
OBSTETRICS

Development and Validation of a Prediction Score for Spinal-anesthesia Induced Hypotension in Cesarean Delivery: A prospective cohort study

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ABSTRACT

Objectives: Spinal anesthesia-induced hypotension is the most common complication in cesarean delivery, which can impede uteroplacental blood flow and may deteriorate maternal and fetal welfare. A good predictor for hypotension can help individualized prophylactic treatment. There is currently no simple and good prediction score for spinal hypotension. We conducted a study to develop and internally validate a risk scoring scheme to predict spinal anesthesia-induced hypotension in cesarean delivery.

Materials and Methods: We performed a prognostic clinical prediction model in a prospective cohort design. The parturients who underwent cesarean delivery using spinal anesthesia were included. The outcome was spinal anesthesia-induced hypotension. Predictors included patients' baseline characteristics, pregnancy details, and preoperative hemodynamic results. Multivariable logistic regression was used for score derivation. Model discrimination and calibration were assessed. The risk score was categorized into low-, moderate-, and high-risk groups.

Results: For 712 parturients who underwent cesarean delivery, a risk score was developed from three predictors: stroke volume index, baseline heart rate, and uterine contraction. The area under the receiver operating characteristic curve was 0.715 (95% confidence interval 0.676-0.754). The risk scores ranged from 0 to 7. When the scores were classified into low- (< 2.5),

moderate- (2.5-4.5), and high- (> 4.5) risk groups, the probability of developing hypotension increased from 21.88% in low-risk to 79.95% in the high-risk group.

Conclusion: A risk score developing from stroke volume index, baseline heart rate, and uterine contraction may help predict spinal hypotension in cesarean delivery and guide individualized prophylactic therapy.

Keywords: prediction score, spinal-anesthesia induced hypotension, cesarean delivery.

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Received: 22 April 2023, **Revised:** 11 July 2023, **Accepted:** 31 July 2023

เกณฑ์การทำนายการเกิดภาวะความดันโลหิตต่ำจากการฉีดยาชาเข้าช่องไขสันหลัง สำหรับการผ่าตัดคลอดทางหน้าท้อง

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บทคัดย่อ

วัตถุประสงค์: เพื่อหาเกณฑ์การทำนายของการเกิดภาวะความดันโลหิตต่ำจากการฉีดยาชาเข้าช่องไขสันหลังสำหรับการผ่าตัดคลอดทางหน้าท้อง

วัสดุและวิธีการ: ทำการศึกษาแบบ prospective cohort ในหญิงตั้งครรภ์ที่มารับการผ่าตัดคลอดทางหน้าท้องโดยใช้วิธีให้ยาระงับความรู้สึกด้วยการฉีดยาชาเข้าช่องไขสันหลัง ตัวแปรทำนาย ได้แก่ ข้อมูลพื้นฐานและhemodynamic parameters ของหญิงตั้งครรภ์ ผู้วิจัยใช้ Noninvasive ultrasound cardiac output monitoring (USCOM) ในการวัด stroke volume index (SVI), cardiac index (CI), and systemic vascular resistance index (SVRI) ข้อมูลที่ได้นำไปวิเคราะห์โดยใช้ multivariable logistic regression model ในการสร้างคะแนนเพื่อใช้เป็นเกณฑ์การทำนาย จากนั้นนำคะแนนที่ได้ไปแบ่งหญิงตั้งครรภ์เป็นกลุ่มความเสี่ยงระดับต่างๆ

ผลการศึกษา: จากข้อมูลของหญิงตั้งครรภ์ที่มารับการผ่าตัดคลอดทางหน้าท้องโดยใช้วิธีให้ยาระงับความรู้สึกด้วยการฉีดยาชาเข้าช่องไขสันหลังจำนวน 712 ราย สามารถพัฒนาคะแนนการทำนายการเกิดภาวะความดันโลหิตต่ำจากการฉีดยาชาเข้าช่องไขสันหลังได้จากสามปัจจัยซึ่ง ได้แก่ stroke volume index อัตราการเต้นของหัวใจพื้นฐานและภาวะการหดตัวของกล้ามเนื้อดลูก ค่า area under the receiver operating characteristic curve ของคะแนนการทำนายอยู่ที่ 0.715 (95% confidence interval 0.676-0.754) โดยค่าคะแนนการทำนายอยู่ระหว่าง 0 ถึง 7 คะแนน ซึ่งสามารถแบ่งตามระดับความเสี่ยงของการเกิดภาวะความดันโลหิตต่ำเป็นน้อย (คะแนนรวมน้อยกว่า 2.5) ปานกลาง (คะแนน 2.5 ถึง 4.5) และสูง (คะแนนมากกว่า 4.5) โอกาสของการเกิดภาวะความดันโลหิตต่ำจะเพิ่มจากร้อยละ 21.88 ในกลุ่มเสี่ยงต่ำเป็นร้อยละ

