

# Increased Pulse Wave Velocity as a Predictor of Intraoperative Hypotension in Hypertensive Patients Undergoing Spinal Anaesthesia

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## ABSTRACT

**Objective:** To investigate whether intra-operative hypotension could be predicted with pulse wave velocity (PWV) if measured preoperatively.

**Study Design:** Descriptive analytical study.

**Place and Duration of the Study:** The University Hospital in Turkiye between September 2021 and September 2022.

**Methodology:** All patients aged 30 years and older, whose physical status was graded as I or II according to the American Society of Anaesthesiologists (ASA) classification, were scheduled for elective lower extremity surgery under spinal anaesthesia (SA). Patients previously diagnosed with hypertension (HT) and/or using antihypertensive medication constituted the HT group, and patients with a preoperative systolic blood pressure (SBP) with a value of <140 mmHg constituted the control group. Arterial stiffness measurements of the patient and control groups were performed using the Oscillo metric device [Mobil-O-Graph]. The SBP and diastolic blood pressure (DBP) values were measured. A 20% or more decrease in systolic blood pressure (SBP) compared to the baseline SBP indicated spinal anaesthesia-related hypotension (SARH).

**Results:** The PWV was higher in the HT group than the control group ( $p < 0.001$ ). The rates of patients that developed hypotension at the 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 20<sup>th</sup>, and 30<sup>th</sup> minutes of SA were also higher in the HT group than in the control group ( $p < 0.05$ ). The PWV value was significantly higher in patients with SARH than those without SARH at the 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 20<sup>th</sup>, and 30<sup>th</sup> minutes after SA ( $p = 0.001$ ,  $p = 0.001$ ,  $p = 0.002$ ,  $p = 0.001$ , and  $p = 0.001$ , respectively).

**Conclusion:** Preoperative PWV may be an effective biomarker in predicting spinal anaesthesia-related hypotension in hypertensive patients.

**Key Words:** Hypotension, Hypertension, Adult, Haemodynamic, Spinal anaesthesia.

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## INTRODUCTION

Spinal anaesthesia (SA) is a temporary and central-regional method of anaesthesia that involves the injection of local anaesthetics into the subarachnoid space, either as a stand-alone or in combination with additional medicines. The most common and severe complication of SA, which is widely used in abdominal, pelvis, perineum, and lower extremity surgeries, and in patients with chronic lung disease, is hypotension.<sup>1-4</sup>

There are various definitions of hypotension seen in adult patients in the literature. According to the most commonly used definition of hypotension, a 20% or more decrease in systolic blood pressure (SBP) compared to the baseline SBP indicates hypotension.<sup>5</sup>

It has been reported that the incidence of hypotension in elderly patients over 50 is 75% compared to 36% in young patients.<sup>5</sup> Various mechanisms play a role in the development of spinal anaesthesia-related hypotension (SARH). Anaesthesia-induced sympathetic block and vasodilation in the arteries-arterioles in the block areas cause a decrease in blood flow in other parts of the body. Hypotension is especially common in elderly patients who are haemodynamically unstable and have arterial stiffness (AS).<sup>5,6</sup>

Non-invasive pulse wave velocity (PWV) measurement has been used safely to assess AS in adult patients for many years. It is known that AS, the incidence of which increases with age, is associated with hypotension. In this context, this study was carried out to investigate whether preoperatively measured PWV is associated with intraoperative hypotension in hypertensive and normotensive patients undergoing SA.

