Ultrasound Obstet Gynecol 2017; **49**: 756–760
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.17455

Multicenter screening for pre-eclampsia by maternal factors and biomarkers at 11–13 weeks' gestation: comparison with NICE guidelines and ACOG recommendations

N. O'GORMAN[1], D. WRIGHT[2], L. C. POON[1,3#], D. L. ROLNIK[1], A. SYNGELAKI[1], M. DE ALVARADO[1,4], I. F. CARBONE[5], V. DUTEMEYER[6], M. FIOLNA[1,7], A. FRICK[1,8], N. KARAGIOTIS[1], S. MASTRODIMA[1,9], C. DE PACO MATALLANA[10], G. PAPAIOANNOU[11], A. PAZOS[12], W. PLASENCIA[13] and K. H. NICOLAIDES[1#]

[1]*Harris Birthright Center for Fetal Medicine, King's College Hospital, London, UK;* [2]*Institute of Health Research, University of Exeter, Exeter, UK;* [3]*Chinese University of Hong Kong, Hong Kong, China;* [4]*Homerton University Hospital, London, UK;* [5]*Ospedale Maggiore Policlinico, Milan, Italy;* [6]*Centre Hospitalier Universitaire Brugmann, Université Libre de Bruxelles, Brussels, Belgium;* [7]*Medway Maritime Hospital, Gillingham, UK;* [8]*Lewisham University Hospital, London, UK;* [9]*North Middlesex University Hospital, London, UK;* [10]*Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain;* [11]*Attikon University Hospital, Athens, Greece;* [12]*Hospital Universitario San Cecilio, Granada, Spain;* [13]*Hospiten Group, Tenerife, Canary Islands, Spain*

KEYWORDS: Bayes' theorem; first-trimester screening; mean arterial pressure; placental growth factor; pre-eclampsia; pregnancy-associated plasma protein-A; pyramid of pregnancy care; survival model; uterine artery Doppler

ABSTRACT

Objective *To compare the performance of screening for pre-eclampsia (PE) based on risk factors from medical history, as recommended by NICE and ACOG, with the method proposed by The Fetal Medicine Foundation (FMF), which uses Bayes' theorem to combine the* a-priori *risk from maternal factors, derived by a multivariable logistic model, with the results of various combinations of biophysical and biochemical measurements.*

Methods *This was a prospective multicenter study of screening for PE in 8775 singleton pregnancies at 11–13 weeks' gestation. A previously published FMF algorithm was used for the calculation of patient-specific risk of PE in each individual. The detection rates (DRs) and false-positive rates (FPRs) for delivery with PE < 32, < 37 and ≥ 37 weeks were estimated and compared with those derived from application of NICE guidelines and ACOG recommendations. According to NICE, all high-risk pregnancies should be offered low-dose aspirin. According to ACOG, use of aspirin should be reserved for women with a history of PE in at least two previous pregnancies or PE requiring delivery < 34 weeks' gestation.*

Results *In the study population, 239 (2.7%) cases developed PE, of which 17 (0.2%), 59 (0.7%) and 180 (2.1%) developed PE < 32, < 37 and ≥ 37 weeks, respectively. Screening with use of the FMF algorithm based on a combination of maternal factors, mean arterial pressure (MAP), uterine artery pulsatility index (UtA-PI) and serum placental growth factor (PlGF) detected 100% (95% CI, 80–100%) of PE < 32 weeks, 75% (95% CI, 62–85%) of PE < 37 weeks and 43% (95% CI, 35–50%) of PE ≥ 37 weeks, at a 10.0% FPR. Screening with use of NICE guidelines detected 41% (95% CI, 18–67%) of PE < 32 weeks, 39% (95% CI, 27–53%) of PE < 37 weeks and 34% (95% CI, 27–41%) of PE ≥ 37 weeks, at 10.2% FPR. Screening with use of ACOG recommendations detected 94% (95% CI, 71–100%) of PE < 32 weeks, 90% (95% CI, 79–96%) of PE < 37 weeks and 89% (95% CI, 84–94%) of PE ≥ 37 weeks, at 64.2% FPR. Screening based on the ACOG recommendations for use of aspirin detected 6% (95% CI, 1–27%) of PE < 32 weeks, 5% (95% CI, 2–14%) of PE < 37 weeks and 2% (95% CI, 0.3–5%) of PE ≥ 37 weeks, at 0.2% FPR.*

