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Research Article

Perfusion Index and its Relation to Hypotension of Parturients Undergoing Cesarean Section Under Spinal Anesthesia: An Observational Study

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Abstract

Background and Objective: Spinal anesthesia is preferred for cesarean deliveries; however, it causes hypotension in parturients. Clinicians prefer several methods to predict hypotension in parturients after spinal anesthesia. Generally, a non-invasive oscillometric method for the measurement of blood pressure is recommended for parturients; however, this method is unable to detect hypotensive episodes promptly. The objectives of this study were to establish a correlation between the intra-operative perfusion index and intra-operative hypotension in parturients undergoing cesarean section under spinal anesthesia. **Materials and Methods:** Total of 185 parturients who underwent cesarean section under spinal anesthesia (epidural ropivacaine) were included in the analysis. A drop of $\geq 20\%$ in mean arterial blood pressure from baseline or < 65 mmHg a diastolic blood pressure was considered hypotension. A total of 10 mg bolus of ephedrine was administered intravenously for hypotension. **Results:** After administration of spinal anesthesia to parturients, diastolic blood and mean arterial blood pressures ($p < 0.0001$ for both) decreased and perfusion index ($p = 0.0004$) increased compared to their pre-operative conditions. A total of 120 (65%) parturients had an intra-operative perfusion index ≥ 3 and 65 (35%) parturients had an intra-operative perfusion index < 3 . Unlike parturients with an intra-operative perfusion index < 3 , parturients who had an intra-operative perfusion index ≥ 3 required administration of bolus ephedrine injection during cesarean section procedures ($p < 0.0001$). Mean arterial blood pressure of parturients before cesarean section, intra-operative diastolic blood pressure, mean arterial blood pressure before administration of bolus ephedrine injection and changes in diastolic blood and mean arterial blood pressures of parturients after administration of spinal anesthesia were negatively correlated with perfusion index ($p < 0.0001$ for all). **Conclusion:** The perfusion index is a useful tool for predicting intra-operative hypotension and its episodes in parturients undergoing cesarean section under spinal anesthesia.

Key words: Adrenergic receptor activity, anesthesia, cesarean section, ephedrine, hypotension, neonate, obstetrics, parturient, perfusion index, spinal anesthesia

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Advanced maternal age and previous cesarean section increase the chances for cesarean section in Chinese women¹. Spinal anesthesia is generally preferred for cesarean delivery². In addition, spinal anesthesia causes less blood loss and is safer for neonates during cesarean deliveries³. However, spinal anesthesia causes hypotension⁴. In normal people incidence of hypotension after spinal anesthesia is 16-33%⁵; however, in pregnant women after spinal anesthesia for cesarean deliveries, chances of hypotension would be 75%⁶. Severe hypotension increases the risks of acidosis and bradycardia². The duration of hypotension is worse than the degree of hypotension in obstetric anesthesia⁷. Therefore, the prevention and treatment of hypotension during spinal anesthesia for cesarean deliveries are of prime importance⁸.

Clinicians prefer several methods to predict hypotension in parturients after spinal anesthesia. Generally, the non-invasive oscillometric method for the measurement of blood pressure is recommended for parturients⁷; however, this method is unable to detect hypotensive episodes promptly². In addition, periods of hypotension could be missed in the non-invasive oscillometric method for the measurement of blood pressure⁴.

The perfusion index is a dimensionless parameter and is the ratio of pulsatile blood flow to non-pulsatile blood flow in parturients². The value was measured using a pulse oximeter, ranging from 0.02 to 20 and normal values ranged between 1 and 10⁹. This is an indicator of peripheral perfusion at the sensor site¹⁰.

The objective of this retrospective study was to establish a correlation between the intra-operative perfusion index and intra-operative hypotension in parturients undergoing cesarean section under spinal anesthesia. In addition, the study evaluated the requirement of vasopressors regarding the perfusion index.

MATERIALS AND METHODS

Study area: Retrospective study is preformed from medical records of women who underwent cesarean section under spinal anesthesia at the department of anesthesiology, the Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, China from March 17, 2019 to December 19, 2020.

