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Risk factors of more severe hypotension after spinal anesthesia for cesarean section

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Abstract

Background: The aim of this study was to examine the risk factors associated with the use of vasopressors to prevent hypotension that occurs after spinal anesthesia during cesarean section. Although the prophylactic use of vasopressors is already suggested as routine care in many parts of the world, the occurrence of spinal anesthesia-induced hypotension (SAIH) is still common in parturients.

Methods: This retrospective study included parturients receiving elective cesarean deliveries under spinal anesthesia from April 2016 to March 2020. Risk factors related to ephedrine dosage were analyzed using a hurdle model, and risk factors related to SAIH were further analyzed with logistic regression.

Results: Five risk factors, namely maternal body mass index (BMI, $p < 0.001$), baseline systolic blood pressure (SBP, $p < 0.001$), baseline heart rate (HR, $p = 0.047$), multiparity ($p = 0.003$), and large fetal weight ($p = 0.005$) were significantly associated with the requirement for ephedrine. Furthermore, a higher ephedrine dosage was significantly associated with maternal BMI ($p < 0.001$), baseline SBP ($p < 0.001$), baseline HR ($p < 0.001$), multiparity ($p = 0.027$), large fetal weight ($p = 0.030$), maternal age ($p = 0.009$), and twin pregnancies ($p < 0.001$). Logistic regression analysis also showed that the same five risk factors—maternal BMI ($p = 0.030$), baseline SBP ($p < 0.001$), baseline HR ($p < 0.001$), multiparity ($p < 0.001$), and large fetal weight ($p < 0.001$)—were significantly associated with SAIH, even in cases where vasopressors were administered.

Conclusion: These findings can be useful for clinicians when deciding the dose of prophylactic ephedrine or phenylephrine to prevent SAIH.

Keywords: Birth weight; Cesarean section; Risk factor

1. INTRODUCTION

Neuraxial anesthesia is the preferred technique of anesthesia for women undergoing cesarean delivery,[1] and it is used in more than 90% of elective cesarean deliveries in the United States and Canada.[2] Compared to general anesthesia, the advantages of neuraxial anesthesia include minimizing maternal morbidity, allowing the parturient to be awake for the birth, minimizing the use of intraoperative systemic medications and transfer to the fetus, and avoiding airway instrumentation.

Among the different types of neuraxial anesthesia, Riley et al[3] demonstrated that single-shot spinal anesthesia was superior to epidural anesthesia for the vast majority of patients, as it can be performed quickly, requires lower doses of analgesics and anxiolytics, and is associated with a lower complication rate. Consequently, single-shot spinal anesthesia has become the technique of choice for elective cesarean deliveries in most countries.[2,4,5]

For cesarean delivery, a sensory level from the sacral dermatomes to T4 is required.[6] Owing to the rapid onset and extensive spread of anesthesia, sympathetic blockade may produce an abrupt decrease in maternal arterial blood pressure, and hypotension following spinal anesthesia during cesarean section can cause both maternal and fetal/neonatal adverse effects.[7–9] Although several management techniques including intravenous fluid preloading or co-loading (15 mL/kg or approximately 1 L[10]), the administration of prophylactic vasopressors,[10,11] and patient positioning are used to prevent hypotension following spinal anesthesia, they may not be sufficient, and the reported hypotension rate varies from 29% to 80% based on the definition.[12,13]

In a systematic review,[13] Yu et al classified the predictive factors of post-spinal anesthesia-induced hypotension (SAIH) into seven domains: demographic characteristics, baseline hemodynamic parameters, sympathovagal balance indices, postural stress testing, peripheral perfusion indices, blood volume and fluid responsiveness indices, and genetic polymorphisms. Most previous studies have focused on demographic characteristics such as maternal weight and body mass index (BMI)[14–16] and baseline hemodynamic parameters such as baseline heart rate (HR)[15] and baseline systolic blood pressure (SBP)[17–19] to predict post-SAIH, however the results have been inconclusive.

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Therefore, we conducted this retrospective study to investigate the factors associated with the need for higher doses of vasopressors in women undergoing cesarean section.

