Maternal cardiovascular function and risk of intrapartum fetal compromise in women undergoing induction of labor: a pilot study

Erkan Kalafat[1,2], Imogen Barratt[1], Alishba Nawaz[1], Basky Thilaganathan[1,3], Asma Khalil[1,3]

[1]Fetal Medicine Unit, St George's Hospital, St George's University of London, UK. Cranmer Terrace, London SW17 0RE

[2]Middle East Technical University, Department of Statistics, Ankara, TURKEY

[3]Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, Cranmer Terrace, London SW17 0RE, UK.

Corresponding author:
Professor Asma Khalil
Fetal Maternal Medicine Unit
St George's University of London
London SW17 0RE
E-mail: akhalil@sgul.ac.uk; asmakhalil79@googlemail.com

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CONTRIBUTION

What are the novel findings of this work?

Low maternal stroke volume and high vascular resistance are associated with intrapartum fetal compromise in women undergoing induction of labor. Cardiovascular assessment improved the detection of operative delivery in addition to maternal characteristics.

What are the clinical implications of this work?

In women undergoing labor induction, women's cardiovascular function could be a useful candidate for predicting fetal compromise. Cardiovascular assessment may help with risk stratification of women undergoing labor induction.

ABSTRACT

OBJECTIVE: Identification of the fetus at risk of intrapartum compromise has many benefits. Impaired maternal cardiovascular function is associated with placental hypoperfusion intrapartum fetal distress. The main aim of this study was to assess the predictive accuracy of maternal hemodynamics for the risk of operative delivery due to presumed fetal compromise in women undergoing induction of labour (IOL).

METHODS: In this prospective cohort study patients were recruited between November 2018 and January 2019. Women undergoing IOL were invited to participate in the study. A non-invasive ultrasonic cardiac output monitor (USCOM-1A) was used for the cardiovascular evaluation. The study outcome was operative delivery due to presumed fetal compromise, which included cesarean or instrumental delivery for abnormal fetal heart monitoring. Regression analysis was used to test the association between cardivascular markers, as well as the maternal characteristics and the risk of operative delivery for presumed fetal compromise. The ROC curve analysis was used to assess the predictive accuracy of the cardivascular markers for the risk of operative delivery for presumed fetal compromise.

RESULTS: A total of 99 women were recruited and four women were later excluded from the analysis due to semi-elective cesarean section (n=2) and failed IOL (n=2). The rate of operative delivery due to presumed fetal compromise was 28.4% (27/95). Women who delivered without suspected fetal compromise were more likely to be multiparous (52.9% vs 18.5%, p=0.002). Women who underwent operative delivery due to presumed fetal compromise had significantly lower cardiac index (CI) (median: 2.50 L/min/m^2 vs. 2.60 L/min/m^2, p=0.039) and higher systemic vascular resistance (SVR) (median: 1480.0 mmHg.min.mL^{-1}/m^2 vs. 1325.0 mmHg.min.mL^{-1}/m^2, p=0.044) compared to controls. The baseline model (multiparity only) showed poor predictive accuracy with an area under the curve (AUC) value of 0.67 (95% CI: 0.58-0.77). The addition of stroke volume index (SVI) <36 ml/m2, systemic vascular resistance (SVR) >7.2 logs or SVR index (SVRI) >7.7 logs significantly improved the baseline model (p=0.012, p=0.026 and p=0.012, respectively).

CONCLUSION: In this pilot study, we demonstrated that pre-labour maternal cardiovascular assessment in women undergoing IOL could be useful for assessing the risk of intrapartum fetal compromise necessitating operative delivery. The addition of SV, SVR and SVRI significantly improved the predictive accuracy of the baseline antenatal model.