Ethics approval and consent to participate: This study was designed by the authors. This study was approved by the

Ethics Committee of the Women and Children's Hospital, School of Medicine, Xiamen University (approval number: KY-2023-142-K01). The study follows the laws of China and the v2008 Declarations of Helsinki. As this was a retrospective study, informed consent was waived by the institutional review board.

Inclusion criteria: Parturients who underwent cesarean section under spinal anesthesia.

Exclusion criteria: Parturients who had no complete details of records in the hospital.

Anesthesia technique: None of the subjects received any premedication. When parturient arrived in the operating room, oxygen was routinely delivered via a face mask at 3 L/min and an intravenous cannula was inserted into the forearm vein. Electrocardiography (ECG), Non-Invasive Blood Pressure (NIBP) and Oxygen Saturation (SpO₂) were monitored continuously. In the left lateral position, combined spinal-epidural (CSE) anesthesia was performed at the L3-4 interspace using the needle-through-needle technique. Epidural puncture penetrated the epidural space using a blunt 18-G epidural needle. The site of the epidural space was confirmed using the loss-of-resistance to saline technique. A pencil-tip 25-G spinal needle was then pierced into the subarachnoid space through the epidural needle. After withdrawal of the clear cerebrospinal fluid, 2 mL of 13 mg ropivacaine was administered. The epidural catheter was placed cephalad to a depth of 3-4 cm. In cases of local anesthetic systemic toxicity or high neuro blockade, a test dose of 2% lidocaine with 3.0 mL of 1/200,000 adrenaline administered to identify intrathecal misplacement. If the epidural catheter or CSE failed to meet surgical requirements, the parturient was removed from the study. During the operation, if the patient's pain score (visual analog scale) was >3 or visceral traction response occurred, an additional 5 mL of 2% lidocaine was administered, repeated every 5 min, if necessary. Midazolam (2 mg) was administered intravenously if the patient experienced nervousness. Additional midazolam and lidocaine doses were also recorded. At the end of the surgery, the allocated study medications were administered epidurally for >60 sec.

Hypotension and treatment: A drop of 20% or more in mean arterial blood pressure (normal value: 70 to 100-mm Hg) from baseline or below 65 mmHg of diastolic blood pressure was considered hypotension. A bolus of ephedrine (10 mg) was

administered intravenously for hypotension or decreased mean arterial blood pressure or diastolic blood pressure. Atropine was administered if the heart rate was less than 60 beats/min⁴.

Adverse effects of parturients and neonates: Any reported unwanted effects on parturients and neonates during and after the cesarean section procedure were collected and analyzed.

Bradycardia: A heart rate less than 60 times a minute was considered as bradycardia.

Statistical analysis: InStat 3.01 (GraphPad Software Inc., San Diego, California, United States of America) was used for the statistical analysis. Categorical, continuous normal and continuous non-normal variables are presented as frequencies with percentages in parentheses, Mean $\pm$ Standard Deviation (SD) and medians with Q3-Q1 in parentheses. Kolmogorov and Smirnov tests were used to check the normality of continuous variables. The Mann-Whitney test was used for the

statistical analysis of continuous non-normal variables. Chi-square (χ^2 -test with Yates correction) or Fisher's exact test was used for statistical analysis of categorical variables. Spearman's rank correlation was developed between changes in hemodynamic parameters and changes in the perfusion index. All results were considered statistically significant at $p < 0.05$.

RESULTS

Study population: From March 17, 2019 to December 19, 2020, 205 women underwent cesarean section under spinal anesthesia at the Department of Anesthesiology, the Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen, China and the referring hospitals. Among them, complete variables were not available for 20 women. Therefore, these women were excluded from this study. Medical records of hemodynamic parameters of 185 parturients who underwent cesarean section under spinal anesthesia were included in the analysis. The flowchart of the study was shown in Fig. 1.