2. METHODS

2.1. Patient selection

This study was approved by the Institutional Review Board of Taipei Veterans General Hospital, Taipei, Taiwan. The need for written informed consent was waived as all data were deidentified before analysis. We carefully reviewed the electronic medical records of parturients undergoing elective cesarean deliveries under spinal anesthesia from April 2016 to March 2020. The exclusion criteria were anesthesia induction technique other than single-shot spinal anesthesia, such as general anesthesia, epidural anesthesia, combined spinal-epidural anesthesia, or combined inhalation anesthesia. Parturients with preexisting hypertension, pregnancy-induced hypertension, preeclampsia, and baseline SBP <90 mmHg were also excluded.

2.2. Anesthesia and hypotension management

All of the parturients received volume preloading with at least 1 L of crystalloids and baseline blood pressure and HR were measured in the supine position before the induction of spinal anesthesia. Spinal anesthesia was induced in the right lateral position at the level of lumbar spine 3 to 4 or 4 to 5 interspaces with 0.5% hyperbaric bupivacaine without fentanyl through a 27- or 25-gauge spinal needle. Oxygen was supplied via a nasal cannula. The dose of prophylactic ephedrine was decided according to the anesthesiologist in charge. After the intrathecal injection, blood pressure and HR were measured at least every 5 minutes until the end of the surgery, and the sensory block level was assessed by pinprick test. Additional vasopressors were administered to manage postspinal hypotension, while norepinephrine or epinephrine were preserved for more severe cardiovascular compromise.

2.3. Hemodynamic measurements, data collection, and endpoints

Intraoperative data including vital signs, vasopressor dosage, amount of fluid administration, urine output, and blood loss were recorded by the anesthetic nurses in charge. The patients' vital signs after they had been transferred to our post-anesthesia care unit were also recorded.

Maternal demographic data including age, height, weight, BMI, comorbidities, obstetric history, and birth records such as birth weight and Apgar scores were also collected through an electronic medical chart review by anesthesiologists not involved in the statistical analysis. After the data had been collected, random samples were examined by the authors to ensure data quality. The primary endpoint was risk factors related to the ephedrine dosage before delivery. The secondary endpoint was risk factors related to SAIH. In this study, any episode of SBP <90 mmHg that developed during the period between spinal anesthesia and childbirth was defined as SAIH.

Because twin pregnancies were included in the analysis, the fetal birth weight was classified into three groups: total birth weight, large fetal weight, and small fetal weight. In singleton pregnancies, total birth weight was equal to the large fetal weight as there was only one baby. In twin pregnancies, the weight of the heavier baby was recorded as the large fetal weight, and the weight of the smaller baby was recorded as the small fetal weight. Therefore, total birth weight was equal to the sum of the big and small fetal weights in twin pregnancies. For Apgar score analysis in twin pregnancies, we only chose the baby with the inferior score.

2.4. Statistical analysis

A hurdle model utilizing backward model selection in R statistical software (version 4.1.2, R Core Team, 2021) with a significance level of 0.05 as the exit criterion was used for the primary endpoint (factors associated with ephedrine dosage). Risk factors for ephedrine requirement were analyzed using a zero-count process, and the factors associated with the dosage of ephedrine were analyzed using a positive-count process.

Binary logistic regression analysis was performed with SPSS (version 25; IBM, Armonk, NY) for the risk factors associated with the development of SAIH. Maternal age, height, weight, BMI, American Society of Anesthesiologists Physical Status (ASA PS) classification, gestational age, baseline SBP, baseline HR, intrathecal Bupivacaine dosage, nulliparity/multiparity, singleton/twin pregnancies, diabetes mellitus/gestational diabetes mellitus, total birth weight, large fetal weight, and the smaller baby weight were included as covariates in a forward stepwise model (likelihood ratio) selection strategy with entry and exit significance levels of 0.05 and 0.1, respectively. Model performance was assessed using receiver operating characteristic (ROC) curve analysis with the probability of post-SAIH calculated from the logistic regression analysis.

For data management, we used Microsoft Excel 2013 (Microsoft Corp., Redmond, WA), and for statistical analyses, we used SPSS version 25 (IBM Corp., Armonk, NY) and R statistical software, version 4.1.2 (R Core Team, 2021). Models were selected according to the Akaike information criterion (AIC, lower scores indicate better fit). Statistical significance was assumed for $p < 0.05$.