79.95 ในกลุ่มเสี่ยงสูง

สรุป: เกณฑ์การทำนายที่ประกอบด้วย stroke volume index อัตราการเต้นของหัวใจพื้นฐานและภาวะการหดตัวของกล้ามเนื้อสามารถช่วยทำนายการเกิดภาวะความดันโลหิตต่ำจากการฉีดยาชาเข้าช่องไขสันหลังสำหรับการผ่าตัดคลอดทางหน้าท้อง และอาจช่วยชี้แนะวิสัญญีแพทย์ในการใช้ยาเพิ่มความดันเพื่อป้องกันการเกิดภาวะความดันโลหิตต่ำในผู้ป่วยที่ได้รับการผ่าตัดคลอดทางหน้าท้องตามระดับความเสี่ยงที่คำนวณได้ในแต่ละคน

คำสำคัญ: ภาวะความดันโลหิตต่ำ, การผ่าตัดคลอดทางหน้าท้อง, การฉีดยาชาเข้าช่องไขสันหลัง

Introduction

Spinal anesthesia is a common anesthetic technique for cesarean delivery owing to its safety for maternal and fetal aspects^(1, 2). However, the most common complication of this technique is spinal anesthesia-induced hypotension (SIH), which occurs in approximately 30 - 80% of cases. Hypotension before delivery can impede uteroplacental blood flow and may deteriorate maternal and fetal welfare. Despite the widespread use of fluid co-loading and prophylactic vasopressors, the risk of SIH in cesarean delivery cannot be completely eliminated⁽³⁾. Additionally, reactive maternal hypertension may occur⁽⁴⁾. While phenylephrine is the vasopressor of choice to prevent SIH, it may not be available in all hospitals. Other vasopressors, such as norepinephrine and metaraminol, have not been widely recommended as first-line drugs for preventing SIH. Therefore, the consideration of using these alternative vasopressors as a replacement for phenylephrine is necessary.

The prediction of SIH can assist anesthesiologists in selecting appropriate parturients for prophylactic vasopressor use and to avoid reactive hypertension. Several studies have identified predictors of SIH in cesarean deliveries. These include demographic data⁽⁵⁾ (e.g., body mass index (BMI), maternal weight gain during pregnancy), baseline hemodynamic parameters (e.g., baseline heart rate⁽⁶⁾, baseline blood pressure), baseline sympathovagal balance indices (e.g., maternal heart rate variability⁽⁷⁾, pulse rate

variability), postural stress testing (e.g., supine stress test^(8, 9), peripheral perfusion indices (e.g., perfusion index⁽¹⁰⁾, cerebral oxygen saturation⁽¹¹⁾, blood volume and fluid responsiveness indices (e.g., inferior vena cava collapsibility index⁽¹²⁾, Pleth variability index⁽¹³⁾, passive leg raising test⁽¹⁴⁾, and genetic polymorphism⁽⁵⁾). However, most studies have small sample sizes, and the predictive power varies. Additionally, some parameters are not suitable for prediction because the elapsed time between prediction and the onset of hypotension is too short.

Currently, there is no single simple tool that serves as a good predictor of SIH. Combining multiple predictors into a prediction score may aid in developing a more effective prediction tool. Bishop et al introduced the pulse rate, age, and mean arterial pressure (PRAM) score, which used only preoperative risk factors to predict hypotension following obstetric spinal anesthesia⁽¹⁵⁾. However, the predictive ability of the PRAM score was found to be poor (area under the receiver operating characteristic curve (AUROC) 0.626).

We conducted a study to develop and internally validate a risk scoring scheme, called the spinal anesthesia-induced hypotension (SIH) score, to predict SIH during cesarean delivery. The predictors considered in the score included maternal baseline characteristics, preoperative physical examination results, and other relevant details associated with the development of SIH.

Since blood pressure is directly influenced by cardiac output and systemic vascular resistance, we included physiological parameters as predictors, namely stroke volume index (SVI), cardiac index (CI), systemic vascular resistance index (SVRI), and flow time corrected (FTc). To obtain these parameters, we utilized noninvasive ultrasound cardiac output monitoring (USCOM). USCOM has been commonly employed in obstetric research for measuring hemodynamic indices. It is a simple, noninvasive, and cost-effective method. The learning curve for USCOM is steep, and good inter-rater reliability can be achieved after a short training period⁽¹⁶⁾.

Materials and Methods

This prospective cohort study was conducted at King Chulalongkorn Memorial Hospital, which is an academic tertiary care center in Bangkok, Thailand. The study protocol was approved by the Chulalongkorn University Institutional Review Board (Med Chula IRB 1543/2560). Written informed consent was obtained from all the participants. This study was conducted between August 2017 and August 2018. Reporting and analysis of study results were conducted according to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) checklist⁽¹⁷⁾.