## METHODOLOGY

This prospective study was conducted between September 2021 and 2022 after approval by the University's Ethics Committee (2021/139, NCT05537246). Study subjects included ASA I-II

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patients who underwent lower extremity surgery with spinal anaesthesia (SA) and age of 30 years or old. Considering the effect size for PWV as 1.2, alpha as 0.05, and statistical power as 80%, it was determined that at least 84 patients were required to conduct the study.<sup>7</sup> Patients were excluded from the study if diagnosed with vasculitis, peripheral arterial disease, renal dysfunction or allergic to the medicines to be used, for whom SA was contraindicated, or was determined to have a sensory block level of T4 and above after SA, or had undergone cardiovascular or neurological surgery in the last six months. Written informed consent was obtained from all patients. AS measurements of the patient and control groups were performed using the Oscillo metric device [Mobil-O-Graph pulse wave analysis (PWA)].<sup>8</sup> After obtaining consent from all patients, AS measurements of the patient and control groups were made with the Oscillo metric device [Mobil-O-Graph PWA].<sup>9</sup> Patients previously diagnosed with hypertension (HT) and/or using antihypertensive medication constituted the HT group, and patients with a clinical SBP value of <140 mmHg constituted the control group. All HT patients received their antihypertensive treatment before surgery. Patients received a 5 ml/kg intravenous (IV) infusion of crystalloids in the preoperative evaluation room. After the first measurement, the study participants were placed in the required position for SA and the intervention area was cleaned with 10% povidone iodine.

Skin anaesthesia was achieved in all patients with 2% lidocaine at the L4-5 vertebrae level. A dose of 12.5 mg 0.5% hyperbaric bupivacaine was administered after the cerebrospinal fluid (CSF) was detected by the median approach using a 25-gauge Quinke-spinal needle. Subsequently, the patient was quickly placed in the supine position. Surgery was started as it was determined that the sensory block level reached T8-10 with the pinprick test. Ten patients with a sensory block level of T4 and above were excluded from the study.

The SBP, DBP, mean arterial pressure (MAP), pulse, and saturation of peripheral oxygen (SpO<sub>2</sub>) values were measured and recorded with the Dateks-Ohmeda Avance CS<sub>2</sub> pro anaesthesia machine at the preoperative, 1<sup>st</sup>, 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 20<sup>th</sup>, and 30<sup>th</sup> minutes after the SA was administered. During the operation, oxygen support was provided at a rate of 2L/min with a nasal cannula. All patients were kept under observation in the postoperative recovery room for 30 minutes after the operation was performed. Anaesthesia administration and haemodynamic data evaluation were performed by the anaesthesiologist blinded to patient groups. The difference in SBP (%) was calculated with the SPSS programme in the postoperative period ( $[(\text{Preoperative SBP} - \text{SBP others time}) / \text{preoperative SBP}] \times 100$ ).

When hypotension was detected, 5 mg ephedrine was administered. Additionally, 0.5 mg of atropine was administered intravenously to the patients with a heart rate of 45 beats per minute. The medicines administered were recorded in the case follow-up forms.

The conformity of the quantitative data to the normal distribution was conducted with the Kolmogorov-Smirnov test. The variables determined to conform to the normal distribution were compared between the groups using the independent samples t-test, and the results of the comparisons were reported using mean and standard deviation (SD) values. On the other hand, the variables that were determined not to conform to the normal distribution were compared between the groups using the Mann-Whitney U test, and the results of the comparisons were reported using median (25<sup>th</sup>-75<sup>th</sup> percentiles) values. The qualitative variables were compared between the groups using the Chi-square test, and the results of the comparisons were reported using frequency (%) values. Logistic regression analysis was used to determine the risk factors affecting hypotension, and receiver operating characteristics (ROC) curve analysis was used to examine the effect of PWV in differentiating SARH. Probability (p) statistics of <0.05 were deemed to indicate statistical significance.

## RESULTS

The overall study group consisted of 124 patients aged between 31 and 81 (mean 57.9 ± 10.3) years. Of these patients, 70 (56.5%) with hypertension constituted the HT group, and 54 age- and gender-matched patients constituted the control group. SARH was observed in 40.3% (50/124) out of all patients.

The comparison of the demographic and clinical data indicated that body weight, body mass index (BMI) value, PWV, and AUI@75 data and rate of patients with SARH were all significantly higher in the HT group (p < 0.05, Table I).

It was determined that 46 (65.7%) HT patients received antihypertensive treatment. The most commonly used antihypertensive treatment was beta-adrenoreceptor blocking agent (beta-blocker) treatment.