3. RESULTS

3.1. Patient characteristics

Patient selection is shown in the flowchart in Fig. 1. A total of 1175 parturients underwent elective cesarean section under spinal anesthesia between April 2016 and March 2020 at our hospital. Of these parturients, 174 with preexisting hypertension, pregnancy-induced hypertension, or preeclampsia, and two with a baseline SBP <90 mmHg were excluded. The remaining 999 parturients with 1108 live childbirths (two intrauterine fetal deaths) were analyzed in this study. As presented in Table 1, the parturients had a median age of 35 years, and the majority were ASA PS class II or III (93.9% and 6.1%, respectively). Most of the births were late preterm or term gestational age (14.8% and 79.8%, respectively). The major reason for cesarean section was a previous history of cesarean section (39.8%), followed by fetal malpresentation (19.3%), dysfunctional labor (7%), previous history of myomectomy (5.8%), and placenta previa/accrete (4.6%). The overall incidence of post-SAIH in this study was 42.9%. Overall, 650 of the parturients received ephedrine after spinal anesthesia. For more severe hypotension, epinephrine and norepinephrine were used in one and five parturients, respectively.

3.2. Risk factors associated with the requirement for ephedrine and dosage

The zero-count process and positive-count process were fitted with a binary logistic regression model and a negative binomial model, respectively, according to the AIC results. As presented in Table 2, five risk factors associated with the requirement for ephedrine, namely maternal BMI ($p < 0.001$), baseline SBP ($p < 0.001$), baseline HR ($p = 0.047$), multiparity ($p = 0.003$), and large fetal weight ($p = 0.005$) were identified in the zero-count process. These five factors, maternal BMI ($p < 0.001$), baseline SBP ($p < 0.001$), baseline HR ($p < 0.001$), multiparity ($p = 0.027$), and large fetal weight ($p = 0.030$), with two additional factors of maternal age ($p = 0.009$) and twin pregnancy ($p < 0.001$) were associated with ephedrine dosage.

