Original Research Article

INVESTIGATION OF HEART RATE VARIABILITY AND THE REQUIREMENT FOR VASOPRESSORS RELATIONSHIP DUE TO HYPOTENSION IN PATIENTS UNDERGOING CAESAREAN SECTION WITH SPINAL ANESTHESIA

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ABSTRACT

Introduction: The most common effect of spinal anesthesia applied in cesarean section operations is hypotension. It is very important to prevent hypotension due to fetal bradycardia, acidosis, and maternal effects. **Objective**: This research was conducted to predict and prevent maternal hypotension in pregnant women undergoing elective cesarean section with spinal anesthesia by measuring heart rate variability parameters about hypotension. **Methods:** The study included pregnant women aged 18-45 with ASA 2 classification who underwent elective cesarean section with spinal anesthesia. Using the 'CorSense Heart Rate Variability Finger Sensor by Elite HRV' device and its smartphone application, 102 volunteer pregnant patients were monitored for 5 minutes in the recovery unit, and their data were recorded. After the administration of spinal anesthesia, patients who exhibited a decrease in systolic blood pressure of 20% or more from their baseline values received intravenous ephedrine in 10 mg bolus doses at each instance of low blood pressure measurements. Patients who received a total of 20 mg or more ephedrine doses or more as needed were designated as 'Group 1,' while patients who received less than 20 mg or no ephedrine were classified as 'Group 2.' **Results:** This study was completed with a total of 102 pregnant patients With 46 patients in Group 1 and 56 patients in Group 2, the relevant parameters that showed a statistically significant difference between patient groups were subjected to ROC analysis for predicting hypotension. It was determined that patients with high HF POWER and TOTAL POWER values had a greater need for vasopressors due to hypotension following spinal anesthesia ($p<0.05$). **Conclusion:** In the research, these values are believed to have the potential to predict hypotension in patients undergoing cesarean sections with spinal anesthesia.

Keywords: Heart Rate Variability; Hypotension; Childbirth Complications; Pregnant; Spinal Anesthesia

ABSTRAK

Pendahuluan: Efek paling umum dari anestesi spinal yang diterapkan pada operasi sesar adalah hipotensi. Sangat penting untuk mencegah hipotensi karena bradikardia janin, asidosis, dan efek maternal. Tujuan: Penelitian ini dilakukan untuk memprediksi dan mencegah hipotensi maternal pada wanita hamil yang menjalani operasi sesar elektif dengan anestesi spinal dengan mengukur parameter variabilitas detak jantung terkait hipotensi. **Metode:** Penelitian ini melibatkan wanita hamil berusia 18-45 tahun dengan klasifikasi ASA 2 yang menjalani operasi sesar elektif dengan anestesi spinal. Menggunakan perangkat 'CorSense Heart Rate Variability Finger Sensor by Elite HRV' dan aplikasi *smartphone* nya, 102 pasien hamil sukarelawan dipantau selama 5 menit di unit pemulihan, dan data mereka dicatat. Setelah pemberian anestesi spinal, pasien yang menunjukkan penurunan tekanan darah sistolik sebesar 20% atau lebih dari nilai awal mereka menerima ephedrine intravena dalam dosis bolus 10 mg pada setiap pengukuran tekanan darah rendah. Pasien yang menerima total dosis ephedrine sebanyak 20 mg atau lebih atau lebih sesuai kebutuhan dianggap sebagai 'Kelompok 1,' sedangkan pasien yang menerima kurang dari 20 mg atau tidak ada ephedrine diklasifikasikan sebagai 'Kelompok 2.' **Hasil:** Penelitian ini diselesaikan dengan total 102 pasien hamil. Dengan 46 pasien di Kelompok 1 dan 56 pasien di Kelompok 2, parameter yang relevan yang menunjukkan perbedaan yang signifikan secara statistik antara kelompok pasien dikenai analisis ROC untuk memprediksi hipotensi. Ditemukan bahwa pasien dengan nilai HF POWER dan TOTAL POWER yang tinggi

memiliki kebutuhan yang lebih besar untuk vasopresor akibat hipotensi setelah anestesi spinal (p<0,05). **Kesimpulan:** Dalam penelitian ini, hasil-hasil tersebut diyakini memiliki potensi untuk memprediksi hipotensi pada pasien yang menjalani operasi sesar dengan anestesi spinal.