Systolic blood pressure was higher in the hypertension group than the controls at every moment evaluated after the spinal anaesthesia (p < 0.05, Figure 1A). However, DBP was higher only at 5<sup>th</sup> and 10<sup>th</sup> minutes of SA in the hypertension group than in the control group (p < 0.05, Figure 1B).

The frequency of SARH was significantly high in the HT group (HT 58.5%, control 16.6%, p < 0.001). Patients with SARH were significantly older and shorter than patients without SARH and had significantly higher BMI values (p < 0.05). The decrease in SBP reached the level of hypotension (≥20%) at the 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, and 20<sup>th</sup> minutes after SA (p < 0.001). Furthermore, PWV and AUI values were significantly higher in patients with SARH than those without SARH (p < 0.001, Table II). All PWV values, except PWV, measured one minute after the spinal anaesthesia, were higher in the with SARH group than those in the without SARH group (p = 0.001, p = 0.001, p = 0.002, p = 0.001, and p = 0.001, respectively).

**Table I: Distribution of demographic and clinical characteristics and AS data by the study groups.**

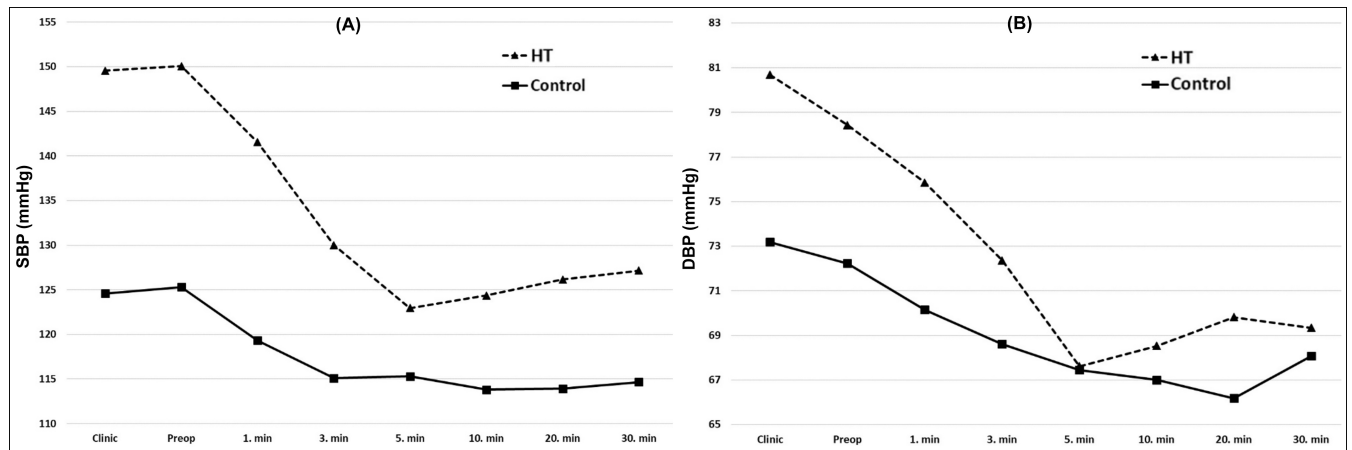
Characteristics	HT (n = 70)	Control (n = 54)	p-value
Age (year)	59.5 ± 8.8	56 ± 11.7	0.073 <sup>a</sup>
Gender (Male / Female) n (%)	26/44 (37.1 / 62.9)	23/31 (42.6 / 57.4)	0.667 <sup>b</sup>
Body weight (kg)	81.1 ± 13.8	74.8 ± 13.7	0.012 <sup>a</sup>
Height (cm)	162 (158 - 170.2)	164.5 (160 - 170.2)	0.161 <sup>c</sup>
BMI (kg/m <sup>2</sup> )	30.4 ± 5.4	27.3 ± 4.9	0.002 <sup>a</sup>
SARH (Y/N) n (%)	41/29 (58.5 / 41.5)	9/45 (16.6 / 83.4)	<0.001 <sup>b</sup>
SARH_1min n (%)	7 (10)	1 (1.9)	0.136 <sup>b</sup>
SARH_3min n (%)	25 (35.7)	5 (9.3)	0.001 <sup>b</sup>
SARH_5min n (%)	31 (44.3)	7 (13)	<0.001 <sup>b</sup>
SARH_10min n (%)	26 (37.1)	4 (7.4)	<0.001 <sup>b</sup>
SARH_20min n (%)	23 (32.9)	5 (9.3)	0.004 <sup>b</sup>
SARH_30min n (%)	18 (25.7)	5 (7.4)	0.016 <sup>b</sup>
Clinic-SBP (mmHg)	150 (141.7 - 159)	127.5 (118.7 - 135)	<0.001 <sup>c</sup>
Clinic-DBP (mmHg)	79 (73 - 88.2)	73.5 (64 - 81)	0.001 <sup>c</sup>
PWV (m/s)	9.5 ± 1.5	7.2 ± 1.4	<0.001 <sup>a</sup>
Aix@75 (%)	32 ± 10.3	25.1 ± 10	<0.001 <sup>a</sup>