INTRODUCTION

Induction of labor (IOL) is a common practice with approximately 20% of all pregnancies requiring IOL prior to the onset of spontaneous labor[1]. IOL is unlikely to decline in the near future due to the recent evidence demonstrating benefits in both low-risk and high-risk populations[2-4]. Emergency cesarean section (CS) occurs in up to 30% of all women undergoing IOL. Furthermore, it is associated with increased maternal morbidity[5-7]. Pre-labor prediction of the need for operative delivery is desirable for both the pregnant women and healthcare professionals. A number of antenatal and intrapartum variables are associated with the risk of operative delivery for presumed fetal compromise[8]. We have previously proposed a model incorporating both intrapartum variables and the cerebroplacental ratio (CPR) to assess the risk of operative delivery in suspected small-for-gestational age (SGA) fetuses[8]. When tested in an external validation study, the model showed good predictive accuracy in suspected SGA fetuses[9]. Although several studies suggest that a low CPR is associated with the risk of operative delivery, the value of CPR is yet to be established in low-risk pregnancies[10-13].

Maternal hemodynamic assessment is becoming more popular in view of the recent evidence of a maladaptive cardiovascular response in the pregnancies complicated by placental syndromes such as hypertensive disorders and fetal growth restriction[-16]. In a recent study, Valensise *et al*. demonstrated that women with low cardiac output (CO) and increased systemic vascular resistance (SVR) had an 8-10 fold increased risk of developing intrapartum complications [17]. Uterine hypoperfusion was suggested as a causative factor[17].

The assessment of the maternal and fetal haemodynamic profile, in combination with the maternal risk factors, could be a strong predictor of fetal distress. This would allow targeted monitoring, advanced preparation and optimisation of timing of intervention with CS or instrumental delivery to prevent serious maternal or fetal complications and reduce healthcare costs. The aim of current study was to assess the predictive accuracy of maternal hemodynamics for the risk of operative delivery due to presumed fetal compromise in women undergoing IOL.

METHODS

This was a prospective cohort study conducted at St. George's University Hospital in London. The recruitment took place between November 2018 and January 2019. Women planned for IOL were invited to participate in the study. Indications for IOL were post-term gestation (above 41 weeks' gestation), suspected SGA fetus, hypertensive disorders of pregnancy, maternal diabetes and other maternal systemic diseases. The exclusion criteria consisted of multiple pregnancy, elective cesarean section due to maternal request or breech presentation and pregnancies complicated by genetic or structural abnormalities. Women included in the study were followed-up at St. George's University hospital in accordance with routine antenatal management protocols.

A non-invasive ultrasonic cardiac output monitor (USCOM-1A®) that has been validated against echocardiography in pregnancy was used for the cardiovascular evaluation of eligible women[18]. All haemodynamic assessments were performed in the same room, under standardized conditions for the entire cohort within 24 hours of planned IOL. Maternal height, weight and brachial blood pressure were obtained prior to hemodynamic assessment. Blood pressure was obtained using an upper arm automatic blood pressure (BP) monitor (Microlife®, Microlife AG Swiss Corporation, Switzerland), in a semi-recumbent position and using an appropriate sized cuff. Mean arterial pressure (MAP) was calculated as (2xdiastolic blood pressure + systolic blood pressure)/3. USCOM-1A® utilizes continuous wave Doppler, with a non-imaging probe in the suprasternal notch to obtain velocity time integrals (VTI) of transaortic blood flow at the left ventricular outflow tract. Using an anthropometric algorithm, which correlates the outflow tract diameter with the patient's given height, USCOM-1A® uses the VTIs to compute the stroke volume (SV) and produce a complete hemodynamic profile, including heart rate (HR), cardiac output (CO) and systemic vascular resistance (SVR). Each Doppler acquisition used for analysis had a minimum of 2 consecutive Doppler profiles (cardiac cycles). Acquisitions with the least amount of interference and the best quality VTIs, deemed by the study investigators to best represent transaortic blood flow, were obtained in the device's flowtracer mode. CO, SV and SVR were measured using the USCOM-A1® device and the corresponding weight adjusted indices were calculated. All the maternal hemodynamic parameters were concealed from the clinicians who are in charge of the antenatal and the intrapartum management in order to minimise the risk of bias.