Conclusion *Performance of screening for PE at 11–13 weeks' gestation by the FMF algorithm using a combination of maternal factors, MAP, UtA-PI and PlGF, is by far superior to the methods recommended by NICE and ACOG. Copyright © 2017 ISUOG. Published by John Wiley & Sons Ltd.*

Correspondence to: Prof. K. H. Nicolaides, Fetal Medicine Research Institute, King's College Hospital, 16–20 Windsor Walk, London SE5 8BB, UK (e-mail: kypros@fetalmedicine.com)

L.C.P. and K.H.N. are joint senior authors.

Accepted: 8 February 2017

INTRODUCTION

The traditional approach to screening for pre-eclampsia (PE) is to identify risk factors from maternal demographic characteristics and medical history (maternal factors)[1,2]. In the UK, the National Institute for Health and Care Excellence (NICE) has issued guidelines recommending that women should be considered to be at high risk of developing PE if they have any one high-risk factor or any two moderate-risk factors; high-risk factors are history of hypertensive disease in previous pregnancy, chronic kidney disease, autoimmune disease, diabetes mellitus or chronic hypertension and moderate-risk factors are first pregnancy, age ≥ 40 years, interpregnancy interval > 10 years, body mass index (BMI) at first visit of ≥ 35 kg/m^2 or family history of PE[1]. In the USA, according to the American College of Obstetricians and Gynecologists (ACOG), taking a medical history to evaluate for risk factors is currently the best and only recommended screening approach for PE; risk factors are nulliparity, age > 40 years, BMI ≥ 30 kg/m^2, conception by *in-vitro* fertilization, history of previous pregnancy with PE, family history of PE, chronic hypertension, chronic renal disease, diabetes mellitus, systemic lupus erythematosus or thrombophilia[2]. Consequently, the approaches recommended by NICE and ACOG essentially treat each risk factor as a separate screening test, with additive detection rate (DR) and screen-positive rate. According to NICE, all high-risk pregnancies should be offered low-dose aspirin. According to ACOG, use of aspirin should be reserved for women with history of PE in two or more previous pregnancies or PE requiring delivery < 34 weeks' gestation[3].

An alternative approach to screening, developed by The Fetal Medicine Foundation (FMF), allows estimation of individual patient-specific risks of PE requiring delivery before a specified gestation, with the use of Bayes' theorem to combine the *a-priori* risk from maternal factors, derived by a multivariable logistic model, with the results of various combinations of biophysical and biochemical measurements[4,5]. In a previous study, we used data from prospective screening in 35 948 singleton pregnancies at 11–13 weeks to develop an algorithm for the calculation of patient-specific risk of PE[5]. Combined screening by maternal factors, mean arterial pressure (MAP), uterine artery pulsatility index (UtA-PI) and serum placental growth factor (PlGF) achieved detection rates (DRs) of delivery with PE < 32, < 37 and ≥ 37 weeks of 89%, 75% and 47%, respectively, at a false-positive rate (FPR) of 10%[5]. A limitation of the study is that the performance of screening by a model derived and tested using the same dataset may be overestimated. However, a recent multicenter study in 8775 singleton pregnancies confirmed the validity of the algorithm and reported DRs of 100% (95% CI, 80–100%), 75% (95% CI, 62–85%) and 43% (95% CI, 35–50%) for PE delivering < 32, < 37 and ≥ 37 weeks, respectively, at a 10% FPR[6].

The objective of this study was to examine the performance of screening based on risk factors from medical history, as recommended by NICE[1] and ACOG[2,3], using the method proposed by the FMF.