Study Population

Parturients scheduled for cesarean delivery under spinal anesthesia at King Chulalongkorn Memorial Hospital during the daytime shift (8.00-16.00) were invited to participate. Participants were aged 18 years or older, had a gestational age of 36 weeks or more, and were capable of giving informed consent. Exclusion criteria included parturients with cardiovascular disease or severe systemic disease, hypertensive disorders, extreme body weight (less than 40 kg or greater than 120 kg), extreme height (less than 145 cm or greater than 180 cm), emergency cesarean delivery without sufficient time for data collection, likelihood of excessive blood loss during the pre-delivery period, compromised fetus, and

situations where data could not be collected from USCOM. Parturients with incomplete or failed spinal anesthesia who required additional intravenous sedation or general anesthesia before clamping the umbilical cord were excluded from the analysis.

Data collection

After confirming patient eligibility, data collectors who were not involved in anesthetic management recorded the details of predictor variables.

Predictor variables included (1) baseline characteristics (age, body weight, height, BMI, underlying disease), (2) pregnancy details (gestational age, maternal weight gain, fetal presentation, single or multiple pregnancies, head engagement, uterine contraction, emergency or elective surgery, fasting duration, intravenous fluid administration), (3) preoperative assessment (baseline systolic blood pressure, heart rate, supine stress test, USCOM parameters [SVI, SVRI, and CI]), and (4) other details (experience of anesthesiologists).

Baseline systolic blood pressure (SBP) and heart rate (HR) were measured after a 10-minute rest in a supine position with a wedge under the right lumbar area. SBP and HR were calculated as the means of three consecutive measurements, with values not differing by more than 10%. GE® CARESCAPE B650 monitors were used with a blood pressure cuff placed on the right arm, opposite the intravenous catheter site.

The supine stress test (SST) followed a methodology from a previous study⁽⁹⁾. Baseline blood pressure and heart rate were measured after a 10-minute rest in the left lateral position. Parturients were then moved to the supine position for five minutes, with blood pressure measured every minute and continuous heart rate monitoring.

SST is considered positive if any of the following criteria are met:

1. Maternal heart rate increases by more than 10 beats per minute compared to baseline for at least one consecutive minute.
2. Systolic arterial blood pressure decreases

by more than 15 mmHg compared to baseline for at least two consecutive minutes.

3. Signs of hypotension associated with the supine position, such as hip flexion and crossing of legs, are observed.

4. Symptoms of hypotension related to the supine position, such as nausea, vomiting, and dizziness, necessitate a change in position.

Hemodynamic parameters from USCOM were measured by five trained anesthesiologists (WT, KK, PP, TP, PS) with experience in at least 50 cases, as recommended⁽¹⁶⁾. USCOM was routinely used in their practice. SVI, CI, and SVRI were measured using the ultrasound non-invasive cardiac output monitor (USCOM®, USCOM Ltd, Sydney, Australia) with the suprasternal notch approach. During the measurement period, patients were positioned in supine with a wedge placed under the right lumbar area.

The spinal anesthetic technique and management followed our institute's protocol. An 18G intravenous catheter was inserted in the left hand or arm. Co-loading with warm-acetated Ringer's solution (10 ml/kg) was performed. Spinal anesthesia was induced in the left lateral position at lumbar interspace L2-3 or L3-4 using a Quincke No 27G needle. Hyperbaric bupivacaine (11 mg) and 0.2 mg morphine were used as local anesthetics. Bupivacaine dosage was adjusted based on maternal height (< 150 cm: 10 mg, > 165 cm: 12 mg). Supplemental oxygen was administered when maternal SpO₂ dropped below 95%.

Following intrathecal injection, the parturient assumed a supine position with a wedge supporting the right lumbar area, creating a 15-degree left uterine tilt. Noninvasive blood pressure was measured at one-minute intervals until umbilical cord clamping. Sensory block levels were assessed at post-injection. Continuous monitoring included ECG, HR, and SpO₂. Incidences of hypotension and bradycardia were recorded. Anesthesiologists who performed the spinal anesthesia were considered inexperienced during their first year of residency.

The primary outcome was SIH which was

defined as either "systolic blood pressure < 80% of baseline value" or "systolic blood pressure < 100 mmHg with signs or symptoms of hypoperfusion such as nausea, vomiting, and dizziness"⁽¹⁸⁾. The assessment of SIH focused on the period from intrathecal injection to umbilical cord clamping.

Standard treatment protocols were implemented for hypotension and bradycardia: Intravenous administration of 100 mcg phenylephrine for hypotension with HR ≥ 60 bpm, 6 mg ephedrine for hypotension with HR < 60 bpm, and 0.6 mg atropine for hypotension with HR < 50 bpm. Anesthetic management after umbilical cord clamping was determined by the primary anesthesiologist in charge of the patient.

Sample size estimation

We aimed to include 20 parameters in the model based on the "10 events per parameter rule of thumb"⁽¹⁹⁾. The observed incidence of SIH at our institute ranged from 30% to 60%. Considering a dropout rate of 10%, the recommended minimum sample size should have been 734 participants. However, a total of 744 participants were enrolled in this study.

