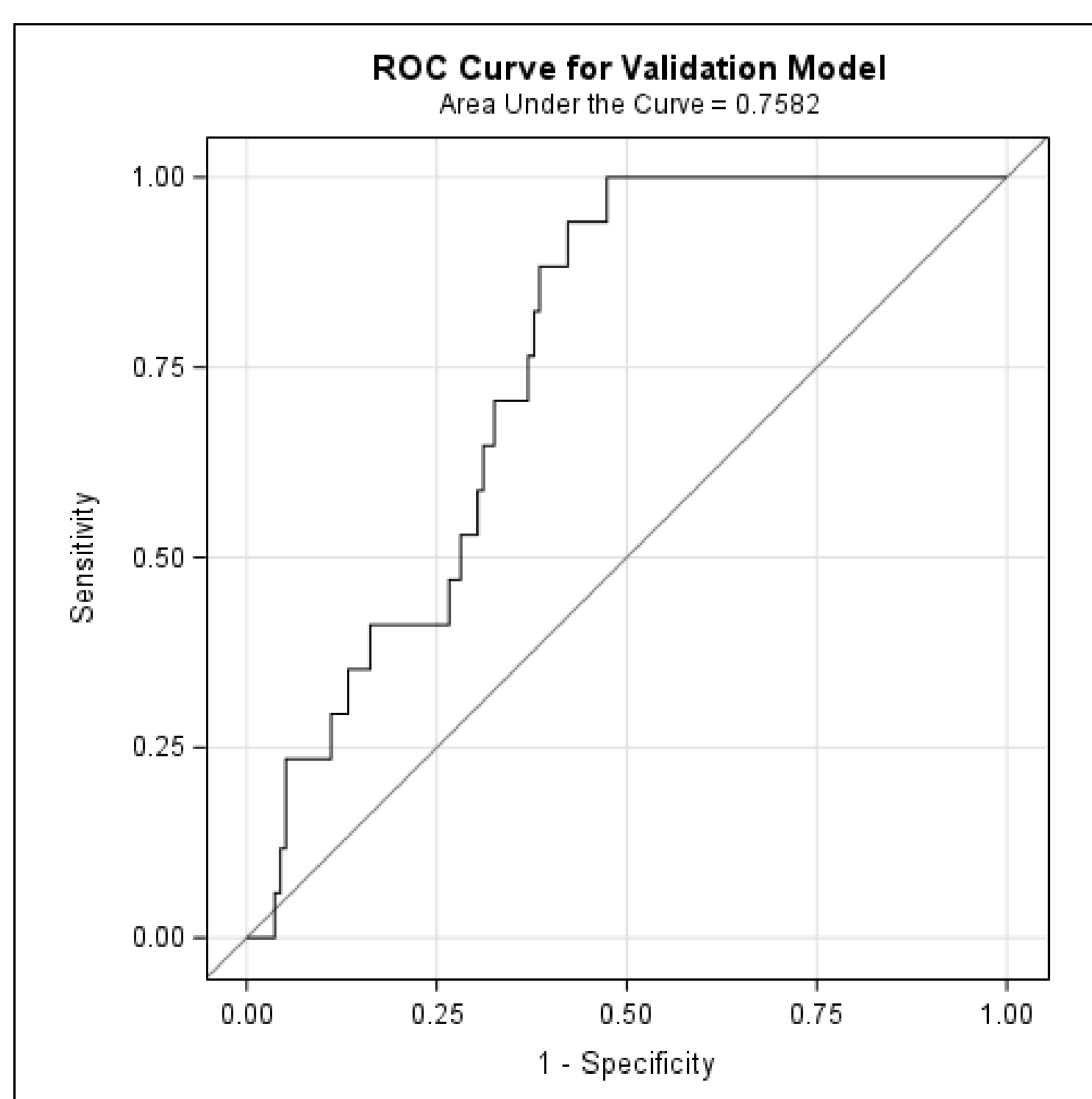
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