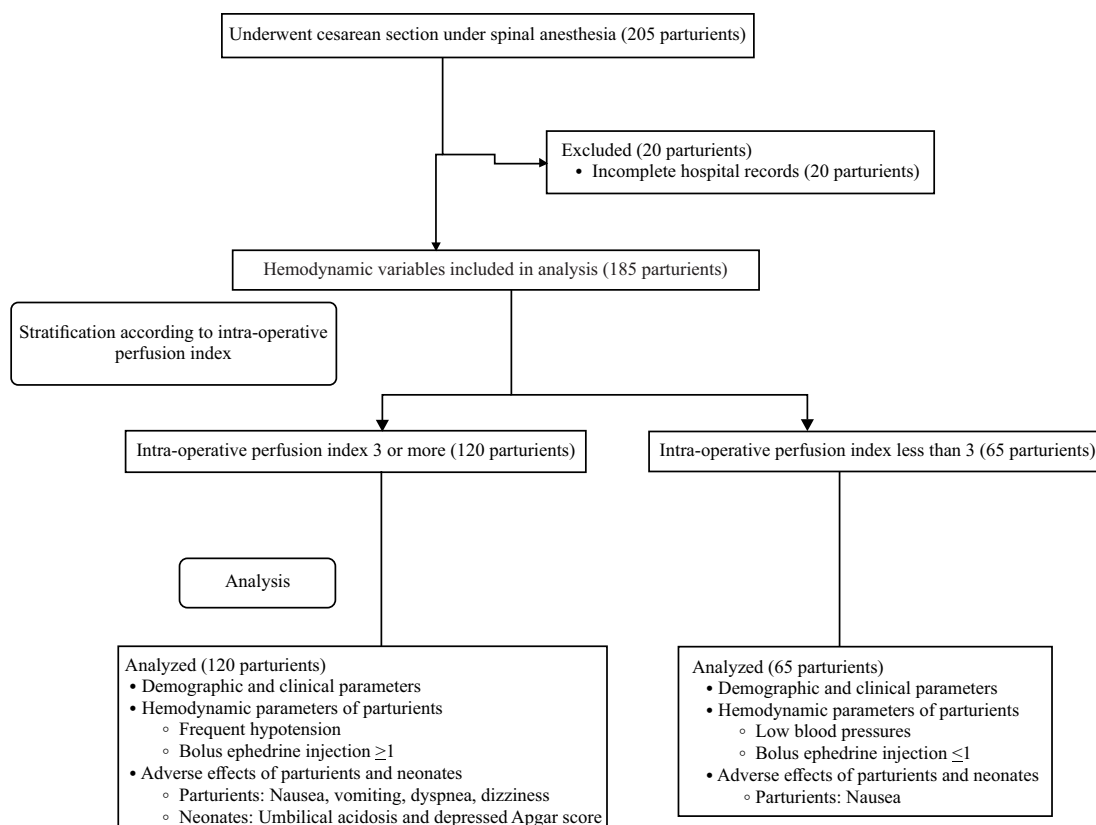


Fig. 1: Study flow chart

Table 1: Demographic and clinical parameters before cesarean section and operative parameters of parturients

Parameter	Cohort					Comparison between cohorts		
	Total	≥3	<3	p-value	df	Test value		
Intraoperative perfusion index	185	120	65					
Number of parturients	27 (27.5-25.5)	26 (27.5-25.5)	27 (27.5-25.5)	0.8011 (Mann-Whitney test)	N/A	3812		
Age of parturients (years)	37 (37.75-36.5)	37 (37.75-36.5)	37 (38-36.5)	0.2291 (Mann-Whitney test)	N/A	3482		
Gestational age (weeks)	114 (62)	80 (67)	34 (52)	0.0786 (χ^2 -test with Yates correction)	1	3.094		
	71 (38)	40 (33)	31 (48)					
Hemoglobin (g)	11.7 (12.15-10.9)	11.8 (12.2-10.5)	11.5 (12-11)	0.6178 (Mann-Whitney test)	N/A	3726		
Body mass index (kg/m ²)	25.2 (25.6-24.8)	25.3 (25.6-24.85)	25.2 (25.5-24.7)	0.5184 (Mann-Whitney test)	N/A	3675		
Administration of bolus ephedrine injection during cesarean section procedures	30 (16)	0 (0)	30 (46)	<0.0001 (χ^2 -test for independence)	3	76.978		
	118 (64)	83 (69)	35 (54)					
	22 (12)	22 (18)	0 (0)					
	15 (8)	15 (13)	0 (0)					
Preoperative perfusion index	3.2 (3.25-3.1)	3.2 (3.25-3.1)	3.18 (3.25-3.11)	0.226 (Mann-Whitney test)	N/A	0		
Preoperative diastolic blood pressure (mmHg)	80 (81-80)	80 (81-80)	80 (81-80)	0.3556 (Mann-Whitney test)	N/A	3581		
Preoperative mean arterial blood pressure (mmHg)	76 (78-72)	75 (78-72)	77 (78-73)	0.2462 (Mann-Whitney test)	N/A	3497		
Ethnicity	169 (91)	109 (91)	60 (92)					
	14 (8)	10 (8)	4 (6)	0.7911 (χ^2 -test for independence)	2	0.4686		
	2 (1)	1 (1)	1 (2)					