Kata Kunci: Variabilitas Denyut Jantung; Hipotensi; Komplikasi Persalinan; Hamil; Anestesi Spinal

INTRODUCTION

Spinal anesthesia is frequently preferred in cesarean section procedures due to its ease of application, rapid onset of action, and advantages such as reduced intraoperative blood loss compared to general anesthesia. Hypotension, one of the complications of spinal anesthesia, occurs in one-third of pregnant women. Intraoperative hypotension, associated with serious complications in the mother such as perioperative acute kidney injury and myocardial ischemia, has been noted to have adverse neurological effects on the fetus in the first hours after birth and can lead to fetal acidemia ([1]). Therefore, predicting and preventing significant hypotension with unwanted effects on the pregnant woman and the fetus is of paramount importance for morbidity and mortality.

In the literature, numerous studies aim to predict and intervene early in intraoperative hypotension following cesarean section under spinal anesthesia. However, these studies have often been insufficient in predicting hypotension or have used methods that lack clinical convenience ([2–4]).

Heart Rate Variability Measurements

Even at a regular rhythm, there is a few milliseconds difference between each heartbeat, known as 'heart rate variability' (HRV). HRV is an important parameter that demonstrates the interaction between cardiac and cerebral systems and is used to obtain detailed information about the autonomic nervous system's control of the heart.

The likelihood of developing hypotension due to spinal anesthesia is higher in patients with pre-existing autonomic dysfunction. Some studies have suggested that hypotension observed in cesarean sections under spinal anesthesia in pregnant women can be predicted using parameters related to HRV, but there are also conflicting results from other studies ([5]).

This research aims to predict significant hypotension that may occur after the administration of spinal anesthesia in pregnant women undergoing elective cesarean section by measuring heart rate variability using a non-invasive device that is clinically convenient. This approach seeks to identify patients at risk of hypotension in advance, allowing for early intervention to reduce the duration and severity of hypotension.

MATERIALS AND METHODS
Ethical Approval and Study Design

This study was initiated after obtaining ethical approval from the Erciyes University Non-Invasive Clinical Research Ethics Committee (2022/698). The study is a non-interventional descriptive observational study with a post-hoc analysis investigating the relationship between heart rate variability and the need for vasopressors due to hypotension in patients undergoing cesarean section between October 2022 and March 2023 in the operating theater unit of Kayseri Erciyes University Hospital.

Study Participants

The study included pregnant women aged 18-45 with ASA 2 classification, who were scheduled for elective cesarean section. Patients with hypertension or any other heart disease during pregnancy, those using medications that could affect heart rate, those undergoing other intraoperative anesthetic techniques, those with contraindications for spinal anesthesia, those who experienced significant blood loss before or during the operation, and those for whom the use of ephedrine was contraindicated were excluded from the study.

Data Collection and Analysis

For the study, the 'CorSense Heart Rate Variability Finger Sensor by Elite HRV' device, which provides heart rate variability measurements through digital pulse wave analysis from the fingertip, was ordered from abroad and obtained for use. Subsequently, the device's existing smartphone application was installed on the research phone. 102 volunteer pregnant patients who had no exclusion criteria and underwent cesarean section under spinal anesthesia in the operating room of Erciyes University between October 2022 and March 2023 were included in the sample after obtaining their consent. All the patients were monitored with the device in the recovery unit at rest. Heart rate variability and parameters were calculated using the data obtained from 5-minute measurements, based on studies indicating correlations between measurements obtained from 24-hour electrocardiographic records and calculations from 5-minute measurements (6). All data were recorded in the phone application without grouping for each patient.

Patients taken to the operating table underwent standard monitoring, including ECG, non-invasive blood pressure, and saturation. All measurements were performed with patients in the supine position. Fluid loading was performed with approximately 1000 ml of crystalloid solution before the procedure and continued with crystalloid infusion during the operation. Patients without the need for intraoperative sedation were included in the study.

Spinal Anesthesia Procedure

Baseline systolic blood pressure values measured before the operation were recorded as 'pre-procedural values' for each patient. Spinal anesthesia was provided with a dose of 0.5% hyperbaric bupivacaine calculated according to the patient's height, using the formula (0.06 x patient's height in cm = bupivacaine dose in mg), administered through a Quincke 25-gauge spinal needle at the L3-4 intervertebral space with the patient in a sitting position, head down (7). A pin-prick test was applied to measure the sensory block level and patients who did not reach the T6 level within 20 minutes or developed a block at levels higher than T4 were excluded from the study. Patients' blood pressure and pulse were noted at specified stages: before spinal anesthesia (pre-procedure), immediately after spinal anesthesia (0 minutes), 1 minute after spinal anesthesia (1 minute), 3 minutes, 5 minutes, 15 minutes, and 30 minutes after spinal anesthesia.