Statistical analysis

Baseline characteristics were compared using appropriate statistical tests (e.g., Student's t-test, Fisher's exact test). Discrimination was assessed using the AUROC.

To develop, derive scores, and validate the model, the following steps were taken: initial univariable logistic regression analysis to explore predictor variables' relationship with SIH, selecting predictors with a p value < 0.1 for inclusion in the multivariable logistic regression model while assessing multicollinearity. Backward elimination logistic regression was performed on the multivariable model, retaining variables with a p value < 0.05. Regression coefficients from the final model were transformed into scores to establish the predictive model. Each parturient received a risk score (SIH score) based on

this model. Performance assessment included discrimination using AUROC and calibration using the Hosmer-Lemeshow tests.

Risk stratification was conducted, classifying patients into low-, moderate-, and high-risk groups based on the clinical risk score classification.

Internal validation was conducted using bootstrapping with stepwise variable selection, which involved generating 1,000 random samples with replacement from the original dataset to estimate optimism. To handle the small amount of missing data, complete case analysis was employed.

Statistical analyses were carried out using STATA-15 software.

Results

Among the 1,281 initially eligible parturients, 744 were enrolled in the study after excluding certain participants. Out of these, 32 cases (4.3%) encountered failed or incomplete spinal anesthesia, requiring additional sedation or conversion to general anesthesia. Consequently, the final analysis involved 712 parturients, and the recruitment process and study flow are illustrated in Fig. 1.

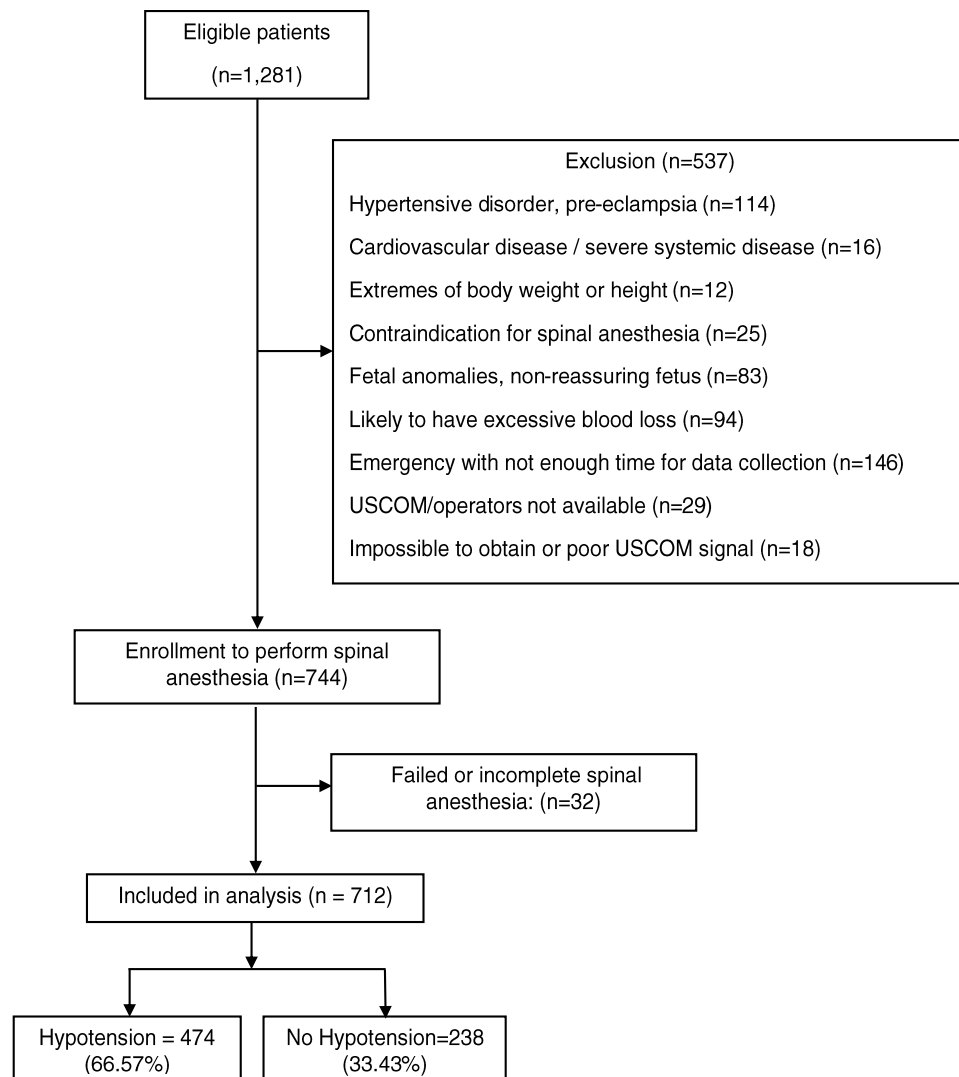


Fig. 1. Study flow diagram.