Variables are demonstrated as medians with Q3-Q1 in parentheses or frequencies with percentages in parentheses, Normal value of mean arterial blood pressure: 70 to 100 mm Hg. All results were declared significant if p<0.05; df: Degree of freedom, N/A: Not applicable and Test value (Mann-Whitney statistics for Mann-Whitney test and χ^2 -value for χ^2 -test)

Table 2: Hemodynamic parameters of parturients before cesarean section, before administration of bolus ephedrine injection and changes

Level	Perfusion index				Diastolic blood pressure (mmHg)				Mean arterial blood pressure (mmHg)			
	185	185	185	p-value	r	95% CI	185	p-value	r	95% CI	185	p-value
Numbers of parturients	3.2 (3.25-3.1)	80 (81-80)	80 (81-80)	0.8869	0.0105	-0.1382 to 0.1588	76 (78-72)	0.0002	-0.2682	-0.4007 to -0.1247	76 (78-72)	0.0002
Before cesarean section	2.6 (3.3-3)	65 (76-62)	65 (76-62)	<0.0001	-0.9672	-0.9756 to -0.9560	60 (72.5-61)	<0.0001	-0.9157	-0.9368 to -0.8879	60 (72.5-61)	<0.0001
Before administration of bolus ephedrine injection	0 (-0.58 to 0.15)	-16 (-18 to -5)	-16 (-18 to -5)	<0.0001	-0.911	-0.9332 to -0.8818	-12 (-16 to -3.5)	<0.0001	-0.7219	-0.7861 to -0.6422	-12 (-16 to -3.5)	<0.0001
Change after administration of spinal anesthesia	0.0004 (Mann-Whitney test)	<0.0001 (Mann-Whitney test)	<0.0001 (Mann-Whitney test)	N/A	N/A	N/A	<0.0001 (Mann-Whitney test)	N/A	N/A	N/A	<0.0001 (Mann-Whitney test)	N/A
Comparison between before cesarean section and before administration of bolus ephedrine injection	13.455	2.286	2.286	N/A	N/A	N/A	4.195	N/A	N/A	N/A	4.195	N/A

Variables are demonstrated as medians with Q3-Q1 in parentheses, Spearman rank correlation was developed among changes in hemodynamic parameters and changes in the perfusion index, CI: Confidence interval, r: Spearman rank correlation constant and all results were declared significant if p<0.05

Demographic and clinical parameters: A total of 120 (65%) parturients had an intra-operative perfusion index of 3 or more and 65 (35%) parturients had an intra-operative perfusion index of <3. Parturients had a minimum age of 23 years and a maximum age of 29 years. The gestational age of the parturients was a minimum of 36 weeks and a maximum of 39 weeks. Unlike parturients who had an intra-operative perfusion index of less than 3, parturients who had an intra-operative perfusion index of 3 or more required administration of bolus ephedrine injection during cesarean section procedures ($p < 0.0001$, χ^2 -test for independence). There were no significant differences between the age of parturients, gestational age, hemoglobin content, body mass index, pre-operative diastolic blood pressure and pre-operative mean arterial blood pressure between parturients who had an intra-operative perfusion index ≥ 3 and those who had an intra-operative perfusion index <3 ($p > 0.05$). The details of the demographic and clinical parameters before cesarean section and the operative parameters of the parturients were reported in Table 1.

Hemodynamic parameters of parturients: After administration of spinal anesthesia, diastolic blood and mean arterial blood pressures of parturients were decreased and the perfusion index of parturients was increased compared to their pre-operative conditions. The mean arterial blood pressure of parturients before cesarean section, diastolic blood pressure and mean arterial blood pressure before administration of bolus ephedrine injection were negatively correlated with the perfusion index. In addition, changes in diastolic blood pressure and mean arterial blood pressure of parturients after administration of spinal anesthesia were negatively correlated with the change in the perfusion index ($p < 0.0001$ for both, spearman rank correlation).