METHODS

This was a prospective, non-intervention, multicenter study in singleton pregnancies at 11 + 0 to 13 + 6 weeks' gestation in women booking for routine pregnancy care in one of 12 maternity hospitals in five different countries: King's College Hospital, London, UK; Medway Maritime Hospital, Gillingham, UK; Homerton University Hospital, London, UK; North Middlesex University Hospital, London, UK; Southend University Hospital, Essex, UK; Lewisham University Hospital, London, UK; Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain; Hospital Universitario San Cecilio, Granada, Spain; Hospiten Sur, Tenerife, Spain; Centre Hospitalier Universitaire Brugmann, Brussels, Belgium; Attikon University Hospital, Athens, Greece; and Ospedale Maggiore Policlinico, Milan, Italy. The women were screened between February and September 2015 and gave written informed consent to participate in the study, which was approved by the National Health Service Research Ethics Committee in the UK and the Ethics Committee of each participating hospital in other countries. The results from screening were not made available to the patients or their physicians.

Maternal factors were recorded as described previously[4] and MAP and UtA-PI were measured using standardized protocols[7,8]. Serum pregnancy-associated plasma protein-A (PAPP-A) and PlGF concentrations were measured by an automated device (PAPP-A and PlGF 1-2-3™ kits, DELFIA® Xpress random access platform; PerkinElmer Inc. Wallac Oy, Turku, Finland). Measured values of MAP, UtA-PI, PAPP-A and PlGF were expressed as multiples of the median, adjusting for those characteristics found to provide a substantive contribution to the $\log_{10}$-transformed value, including maternal factors, in the prior model[9–12].

The outcome measure was PE, as defined by the International Society for the Study of Hypertension in Pregnancy[13]. Data on pregnancy outcome were collected from the hospital maternity records of the women. The obstetric records of all women with pre-existing or pregnancy-associated hypertension were examined to determine if the condition was PE.

The FMF algorithm was used for the calculation of patient-specific risks of delivery with PE delivering < 32, < 37 and ≥ 37 weeks' gestation using maternal factors and various combinations of maternal factors and biomarkers[4,5]. DR, with 95% CI, at a FPR of 10% was estimated. Similarly, the maternal characteristics and medical history of each patient were examined to determine whether they were screen positive or negative according to the NICE[1] and ACOG[2,3] guidelines; the DR, with 95% CI, of delivery with PE delivering < 32, < 37 and ≥ 37 weeks' gestation and the FPR were then estimated.

The statistical software package R was used for data analyses[14].

RESULTS

In the study population, 239 (2.7%) cases developed PE, of which 17 (0.2%), 59 (0.7%) and 180 (2.1%) developed PE < 32, < 37 and ≥ 37 weeks, respectively, and 8536 cases were without PE. Baseline demographic and clinical characteristics of participants are shown in Table S1.

The performance of screening by the FMF algorithm[4,5] and the methods advocated by NICE[1] and ACOG[2,3] are summarized in Table 1. Combined screening by maternal factors, MAP, UtA-PI and PlGF[4,5] detected 100% (95% CI, 80–100%) of PE < 32 weeks, 75% (95% CI, 62–85%) of PE < 37 weeks and 43% (95% CI, 35–50%) of PE ≥ 37 weeks, at a 10.0% FPR. The receiver–operating characteristics curves are shown in Figure 1.

Screening with use of NICE guidelines[1] detected 41% (95% CI, 18–67%) of PE < 32 weeks, 39% (95% CI, 27–53%) of PE < 37 weeks and 34% (95% CI, 27–41%) of PE ≥ 37 weeks, at a 10.2% FPR. Screening with use of ACOG recommendations[2] detected 94% (95% CI, 71–100%) of PE < 32 weeks, 90% (95% CI, 79–96%) of PE < 37 weeks and 89% (95% CI, 84–94%) of PE ≥ 37 weeks, at a 64.2% FPR. The results of the methods advocated by NICE[1] and ACOG[2,3] are illustrated in Figure 1. Screening based on the ACOG recommendations for use of aspirin[3] detected 6% (95% CI, 1–27%; 1/17) of PE < 32 weeks, 5% (95% CI, 2–14%; 3/59) of PE < 37 weeks and 2% (95% CI, 0.3–5%; 3/180) of PE ≥ 37 weeks, at a 0.2% (19/8536) FPR.

