OBSTETRICS

Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks gestation

Neil O'Gorman, MD; David Wright, PhD; Argyro Syngelaki, RM; Ranjit Akolekar, MD; Alan Wright, PhD; Leona C. Poon, MD; Kypros H. Nicolaides, MD

BACKGROUND: Preeclampsia affects approximately 3% of all pregnancies and is a major cause of maternal and perinatal morbidity and death. In the last decade, extensive research has been devoted to early screening for preeclampsia with the aim of reducing the prevalence of the disease through pharmacologic intervention in the high-risk group starting from the first trimester of pregnancy.

OBJECTIVE: The purpose of this study was to develop a model for preeclampsia based on maternal demographic characteristics and medical history (maternal factors) and biomarkers.

STUDY DESIGN: The data for this study were derived from prospective screening for adverse obstetric outcomes in women who attended for their routine first hospital visit at 11-13 weeks gestation in 2 maternity hospitals in England. We screened 35,948 singleton pregnancies that included 1058 pregnancies (2.9%) that experienced preeclampsia. Bayes theorem was used to combine the a priori risk from maternal factors with various combinations of uterine artery pulsatility index, mean arterial pressure, serum pregnancy-associated plasma protein-A, and placental growth factor multiple of the median values. Five-fold cross validation was used to assess the performance of screening for preeclampsia that delivered at <37 weeks gestation (preterm-preeclampsia) and ≥37 weeks gestation (term-preeclampsia) by models that combined maternal factors with individual biomarkers and their combination with screening by maternal factors alone.

RESULTS: In pregnancies that experienced preeclampsia, the values of uterine artery pulsatility index and mean arterial pressure were increased, and the values of serum pregnancy-associated plasma protein-A and placental growth factor were decreased. For all biomarkers, the deviation from normal was greater for early than late preeclampsia; therefore, the performance of screening was related inversely to the gestational age at which delivery became necessary for maternal and/or fetal indications. Combined screening by maternal factors, uterine artery pulsatility index, mean arterial pressure, and placental growth factor predicted 75% (95% confidence interval, 70-80%) of preterm-preeclampsia and 47% (95% confidence interval, 44-51%) of term-preeclampsia, at a false-positive rate of 10%; inclusion of pregnancy-associated plasma protein-A did not improve the performance of screening. Such detection rates are superior to the respective values of 49% (95% confidence interval, 43-55%) and 38% (34-41%) that were achieved by screening with maternal factors alone.

CONCLUSION: Combination of maternal factors and biomarkers provides effective first-trimester screening for preterm-preeclampsia.

Key words: Bayes theorem, first trimester screening, mean arterial pressure, placental growth factor, preeclampsia, pregnancy-associated plasma protein-A, uterine artery

Preeclampsia affects 2-3% of all pregnancies and is a major cause of maternal and perinatal morbidity and death.[1,2] In the last decade extensive research has been devoted to screening for preeclampsia with the aims of (1) to reduce the prevalence of the disease through pharmacologic intervention in the high-risk group[3,4] and (2) to minimize adverse perinatal events for those who experience preeclampsia by the determination of the appropriate time and place for delivery.[5] The traditional approach to screening for preeclampsia

EDITORS' CHOICE

is to identify risk factors from maternal demographic characteristics and medical history (maternal factors), but such an approach can identify only 35% of all preeclampsia and approximately 40% of preterm-preeclampsia, at false-positive rate (FPR) of 10%.[6,7]

An alternative approach to screening, which allows estimation of individual patient- specific risks of preeclampsia that requires delivery before a specified gestation, is to use Bayes theorem to combine the a priori risk from maternal characteristics and medical history (maternal factors) with the results of various combinations of biophysical and biochemical measurements that are made at different times during pregnancy.[8,9] We adopted this approach using a competing risk model for the time to delivery with preeclampsia. This model assumes that, if the pregnancy was to continue indefinitely, all women would experience preeclampsia; whether they do so before a specified gestational age depends on competition between delivery before or after the development of preeclampsia.[8] The effect of maternal factors is to modify the mean of the distribution of gestational age at delivery with preeclampsia so that, in pregnancies that are at low-risk for preeclampsia, the gestational age distribution is shifted to the right with the implication that, in most pregnancies, delivery actually will occur before the development of preeclampsia. In high-risk pregnancies the distribution is shifted to the left, and the smaller the mean gestational age, the higher is the risk for preeclampsia. The distribution of biomarkers is specified conditionally on the gestational age at delivery with preeclampsia. For any women with specific maternal factors

Cite this article as: O'Gorman N, Wright D, Syngelaki A, et al. Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks gestation. Am J Obstet Gynecol 2016; 214:103.e1-12.

