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EDITORIAL COMMENT

Can Artificial Intelligence Make Maternal Cardiac Risk Prediction a Walk in the Park?

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Severe maternal morbidity (SMM) during delivery hospitalizations continues to rise in the United States, increasing more than 20% from 2008 through 2020.[1] Cardiovascular SMM has mirrored this increase.[2] In addition to mortality, SMM is associated with increased hospital stay length, medical care costs, and long-term adverse health consequences. Cardiac SMM is the highest in those without previously documented cardiac disease and frequently appears to be preventable.[2,3] Early accurate prediction of patients likely to have cardiac complications provides a window of opportunity to improve maternal cardiovascular outcomes.

Machine learning algorithms can consider a greater number and complexity of variables than traditional measures for predictive analysis. These techniques are increasingly applied to large health care data sets to build predictive models.[4] In this issue of *JACC: Advances*, Zahid et al[5] used artificial intelligence to analyze data on 2.3 million delivery hospitalizations from the 2016 to 2020 National Inpatient Sample of the Health Care Cost and Utilization Project to identify individuals at risk of acute peripartum cardiac complications at the time of delivery. They developed a Prediction of Acute Risk for Cardiovascular Complications in the Peripartum Period Score for a composite end point measure of cardiovascular complications based on International Classification of Diseases-10th Revision codes present at time of admission. Adverse outcomes included preeclampsia/eclampsia, peripartum cardiomyopathy, acute heart failure, acute coronary syndrome, thromboembolism, arrhythmias, and renal complications. A training data set (70%) was used for score creation, a validation set (20%) for interim evaluation, and a testing set (10%) to determine final performance metrics resulting in a receiver operating characteristic curve of 0.68 (95% CI: 0.68-0.69). The most important predictors (in decreasing point order of importance) included pre-existing heart failure, history of stroke, electrolyte imbalances, pre-existing diabetes or gestational diabetes, obesity, coagulopathy, cesarean delivery, multiple gestation, age <20 or >34 years, nonelective admission, and low median income.

Most currently used predictive models for pregnancy-associated cardiovascular complications are based on registry data, cohort data, or expert advice. The populations included in the cohort or registry are often more narrowly defined and not representative of all pregnant people. For example, modified World Health Organization criteria attribute risk based on lesion-specific diagnoses. Risk assessment was initially based on an expert multidisciplinary panel but was subsequently validated in 2,742 patients participating in the Registry of Cardiac Disease.[6,7] CARPREG II (Cardiac Disease in Pregnancy) is based on 10 maternal risk factors in close to 2,000 pregnancies in women with known cardiovascular disease (CVD).[8] The Zwangerschap bij Aangeboren Hartafwijking scale is a weighted risk score that predicts cardiovascular adverse outcomes in 1802 pregnant and postpartum women with congenital heart disease.[9] Since these scoring systems were derived from patients with known prior cardiac disease, they may not accurately address patients whose CVD develops de novo during pregnancy.

The American College of Obstetrics and Gynecology has proposed screening women with concerning symptoms and vital signs derived from an analysis of

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maternal deaths from CVD by the California Maternal Quality Care Collaborative. The tool kit was validated internally and identified approximately 90% of maternal deaths.[10,11] "Red flags" for urgent screening include shortness of breath at rest, O_2 saturation <94%, blood pressure > 160/90 mm Hg, or a resting heart rate >120 beats/min. Unfortunately, if we wait until these signs develop, the patient is likely to have morbidity already. Lesser abnormalities were also recommended for further investigation such as less severely abnormal vital signs, concerning symptoms, or presence of several risk factors (eg, older age, Black race, obesity, hypertension or diabetes, and prior substance use). Performance of the California Screening Tool was assessed in a general obstetric population of 846 women in two academic medical centers, with a screen positive rate of 8% and an overall positive rate of 1.5%. CVD was present in 30% of those with positive screens who completed follow-up. Surprisingly, the positive screen rate was higher in the center with a lower "true positive rate."[12] Low positive rate may have been related to screening bias, lack of a control group, or failure of many patients with an initial positive screen to complete full testing. This tool is currently undergoing wider validation.

An advantage of this study is its utilization of recent data from an extremely large, well-vetted database (the National Inpatient Sample). Moreover, the investigators were able to adjust predicted risk score cutoffs to modulate sensitivity and specificity, as well as positive predictive and negative predictive values. Using a risk cut-off of 5.0%, a score cut-off of 4, and identification of 52% of high-risk patients, sensitivity was 73.3% (95% CI: 72.8%-73.8%), specificity was lower at 49.5%, and accuracy was 51.2% (95% CI: 51.1%-53.3%). This will need to be compared with results based on the algorithm suggested by the California Screening Tool. Prioritization of increased detection of true positives, even at the extent of increased false positives, is a reasonable strategy for maternal CVD, given current high maternal morbidity and mortality. Moreover, the negative predictive value of 96.1% (95% CI: 96.0%-96.2%) suggests lower-risk patients were truly at minimal risk. Another advantage is that the investigators were able to incorporate socioeconomic and racial-ethnic variables.

As the authors note, incorporation of predictive models into the electronic medical record has the potential to enhance quality improvement initiatives by making them immediately available at the point of care, which obviates the need for clinicians to calculate the risk manually. However, the benefit of this approach to subsequent health outcomes still needs to be proven.

A weakness of this predictive model is that some variables chosen for the model may not be as clinically useful in early pregnancy. For example, nonelective admission or electrolyte disorder (eg, acid-base disorder) may be surrogates for patients with acute cardiac morbidity at the time of admission and represent a "red flag," which is less helpful in defining the need for early screening. Moreover, some risk factors identified have been recognized from standard retrospective analysis—underlying comorbidities such as diabetes, renal disease, hypertension, pre-existing heart failure, or stroke—and already should have prompted intensive follow-up for CVD during pregnancy.

All large database analyses, including this one, are subject to coding errors in the International Classification of Diseases-10th Revision (ICD-10) diagnosis system. We do not have the luxury of a full chart review, as can be done in a registry or cohort analysis, to assure accuracy of diagnosis. Moreover, only delivery hospitalizations are addressed. Ideally, this predictive model should extend into the "fourth trimester," where most cardiovascular complications are known to occur—a goal for future research.

Finally, identification prior to admission for delivery will be the key. Future models that incorporate lab values and pregnancy imaging data have the potential for even better predictive capabilities. Once these algorithms are fully developed and refined, they are expected to surpass the current cardiac risk stratification scores used in pregnancy. Despite weaknesses, using machine learning algorithms in artificial intelligence holds significant promise for enhancing our ability to identify individuals at risk, leading to early intervention and improved outcomes during pregnancy and the postpartum period.

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AWD00004314 (137168-1); is an unpaid consultant for the Illinois Maternal Mortality Committee, serves on the steering committee, and is a site investigator for the REBIRTH trial of bromocriptine for peripartum cardiomyopathy; and has received honoraria for giving academic talks for the American Heart Association and for cardio-obstetrics conferences. Dr Jayaram has reported that she has no relationships relevant to the contents of this paper to disclose.

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