DISCUSSION

Main findings

The findings of this prospective multicenter validation study demonstrate that the performance of first-trimester screening for PE by the FMF algorithm, in which the patient-specific risk is derived from a combination of maternal factors, MAP, UtA-PI and PlGF[4,5], is by far superior to the methods advocated by NICE[1] and ACOG[2,3]. In screening by the FMF algorithm, the DRs of delivery with PE < 32, < 37 and ≥ 37 weeks' gestation were 100%, 75% and 43%, respectively, at a FPR of 10.0%. The respective DRs in screening according to NICE guidelines[1] were 41%, 39% and 34%, at a FPR of 10.2%. In the case of ACOG recommendations[2], about two-thirds of the population were classified as screen positive; the DRs of delivery with PE < 32, < 37 and ≥ 37 weeks were 94%, 90% and 89%, respectively, at a FPR of 64.2%. In screening based on the ACOG recommendations for use of aspirin[3], the DRs of delivery with PE < 32, < 37 and ≥ 37 weeks were 6%, 5% and 2%, respectively, at a FPR of 0.2%.

Study limitations

The main limitation of the study relates to the low incidence of delivery with PE with the inevitable wide confidence intervals obtained for performance of screening. Nevertheless, the values obtained in the validation study are very similar to those in the dataset of 35 948 pregnancies that was used for development of the algorithm[5].

Table 1 Detection rate of pre-eclampsia (PE) delivering < 32, < 37 or ≥ 37 weeks' gestation in validation dataset using screening algorithm developed by The Fetal Medicine Foundation (FMF)[5] based on maternal factors and combinations of biomarkers, and using recommendations of National Institute of Health and Care Excellence (NICE)[1] and American College of Obstetricians and Gynecologists (ACOG)[2,3]

	DR (%) of PE with delivery at:		
Screening method	*< 32 weeks*	*< 37 weeks*	*≥ 37 weeks*
FMF algorithm (FPR = 10.0%)			
Maternal factors	53 (28–77)	41 (28–54)	37 (30–45)
Maternal factors plus:			
MAP	71 (44–90)	47 (34–61)	37 (30–45)
UtA-PI	82 (57–96)	61 (47–73)	39 (32–47)
PAPP-A	59 (33–82)	47 (34–61)	37 (30–44)
PlGF	88 (64–99)	63 (49–75)	39 (32–46)
MAP, UtA-PI	94 (71–100)	71 (58–82)	41 (34–49)
MAP, PAPP-A	76 (50–93)	49 (36–63)	40 (33–48)
MAP, PlGF	88 (64–99)	69 (56–81)	43 (36–51)
UtA-PI, PAPP-A	82 (57–96)	66 (53–78)	40 (33–48)
UtA-PI, PlGF	100 (80–100)	75 (62–85)	39 (32–47)
PlGF, PAPP-A	88 (64–99)	66 (53–78)	39 (32–47)
MAP, UtA-PI, PAPP-A	94 (71–100)	69 (56–81)	42 (35–50)
MAP, PAPP-A, PlGF	88 (64–99)	69 (56–81)	43 (36–51)
MAP, UtA-PI, PlGF	100 (80–100)	75 (62–85)	43 (35–50)
UtA-PI, PAPP-A, PlGF	100 (80–100)	75 (62–85)	38 (31–46)
MAP, UtA-PI, PAPP-A, PlGF	100 (80–100)	80 (67–89)	43 (35–50)
NICE[1] (FPR = 10.2%)	41 (18–67)	39 (27–53)	34 (27–41)
ACOG[2] (FPR = 64.2%)	94 (71–100)	90 (79–96)	89 (84–94)
ACOG aspirin[3] (FPR = 0.2%)	6 (1–27)	5 (2–14)	2 (0.3–5)

Values in parentheses are 95% CI. DR, detection rate; FPR, false-positive rate; MAP, mean arterial pressure; PAPP-A, pregnancy-associated plasma protein-A; PlGF, placental growth factor; UtA-PI, uterine artery pulsatility index.