A dinoprostone vaginal insert (10mg) was used for induction of labour in all the pregnancies. The pessary was removed after the commencement of labor which was diagnosed when cervical change associated with regular painful contractions is present. If labor failed to commence after 24 hours, vaginal insert was removed. Oxytocin infusion was commenced at least 30 minutes after the removal of vaginal pessary, if further labor augmentation was deemed necessary by the attending physician. Cardiotocography tracings were evaluted according to the National Institute for Health and Care Excellence guidelines[19]. Epidural analgesia was commenced for women in active labor who were unable to cope with the pain. The study outcome was operative delivery due to presumed fetal compromise, which included cesarean or instrumental delivery for abnormal fetal heart monitoring. The remaining women who had any type of delivery without an abnormal fetal heart tracings were included in the control group. The diagnosis of fetal compromise was based on CTG abnormalities [19], ST analysis abnormalities, abnormal fetal scalp blood sample pH, or a combination of these. Intrapartum characteristics and neonatal outcome were routinely recorded in the maternity electronic records by the clinical team. Antepartum data and ultrasound parameters were obtained from the maternity and ultrasound electronic records.

Statistical analysis

All continuous variables were tested for normality assumptions using Shapiro-Wilk test. Continuous variables were presented as median and interquartile range regardless of distribution assumptions. Categorical data were presented as number and percentage. Wilcoxon rank-sum test, t-test, chi-square test and Fisher's exact tests were used for group comparisons where appropriate.

Firstly, the association of operative delivery due to presumed fetal compromise with cardiovascular and other antenatal or intrapartum variables was examined using univariate regression. Secondly, the adjusted effects of cardiovascular variables were tested with multivariate regression after adjusting for antenatal variables which were significantly associated with the outcome. A baseline model was developed using significant antepartum variables and then cardiovascular assessment variables were added to the baseline model. The Receiver operating characteristics (ROC) curves for the baseline model and combined models were obtained. The area under the curve (AUC) values of each combined model was

compared to the baseline model for statistically significant improvement in model accuracy using De Long's test.

P values below 0.05 were considered statistically significant and all tests were two-tailed. R for statistical computing software (version 3.5.2, R Foundation For Statistical Computing, Vienna, Austria) was used for all analyses[20].

RESULTS

Study population

A total of 99 women were recruited and four women were later excluded from the analysis due to elective cesarean (n=2) and failed IOL (n=2). The baseline and intrapartum characteristics of the participants along with their cardiovascular assessment variables are presented in Table 1. The rate of operative delivery due to presumed fetal compromise was 28.4% (27/95). Women who delivered without suspected fetal compromise were more likely to be multiparous (52.9% vs 18.5%, p=0.002) and Caucasian (73.5% vs 51.9%, p=0.023). There were no other significant differences between the group who had operative delivery for fetal distress and the group who experienced vaginal birth.

Antenatal ultrasound scan within a month of planned IOL did not reveal any significant differences between the operative delivery and control groups, including the estimated fetal weight percentile (median: 61.9 vs. 53.2, p=0.693) or suspected SGA fetus (11.1% vs. 5.9%, p=0.378).

Maternal hemodynamic parameters

Women who underwent operative delivery due to presumed fetal compromise had significantly lower cardiac index (CI) (median: 2.50 L/min/m^2 vs. 2.60 L/min/m^2, p=0.039) and higher SVR (median: 1480.0 mmHg.min.mL^{-1}/m^2 vs. 1325.0 mmHg.min.mL^{-1}/m^2, p=0.044) compared to controls. No significant differences were observed between the operative delivery and control groups regarding maternal CO (median: 4.7 L/min vs 5.0 L/min, p=0.189), SV (median: 32.0 ml vs. 34.0 ml, p=0.099) and systemic vascular resistance index (SVRI) (median: 2769.0 mmHg.min.mL^{-1} vs. 2578.0 mmHg.min.mL^{-1}, p=0.059). The operative delivery group had a higher rate of epidural analgesia (81.5% vs. 42.6%, p<0.001), intrapartum pyrexia (22.2% vs. 5.9%, p=0.019) and neonatal intensive care unit admission (25.9% vs. 0.0%, p<0.001).