The details of the hemodynamic parameters of parturients before cesarean section, before administration of bolus ephedrine injection and changes were reported in Table 2.

Adverse effects of parturients and neonates: None of the women reported bradycardia. A total of 45 (24%) parturients experienced nausea, 5 (3%) parturients experienced vomiting, 3 (2%) parturients experienced dyspnea, 5 (3%) parturients experienced dizziness and 6 (3%) parturients experienced decreased levels of consciousness during cesarean section procedure. A total of 2 (1%) neonates reported acidosis and Apgar scores of four (2%) neonates were decreased. Parturients who had an intra-operative perfusion index ≥ 3 before ephedrine administration reported nausea, vomiting, dyspnea and dizziness and their neonates reported umbilical acidosis and depressed Apgar scores. The details of the adverse effects on parturients and neonates during and after the cesarean section procedure were reported in Table 3.

DISCUSSION

In the current study after administration of spinal anesthesia, the diastolic blood pressure and mean arterial blood pressure of parturients decreased. Pre-operative labor pain is associated with hypotension⁷. High pre-operative anxiety decreases diastolic blood pressure¹¹. Spinal anesthesia causes peripheral vasodilatation and venous pooling of blood, leading to hypotension^{12,13}. A gravid uterus with subsequent aortocaval compression that causes low mean arterial pressure exacerbates these effects (hypotension)¹⁴. Decreased responsiveness to vasopressors during pregnancy, with increased sensitivity of nerve fibers to local anesthetics, contributes to severe hypotension after spinal anesthesia for lower-segment cesarean sections¹². After administration of

Table 3: Adverse effects of parturients and neonates during and after cesarean section procedure

Event	Cohort			Comparison between cohorts		
	Total	≥ 3	<3			
Intra-operative perfusion index						
Number of parturients	185	120	65	p-value	Relative risk	95% CI
Nausea	45 (24)	35 (29)	10 (15)	0.0478	1.281	1.0430 to 1.573
Vomiting	5 (3)	5 (3)	0 (0)	0.1638	1.565	1.4020 to 1.747
Dyspnea	3 (2)	3 (3)	0 (0)	0.5530	1.556	1.3960 to 1.734
Dizziness	5 (3)	4 (3)	1 (1)	0.6584	1.241	0.7903 to 1.950
Decreased level of consciousness of parturients	6 (3)	6 (5)	0 (0)	0.0921	1.570	1.4060 to 1.754
Neonatal umbilical acidosis	2 (1)	2 (2)	0 (0)	0.5417	1.551	1.3930 to 1.727
Depressed Apgar scores of neonates	4 (2)	4 (3)	0 (0)	0.2992	1.560	1.3990 to 1.740

Variables are demonstrated as frequencies with percentages in parentheses, Fisher's exact test was used for statistical analysis, All results were declared significant if $p < 0.05$ and CI: Confidence interval (using the approximation of Katz.)

spinal anesthesia, hypotension in parturient is a common phenomenon during cesarean section procedures.

Mean arterial blood pressure before administration of bolus ephedrine injection and changes in diastolic blood pressure and mean arterial blood pressure after administration of spinal anesthesia in the current study were negatively correlated with the perfusion index. The results of the correlation of hypotension with the perfusion index are consistent with those of prospective observational studies^{2,15,16} but were not consistent with those of a prospective observational study¹⁷. After administration of spinal anesthesia to parturients during cesarean section, peripheral pooling of blood causes reduced venous return and decreased cardiac output². Methodological discrimination is responsible for the contradictory results of the current study to those of a prospective observational study¹⁷. A decreased vascular tone increases the perfusion index¹⁸. Intra-operative hypotension in parturients during cesarean section is negatively correlated with perfusion index.

During cesarean section, a bolus ephedrine injection was administered for parturients in the current study. The results of the vasopressor agent (10 mg bolus ephedrine injection) in the current study were consistent with those of prospective observational studies^{4,15}. Ephedrine injection was required only if hypotension (as defined by the protocol)⁴ was reported in parturients. Therefore, bolus injection was administered instead of infusion. Additionally, bradycardia has not yet been reported. In such conditions, a small dose of bolus ephedrine injection is convenient for managing hypotension and cost-effective for parturients with ephedrine. Bolus ephedrine could be preferred over other α -agonist drugs and their formulations if there is no risk of bradycardia.