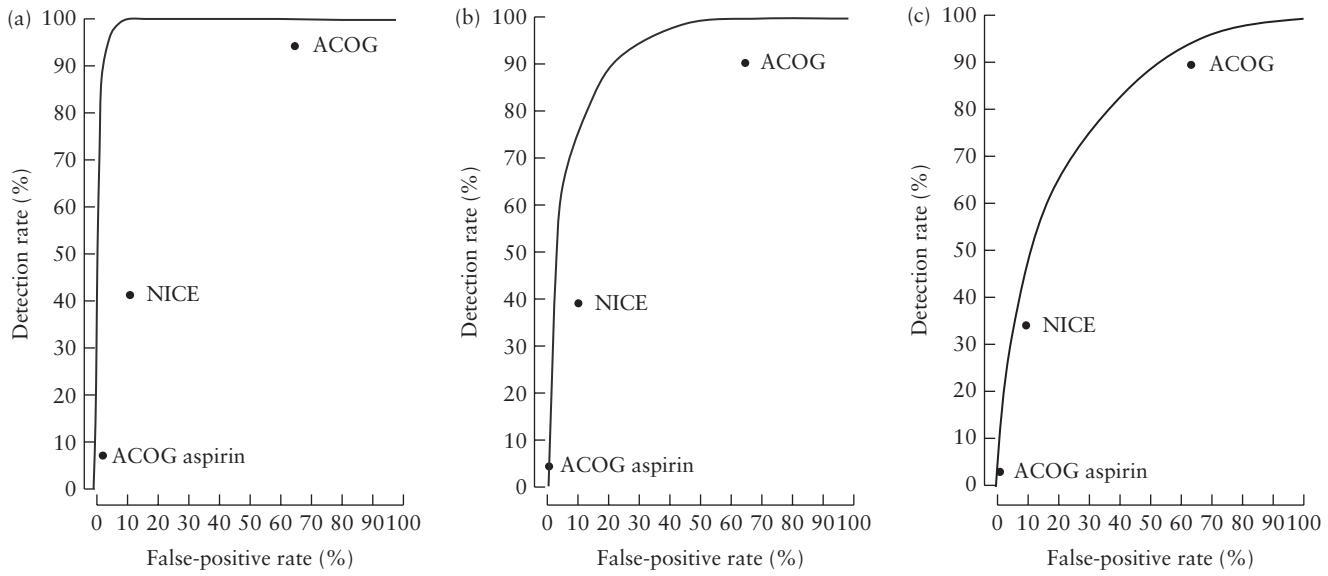


Figure 1 Receiver–operating characteristics curves for prediction of delivery with pre-eclampsia at < 32 weeks (a), < 37 weeks (b) and ≥ 37 weeks (c) of gestation using The Fetal Medicine Foundation algorithm, combining maternal factors, mean arterial pressure, uterine artery pulsatility index and placental growth factor. Performance of screening using the methods of National Institute for Health and Care Excellence (NICE)[1], American College of Obstetricians and Gynecologists (ACOG)[2] and ACOG for use of aspirin[3] are shown.

Implications for practice

In a proposed new pyramid of pregnancy care[15], assessment of risk at 11–13 weeks' gestation aims to identify pregnancies at high risk of developing PE and, through pharmacological intervention with such medications as low-dose aspirin, reduce the incidence of these complications[16–18]. Administration of low-dose aspirin from the first-trimester to those at high risk is effective in prevention of preterm, rather than term, PE[18], and the use of the method advocated by the FMF[4,5] is superior to those recommended by NICE[1] and ACOG[2,3] in identifying the group of pregnancies that could benefit from such therapy. According to FMF and NICE, about 10% of the pregnant population would receive low-dose aspirin and this population would contain 75% of those that will develop preterm PE if selection of the high-risk group was based on the FMF algorithm and only 39% if selection was based on the NICE guidelines. In the case of the ACOG recommendations, 0.2% of the population would receive aspirin and only 5% of cases of preterm PE that would potentially benefit from such therapy would be targeted.