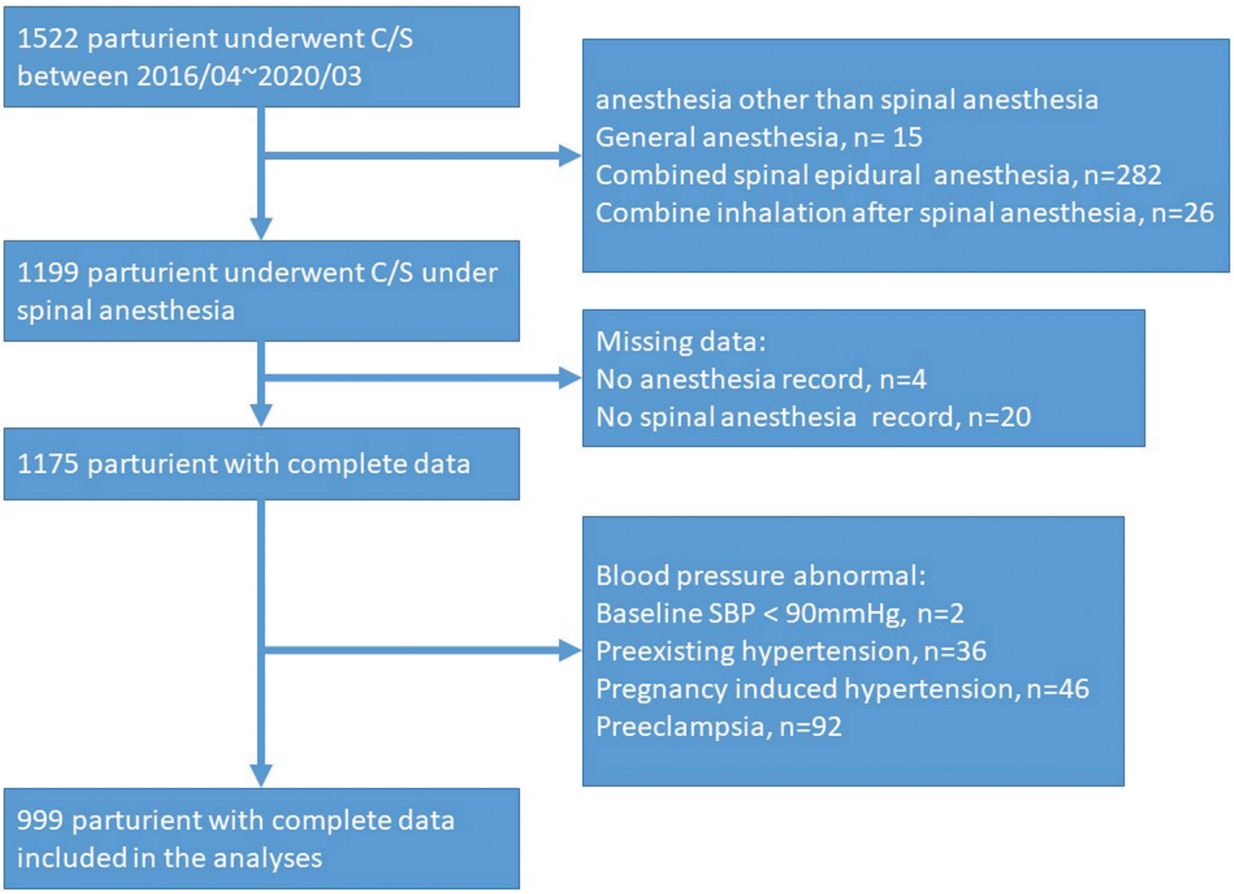

Fig. 1 Patient selection flowchart. C/S = cesarean section; SBP = systolic blood pressure.

Based on the estimated parameters, a simplified risk-scoring system to predict the requirement for ephedrine was developed as:

$$\text{Risk score} = 42 \times (\text{multiparous} = 1,\ \text{nulliparous} = 0) + \text{HR} - 3 \times \text{SBP} + 6 \times \text{BMI} + 3 \times \text{fetal weight (in 100 g)}$$

For parturients with a score of more than 75, prophylactic ephedrine should not be omitted.

The average ephedrine dosage in the parturients without risk factors was 2.2 mg. This dosage increased by 1.02, 0.99, and 1.01 times, respectively, for each unit increase in age, BMI, baseline SBP, and baseline HR. Multiparous and twin pregnancies increased it by 1.11 and 1.38 times, respectively. In addition, every 100 g increase in large fetal weight increased the average ephedrine dose by 1.01 times.

3.3. Univariate analysis of SAIH

Compared to the parturients without SAIH, those with SAIH had a significantly lower baseline SBP (122 [interquartile range = 114-130] vs 130 [120-143] mmHg, $p < 0.001$), heavier large fetal weight (3098 [2742-3345] vs 2930 [2576-3266] g, $p < 0.001$), were more often multiparous (259 [60.4%] vs 261 [45.8%], $p < 0.001$), had a higher percent change in lowest SBP (33 [27-39] vs 19 [12-25]%, $p < 0.001$), and shorter time to lowest SBP after spinal anesthesia (14.9 [10-20] vs 15.9 [10-20] minutes, $p < 0.001$).

3.4. Multivariate logistic regression analysis of SAIH

The results of multivariate logistic regression analysis showed that the independent variables significantly associated with SAIH were maternal BMI (odds ratio [OR]: 1.04, 95% CI, 1.00-1.08, $p = 0.030$), baseline SBP (OR: 0.95, 95% CI, 0.94-0.96, $p < 0.001$), baseline HR (OR: 1.02, 95% CI, 1.01-1.03, $p < 0.001$), multiparity (OR: 1.61, 95% CI, 1.23-2.11, $p < 0.001$), and large fetal weight (OR: 1.04, 95% CI: 1.02-1.06, $p < 0.001$) (Table 3).

4. DISCUSSION

A total of 650 parturients received prophylactic ephedrine treatment in this study, however 429 still developed SAIH. This result suggests that more aggressive prophylactic ephedrine treatment is needed in some parturients.

To the best of our knowledge, this study is the first to use fetal weight as a predictor of prophylactic ephedrine dose and SAIH. Although we used the actual fetal weight in the analysis, the predicted fetal weight could be obtained through prenatal sonography examinations. Further studies are needed to clarify whether predicted fetal weight could also guide the prophylactic vasopressor dosage.