Definition of Hypotension

In this study, a decrease of 20% or more in the baseline systolic blood pressure values measured before the procedure, as measured before the operation, was considered hypotension, following routine practice in the operating room, and ephedrine was administered in intravenous bolus doses of 10

25

mg for patients with low blood pressure measurements. High-dose ephedrine was defined as the intravenous administration of 20 mg or more of ephedrine during the operation. Patients receiving a total of 20 mg or more of ephedrine during the operation were included in 'Group 1', while patients receiving less than 20 mg or no ephedrine were classified as 'Group 2'.

Data Analysis

The data obtained were evaluated using the IBM SPSS 25.0 statistical package program. Descriptive statistics were presented as unit count (n), percentage (%), mean ± standard deviation (mean±sd), median (M), minimum (min), and maximum (max) values. Data distribution was assessed using Q-Q plots, Shapiro-Wilk tests, and histogram graphics. Parametric data were analyzed using Student's t-test for normally distributed data, while non-parametric data were analyzed using the Mann-Whitney U test. Group differences were analyzed using Student's t-test for parametric data, the Mann-Whitney U test for non-parametric data, and ROC analysis. The study was conducted with a 95% confidence interval and a 5% margin of error, and a p-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Descriptive Statistical Analysis Results Between Patient Groups

In this study, 102 patients were included, with 46 (45.1%) in Group 1 and 56 (54.9%) in Group 2. The ages of Group 1 patients ranged from 19 to 44 years, with a mean age of 28.24±5.47 years, while Group 2 patients' ages ranged from 18 to 45 years, with a mean age of 31.32±6.50 years. Based on the measurements

conducted with the device before the operation, Mann-Whitney U Test results revealed statistically significant differences between Group 1 and Group 2 patients in HRV and time-related measurements, including the root mean square of successive differences between normal heartbeats (RMSSD), the standard deviation of the R-R intervals of normal sinus beats (SDNN), the natural logarithm (LN) and the percentage of adjacent the number of pairs of successive NN (R-R) intervals that differ from each other by more than 50 ms (pNN50%). Regarding frequency domain measurements, statistically significant differences were observed between the groups in TOTAL POWER, Low Frequency (LF) / High Frequency (HF), LF POWER, and HF POWER values. Furthermore, there was a statistically significant difference in the ages of patient groups ($p<0.05$) (Table 1).

The average baseline systolic blood pressure values measured before the operation, the average systolic blood pressure values measured during the intraoperative periods, and the average total ephedrine dosage administered throughout the operation following spinal anesthesia were calculated for the patients. Out of the 102 patients participating in the study, 46 patients received ephedrine doses of 20 mg or higher, while 56 patients received ephedrine doses lower than 20 mg or no ephedrine at all. Based on the measurements conducted in both groups, statistically significant differences were observed in the averages of systolic blood pressure values and the total ephedrine doses administered to patients during the measurements performed at 1st, 3rd, and 5th minutes after spinal anesthesia ($p<0.05$) (Table 2).

Hypotension ROC analysis with TOTAL POWER

In the ROC analysis conducted to assess the predictive power of TOTAL POWER for post-spinal anesthesia hypotension in pregnant women, the AUC (95%) value was calculated as 0.905 (0.848-0.963). The cut-off value was determined as 984.07, with a sensitivity of 83% and specificity of 17% (p 0.0001) (Table 3) (Figure 1).

Table 1. Statistical Analysis Results Between Patient Groups

Variable	Group 1 (n=46)			Group 2 (n=56)			z	u	p-value*
	Mean±SD	Min.	Max.	Mean±SD	Min.	Max.			
Age	28.24±5.47	19.00	44.00	31.32±6.50	18.00	45.00	-2.432	927	0.015
HRV	56.87±4.71	46,00	67.00	47.75±7.39	27.00	60.00	-6.311	351	0.000
RMSSD	42.24±13.30	19.87	78.34	24.50±10.29	5.84	50.32	-6.318	348.5	0.000
SDNN	56.30±16.10	31.45	126.73	39.33±13.22	16.48	87.04	-5.542	464	0.000
LN	3.70±0.30	2.99	4.36	3.10±0.48	1.8	3.9	-6.383	339	0.000
pNN50%	16.28±12.95	3.00	48.00	4.66±4.58	0.00	17.00	-6.009	397	0.000
MEANRR	674.80±100.16	472.49	932.00	644.11±94.60	454.43	863.52	-1.244	1103	0.213
TOTAL POWER	1813.82±991.03	448.19	4809.79	628.87±384.51	126.44	1744.61	-7.122	229	0,000
LF/HF	1.53±0.96	0.18	3.88	3.55±3.82	0.37	22.48	-4.422	630.5	0.000
LF POWER	971.30±599.41	266.85	3240.53	434.12±267.61	90.74	1071.72	-5.568	460	0.000
HF POWER	842.52±677.79	181.34	4081.77	194.68±168.77	17.98	890.36	-7.445	181	0.000
LF PEAK	0.09±0.03	0.04	0.15	0.09±0.09	0.04	0.70	-1.323	1091.5	0.186
HF PEAK	0.24±0.08	0.15	0.45	0.25±0.10	0.15	0.48	-0.475	1217.5	0.635