Of the included participants, 474 parturients (66.57%) developed hypotension, while 238 (33.43%) did not. Additionally, 12 patients (1.69%) developed bradycardia. No severe neonatal adverse events were reported. Among the cases, only five (0.7%) had an Apgar score below 7 at one minute, but all of them

improved to a score of 7 or higher at five minutes.

The predictor variables included the baseline characteristics of the parturients, pregnancy details, preoperative assessment, and the inexperienced anesthesiologist were demonstrated with details in Table 1.

Table 1. Patient characteristics.

Characteristics	Hypotension n = 474 (66.57%) Mean (SD)	No hypotension n = 238 (33.43%) Mean (SD)	p value	AUROC (95%CI)
Demographics				
Age (years)	33.30 (4.98)	32.70 (5.02)	0.129	0.53 (0.48 to 0.57)
Maternal weight (kg)	73.07 (11.39)	70.40 (9.93)	0.002	0.57 (0.52 to 0.61)
Body mass index (kg/m ²)	28.98 (4.25)	27.89 (3.79)	< 0.001	0.57 (0.53 to 0.62)
Underlying DM/GDM n (%)	60 (12.66%)	14 (5.88%)	0.006	0.53 (0.51 to 0.55)
Pregnancy information				
Weight gain during pregnancy (kg)	14.17 (5.21)	14.73 (4.90)	0.172	0.47 (0.42 to 0.51)
Multiple pregnancy n (%)	18 (3.8%)	14 (5.88%)	0.249	0.49 (0.47 to 0.51)
Cephalic presentation n (%)	426 (89.87%)	206 (86.55%)	0.186	0.52 (0.49 to 0.54)
GA ≥ 38 weeks n (%)	390 (82.49%)	173 (73.11%)	0.003	0.55 (0.51 to 0.58)
Head engagement n (%)	51 (10.76%)	35 (14.71%)	0.129	0.48 (0.45 to 0.51)
Emergency surgery n (%)	83 (17.51%)	96 (40.34%)	< 0.001	0.61(0.58 to 0.65)
Uterine contraction n (%)	70 (14.80%)	84 (35.29%)	< 0.001	0.61(0.57 to 0.64)
Positive SST n (%)	79 (16.67%)	28 (11.76%)	0.095	0.52 (0.50 to 0.55)
IV fluid before anesthesia n (%)	120 (25.42%)	98 (41.18 %)	< 0.001	0.58 (0.54 to 0.62)
Duration of fasting (min)	654.68 (195.51)	612.79 (255.08)	0.028	0.53 (0.48 to 0.57)
Baseline hemodynamic parameters				
Baseline SBP (mmHg)	113.51 (9.77)	112.94 (10.43)	0.475	0.52 (0.48 to 0.57)
Baseline heart rate (bpm)	82.98 (11.08)	79.85 (10.71)	< 0.001	0.58 (0.54 to 0.63)
SVI (ml/m ²)	45.53 (7.98)	51.01 (8.57)	< 0.001	0.60 (0.57 to 0.64)
CI (L/min/m ²)	3.671 (0.62)	3.87563 (0.67)	< 0.001	0.59 (0.54 to 0.63)
SVRI (dynes · sec/cm ⁵)	1776.97 (357.39)	1678.96 (325.43)	< 0.001	0.58 (0.53 to 0.62)
FTc (ms)	375.77 (34.74)	369.20 (38.37)	0.022	0.55 (0.50 to 0.59)
Intraoperative detail				
Inexperienced anesthesiologist n (%)	301 (65.15%)	158 (67.52 %)	0.533	0.51 (0.47 to 0.55)

SD: standard deviation, GDM: gestational diabetes mellitus, DM: diabetes mellitus, GA: gestational age, SST: supine stress test, IV: intravenous, SBP: systolic blood pressure, SVI: stroke volume index, CI: cardiac index, SVRI: systemic vascular resistance index, FTc: flow time corrected, AUROC: area under the receiver operating characteristic curve.

Predictors showing statistical significance ($p < 0.1$) in univariable analysis were included in the subsequent multivariable analysis. These predictors include BMI, underlying diabetes mellitus/gestational diabetes mellitus (DM/GDM), gestational age, emergency surgery, positive supine stress test, uterine contraction, intravenous injection fluid administration before anesthesia, fasting duration, baseline heart rate, SVI, CI, and SVRI.

The final multivariable model in Table 2 included three predictors: uterine contraction, baseline heart rate > 80 bpm, and SVI. The model demonstrated an AUROC of 0.715. Coefficients and score transformation details are also provided in Table 2. SIH scores ranged from 0 to 7 (Table 3). Fig. 2 illustrates the distribution of cases across different score points for hypotension and no hypotension. The AUROC of the SIH score was 0.715 (95% confidence interval (CI) 0.676-0.754), demonstrating acceptable discriminative ability. This

was significantly better ($p < 0.001$) than the model with only SVI (AUROC 0.643) shown in Fig. 3. The Hosmer-Lemeshow test yielded a p value of 0.639, indicating good model fit. The bootstrapped ROC of the SIH score was 0.660 (95%CI 0.601-0.702%). Fig. 4 highlights how the SIH score corresponds to the actual risk of hypotension.