Maternal factors such as weight, BMI,[14–16] weight gain during pregnancy,[20] abdominal girth, and distance between the symphysis pubis and fundus[21] have been reported to be able to predict SAIH due to aortocaval compression.[16,22–24] However, fetal weight, which was identified as a risk factor for SAIH in this study, may represent this compression more directly. Once the compression exceeds sympathetic compensation ability, more severe hypotension may develop post-spinal anesthesia requiring a higher vasopressor dose. Moreover, older maternal age has been associated with lower

Table 1

Patient baseline characteristics and clinical outcomes

Variable	All	Ephedrine dosage			SAIH		
		Present	Absent		Present	Absent	
	n = 999	n = 650	n = 349	*p*	n = 429	n = 570	*p*
Age, y	35 (32-38)	35 (32-38)	35 (32-38)	NS	35 (32-38)	35 (32-38)	NS
Height, cm	160 (156.8-164)	160 (157-164)	160 (157-164)	NS	160 (157-163)	160 (157-164)	NS
Weight, kg	68 (62-76)	69 (62-76)	67 (61-74)	0.009	68 (62-76)	68 (62-76)	NS
BMI	26.5 (24.2-29.1)	26.8 (24.3-29.5)	26.1 (23.9-28.5)	NS	26.7 (24.4-29.2)	26.3 (24.1-29.1)	NS
Baseline SBP, mmHg	126 (117-137)	124 (115-135)	130 (121-143)	<0.001	122 (114-130)	130 (120-143)	<0.001
Baseline HR, bpm	83 (73-92)	83 (74-92)	83 (73-93)	NS	83 (74-92)	82 (73-92)	NS
Marcaine dose, mg	12 (12-13)	12 (12-13)	12 (12-13)	NS	12 (12-13)	12 (12-13)	NS
Total fetal weight (100 g)	31.30 (27.72-34.66)	31.55 (28.40-34.56)	30.48 (26.56-35.18)	0.042	31.62 (28.52-34.66)	30.97 (27.02-34.66)	0.042
Large fetal weight (100 g)[a]	30.02 (26.36-33.04)	30.80 (27.16-33.34)	28.44 (25.34-32.10)	<0.001	30.98 (27.42-33.45)	29.30 (25.76-32.66)	<0.001
ASA PS classification							
2	938 (93.9)	612 (94.2)	326 (93.4)	NS	402 (93.7)	536 (94)	NS
3	61 (6.1)	38 (5.8)	23 (6.6)	NS	27 (6.3)	34 (6)	NS
Gestational age, wk	38.3 (37.3-39.0)	38.3 (37.4-39.0)	38.1 (36.9-38.9)	NS	38.3 (37.6-39.0)	38.1 (37.0-38.9)	NS
Multiparous	520 (52.1)	372 (57.1)	296 (84.8)	<0.001	259 (60.4)	261 (45.8)	<0.001
Twin pregnancy	111 (11.1)	57 (8.7)	53 (15.2)	0.005	38 (8.9)	73 (12.8)	0.049
Diabetes mellitus	54 (5.6)	33 (5.1)	23 (6.6)	NS	20 (4.7)	36 (6.3)	NS
Apgar scores (1 min)[b]	8 (7-8)	8 (7-8)	8 (7-8)	NS	8 (7-8)	8 (7-8)	NS
Apgar scores (5 min)[b]	9 (9-9)	9 (9-9)	9 (8-9)	NS	9 (9-9)	9 (9-9)	NS
Percent change in lowest SBP, %	25 (17-33)	29 (22-36)	17 (10-13)	<0.001	33 (27-39)	19 (12-25)	<0.001
Time to lowest SBP, min	15.5 (10-20)	15.0 (10-20)	16.3 (10-20)	<0.001	14.9 (10-20)	15.9 (10-20)	<0.001

Data are presented as the median (25th–75th percentile) or number of patients (%). For categorical data, the χ^2 test or Fisher's exact test was used, as appropriate; for continuous data, the Mann-Whitney *U*-test.

ASA PS = American Society of Anesthesiologists Physical Status; HR = heart rate; NS = non-significant; SAIH = Spinal anesthesia-induced hypotension; SBP = systolic blood pressure.

[a]Definition of large fetal weight: in singleton pregnancies, large fetal weight means the total fetal weight; in twin pregnancies, large fetal weight means the weight of the bigger fetus.