Data were expressed as mean and SD or n (%) or median (25<sup>th</sup> - 75<sup>th</sup> percentile). HT: Hypertension, BMI: Body mass index, SARH: Spinal anaesthesia related hypotension, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PWV: pulse wave velocity, Aix: Augmentation index. a: Independent samples t-test. b: Chi-square test. c: Mann Whitney U test.

**Table II: Distribution of demographic and clinical characteristics and haemodynamic data with SARH and without SARH patient groups.**

Characteristics	SARH (+) (n = 50)	SARH (-) (n = 74)	p-value
Age (year)	61.3 ± 8.5	55.6 ± 10.8	0.002 <sup>a</sup>
Gender (Male / Female) n (%)	16/34 (32 / 68)	33/41(44.6 / 55.4)	0.222 <sup>b</sup>
Group HT / control n(%)	41/9 (58.5 / 16.6)	29/45 (41.5 / 83.4)	<0.001 <sup>b</sup>
Body weight (kg)	80.4 ± 14.5	77 ± 13.7	0.197 <sup>a</sup>
Height (cm)	160 (150 - 167.2)	165 (160 - 172)	0.006 <sup>c</sup>
BMI (kg/m <sup>2</sup> )	30.6 ± 5.9	28 ± 4.8	0.008 <sup>a</sup>
Preoperative heart rate	80.1 ± 12.2	79.7 ± 13.5	0.889 <sup>a</sup>
Clinic SBP (mmHg)	150 ± 18	130.6 ± 16.2	<0.001 <sup>a</sup>
SBP_preoperative (mmHg)	149.4 ± 19.8	132.4 ± 18.2	<0.001 <sup>a</sup>
SBP_1 min. (mmHg)	137.9 ± 23.4	127.7 ± 18.3	0.008 <sup>a</sup>
SBP_3 min. (mmHg)	119.8 ± 23.9	125.9 ± 17	0.123 <sup>a</sup>
SBP_5 min. (mmHg)	110.2 ± 20.3	125.9 ± 16	<0.001 <sup>a</sup>
SBP_10 min. (mmHg)	114.9 ± 20.5	123 ± 17	0.019 <sup>a</sup>
SBP_20 min. (mmHg)	118.2 ± 18.5	122.5 ± 16.4	0.175 <sup>a</sup>
SBP_30 min. (mmHg)	120.8 ± 17.2	122.2 ± 15.4	0.637 <sup>a</sup>
SBP_preop-SBP_1 min. difference (%)	3.6 (0.4 - 14)	2.6 (-1.4 - 7.4)	0.08 <sup>c</sup>
SBP_preop-SBP_3 min. difference (%)	20.8 (5.9 - 26.9)	4.8 (-1.1 - 11.9)	<0.001 <sup>c</sup>
SBP_preop-SBP_5 min. difference (%)	26.9 (17.8 - 35)	4.8 (0 - 9.1)	<0.001 <sup>c</sup>
SBP_preop-SBP_10 min. difference (%)	25.1 (12.4 - 32)	6.8 (0.6 - 13.9)	<0.001 <sup>c</sup>
SBP_preop-SBP_20 min. difference (%)	21.3 (9.5 - 29.3)	6.2 (1.7 - 15.9)	<0.001 <sup>c</sup>
SBP_preop-SBP_30 min. difference (%)	17.6 (10.2 - 26.3)	7.2 (0.9 - 13.4)	<0.001 <sup>c</sup>
PWV (m/s)	9.4 ± 1.5	7.8 ± 1.8	<0.001 <sup>a</sup>
Aix@75 (%)	33 ± 9.7	26.3 ± 10.5	<0.001 <sup>a</sup>