In this study, SIH scores were classified into three groups (Table 3) based on two cutoff points for the SIH risk score, determining low, moderate, and high-risk categories: scores 0-2 (low-risk), scores 2.5-4.5 (moderate-risk), and scores 5-7 (high-risk). The probabilities of hypotension were 21.88% (low-risk), 54.05% (moderate-risk), and 79.95% (high-risk), showing statistically significant differences ($p < 0.001$). These findings demonstrated the association between the SIH risk score and hypotension likelihood, emphasizing its utility for identifying patients at varying risk levels and informing clinical decision-making.

Table 2. Multivariable risk predictors, logit coefficients, and score transformation.

Predictor	Odds ratio	95%CI	p value	Coefficient	Score
Uterine contraction					
Yes					0
No	3.226	2.187 to 4.758	< 0.001	1.171	2
Heart rate (bpm)					
≤ 80					0
> 80	1.702	1.208 to 2.399	0.002	0.532	1
Stroke volume index (ml/ m ² / beat)					
> 60					0
45 to 60	3.758	1.881 to 7.913	< 0.001	1.350	2.5
< 45	8.785	4.128 to 18.696	< 0.001	2.173	4

CI: confidence interval

Table 3. Distribution of hypotension vs. no hypotension in low, moderate, and high probability categories.

Probability category	Risk score	Hypotension (n = 474) n (%)	No hypotension (n = 238) n (%)	p value
Low	0-2	7 (21.88)	25 (78.13)	< 0.001
Moderate	2.5-4.5	160 (54.05)	136 (45.95)	
High	5-7	307 (79.95)	77 (20.05)	

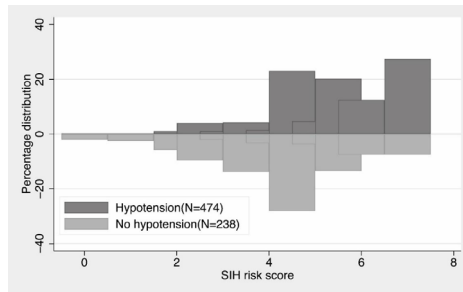


Fig. 2. Percentage distribution of spinal anesthesia-induced hypotension (SIH) risk scores categorized by hypotension and no hypotension.

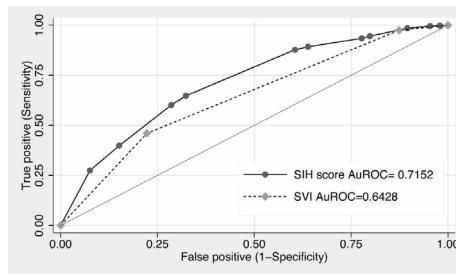


Fig. 3. Receiver operating characteristic curve for the prediction of spinal anesthesia-induced hypotension, comparison of the spinal anesthesia-induced hypotension (SIH) score, and stroke volume index (SVI) obtained from ultrasound cardiac output monitoring (USCOM).

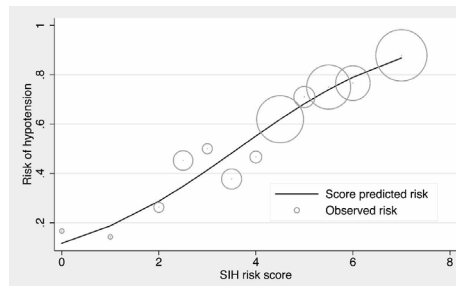


Fig. 4. Observed risk for each score point (circle) versus predicted risk (solid line) of spinal anesthesia-induced hypotension (SIH). The size of the circle represents the number of patients at each score point.

Discussion

Predicting SIH is difficult because of the complex mechanisms of SIH during cesarean delivery. Several previous studies failed to identify a simple good predictor⁽⁵⁾. In our study, we incorporated noninvasive USCOM hemodynamic monitoring to

directly measure the mechanism of hypotension, going beyond preoperative risk factors. The best predictor among the various USCOM parameters was the SVI, but its predictive power was relatively poor (AUROC = 0.643). On the other hand, the SIH risk score, derived from a combination of three predictors: SVI,

uterine contraction, and baseline heart rate demonstrated acceptable predictive performance, with an AUROC of 0.715.

In our study, the baseline SVI emerged as the most prominent predictor. SVI reflects preload, which is a crucial component of blood pressure. This finding underscores the continued significance of fluid status in predicting SIH.

Although CI shows significance in both the univariable and multivariable logistic models, it is highly correlated with SVI. To address the issue of multicollinearity, we decided to exclude CI from the model and instead include SVI. SVI was chosen because it is directly obtained from USCOM. Additionally, CI values are typically very small and often expressed in decimal points, making it challenging to categorize CI effectively. Furthermore, the categorization of CI may not have significant clinical relevance due to its small value.