0002-9378/free
© 2016 Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.ajog.2015.08.034

and biomarker multiple of the median (MoM) values, the posterior distribution of the time to delivery with preeclampsia, assuming that there is no other cause of delivery, is obtained from the application of Bayes theorem.

We have reported previously on the development and performance of a maternal factor–derived algorithm for the prediction of preeclampsia.[7] We have also proposed a model for combining the maternal factor–derived previous risk with the results of uterine artery pulsatility index (PI), mean arterial pressure (MAP), serum placental growth factor (PLGF), and pregnancy-associated plasma protein-A (PAPP-A).[8,9] However, the performance of screening was assessed by simulation from the fitted model, and such an approach generally is biased optimistically because it ignores errors of estimation and departures from the assumed model.

The objective of this study of 35,948 singleton pregnancies, which included 1058 patients (2.9%) who experienced preeclampsia, with complete data on uterine artery PI, MAP, serum PLGF, and PAPP-A, is to examine the potential improvement in performance of screening by maternal factors alone[7] with the addition of each biomarker and combinations of biomarkers. Performance of screening was assessed with the use of 5-fold cross validation.

Methods

Study population

The data for this study were derived from prospective screening for adverse obstetric outcomes in women who were attending for their routine first hospital visit in pregnancy at King's College Hospital and Medway Maritime Hospital, UK. This visit, which was held at 11^{+0} to 13^{+6} weeks gestation, included (1) the recording of maternal characteristics and medical history,[7] (2) measurement of the left and right uterine artery PI by transabdominal color Doppler ultrasound scanning and calculation of the mean PI,[10] (3) measurement of MAP by validated automated devices and standardized protocol,[11] and (4) measurement of serum concentration of PLGF and PAPP-A (DELFIA Xpress system, PerkinElmer Life and Analytical Sciences, Waltham, MA). Gestational age was determined from the fetal crown-rump

TABLE 1
Maternal and pregnancy characteristics in the screening population

Variables	Unaffected (n = 34,890)	Preeclampsia (n = 1058)	*P* value
Maternal age, y[a]	31.3 (26.8–35.0)	31.5 (27.0–35.6)	.34501
Maternal weight, kg[a]	66.5 (59.0–77.0)	72.1 (63.0–86.7)	.37555
Maternal height, cm[a]	164.5 (160.0–169.0)	163.2 (159.0–168.0)	.19445
Body mass index, kg/m^2[a]	24.5 (21.9–28.3)	27.1 (23.5–32.1)	.66575
Gestational age, wk[a]	12.7 (12.3–13.1)	12.7 (12.3–13.1)	.19424
Racial origin, n (%)			< .00001
White	25,315 (72.6)	564 (53.3)	
Afro-Caribbean	6,287 (18.0)	394 (37.2)	
South Asian	1,567 (4.5)	56 (5.3)	
East Asian	829 (2.4)	17 (1.6)	
Mixed	892 (2.6)	27 (2.6)	
Medical history			
Chronic hypertension	421 (1.2)	140 (13.2)	< .00001
Diabetes mellitus	303 (0.9)	22 (2.1)	.00008
Systemic lupus erythematosus/antiphospholipid syndrome	48 (0.1)	5 (0.5)	.01679
Cigarette smokers, n (%)	3,195 (9.2)	68 (6.4)	.00278
Family history of preeclampsia, n (%)	1,428 (4.1)	90 (8.5)	< .00001
Parity, n (%)			< .00001
Nulliparous	16,739 (48.0)	622 (58.8)	
Parous with no previous preeclampsia	17,028 (48.8)	283 (26.8)	
Parous with previous preeclampsia	1,123 (3.2)	153 (14.5)	

Comparisons between outcome groups were by chi-square or Fisher exact test for categoric variables and Mann-Whitney *U* test for continuous variables.

[a] Data are given as median (interquartile range).

O'Gorman et al. Competing risks model in screening for preeclampsia. Am J Obstet Gynecol 2016.

Download English Version:

https://daneshyari.com/en/article/3432311

Download Persian Version:

https://daneshyari.com/article/3432311

Daneshyari.com