The methods of NICE[1] and ACOG[2] treat each maternal factor as a separate screening test with additive DR and FPR. In the FMF method, use of a multivariable logistic model to define the prior risk attributes the appropriate relative importance to each maternal factor and allows estimation of the patient-specific risk of PE requiring delivery before a specified gestation[4]. The prior risk can then be adjusted according to the results of biophysical and biochemical testing[5]. The software for such estimation of prior and adjusted risk is freely available (www.fetalmedicine.com). Recording of maternal history and measurement of blood pressure are universally carried out as part of routine pregnancy care; measurement of MAP requires adherence to a protocol[7] but can be undertaken by healthcare assistants after minimal training, using inexpensive equipment and taking a few minutes to perform. Measurement of UtA-PI requires specific training by sonographers and quality assurance of their results[8]; nevertheless, this test can be undertaken within a few minutes by the same sonographer and machine as part of the routine first-trimester scan. Measurement of serum PlGF can be undertaken on the same machine as free β-human chorionic gonadotropin and PAPP-A, which are widely used in screening for Down syndrome.

ACKNOWLEDGMENT

The study was supported by grants from The Fetal Medicine Foundation (Charity No: 1037116) and by the European Union 7th Framework Programme - FP7-HEALTH-2013-INNOVATION-2 (ASPRE Project # 601852).

REFERENCES

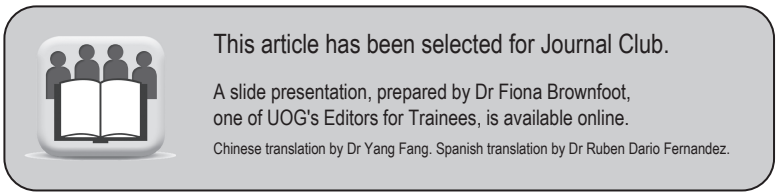
1. National Collaborating Centre for Women's and Children's Health (UK). *Hypertension in Pregnancy: The Management of Hypertensive Disorders During Pregnancy*. London: RCOG Press, 2010.
2. ACOG. First-trimester risk assessment for early-onset preeclampsia. Committee opinion No. 638. *Obstet Gynecol* 2015; **126**: e25–27.
3. American College of Obstetricians and Gynecologists. Task Force on hypertension in pregnancy. *The American College of Obstetricians and Gynecologists*; Washington (DC): 2013; **122**: 1122–1131.
4. Wright D, Syngelaki A, Akolekar R, Poon LC, Nicolaides KH. Competing risks model in screening for preeclampsia by maternal characteristics and medical history. *Am J Obstet Gynecol* 2015; **213**: 62.e1–10.
5. O'Gorman N, Wright D, Syngelaki A, Akolekar R, Wright A, Poon LC, Nicolaides KH. 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–e12.
6. O'Gorman N, Wright D, Liona C. Poon LC, Rolnik DL, Syngelaki A, Wright A, Akolekar R, Cicero S, Janga D, Jani J, Molina FS, De Paco Matallana C, Papantoniou N, Persico N, Plasencia W, Singh M, Nicolaides KH. Accuracy of competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11–13 weeks' gestation. *Ultrasound Obstet Gynecol* 2017; **49**: 751–755.