Data were expressed as mean and SD or n (%) or median (25<sup>th</sup> - 75<sup>th</sup> percentiles). HT: Hypertension, BMI: Body mass index, SARH: Spinal anaesthesia related hypotension, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PWV: Pulse wave velocity, Aix: Augmentation index. a: Independent samples t-test. b: Chi-square test. c: Mann-Whitney U test.



**Figure 1: Comparison of SBP and DBP data between study groups over time (A) Systolic blood pressure (B) Diastolic blood pressure.**

Logistic regression analysis revealed that the presence of HT and advanced age increased the risk of SARH by 6.441 and 1.059 times, respectively, whereas tallness decreased the risk of SARH by 0.933 times ( $p < 0.05$ ). On the other hand, it was found that gender and body weight did not contribute to the development of SARH ( $p > 0.05$ ).

ROC analysis was used to assess the efficacy of preoperative PWV in predicting the development of SARH. Consequently, the optimal cut-off value of PWV in predicting the development of SARH was determined as 8.2 m/s. The corresponding area under the curve (AUC) was found to be 0.753, a statistically significant value ( $p < 0.001$ ). Using the said cut-off value, PWV predicted the development of SARH with 82% sensitivity and 60.8% specificity.

## DISCUSSION

The data suggests that the AS-PWV value can be a predictor of hypotension that may occur in the early intraoperative period in patients who have undergone spinal anaesthesia. The presence of HT and advanced age contributed significantly to the development of SARH. Moreover, the optimal cut-off value of PWV (8.2 m/s) predicted SARH with 82% sensitivity and 60.8% specificity.

The mean age of the overall study group was  $57.9 \pm 10.3$  years. The incidence of HT in the overall study group was 56.5%, higher than the HT rate of 42.3%, found in a comprehensive study conducted in a similar age group in the authors' country.<sup>10</sup> Lifestyle changes, salt-rich diets, and lack of physical exercise have significantly contributed to increased HT in adults in recent years. In parallel, the fact that the BMI value of the overall study group was found to be  $30.4 \pm 5.4$  kg/m<sup>2</sup>, which is close to the obesity threshold, is likely to have contributed to the high incidence of HT in the study group.

Hypotension may develop in elderly patients depending on the technique preferred in spinal anaesthesia and comorbid conditions. Since the definition of hypotension is different in the studies, the incidence of general anaesthesia and spinal anaesthesia hypotension is in a very wide range in the literature.<sup>5,11-13</sup> In this study, a decrease of 20% or more in SBP compared to the baseline value, one of the most widely used criteria for hypotension in the literature, was deemed to indicate hypotension. Similar to the incidence of SARH in the literature, the incidence of SARH was high in the entire study group and HT group (40.3% and 58.6%, respectively). Advanced age, obesity, and sensory block level were reported as the risk factors in the development of SARH in the literature. Similarly, it was determined that the patients with SARH were older than the patients without SARH in the present study. In elderly patients, insufficient increase in heart rate in response to the hypotension and an insufficient peripheral vascular resistance may cause SARH.

