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Risk of operative delivery for intrapartum fetal compromise in small-for-gestational-age fetuses at term: an internally validated prediction model

Erkan Kalafat, MD; Jose Morales-Rosello, MD; Basky Thilaganathan, MD, PhD, FRCOG; Fathema Tahera, BSc; Asma Khalil, MD, MRCOG

BACKGROUND: Small-for-gestational-age fetuses are at an increased risk of intrapartum fetal compromise requiring operative delivery. Factors associated with the risk of intrapartum fetal compromise are yet to be established, and a comprehensive model accounting for both the antenatal and intrapartum variables is lacking.

OBJECTIVE: We aimed to develop and validate a predictive model for the risk of operative delivery for presumed intrapartum fetal compromise in fetuses suspected to be small for gestational age at term.

STUDY DESIGN: This was a single-center cohort study of small-forgestational-age fetuses, defined as estimated fetal weight below the 10th centile in singleton pregnancies at term. The variables included known risk factors for operative delivery because of fetal compromise: maternal characteristics, estimated fetal weight, abdominal circumference, Doppler parameters, gestational age at delivery, induction of labor, and intrapartum risk factors (presence of meconium, augmentation of labor using oxytocin, the use of epidural analgesia, intrapartum pyrexia, and hemorrhage). The receiver-operating characteristics curve analysis was used to investigate the predictive accuracy. Internal validation of the models was performed with bootstrapped data sets.

RESULTS: A total of 927 term pregnancies with 18.7% operative deliveries were included. The antenatal model (area under the curve, 0.69; 95% confidence interval. 0.65–0.73) using only the antenatal risk factors included parity, abdominal circumference centile, gestational age at delivery beyond 39 weeks' gestation, and the cerebroplacental ratio multiples of median. The combined model (area under the curve, 0.76; 95% confidence interval, 0.72-0.80), using both the antenatal and intrapartum risk factors, included the gestational age at delivery beyond 39 weeks' gestation (odds ratio, 1.62; 95% confidence interval, 1.14-2.56), the cerebroplacental ratio multiples of median (odds ratio, 0.38; 95% confidence interval, 0.18–0.79), parity (odds ratio 0.35; 95% confidence interval, 0.22-0.54), induction of labor (odds ratio 1.63; 95% confidence interval, 1.11-2.40), augmentation using oxytocin (odds ratio, 1.84; 95% confidence interval, 1.23-2.73) and the use of epidural analgesia (odds ratio, 2.80; 95% confidence interval, 1.94-4.04). The results indicate that the model has good discrimination and, according to the Hosmer-Lemeshow test, has good fit (P = .591).

CONCLUSION: The prediction model demonstrates 6 important risk factors that are associated with the risk of operative delivery for fetal compromise in small-for-gestational-age fetuses at term. The model shows good discrimination and fit and has the potential to be used for clinical decision making and to counsel women about their individual intrapartum risk.

Key words: cerebroplacental ratio, Doppler, emergency cesarean delivery, fetal distress, fetal growth restriction, forceps, operative delivery, small for gestational age

anagement of fetuses presumed to be small for gestational age (SGA) at term continues to be the focus of much recent debate and research. One of the main challenges arises from the fact that the estimated fetal weight (EFW) alone is not a good proxy for the diagnosis of fetal growth restriction and is a poor predictor of intrapartum fetal compromise in SGA pregnancies.^{1,2}

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Previous studies have identified certain antenatal risk factors, in particular SGA and low cerebroplacental ratio (CPR), which increase the risk of operative delivery.³⁻⁶ Although these studies are informative about possible antenatal markers of fetal compromise, the intrapartum events are likely to be equally, or even more, important in determining the mode of delivery and neonatal outcome.⁵⁻⁷ Furthermore, it is possible that the combination of both antenatal and intrapartum risk factors may improve on their individual predictive accuracy.

Despite the need for tools to aid clinical decision making, a comprehensive prediction model for assessing the risk of operative delivery for intrapartum fetal compromise in SGA fetuses is yet to be established. If validated,

such a prediction model could help in the identification of the pregnancies at highest risk of intrapartum fetal compromise, enabling appropriate management of at-risk fetuses as well as facilitating appropriate individualized antenatal counseling.

The main aim of this study was to develop an integrated prediction model combining antenatal and intrapartum parameters for the evaluation of their predictive accuracy for the risk of operative delivery for presumed intrapartum fetal compromise. In some circumstances, the decision regarding the timing and mode of delivery might have to rely on antenatal parameters only. Therefore, we also aimed to develop an integrated prediction model combining antenatal parameters only.