Risk factors associated with operative delivery for intrapartum fetal distress

Multiparity was the only antenatal variable that showed a significant association with the risk of operative delivery in univariate regression model (OR 0.20; 95% CI 0.06-0.56, p=0.003) (Table 2). In the univariate analysis, a CI <2.9 L/minute (p=0.043), SV <65 mL (p=0.027),

stroke volume index (SVI) <36 ml/m^2 (p=0.014), SVR >7.2 logs (p=0.020) and SVRI >7.7 logs (p=0.023) were significantly associated with the risk of operative delivery.

The baseline model was developed using multiparity as the sole antenatal variable with statistical significance. The baseline model showed poor predicted accuracy with an area under the curve (AUC) value of 0.67 (95% CI: 0.58-0.77) (Table 3). The addition of SVI <36 ml/m2, SVR>7.2 logs and SVRI>7.7 logs significantly improved the baseline model (p=0.012, p=0.026 and p=0.012, respectively) (Table 3 & Figure 1a-1c). However, the predictive capabilities of these models remained modest with AUC values of 0.73 (95% CI: 0.64-0.82), 0.73 (95% CI: 0.63-0.84) and 0.73 (95% CI: 0.64-0.82) for the combined models with SV, SVR and SVRI, respectively (Table 3). Conditional probability plots revealed a linear relationship of risk change with SV, SVR and SVRI (Supplementary Figure 1a-1c).

DISCUSSION

In this cohort study, we demonstrated that pre-labour maternal cardiovascular assessment could be useful for assessing the risk of intrapartum fetal compromise necessitating operative delivery. The addition of SV, SVR and SVRI significantly improved the predictive capability of the baseline antenatal model in women undergoing IOL.

Our study has several strengths. Firstly, the cardiovascular assessment results were concealed from the antenatal and labor management team eliminating the risk of intervention bias. Secondly, women were evaluated prior to IOL in standardized conditions that minimizes the risk of environmental conditions (heat, labour pain etc.) affecting the cardiovascular parameters. Thirdly, the prospective study design ensures that all the relevant parameters were consistently recorded with no missing data within the study cohort.

Our study also has several limitations. The Doppler variables are associated with the risk of intrapartum compromise in SGA fetuses and some studies suggest a similar relationship in low-risk fetuses as well [8,10-13]. We did not adjust the cardiovascular assessment variables for Doppler measurements that could have changed the impact of cardiovascular assessment. Furthermore, intrapartum variables had a strong relationship with intrapartum compromise in our study that was not incorporated into the multivariable model. We intentionally excluded variables that cannot be known prior to IOL from the model, as these variables are unlikely to be useful for antenatal risk assessment. Moreover, the statistical analysis is not adequately powered for a multivariate regression analysis. Finally, the operative delivery decision involves human factor that cannot be accounted for in a statistical analysis. However, adherence to the published management guidelines in our institution would minimize this confounding factor[19].

In this study, women of Caucasian ethnicity were found to be less likely to undergo operative delivery due to presumed fetal distress. Conversely, Asian and Afro-Caribbean women were more likely to experience fetal distress and Asian ethnicity was found to be a significant predictor of fetal distress. These findings are consistent with that of Khalil *et al*, who, in a study consisting of 76,158 pregnancies, found women of Afro-Caribbean and Asian ethnicity to be at significantly greater risk of a range of adverse labour outcomes, including emergency CS [21]. Furthermore, Familiari *et al* found non-Caucasian ethnicity to be significantly associated with the risk of stillbirth [22]. A number of mechanisms by which

ethnicity may influence pregnancy include genetics, socioeconomic status, access to healthcare, maternal age, parity, obesity and smoking [23]. Future studies should aim to confirm the cause of this disparity and investigate methods of improving labour outcomes in Asian and Afro-Caribbean women.