7. Poon LC, Zymeri NA, Zamprakou A, Syngelaki A, Nicolaides KH. Protocol for measurement of mean arterial pressure at 11–13 weeks' gestation. *Fetal Diagn Ther* 2012; **31**: 42–48.
8. Plasencia W, Maiz N, Bonino S, Kaihura C, Nicolaides KH. Uterine artery Doppler at 11 + 0 to 13 + 6 weeks in the prediction of pre-eclampsia. *Ultrasound Obstet Gynecol* 2007; **30**: 742–749.
9. Wright A, Wright D, Ispas A, Poon LC, Nicolaides KH. Mean arterial pressure in the three trimesters of pregnancy: effects of maternal characteristics and medical history. *Ultrasound Obstet Gynecol* 2015; **45**: 698–706.
10. Tayyar A, Guerra L, Wright A, Wright D, Nicolaides KH. Uterine artery pulsatility index in the three trimesters of pregnancy: effects of maternal characteristics and medical history. *Ultrasound Obstet Gynecol* 2015; **45**: 689–697.
11. Wright D, Silva M, Papadopoulos S, Wright A, Nicolaides KH. Serum pregnancy associated plasma protein-A in the three trimesters of pregnancy: effects of maternal characteristics and medical history. *Ultrasound Obstet Gynecol* 2015; **46**: 42–50.
12. Tsiakkas A, Duvdevani N, Wright A, Wright D, Nicolaides KH. Serum placental growth factor in the three trimesters of pregnancy: effects of maternal characteristics and medical history. *Ultrasound Obstet Gynecol* 2015; **45**: 591–598.
13. Brown MA, Lindheimer MD, de Swiet M, Van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: Statement from the international society for the study of hypertension in pregnancy (ISSHP). *Hypertens Pregnancy* 2001; **20**: IX–XIV.
14. R Development Core Team. *R. A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. 2011; ISBN 3-900051-07-0, http://www.R-project.org/.
15. Nicolaides KH. Turning the pyramid of prenatal care. *Fetal Diagn Ther* 2011; **29**: 183–196.
16. Bujold E, Roberge S, Lacasse Y, Bureau M, Audibert F, Marcoux S, Forest JC, Giguère Y. Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. *Obstet Gynecol* 2010; **116**: 402–414.
17. Roberge S, Nicolaides K, Demers S, Villa P, Bujold E. Prevention of perinatal death and adverse perinatal outcome using low-dose aspirin: a meta-analysis. *Ultrasound Obstet Gynecol* 2013; **41**: 491–499.
18. Roberge S, Villa P, Nicolaides K, Giguère Y, Vainio M, Bakthi A, Ebrashy A, Bujold E. Early administration of low dose aspirin for the prevention of preterm and term pre-eclampsia: a systematic review and meta-analysis. *Fetal Diagn Ther* 2012; **31**: 141–146.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Characteristics of women with normal singleton pregnancy and of those who developed pre-eclampsia (PE) with delivery < 32 weeks, < 37 weeks or ≥ 37 weeks



Ultrasound Obstet Gynecol 2017; **49**: 756–760
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.17455

Cribado multicéntrico de preeclampsia a partir de factores maternos y biomarcadores a las 11-13 semanas de gestación: comparación con las directrices de NICE y las recomendaciones de ACOG

RESUMEN

Objetivo Comparar el desempeño del cribado de preeclampsia (PE) a partir de factores de riesgo del historial clínico, siguiendo las recomendaciones de NICE y ACOG, con el método propuesto por The Fetal Medicine Foundation (FMF), que utiliza el teorema de Bayes para combinar el riesgo *a priori* de los factores maternos, estimado en función de un modelo logístico multivariable, con los resultados de diversas combinaciones de medidas biofísicas y bioquímicas.

Métodos La investigación fue un estudio multicéntrico prospectivo del cribado de PE en 8775 embarazos con feto único a las 11–13 semanas de gestación. Se utilizó un algoritmo ya publicado por la FMF para el cálculo del riesgo específico de PE para cada paciente. Se estimaron las tasas de detección (TD) y las tasas de falsos positivos (TFP) para el parto con PE <32, <37 y ≥37 semanas y se compararon con las tasas obtenidas mediante la aplicación de las directrices de NICE y las recomendaciones de ACOG. Según NICE, todos los embarazos de alto riesgo deberían recibir una dosis baja de aspirina. De acuerdo con ACOG, el uso de aspirina se debería reservar para las mujeres con antecedentes de PE en al menos dos embarazos previos o PE que requiere inducción del parto a <34 semanas de gestación.