[b]For twins, the babies with inferior Apgar scores are presented.

Table 2

Results of the hurdle model

Zero count process	β	SE	OR (95% CI)	*p*
(Intercept)	0.750	0.953	2.118 (0.327-13.720)	0.431
Age	0.007	0.015	1.007 (0.977-1.038)	0.644
BMI	0.064	0.020	1.066 (1.026-1.108)	0.001
Baseline SBP	−0.032	0.005	0.969 (0.959-0.978)	<0.001
Baseline HR	0.010	0.005	1.010 (1.000-1.021)	0.047
Multiparous	0.421	0.144	1.524 (1.149-2.019)	0.003
Twin pregnancy	−0.202	0.229	0.817 (0.522-1.279)	0.376
Large fetal weight	0.034	0.012	1.034 (1.010-1.058)	0.005
Positive-count process				
(Intercept)	2.203	0.317	9.056 (4.867-16.849)	0.000
Age	0.014	0.005	1.014 (1.004-1.025)	0.009
BMI	0.022	0.006	1.022 (1.009-1.035)	0.001
Baseline SBP	−0.010	0.002	0.990 (0.987-0.993)	<0.001
Baseline HR	0.006	0.002	1.006 (1.003-1.010)	<0.001
Multiparous	0.108	0.049	1.114 (1.012-1.225)	0.027
Twin pregnancy	0.323	0.089	1.381 (1.160-1.644)	<0.001
Large fetal weight	0.009	0.004	1.009 (1.001-1.018)	0.030
Log, θ	1.20	0.07		<0.001

The zero-count process represents the factors associated with ephedrine requirement; the positive-count process represents the factors associated with the ephedrine dosage.

β = regression coefficients; BMI = body mass index; HR = heart rate; OR = odds ratio; SBP = systolic blood pressure.

baseline SBP in the second and third trimesters.[25] In addition, the magnitude of the decrease in systemic vascular resistance secondary to pregnancy has been reported to be greater in multiparous women compared to nulliparous women,[26,27] resulting in lower baseline SBP. A higher baseline HR has also been associated with a significantly increased incidence of hypotension following spinal anesthesia.[19,28,29]

Compared to singleton pregnancies, twin pregnancies have been associated with greater left atrial diameter, greater left ventricular end-diastolic diameter, more volume overload,[30] 15% higher cardiac output,[31,32] lower total vascular resistance,[32] and comparable SBP.[33] In this study, we also found that the parturients with twin pregnancies needed a 1.38-fold higher dose of prophylactic ephedrine than those with a singleton pregnancy.

Table 3

Results of logistic regression analysis—independent variables and variable categories significantly associated with spinal anesthesia-induced hypotension

	β	SE	SD β	OR (95% CI)	p
BMI	0.041	0.019	0.068	1.04 (1.00-1.08)	0.030
Baseline SBP	−0.050	0.005	−0.319	0.95 (0.94-0.96)	<0.001
Baseline HR	0.021	0.005	0.123	1.02 (1.01-1.03)	<0.001
Multiparous	0.477	0.139	0.100	1.61 (1.23-2.11)	<0.001
Large fetal weight	0.037	0.012	0.104	1.04 (1.01-1.06)	<0.001
					AUC = 0.712

β = regression coefficients; AUC = area under the curve; BMI = body mass index; HR = heart rate; OR = odds ratio; SBP = systolic blood pressure; STD β = standardized regression coefficients.

Although the use of prophylactic vasopressor treatment is already suggested as routine care in many areas, clinicians may sometimes hesitate or omit such treatment due to the presence of normal vital signs. We developed a simplified risk-scoring system with the following formula:

$$\text{Risk score} = 42 \times (\text{multiparous} = 1,\ \text{nulliparous} = 0) + \text{HR} - 3 \times \text{SBP} + 6 \times \text{BMI} + 3 \times \text{fetal weight (in 100 g)}$$

For parturients with a score of more than 75, prophylactic ephedrine should not be omitted.

