

“New Paths to Learn to Travel”: Artificial Intelligence to Predict Preeclampsia

“Nuevos caminos para aprender a transitarlos”: Inteligencia artificial para predecir preeclampsia

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In 2018 the Senate and the Chamber of Deputies of Argentina, declared May 22 as the “National Preeclampsia Awareness Day” (PE).

There were several reasons for this measure. One of the main ones was that hypertensive disorders of pregnancy (HDP), especially PE, one of the most severe and frequent presenting phenotypes, is responsible for 15.2% of maternal mortality in Argentina (3.9 out of 10 000 live births); another predominant factor for the spread of this entity was that its origin is unknown, there being many challenges for prediction, prevention, and treatment. (1)

Although there are several theories that attempt to explain the pathophysiology of HDP, (2) they do not do so completely, which is why every researcher studying the subject aims to find markers for the early prediction of PE and thus prevent its complications.

Due in large part to the multiple mechanisms involved in the production of HDP, early markers with high diagnostic sensitivity and specificity have not yet been established, leaving open ground for research in this aspect. (3)

Olano et al. had the purpose of finding an early PE marker and in this *Argent J Cardiol* issue have published a novel study, using artificial intelligence (AI) as a method, still little widespread in Argentina at least in this area of medicine, but with enormous potential for development and application in the near future.(4)

For this purpose, they carried out a prospective, observational study, which included 112 high-risk pregnant women, from a sample of 1155 patients, who were in weeks 10 to 16 of gestation and without pharmacological treatment. They were evaluated with impedance cardiography, pulse wave velocity, and 24-hour ambulatory blood pressure monitoring. Among the 112 patients, 17 presented PE, considered as the

primary endpoint. The data obtained were analyzed using traditional statistics and some of them, such as those obtained by impedance cardiography, by Machine Learning with j48 classification tree to obtain a PE prediction algorithm in the first trimester of pregnancy.

The authors conclude that the arterial compliance index, which was the main node of the algorithm, together with the variables indicative of alteration in myocardial contractility, such as cardiac index, systolic work index, ejection time ratio and Heather index were early predictors of a hemodynamic pattern of PE risk.

To date, the main therapeutic measure we have to prevent the progression to PE is the indication of low doses of acetylsalicylic acid (ASA) between weeks 12 and 16 of pregnancy, only in a selected high-risk population. (5)

Risk stratification, in this case high risk of PE, is not uniform in clinical practice or in guidelines dedicated to this topic. Prediction of PE only by clinical history detects the disease in 40% of cases. (6) This is the reason why the authors of the ASPRE study, (5) who demonstrated the effectiveness of early treatment with ASA to prevent PE, evaluated the risk of the included population, with other complementary methods such as uterine artery Doppler, placental markers and office blood pressure, thus increasing the risk prediction to 80%, mainly in early-onset PE, which is the one that benefits the most from ASA treatment.

In the publication by Olano et al., it is not clear how they evaluated the risk of the patients included, which is a determining and necessary point when indicating the hemodynamic evaluation proposed by the authors.

Another information that is not described in the

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text is about treatment or not with ASA, especially considering that they were high risk patients, making it extremely likely that part of the included population had received it, which could influence the results.

Of the 17 patients who progressed to PE, only in 3 cases PE developed before 34 weeks of pregnancy, the rest presented it late. In previous publications, (7,8) a different hemodynamic pattern has been described between these two entities: early PE is characterized by elevated peripheral resistance and decreased stroke volume measured by impedance cardiography. The early identification of this hemodynamic pattern becomes important since early-onset PE has a worse prognosis, but it is the one that benefits the most from the early indication of ASA.

A hypothesis of interest to confirm is that patients who develop late PE have altered contractile function indices, with a different hemodynamic pattern from those with early onset.

Among the limitations of this work we have, in the first instance, the lack of evaluation of clinical data indicative of PE risk, and the small number of patients. It would be interesting and diagnostically useful, to confirm the results of this study with a larger sample, as well as, in a later phase, to verify the clinical usefulness of the myocardial contractility indices chosen in the algorithm through AI, to thus add another complementary method to the simple routine interrogation to assess the risk of PE.

However, impedance cardiography is not a widely used technique in our setting, except in the field of hypertension specialists.