Resultados En la población estudiada, 239 (2,7%) casos desarrollaron PE, de los cuales 17 (0,2%), 59 (0,7%) y 180 (2,1%) desarrollaron PE <32, <37 y ≥37 semanas, respectivamente. El cribado mediante el uso del algoritmo de FMF, basado en una combinación de factores maternos, la presión arterial media (PAM), el índice de pulsatilidad de la arteria uterina (UtA-PI) y el factor de crecimiento placentario sérico (PlGF) detectó el 100% (IC 95%, 80–100 %) de la PE <32 semanas, el 75% (IC 95%, 62–85%) de la PE <37 semanas y el 43% (IC 95%, 35–50%) de la PE ≥37 semanas, con una TFP del 10%. El cribado siguiendo las directrices de NICE detectó el 41% (IC 95%, 18–67%) de la PE <32 semanas, el 39% (IC 95%, 27–53%) de la PE <37 semanas y el 34% (IC 95%, 27–41%) de la PE ≥37 semanas, con una TFP del 10,2%. El cribado siguiendo las recomendaciones de ACOG detectó el 94% (IC 95%, 71–100%) de la PE <32 semanas, el 90% (IC 95%, 79–96%) de la PE <37 semanas y el 89% (IC 95%, 84–94%) de la PE ≥37 semanas, con una TFP del 64,2%. El cribado basado en las recomendaciones de ACOG para el uso de aspirina detectó el 6% (IC 95%, 1–27%) de la PE <32 semanas, el 5% (IC 95%, 2–14%) de la PE <37 semanas y el 2% (IC 95%, 0,3–5%) de la PE ≥ 37 semanas, con una TFP del 0,2%.

Conclusión El desempeño del cribado de PE a las 11–13 semanas de gestación mediante el algoritmo de FMF, utilizando una combinación de factores maternos, PAM, UtA-PI y PlGF, es muy superior a los métodos recomendados por NICE y ACOG.

根据母体因素和生物标志物在孕11~13周时多中心筛查子痫前期：与NICE指南和ACOG建议的比较

目的：NICE和ACOG推荐根据病史获得的危险因素筛查子痫前期（pre-eclampsia，PE），我们将其与胎儿医学基金会（Fetal Medicine Foundation，FMF）提出的方法进行比较，FMF的方法采用贝叶斯原理，将从多变量logistic模型获得的母体因素先验风险与结合各种生物物理和生物化学检测方法得到的结果联合。

方法：本研究为前瞻性多中心研究，对8775例孕11~13周的单胎妊娠进行PE筛查。采用之前发表的FMF计算方法计算每名孕妇的患者特异的PE风险。估计PE发病孕周<32周、<37周和≥37周的检出率（detection rates，DRs）和假阳性率（false-positive rates，FPRs），并与采用NICE指南和ACOG建议得到的结果进行比较。根据NICE，所有高危孕妇均应给予小剂量阿司匹林。根据ACOG，仅至少之前两次妊娠出现PE或在孕34周前分娩的PE孕妇需要服用阿司匹林。

结果：研究人群中，239例（2.7%）出现PE，其中分别有17例（0.2%）、59例（0.7%）和180例（2.1%）在<32周、<37周和≥37周时出现PE。采用根据联合母体因素、平均动脉压（mean arterial pressure，MAP）、子宫动脉搏动指数（uterine artery pulsatility index，UtA-PI）和血清胎盘生长因子（placental growth factor，PlGF）的 FMF计算方法进行筛查，PE发病孕周<32周、<37周和≥37周的检出率分别为100%（95% CI，80%~100%）、75%（95% CI，62%~85%）和43%（95% CI，35%~50%），FPR为10.0%。采用NICE指南进行筛查，PE发病孕周<32周、<37周和≥37周的检出率分别为41%（95% CI，18%~67%）、39%（95% CI，27%~53%）和34%（95% CI，27%~41%），FPR为10.2%。采用ACOG建议进行筛查，PE发病孕周<32周、<37周和≥37周的检出率分别为94%（95% CI，71%~100%）、90%（95% CI，79%~96%）和89%（95% CI，84%~94%），FPR为64.2%。根据ACOG建议给予阿司匹林，PE发病孕周<32周、<37周和≥37周的检出率分别为6%（95% CI，1%~27%）、5%（95% CI，2%~14%）和2%（95% CI，0.3%~5%），FPR为0.2%。

结论：采用联合母体因素、MAP、UtA-PI和PlGF的FMF计算方法在孕11~13周时筛查PE，其筛查效果明显优于NICE和ACOG推荐的方法。