There were some limitations to this study. First, although prophylactic phenylephrine infusion is already routine care in many parts of the world, phenylephrine is not available at our hospital, and we administer prophylactic vasopressors with bolus ephedrine. To provide an ephedrine dosage prediction formula was, therefore, not a goal of this study. Second, this study was conducted at a tertiary hospital, and so the number of high-risk pregnancies including those with advanced maternal age (34.7 ± 4.6 years old), maternal comorbidities (such as diabetes mellitus [1%] and gestational diabetes [4.4%]), and preterm labor (term pregnancies [79.8%]) may be higher than in the normal population. In addition, the maternal body habitus varies between countries and races, and so the generalizability of the results may be limited. Third, due to the retrospective design of the study, unknown confounders remain an inevitable problem. Furthermore, 25% of the parturients in our study were referred from local clinics, and their sonography reports of prenatal predicted fetal weight were not available in our electronic medical records system. Consequently, we could not analyze correlations between prenatal predicted fetal weight and actual fetal weight, and further studies are needed.

In conclusion, we identified seven risk factors for a higher ephedrine dosage, namely maternal BMI, baseline SBP, baseline HR, multiparity, fetal weight, maternal age, and twin pregnancies. A higher prophylactic vasopressor dosage should be administered in high-risk parturients. According to our proposed simplified risk scoring system, prophylactic ephedrine should not be omitted in parturients with a score of more than 75, even if their vital signs are normal.

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REFERENCES

1. Benhamou D, Wong C. Neuraxial anesthesia for cesarean delivery: what criteria define the "optimal" technique? *Anesth Analg* 2009;109:1370–3.
2. Bucklin BA, Hawkins JL, Anderson JR, Ullrich FA. Obstetric anesthesia workforce survey: twenty-year update. *Anesthesiology* 2005;103:645–53.
3. Riley ET, Cohen SE, Macario A, Desai JB, Ratner EF. Spinal versus epidural anesthesia for cesarean section: a comparison of time efficiency, costs, charges, and complications. *Anesth Analg* 1995;80:709–12.
4. Benhamou D, Bouaziz H, Chassard D, Ducloy JC, Fuzier V, Laffon M, et al. Anaesthetic practices for scheduled caesarean delivery: a 2005 French national survey. *Eur J Anaesthesiol* 2009;26:694–700.
5. Shibli KU, Russell IF. A survey of anaesthetic techniques used for caesarean section in the UK in 1997. *Int J Obstet Anesth* 2000;9:160–7.
6. Craft JB, Jr, Roizen MF, Dao SD, Edwards M, Gilman R. A comparison of T4 and T7 dermatomal levels of analgesia for caesarean section using the lumbar epidural technique. *Can Anaesth Soc J* 1982;29:264–9.
7. Hollmen AI, Jouppila R, Koivisto M, Maatta L, Pihlajaniemi R, Puukka M, et al. Neurologic activity of infants following anesthesia for cesarean section. *Anesthesiology* 1978;48:350–6.
8. Corke BC, Datta S, Ostheimer GW, Weiss JB, Alper MH. Spinal anaesthesia for Caesarean section. The influence of hypotension on neonatal outcome. *Anaesthesia* 1982;37:658–62.
9. Ilies C, Kiskalt H, Siedenhans D, Meybohm P, Steinfath M, Bein B, et al. Detection of hypotension during caesarean section with continuous non-invasive arterial pressure device or intermittent oscillometric arterial pressure measurement. *Br J Anaesth* 2012;109:413–9.
10. Kinsella SM, Carvalho B, Dyer RA, Fernando R, McDonnell N, Mercier FJ, et al; Consensus Statement Collaborators. International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. *Anaesthesia* 2018;73:71–92.
11. Heesen M, Kolhr S, Rossaint R, Straube S. Prophylactic phenylephrine for caesarean section under spinal anaesthesia: systematic review and meta-analysis. *Anaesthesia* 2014;69:143–65.
12. Hasanin A, Amin S, Refaat S, Habib S, Zayed M, Abdelwahab Y, et al. Norepinephrine versus phenylephrine infusion for prophylaxis against post-spinal anaesthesia hypotension during elective caesarean delivery: a randomised controlled trial. *Anaesth Crit Care Pain Med* 2019;38:601–7.
13. 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.
14. Xu Z, Xu T, Zhao P, Ma R, Zhang M, Zheng J. Differential roles of the right and left toe perfusion index in predicting the incidence of post-spinal hypotension during cesarean delivery. *Anesth Analg* 2017;125:1560–6.
15. Jeon YT, Hwang JW, Kim MH, Oh AY, Park KH, Park HP, et al. Positional blood pressure change and the risk of hypotension during spinal anesthesia for cesarean delivery: an observational study. *Anesth Analg* 2010;111:712–5.
16. Yeh PH, Chang YJ, Tsai SE. Observation of hemodynamic parameters using a non-invasive cardiac output monitor system to identify predictive indicators for post-spinal anesthesia hypotension in parturients undergoing cesarean section. *Exp Ther Med* 2020;20:168.