A number of studies have identified SVR as a key predictor of intrapartum complications, including fetal distress. Valensise *et al.* demonstrated a raised SVR to be significantly associated with fetal distress and Vasapollo *et al*. determined an elevated SVR to be the best predictor of intrapartum complications[17,24]. Tiralongo *et al.* demonstrated a significantly greater occurrence of complications and poorer outcomes in the group with SVR greater than 1200mmHg.min.mL $^{-1}$[25]. In terms of SVR, our findings are in agreement with that of previous studies, with the operative delivery due to presumed fetal compromise group having a significantly higher median SVR than the delivery without fetal compromise group[17]. It has been suggested that, under normal circumstances, vascular remodelling of the spiral arteries allows for a decrease in SVR and thus improved blood flow, which reduces the chances of the fetus suffering from hypoxia[17]. The absence of this adaptation, which leads to an increased risk of fetal distress, is manifested as an elevated SVR, which provides an explanation of the etiology of the aforementioned SVR findings.

Evidence suggests that CO is a significant predictor of fetal distress. For example, Valensise et al found an 8-10 fold increase in intrapartum complications in patients with a lower CO and Tiralongo et al found a higher CO to predict better maternal and neonatal outcome[17,25]. CO, the volume of blood being ejected from the heart per minute, reflects cardiovascular performance. A lower CO, and thus a lower CI, indicates suboptimal cardiovascular performance and reduced placental perfusion, thus increasing the risk of fetal distress. Although our findings did not demonstrate a significant difference in CO between the two groups as expected, the median CI was found to be significantly lower in the operative delivery due to presumed fetal compromise group. This suggests that, in our cohort, CO values were affected by the participants' height and weight, which is corroborated by the findings of Vinayagam et al, who found CO to be significantly influenced by maternal age, height and weight[26]. Another possible reason for the lack of significant CO findings is inferior vena cava (IVC) compression due to the fact that the

assessment was carried out in the semi-recumbent position[27]. Future studies should assess the effect of carrying out hemodynamic assessment with USCOM® in the left lateral position, which has been suggested to relieve IVC compression . Moreover, with obesity being an obstetric risk factor[28], a number of our recruited patients were undergoing IOL due to having a high BMI and this is manifested as the average BMI of both groups in our study being higher than that obtained in other relevant studies, such as that of Valensise *et al*[17]. A high BMI may have affected the USCOM® operator's ability to obtain accurate CO measurements. Future studies should continue to explore the relationship between SVR and CO, and fetal distress and the effect of maternal body surface area (BSA) on these parameters.

Many studies now show a close relationship between cardiovascular function and placental syndromes[29-31]. It is also possible that cardiovascular function will affect uteroplacental perfusion without an overt systemic derangement such as preeclampsia[17]. Our findings are in line with Valensise *et al*. demonstrating that poorer maternal cardiovascular function is more likely to require operative delivery due to presumed fetal compromise[17]. Our study includes women undergoing IOL as opposed to Valensise *et al*. that included low-risk women. Despite this difference, our findings were quite similar. Both studies were not large enough to test and adjust for all possible confounders and future studies should aim for larger cohorts..

Conclusions

Women with lower cardiac index and increased peripheral vascular resistance before onset of labour are more likely to require operative delivery due to presumed fetal compromise. In this pilot study, the addition of cardiovascular assessment to the antenatal characteristics improved the detection of operative delivery in women undergoing IOL.

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Figure legends

Figure 1a. The receiver operating characteristics curves of baseline model (solid line) and combined models with cardiac index (dashed line). The addition of cardiac index did not significantly improve the accuracy of baseline model (p=0.070)

Figure 1b. The receiver operating characteristics curves of baseline model (solid line) and combined models with stroke volume (dashed line) and stroke volume index (dotted line). The addition of stroke volume did not significantly improve the accuracy of baseline model, whereas the addition of stroke volume index did (p=0.071 and p=0.012, respectively)

Figure 1c. The receiver operating characteristics curves of baseline model (solid line) and combined models with systemic vascular resistance (dashed line) and systemic vascular resistance index (dotted line). The addition of systemic vascular resistance and systemic vascular resistance index did improve the model accuracy (p=0.026 and p=0.012, respectively)

Supplementary Figure 1a. Conditional probability plot of stroke volume index. The probability of delivery without fetal compromise increased with increasing stroke volume index.