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This was a retrospective cohort study in a 113 single tertiary referral center over a 16 114year period from 1999 through 2015. 115 The ViewPoint database (ViewPoint 116 5.6.8.428; ViewPoint Bildverarbeitung 117 GmbH, Weßling, Germany) was used to 118 identify cases evaluated at the Fetal 119 Medicine Unit (St George's Hospital, 120 London, United Kingdom). 121

The inclusion criteria were singleton 122 pregnancies diagnosed with an SGA 123 fetus, defined as EFW below the 10th 124 centile for gestational age at 36 weeks or 125 beyond. Pregnancies complicated by 126 major structural fetal abnormalities, 127 aneuploidy, or genetic syndromes were 128 excluded from the analysis. In addition, 129 pregnancies that had an elective cesarean 130 delivery and those that had operative 131 delivery (cesarean delivery or instru-132 mental delivery) because of failure to 133 progress in labor or any cause other than 134 presumed fetal compromise were also 135 excluded from the analysis. 136

Gestational age (GA) was calculated 137 from the crown-rump length measure-138 ment at 11-13 weeks and only one (the 139 last) examination per pregnancy was 140 included in the analysis.8 For pregnan-141 cies in which the first ultrasound 142 was performed in the second trimester 143 (>14 weeks' gestation), the pregnancy 144was dated according to the head 145 circumference.9 146

Routine fetal biometry was performed 147 according to a standard protocol and the 148 EFW was calculated using the Hadlock 149 formula.¹⁰ The umbilical artery (UA) 150 and middle cerebral artery (MCA) 151 Doppler waveforms were recorded using 152 color Doppler, and the pulsatility index 153 (PI) was calculated according to a stan-154 dard protocol.^{11,12} In brief, the MCA PI 155 values were obtained in the space at 156 which the artery passes by the sphenoid 157 wing close to the Circle of Willis, and UA 158 PI values were obtained in free loops of 159 umbilical cord. 160

The Doppler measurements were performed within 4 weeks of delivery. The measurements were obtained in the absence of fetal movement and keeping the insonation angle with the examined vessels less than 30°.¹³ The CPR was calculated as the simple ratio between the MCA PI and the UA PI.^{14,15} All Doppler indices were converted into multiples of median (MoM), correcting for GA using reference ranges, and birthweight values were converted into centiles.¹⁶⁻¹⁸

Intrapartum data included whether the labor was induced or spontaneous, presence or absence of meconiumstained liquor (grade 2 or 3), CTG abnormalities (classified according to National Institute for Health and Care Excellence guidelines), ST analysis abnormalities, use of oxytocin for slow progress of labor, intrapartum pyrexia, intrapartum hemorrhage, use of epidural analgesia for labor, and mode of delivery.¹⁹ Data on the maternal baseline characteristics and the pregnancy outcomes were collected from the hospital obstetric records.

The main outcome in this study was the operative delivery for presumed fetal compromise. Operative delivery for presumed fetal compromise included both cesarean delivery and instrumental delivery. The diagnosis of fetal compromise was based on CTG abnormalities, ST analysis abnormalities, abnormal fetal scalp blood sample pH, or a combination of these.²⁰ The study was exempt from review by Wandsworth Research Ethics Committee. Some of the pregnancies reported in this study were included in a previous study.⁵

Statistical analysis

Continuous variables were presented as median with interquartile range, while categorical variables were presented as a fraction of the total with percentages. Distribution assumptions were tested with a Shapiro-Wilk test and QQ plots. Group comparison of variables was made with a Student *t* test, Mann-Whitney *U* test, or χ^2 test where appropriate. Missing variables were imputed with a linear regression model using the missing parameter as the outcome variable and the missing parameter's most likely clinical covariate as the regressor.

Parameters in the models were determined by a forward selection, backward elimination approach. First, a univariable analysis was used to determine the significant associations between the mode of delivery and the variables. After adding all the significant parameters into the model, the least contributory parameters were removed one by one until the model had both good precision and calibration. Multivariable models were built with a variable selection approach.

After adding all variables with significant associations in the univariate model, the final predictors were determined with a backwards elimination in the logistic regression model using Akiake's Information Criterion. Only the parameters that could be obtained prior to delivery were considered eligible for inclusion in the multivariable model. The Hosmer-Lemeshow test was used to test the goodness of fit of models. Q2

The validation of the model was performed using 10,000 bootstrap replicates of the original cohort. Separate data sets of the same sizes were constructed using a bootstrapping technique. The variables were chosen at random with equal sampling probability and with replacement. The predictive value of the final model was assessed with the area under the receiver-operator curve (AUC).

Multiple bootstrapped data sets were analyzed to prevent the overestimation of the regression coefficients and to prevent overfitting. After determining the discrimination power and goodness of fit of the final model receiveroperating characteristic curves and Hosmer test, the probabilities of some clinical examples were calculated to provide a better relationship to the practical uses of the model. The statistical analysis was performed using the RStudio statistical software (version 1.0.136; RStudio, Inc, Boston, MA).

Results

We identified 1061 singleton pregnancies that were eligible for inclusion in the study. In total, 927 women were included in the analysis after excluding major fetal abnormalities, aneuploidy, genetic syndromes, missing delivery records, elective cesarean delivery, and operative delivery for causes other than fetal compromise (n = 134).

The proportion of missing variables in the data set was less than 1%. The incidence of operative delivery for presumed 169

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