17. Riffard C, Viêt TQ, Desgranges FP, Bouvet L, Allaouchiche B, Stewart A, et al. The pupillary light reflex for predicting the risk of hypotension after spinal anaesthesia for elective caesarean section. *Anaesth Crit Care Pain Med* 2018;37:233–8.
18. Fakherpour A, Ghaem H, Fattahi Z, Zaree S. Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: a multinomial logistic regression. *Indian J Anaesth* 2018;62:36–46.
19. Chamchad D, Arkoosh VA, Horrow JC, Buxbaum JL, Izrailtyan I, Nakhamchik L, et al. Using heart rate variability to stratify risk of obstetric patients undergoing spinal anesthesia. *Anesth Analg* 2004;99:1818–21.
20. Ghabach MB, El-Khatib MF, Zreik TG, Matta MS, Mouawad JJ, Karam CJ, et al. Effect of weight gain during pregnancy on heart rate variability and hypotension during caesarean section under spinal anaesthesia. *Anaesthesia* 2011;66:1106–11.
21. Parthasarathy P, Aithal RR, Raghavendra Rao RS, Raghuram S, Ramesh R, Nazneen A. Correlation of symphysiofundal height and abdominal girth with the incidence of hypotension in cesarean section under spinal anesthesia using bupivacaine with fentanyl as adjuvant: a clinical study. *Anesth Essays Res* 2019;13:214–8.
22. Lee SW, Khaw KS, Ngan Kee WD, Leung TY, Critchley LA. Haemodynamic effects from aortocaval compression at different angles of lateral tilt in non-labouring term pregnant women. *Br J Anaesth* 2012;109:950–6.
23. Bieniarz J, Yoshida T, Romero-Salinas G, Curuchet E, Caldeyro-Barcia R, Crottogini JJ. Aortocaval compression by the uterus in late human pregnancy. *Am J Obstet Gynecol* 1969;103:19–31.
24. Eckstein KL, Marx GF. Aortocaval compression and uterine displacement. *Anesthesiology* 1974;40:92–6.
25. Gaillard R, Bakker R, Steegers EA, Hofman A, Jaddoe VW. Maternal age during pregnancy is associated with third trimester blood pressure level: the generation R study. *Am J Hypertens* 2011;24:1046–53.
26. Clapp JF, Capeless E. Cardiovascular function before, during, and after the first and subsequent pregnancies. *Am J Cardiol* 1997;80:1469–73.
27. Rurangirwa AA, Gaillard R, Steegers EA, Hofman A, Jaddoe VW. Hemodynamic adaptations in different trimesters among nulliparous and multiparous pregnant women; the Generation R study. *Am J Hypertens* 2012;25:892–9.
28. Frolich MA, Caton D. Baseline heart rate may predict hypotension after spinal anesthesia in prehydrated obstetrical patients. *Can J Anaesth* 2002;49:185–9.
29. 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.
30. Kametas N. Maternal cardiac function in twin pregnancy. *Obstet Gynecol* 2003;102:806–15.
31. Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. *Circulation* 2014;130:1003–8.
32. Kuleva M, Youssef A, Maroni E, Contro E, Pilu G, Rizzo N, et al. Maternal cardiac function in normal twin pregnancy: a longitudinal study. *Ultrasound Obstet Gynecol* 2011;38:575–80.
33. Adank MC, Broere-Brown ZA, Gonçalves R, Ikram MK, Jaddoe VWV, Steegers EAP, et al. Maternal cardiovascular adaptation to twin pregnancy: a population-based prospective cohort study. *BMC Pregnancy Childbirth* 2020;20:327.