Mann-Whitney U Test   SD: Standard deviation

Hypotension ROC analysis with HF POWER

In the ROC analysis conducted to assess the predictive power of HF POWER for post-spinal anesthesia hypotension in pregnant women, the AUC (95%) value was calculated as 0.925 (0.876-0.975). The cut-off value was determined as 327.05, with a sensitivity of 85% and specificity of 15% (p 0.0001) (Table 3) (Figure 2).

As a result of the significance analyses conducted, the relevant parameters were subjected to ROC analysis. The ROC analysis of TOTAL POWER and HF POWER values revealed that they could be decisive parameters in predicting hypotension in terms of sensitivity and specificity. The intergroup values were found to be significant in the analysis of the average TOTAL POWER and HF POWER values of Group 1 and Group 2 patients, and high sensitivity was observed in the ROC analysis.

Table 2. Average of SBP (Systolic Blood Pressure) Values and Total Amount of Ephedrine Administered Between Patient Groups

	Group 1 (N=46)	Group 2 (N=56)	p-value
Average of Baseline SBP	127,66 ± 12,8	124,54 ± 11,43	0.202
Average SBP at 0-Minute Post-Spinal	114,41 ± 16,04	122,91 ± 20,09	0.022
Average SBP at 1 Minute Post-Spinal	**94,33 ± 15,01**	**118,33 ± 15,25**	**<0,01**
Average SBP at 3 Minutes Post-Spinal	**89,74 ± 15,26**	**115,49 ± 16,30**	**<0,01**
Average SBP at 5 Minutes Post-Spinal	**99,13 ± 16,69**	**116,91 ± 19,2**	**<0,01**
Average SBP at 15 Minutes Post-Spinal	112,3 ± 11,59	116,58 ± 12,04	0.060
Average SBP at 30 Minutes Post-Spinal	115,83 ± 11,08	115,11 ± 11,37	0.803
Average Total Amount of Ephedrine Administered	**23,04 ± 4,65**	**2,36 ± 4,29**	**<0,01**

Notes: Mean±Standard deviation. Systolic blood pressure values were calculated in mmHg and the amount of ephedrine administered was calculated in mg. SBP: systolic blood pressure

Table 3. Hypotension ROC analysis with TOTAL POWER and HF POWER

	AUC (%95)	cut-off	p-value	Sensitivity (%)	Specificity (%)
TOTAL POWER	0,905(0,848-0,963)	984,07	0,00	0,83	0,17
HF POWER	0,925(0,876-0,975)	327,05	0,00	0,85	0,15

Notes: AUC – Area under the curve

In cesarean-section surgeries, the desired outcome of anesthesia is maternal comfort and safety, along with fetal well-being and the maintenance of vital fetal functions without depression (1). In a study utilizing the 'Hypotension Prediction Index' (HPI) for preventing intraoperative hypotension, the guidance of the index did not meet the expectations of significantly reducing intraoperative hypotension (8). In an article related to the predictability of intraoperative hypotension, it was noted that artificial intelligence programs could accurately predict hypotension, but they did not improve clinical outcomes. It was suggested that with the development of 'Augmented Intelligence' programs, the cause of hypotension, including surgical manipulations, could be determined. These programs could guide clinicians regarding the choice of interventions, such as intravenous fluid replacement, vasoactive agents, or inotropic drugs, aiming to prevent hypotension (9).
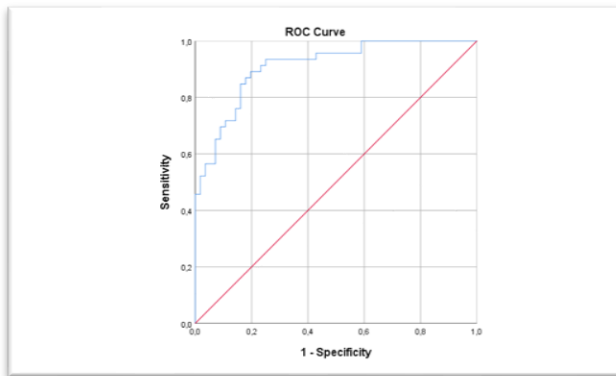
Figure 1. ROC analysis of TOTAL POWER in predicting hypotension