The hemodynamic study of the pregnant woman is an extensive resource to investigate the pathophysiological alterations of HDP, (9,10) and perhaps in the near future, when we have solid evidence, it will be time to apply it or not, as an early diagnostic tool.

In the present work, the resulting PE prediction algorithm included variables other than those indicated as significant by traditional statistics, which, with a larger number of patients, would have been predictors of PE by logistic regression, as previously demonstrated for peripheral resistance index and the cardiac index. (11) The question remains whether the algorithm developed by AI has a power independent of the number of data included, unlike traditional statistics.

The strength of this work is the recruitment of patients in the first trimester of pregnancy for the purpose of early diagnosis, which few previous studies on the subject have demonstrated.

Artificial intelligence is an additional useful tool, but more evidence is needed to include its results in clinical practice. Undoubtedly, the evidence will arrive soon and will contribute with traditional statistics for the implementation of new forms of diagnosis and treatment.

Olano et al. have the privilege of publishing the first work in Argentina on PE prediction through AI. The road is open, although there is still a long way to go.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

REFERENCES

1. <https://www.hcdn.gob.ar/proyectos/proyecto.jsp?exp=5207-D-2018#:~:text=%2D%20Instituyese%20el%20d%C3%ADa%2022%20de,enfermedad%20para%20evitar%20complicaciones%20conexas>.
2. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: Pathophysiology, Challenges, and Perspectives. *Circ Res*. 2019;124:1094-112. <https://doi.org/10.1161/CIRCRESAHA.118.313276>
3. MacDonald TM, Walker SP, Hannan NJ, Tong S, Kaitu'u-Lino TJ. Clinical tools and biomarkers to predict preeclampsia. *EBioMedicine*. 2022;75:103780. <https://doi.org/10.1016/j.ebiom.2021.103780>.
4. Olano RD, Espeche WG, Leiva Sisniegues BC, Carrera Ramos PM, Martínez C, Leiva Sisniegues CE, et al. Artificial Intelligence Modeling with Non-Invasive Hemodynamics to Predict Preeclampsia in High-Risk Pregnancy. *Argent J Cardiol* 2023;91:xxx-xxx. <http://dx.doi.org/10.7775/rac.v91.i5.20675>
5. RRolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C, et al. Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. *N Engl J Med*. 2017;377:613-22. <https://doi.org/10.1056/NEJMoa1704559>
6. Chappell LC, Cluver CA, Kingdom J, Tong S. Pre-eclampsia. *Lancet*. 2021;398:341-54. [https://doi.org/10.1016/S0140-6736\(20\)32335-7](https://doi.org/10.1016/S0140-6736(20)32335-7)
7. Valensise H, Vasapollo B, Gagliardi G, Novelli GP. Early and late preeclampsia: two different maternal hemodynamic states in the latent phase of the disease. *Hypertension*. 2008;52:873-80. <https://doi.org/10.1161/HYPERTENSIONAHA.108.117358>
8. Foo FL, Mahendru AA, Masini G, Fraser A, Cacciatore S, MacIntyre DA, et al. Association Between Prepregnancy Cardiovascular Function and Subsequent Preeclampsia or Fetal Growth Restriction. *Hypertension*. 2018;72:442-50. <https://doi.org/10.1161/HYPERTENSIONAHA.118.11092>
9. Paez OB, Puleio PA, Visser M, Mazzeo S, Antello L, Alderete JR, y cols. La preeclampsia es precedida por alteración de la función cardiovascular. *Rev Argent Cardiol* 2020;88:55-60. <http://dx.doi.org/10.7775/rac.es.v88.i1.17192>
10. Gyselaers W, Vonck S, Staelens AS, Lanssens D, Tomsin K, Oben J, et al. Gestational hypertensive disorders show unique patterns of circulatory deterioration with ongoing pregnancy. *Am J Physiol Regul Integr Comp Physiol*. 2019;316:R210-21. <https://doi.org/10.1152/ajpregu.00075.2018>
11. McLaughlin K, Zhang J, Lye SJ, Parker JD, Kingdom JC. Phenotypes of Pregnant Women Who Subsequently Develop Hypertension in Pregnancy. *J Am Heart Assoc*. 2018;7:e009595. <https://doi.org/10.1161/JAHA.118.009595>