Supplementary Figure 1b. Conditional probability plot of systemic vascular resistance. The probability of delivery without fetal compromise decreased with increasing systemic vascular resistance.

Supplementary Figure 1c. Conditional probability plot of systemic vascular resistance index. The probability of delivery without fetal compromise decreased with increasing systemic vascular resistance index.

Table 1. Baseline characteristics of the two study groups according to whether they had operative delivery due to presumed fetal compromise

Variables	**Operative delivery due to presumed fetal compromise (n=27)**	**Delivery without fetal compromise (n=68)**	**P value ***
Maternal characteristics			
Maternal age, years	33.0 (29.5-37.5)	33.0 (30.8-36.3)	0.832
Self-reported ethnicity			0.023
Caucasian	14 (51.9)	50 (73.5)	
Afro-Caribbean	5 (18.5)	5 (7.4)	
Asian	8 (29.6)	8 (11.7)	
Mixed/Other	0 (0.0)	5 (7.4)	
Comorbidities			.999
Hypertensive disorders of pregnancy	1 (3.7)	4 (5.9)	
Valvular heart disease	0 (0.0)	1 (1.5)	
Chronic kidney disease	0 (0.0)	0 (0.0)	
Body-mass index, kg/m^2	29.3 (26.9-32.5)	28.7 (24.3-33.1)	0.435
Multiparity	5 (18.5)	36 (52.9)	0.002
Assisted reproductive methods	1 (3.7)	4 (5.9)	0.668
Previous cesarean section	1 (3.7)	2 (2.9)	0.848
Smoker	0 (0.0)	3 (4.4)	0.646
Ultrasound characteristics			
Gestational age at ultrasound, weeks	36.6 (36.0-38.4)	37.0 (36.1-39.7)	0.362
Estimated fetal weight, grams	2906.0 (2677.0-3204.0)	2920.0 (2707.0-3272.0)	0.402
Estimated fetal weight, centile	61.9 (17.6-79.1)	53.2 (29.4-76.5)	0.693
Estimated fetal weight $<10^{th}$ centile	3 (11.1)	4 (5.9)	0.378

Cardiovascular assessment			
Cardiac output, L/min	4.70 (4.20-5.20)	5.00 (4.50-5.70)	0.189
Cardiac index, L/min/m^2	2.50 (2.30-2.70)	2.60 (2.28-3.00)	0.039
Stroke volume, mL	60.0 (55.5-64.5)	65.0 (55.8-73.0)	0.117
Stroke volume index, mL/m^2	32.0 (28.5-35.0)	34.0 (29.0-39.0)	0.099
Systemic vascular resistance, dynes.sec/cm^5	1480.0 (1348.0-1648.0)	1325.0 (1150.0-1535.0)	0.044
Systemic vascular resistance index, dynes.sec/cm^5 .m^2	2769.0 (2524.0-3156.0)	2578.0 (2140.0-2932.0)	0.059
Intrapartum characteristics			
Gestational age at birth, weeks	39.3 (38.1-40.1)	39.9 (38.8-41.0)	0.144
Birth weight, grams	3140.0 (2919.0-3750.0)	3440.0 (3095.0-3735.0)	0.174
Birth weight, centile	30.0 (17.2-74.2)	44.0 (23.8-75.1)	0.292
Mode of birth			<0.001
- Instrumental delivery	15 (55.6)	7 (10.3)	
- Cesarean delivery	12 (44.4)	2 (2.9)	
- Vaginal delivery	0 (0.0)	59 (86.8)	
Epidural analgesia	22 (81.5)	29 (42.6)	<0.001
Thick meconium	4 (14.8)	5 (7.4)	0.262
Intrapartum pyrexia	6 (22.2)	4 (5.9)	0.019
Neonatal unit admission	7 (25.9)	0 (0.0)	<0.001