Figure 2. ROC analysis of HF POWER in predicting hypotension

One effective method for preventing hypotension following spinal anesthesia in obstetrics is the administration of ephedrine. Some studies on spinal anesthesia for cesarean delivery have defined a systolic blood pressure drop of 20% or more from baseline as 'hypotension' (3). Yeh, Chang, and Tsai (2020) characterized a 20% drop in systolic blood pressure measured as baseline as a 'hypotension criterion' and administering ephedrine at 20 mg or more as 'high-dose ephedrine' (10). Kang et al. found that the use of ephedrine was essential for preventing maternal hypotension and had a minimal impact on umbilical artery pH. They also suggested the use of 20 mg prophylactic ephedrine infusion for the prevention of maternal hypotension (11). In this study, the usage of ephedrine was considered a predictor of significant hypotension and was used as a criterion for grouping patients.

Some studies have suggested that heart rate variability measurements are related to hypotension following spinal anesthesia in cesarean surgeries. Hanss et al. found in their studies in 2005 and 2006 that patients with higher sympathetic tone were particularly sensitive to hypotension following spinal anesthesia, and an LF/HF ratio greater tha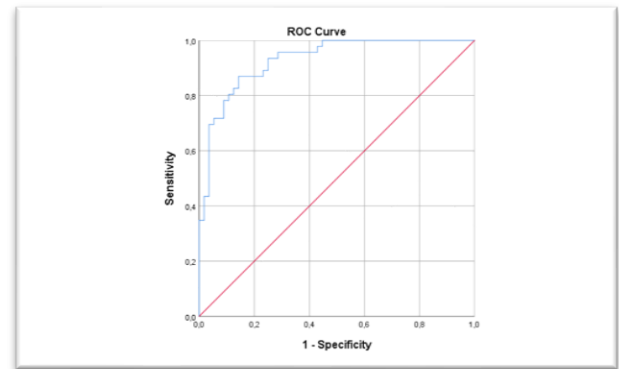n 2.5 was indicative of severe hypotension in pregnant women (9,10). In Bishop et al.'s study from 2017, the LF/HF ratio was identified as an optimal threshold with a value of 2.0 for predicting obstetric spinal hypotension, indicating that heart rate variability analysis techniques have significant potential for predicting and managing hypotension (5). However, in this study, the LF/HF value showed negative significance but did not demonstrate the desired sensitivity in the ROC analysis.

Thomas et al. stated in 2019 that parameters such as SDNN, LF POWER, HF POWER, and LF/HF ratio were essential in predicting the health of the autonomic nervous system (12). In a study conducted by Frandsen et al. in 2022, they found that low TOTAL POWER and HF values measured on the day of surgery were indicative of intraoperative hypotension under general anesthesia (13). Eller in 2007 stated that TOTAL POWER and HF values were associated with atherosclerosis (14). Vinayagam et al. reported in their studies in 2019 that variables like SDNN and RMSSD were independently associated with hypotension and could be useful in predicting hypotension following spinal anesthesia (15). In Shehata et al.'s research from 2019, HRV

was not predictive for hypotension in preeclamptic pregnant women ([16](#)).

This study is limited to patients undergoing cesarean section in the operating room unit of Erciyes University Hospital between October 2022 and March 2023and it is acknowledged that patients may vary in terms of mental stress and anxiety. Despite warning patients to "remain calm" during heart rate variability measurements before entering the operating room, it is unlikely that all patients will be equally unaffected by these factors.

CONCLUSION

This study suggests that elevated TOTAL POWER and HF POWER values, measured by the 'CorSense Heart Rate Variability Finger Sensor by Elite HRV,' indicate a higher likelihood of requiring vasoactive agents for hypotension after spinal anesthesia during cesarean surgery. Despite being an indirect measure of autonomic activity, this device offers a practical means of predicting hypotension in routine cesarean operations. Implementing interventions like preoperative fluid replacement and positioning adjustments for high HF POWER and TOTAL POWER values could mitigate intraoperative hypotension severity. Future research with a larger patient cohort and artificial intelligence integration aims to enhance predictive accuracy for vasoactive agent requirements during elective cesarean surgeries.

Acknowledgment
None.

Conflict of Interest
None of the authors in the study have any conflict of interest.

Authors' Contributions
All authors have contributed to all processes in this research.

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