Parturients who did not develop hypotension (as defined by protocol)⁴ also received a 10 mg bolus ephedrine injection during cesarean section procedures. The aim of cesarean section procedures is to maintain a diastolic blood pressure of 90 mmHg or more to reduce episodes of hypotension⁷. Parturients who did not develop hypotension (as defined by the protocol)⁴ also had a diastolic blood pressure ≤ 80 mmHg after spinal anesthesia. Therefore, they received a 10 mg bolus ephedrine injection during cesarean section procedures. Bolus ephedrine could be recommended in parturients to maintain a diastolic blood pressure during cesarean section under spinal anesthesia.

A total of 37 (20%) parturients required more than one administration of bolus ephedrine injection during cesarean

section procedures. The results of more than one bolus ephedrine injection during cesarean section procedures in the current study are consistent with those of a prospective observational study⁴. Ephedrine has indirect adrenergic receptor activity and weak direct effects on other α -agonist drugs⁷. Therefore, parturients require more than one 10 mg bolus ephedrine injection during cesarean section procedures. Before cesarean section, the diastolic blood pressure of the parturients was not negatively correlated with the perfusion index. Pre-operative parameters of the parturients were at admission to the labor ward, but not just before performing spinal anesthesia. Diastolic blood pressure decreases after entering the labor ward due to anxiety and pre-operative labor pain⁷. In addition, before cesarean section, aortocaval compression in the supine position affects perfusion index recordings¹⁵.

Parturients who had an intra-operative perfusion index ≥ 3 before ephedrine administration and their neonates reported adverse effects during and after cesarean section. Spinal anesthesia leads to acute hypotension that reduces cerebral perfusion, induces transient brainstem ischemia and activates the vomiting center, resulting in vomiting and nausea in parturients⁷. Prolonged hypotension causes dizziness and decreases the level of consciousness in parturients⁷. Hypotension for >2 min is associated with an increase in umbilical venous oxypurines and lipid peroxides, leading to ischemia-reperfusion injuries and neonatal umbilical acidosis⁷. In addition, ephedrine administration is responsible for neonatal umbilical acidosis⁷. Spinal anesthesia and ephedrine treatment for hypotension are responsible for adverse effects on parturients and their neonates during and after cesarean section.

The limitations of the study, for example, observational study and lack of comparisons with other standard methods for measurements of hypotension (e.g., pleth variability index¹³, heart rate¹⁴, ratio of low frequency and high frequency heart rates¹⁷) of parturients during cesarean section procedures. The other limitations of the study, such as cesarean section procedures, were not specified, such as emergency cesarean section procedures and elective cesarean section procedures. Emergency cesarean section procedures result in less hypotension than elective cesarean section procedures⁷.

CONCLUSION

After administration of spinal anesthesia, hypotension in parturients is a common phenomenon during cesarean

section procedures. Intra-operative hypotension in parturients during cesarean section is negatively correlated with perfusion index. Bolus ephedrine could be preferred over other α -agonist drugs and their formulations to maintain the blood pressure of parturients during cesarean section. The perfusion index is a useful tool for predicting intra-operative hypotension and episodes in parturients undergoing cesarean section under spinal anesthesia. Spinal anesthesia and ephedrine treatment are responsible for adverse effects on parturients and their neonates during and after cesarean section.

SIGNIFICANCE STATEMENT

A retrospective study reported that after administration of spinal anesthesia, hypotension in parturients is a common phenomenon during cesarean section procedures. Diastolic blood and mean arterial blood pressure are negatively correlated with the perfusion index after administration of spinal anesthesia. The perfusion index is a useful tool for predicting intra-operative hypotension and episodes in parturients undergoing cesarean section under spinal anesthesia. Spinal anesthesia and ephedrine treatment are responsible for adverse effects on parturients and their neonates during and after cesarean section. The finding will help anesthesiologists uncover critical areas of hemodynamic measurements during obstetric anesthesia that many clinicians have not evaluated.

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