Baseline HR has been identified as a predictor of SIH^(6, 15). Higher baseline HR is believed to indicate increased sympathetic tone and a higher risk of developing hypotension after sympathectomy⁽⁶⁾. In our study, we found that a baseline HR cutoff point of 80 bpm was the best for predicting SIH. Interestingly, uterine contractions during spinal anesthesia were associated with a lower incidence of hypotension, acting as a protective predictor. Autotransfusion during uterine contractions in laboring women has been suggested as a potential mechanism for this protective effect⁽²⁰⁾. The release of catecholamines and stress hormones during labor progression⁽²¹⁾ may also contribute to this protective mechanism.

Our study did not find the supine stress test (SST) to be a significant predictor, despite its previous association with SIH in cesarean delivery^(8, 9). Unlike previous studies that focused on elective surgeries, our study included both elective and emergency cases. In emergency patients, factors like pain from uterine contractions may impact the accuracy of SST results, even though we attempted to perform the test during non-contraction periods. The increase in stress hormones due to pain could potentially affect the SST

results. Consequently, SST may not reliably predict outcomes in emergency cesarean deliveries.

Systemic vascular resistance index (SVRI) did not emerge as a significant predictor in our study. This may be attributed to the fact that SVRI values obtained from USCOM are calculated rather than directly measured. Additionally, the absence of central venous pressure measurement in our data collection could introduce errors in the determination of SVRI values. The three predictors in our model, namely SVI, baseline heart rate, and uterine contraction, reflect fluid status and maternal sympathetic tone, both of which play a direct role in blood pressure regulation. Consequently, the other predictors that did not demonstrate significance are likely indicative of the same underlying mechanism as our three predictors, albeit with weaker correlations. As a result, these predictors were unable to exhibit significance in the multivariable model.

The PRAM score, developed by Bishop et al, utilizes preoperative risk factors to predict obstetric spinal hypotension⁽¹⁵⁾. However, despite its simplicity, the PRAM score exhibits poor discriminative ability (AUROC = 0.626). Additionally, the PRAM score has several limitations. The original study assessed hypotension until 15 minutes after neonatal delivery, potentially confounded by factors such as bleeding and adverse effects of uterotonic agents. Furthermore, the PRAM study allowed anesthesiologists to decide whether to administer prophylactic phenylephrine, which could impact the outcome variable. This discrepancy may explain the substantial difference in hypotension incidence between the PRAM study (30.36%) and our study (66.57%).

To the best of our knowledge, there is currently no existing predictive score with good or acceptable predictive power for hypotension in cesarean delivery. In our study, we developed a SIH risk score based on three parameters, which demonstrated acceptable predictive power (AUROC = 0.715). One of the strengths of our study is the prospective development of the risk score, utilizing a large number of patients and predictors. Furthermore, we combined data from

both maternal characteristics and hemodynamic monitoring, enhancing the comprehensiveness of our approach.

Our study has several limitations. Firstly, it was conducted in a single academic hospital, and the validation was only performed internally. This raises the possibility of overfitting the model, highlighting the importance of external validation in different settings. Secondly, the use of USCOM to obtain the SVI poses challenges due to equipment availability and the need for experienced operators. Although USCOM is a simple, noninvasive, and cost-effective method, a minimum of 50 cases is required for training to achieve the learning curve and ensure good inter-rater reliability. Thirdly, our study included a population of normal healthy parturients, raising questions about its applicability to extreme or unhealthy populations. Developing separate prediction scores for different populations may be more appropriate. Additionally, our study was restricted to daytime shifts, leading to potential data loss during out-of-office hours, particularly in emergency cases. Nonetheless, we included a sufficient number of emergency surgery cases (179 cases, 25.14%). Finally, the discrimination power of our risk score did not reach a very high level. Future studies should explore the complex mechanisms of SIH and identify better predictors for improved risk assessment.

In a resource-limited setting where routine prophylactic therapy with phenylephrine for SIH is unavailable, tailoring prophylactic therapy based on individual risk assessment can contribute to the efficient utilization of resources. This approach can help guide decision-making in selecting patients for prophylactic therapy, prioritizing the high-risk group over the low-risk group.

Further studies should be conducted to evaluate the prophylactic therapy regimen for each individual risk group. For instance, consideration should be given to a higher dose of vasopressor medication or the utilization of combined colloid co-loading⁽²²⁾ in the high-risk group, which has a significant likelihood of developing hypotension (79.95%). Conversely, in the

low-risk group, a lower dose of prophylactic therapy should be considered to mitigate the risk of side effects, such as reactive hypertension.

Conclusion

Our study developed a scoring system for predicting SIH in cesarean delivery, which included three predictors: SVI, baseline heart rate > 80 bpm, and the presence of uterine contractions. Categorizing patients into low-, moderate-, and high-risk groups based on their SIH scores can assist in prioritizing the use of prophylactic therapy in resource-limited settings.