Variables are presented as median (lower and upper quartiles) or as count (percentage). *p values are calculated with either t-test, Wilcoxon rank-sum test, chi-squared test or Fisher's exact where appropriate

Table 2. Results of univariate logistic regression analysis for predicting the risk of operative delivery due to presumed fetal compromise

Variables	**OR (95% CI)**	**P ***
Maternal age, years	0.99 (0.91-1.08)	0.832
Self-reported ethnicity		
- Caucasian	Reference	
- Afro-Caribbean	3.57 (0.88-14.62)	0.069
- Asian	3.57 (1.13-11.47)	0.029
- Mixed/Other	NE	0.992
Body-mass index, kg/m^2	1.02 (0.94-1.10)	0.624
Obesity (Body-mass index >30kg/m^2)	1.14 (0.46-2.81)	0.771
Multiparity	0.20 (0.06-0.56)	0.003
Assisted reproductive methods	0.62 (0.03-4.41)	0.670
Previous cesarean section	1.27 (0.06-13.80)	0.848
Smoker	NE	0.991
Drug use	NE	0.991
Estimated fetal weight, centile	1.00 (0.99-1.02)	0.794
Suspected small for gestational age	1.82 (0.34-8.96)	0.457
Cardiac output, L/min	0.59 (0.31-1.06)	0.090
Cardiac output <5.5 L/min	2.4 (0.86-7.88)	0.115
Cardiac index, L/min/m^2	0.43 (0.15-1.12)	0.096
Cardiac index <2.9 L/min/m^2	3.34 (1.13-12.38)	0.043
Stroke volume, mL	0.97 (0.93-1.00)	0.124
Stroke volume <65 mL	3.03 (1.17-8.59)	0.027
Stroke volume index, ml/m^2	0.95 (0.89-1.02)	0.160
Stroke volume index <36 ml/m^2	4.28 (1.45-15.78)	0.014
Systemic vascular resistance, dynes.sec/cm^5 †	6.18 (0.76-57.23)	0.095
Systemic vascular resistance >7.2 dynes.sec/cm^5 †	3.21 (1.25-9.11)	0.020
Systemic vascular resistance index, dynes.sec/cm^5 .m^2 †	4.34 (6.59-31.41)	0.132
Systemic vascular resistance index >7.7, dynes.sec/cm^5 .m^2 †	10.83 (2.07-199.87)	0.023

Gestational age at delivery, weeks	0.76 (0.55-1.04)	0.093
Epidural analgesia	5.92 (2.14-19.36)	0.001
Thick meconium	2.19 (0.50-8.99)	0.272
Intrapartum pyrexia	4.57 (1.19-19.39)	0.028

NE: not estimable, OR: odds ratio, CI: confidence interval

* Obtained with a generalized linear model using logit link function

†natural log-transformed variable

Table 3. The predictive accuracy as shown by the area under the curve (AUC) values of multivariable models.

Model	**AUC (95% CI)**	**P ***	**AUC (95% CI)‡**	**P *‡**
Baseline model (parity only)	0.67 (0.58-0.77)	NA	0.69 (0.59-0.78)	NA
Baseline + Cardiac index <2.9 L/min/m^2	0.72 (0.61-0.82)	.070	0.73 (0.62-0.84)	.107
Baseline + Stroke volume <65 mL	0.72 (0.62-0.83)	.071	0.74 (0.65-0.85)	.051
Baseline + Stroke volume index <36 ml/m^2	0.73 (0.64-0.82)	.012	0.75 (0.64-0.85)	.019
Baseline + Systemic vascular resistance >7.2 dynes.sec/cm^5 †	0.73 (0.63-0.84)	.026	0.75 (0.64-0.85)	.042
Baseline + Systemic vascular resistance index >7.7 dynes.sec/cm^5 .m^2 †	0.73 (0.64-0.82)	.012	0.74 (0.65-0.83)	.019

CI: confidence interval, NA: not applicable

*Comparison with the baseline model using De Long's test

† natural log-transformed variable

‡Excluding fetuses with a cerebroplacental ratio below 0.6765 multiple of median (n=3).