Acknowledgments

The authors thank Professor Jayanton Patumanond, M.D., MSc., DSc., PhD. for statistical consultation and the anesthetic personnel in the obstetric operating room for facilitating data collection.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Eltzschig HK, Lieberman ES, Camann WR. Regional anesthesia and analgesia for labor and delivery. *N Engl J Med* 2003;348:319-32.
2. Koković JT, Radunovic N, Filimonović D, Nejković L, Arsenijević L, Mirković LJ, et al. Maternal hemodynamic influence on uteroplacental oxygen distribution during cesarean section. *Clin Exp Obstet Gynecol* 2015;42:610-3.
3. Butwick AJ, Columb MO, Carvalho B. Preventing spinal hypotension during Cesarean delivery: what is the latest. *Br J Anaesth* 2015;114:183-6.
4. Fu F, Xiao F, Chen W, Yang M, Zhou Y, Ngan Kee WD, et al. A randomised double-blind dose-response study of weight-adjusted infusions of norepinephrine for preventing hypotension during combined spinal-epidural anaesthesia for Cesarean delivery. *Br J Anaesth* 2020;124:e108-e114.
5. Yu C, Gu J, Liao Z, Feng S. Prediction of spinal anesthesia-induced hypotension during elective cesarean section: a systematic review of prospective observational studies. *Int J Obstet Anesth*

2021;47:103175.

6. Frölich MA, Caton D. Baseline heart rate may predict hypotension after spinal anesthesia in prehydrated obstetrical patients. *Can J Anaesth* 2002;49:185-9.
7. Bishop DG, Cairns C, Grobbelaar M, Rodseth RN. Heart rate variability as a predictor of hypotension following spinal for elective caesarean section: a prospective observational study. *Anaesthesia* 2017;72:603-8.
8. Erango M, Frigessi A, Rosseland LA. A three minutes supine position test reveals higher risk of spinal anesthesia induced hypotension during cesarean delivery. An observational study. *F1000Res* 2018;7:1028.
9. Dahlgren G, Granath F, Wessel H, Irestedt L. Prediction of hypotension during spinal anesthesia for Cesarean section and its relation to the effect of crystalloid or colloid preload. *Int J Obstet Anesth* 2007;16:128-34.
10. Duggappa DR, Lokesh M, Dixit A, Paul R, Raghavendra Rao RS, Prabha P. Perfusion index as a predictor of hypotension following spinal anaesthesia in lower segment caesarean section. *Indian J Anaesth* 2017;61:649-54.
11. Sun S, Liu NH, Huang SQ. Role of cerebral oxygenation for prediction of hypotension after spinal anesthesia for caesarean section. *J Clin Monit Comput* 2016;30:417-21.
12. Elbadry AA, El Dabe A, Abu Sabaa MA. Preoperative Ultrasonographic evaluation of the internal jugular vein collapsibility index and inferior vena cava collapsibility index to predict post spinal hypotension in pregnant women undergoing caesarean section. *Anesth Pain Med* 2022;12:e121648.
13. Yokose M, Mihara T, Sugawara Y, Goto T. The predictive ability of non-invasive haemodynamic parameters for hypotension during caesarean section: a prospective observational study. *Anaesthesia* 2015;70:555-62.
14. Meirowitz N, Katz A, Danzer B, Siegenfeld R. Can the passive leg raise test predict spinal hypotension during cesarean delivery? An observational pilot study. *Int J Obstet Anesth* 2012;21:324-8.
15. Bishop DG, Cairns C, Grobbelaar M, Rodseth RN. Obstetric spinal hypotension: Preoperative risk factors and the development of a preliminary risk score - the PRAM score. *S Afr Med J* 2017;107:1127-31.
16. Hodgson LE, Venn R, Forni LG, Samuels TL, Wakeling HG. Measuring the cardiac output in acute emergency admissions: use of the non-invasive ultrasonic cardiac output monitor (USCOM) with determination of the learning curve and inter-rater reliability. *J Intensive Care Soc* 2016;17:122-8.
17. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD Statement. *Br J Surg* 2015;102:148-58.
18. Klöhr S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anaesthesia for caesarean section: literature search and application to parturients. *Acta Anaesthesiol Scand* 2010;54: 909-21.
19. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373-9.
20. Clark RB. Hypotension and Caesarean section. *Br J Anaesth* 2008;101:882-3.
21. Bonapace J, Gagné GP, Chaillet N, Gagnon R, Hébert E, Buckley S. No. 355-Physiologic Basis of pain in labour and delivery: An evidence-based approach to its management. *J Obstet Gynaecol Can* 2018;40: 227-45.
22. Ripollés Melchor J, Espinosa Á, Martínez Hurtado E, Casans Francés R, Navarro Pérez R, Abad Gurumeta A, et al. Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis. *Minerva Anesthesiol* 2015;81:1019-30.