The relationship between obesity and SARH has been reported in the literature.<sup>14,15</sup> Along these lines, in this study, the mean BMI of patients with SARH ( $30.6 \pm 5.9$  kg/m<sup>2</sup>) was found to be significantly higher than the patients without SARH ( $28 \pm 4.8$ ). On the other hand, a few studies in the literature did not find any relationship between BMI and SARH.<sup>16</sup> It is known that the incidence of hypotension increases at T4 and higher sensory block levels with the development of SARH. Therefore, in this study, the same medicine was administered to all patients at the same dose from a similar level in the sitting position, and patients who developed a sensory block level of T4 and above were excluded from the study.

The sympathetic nervous system activity is increased in HT patients. Sympathetic blockade after SA may cause prolonged and severe hypotension in HT patients. The increase in the incidence of SARH with the presence of HT and advanced age has been reported in previously conducted studies investigating haemodynamic changes after SA in hypertensive and normotensive patients. In contrast, a study comparing the haemodynamic effects of SA administered with hyperbaric bupivacaine did not reveal any significant difference between hypertensive and normotensive patients in terms of the development of SARH.<sup>1</sup> Similar to this study, SARH frequency was found to be higher in the HT group. Therefore, preoperative measures should be taken to ensure haemodynamic stability and reduce the risk of SARH in haemodynamically unstable patients undergoing elective surgery.

In recent years, arterial stiffness has attracted the attention of researchers and its role in the development of cardiovascular diseases has become the focus of interest.

It has been reported that the PWV, the best indicator of AS, can be used as an independent biomarker to predict the future development of cardiovascular diseases.<sup>17</sup> In many studies, PWV was reported to be higher in hypertensive patients than healthy adults.<sup>18,19</sup> In accordance with the literature, PWV was quite high in patients with HT. Increased PWV may be an indicator of increased haemodynamic problems. The high PWV values in HT patients will likely contribute to patient morbidity and mortality in the long term.

There are limited studies in the literature evaluating the incidence of intraoperative hypotension and its relationship with AS in patients with hypertension. Furthermore, these studies addressed the predictive value of preoperative PWV for intraoperative hypotension in patients undergoing general anaesthesia and not SA. Moreover, most of these studies were conducted with very few patients. Nevertheless, most of these studies found that preoperative PWV was associated with intraoperative hypotension.<sup>7,19-21</sup> A recent study conducted with 95 HT patients has speculated that preoperative PWV, which can be easily measured in a non-invasive manner, could be a good predictor of hypotension at the 30<sup>th</sup>

second of intubation during the induction of general anaesthesia. Nonetheless, the study reported that the fact that patients included in the study were mild-risk (ASA I or II) patients, may not allow generalisation of the study results to high-risk patients.<sup>20</sup> This is the first study evaluating the relationship between preoperative PWV and SARH in hypertensive and normotensive patients undergoing SA.

The preoperative PWV was significantly higher in intraoperative with SARH (n = 50) patients than without SARH (n = 74) patients (9.4 ± 1.5 m/s vs. 7.8 ± 1.8 m/s). However, step-wise logistic-regression analysis revealed that PWV did not contribute to the factors affecting the development of SARH. ROC analysis of PWV in predicting hypotension after SA revealed that it is a highly effective biomarker in predicting hypotension but lacks the sensitivity and specificity required for its use as a diagnostic test.

Almost all relevant studies in the literature demonstrated that PWV increases and AS progresses with age.<sup>19,21</sup> Similar to this study, a high correlation was found between PWV and age in both groups.

The study's primary limitation is that only mild-risk (ASA I-II) patients were included in the study. Secondly, patients' lipid profiles that may be associated with AS could not be examined. Thirdly, the anti-hypertensive treatments of the patients in the HT group were not homogeneous. Lastly, the fact that HT patients' diagnosis times and treatment durations were not queried, can be considered another limitation of the study.

## CONCLUSION

The study's findings suggest that preoperative PWV may be an effective biomarker in predicting hypotension after SA in hypertensive patients. Most of the studies conducted so far on AS have been conducted in the field of cardiology. Therefore, prospective, multicentre, large-scale studies are needed to elucidate the relationship between anaesthesia and AS.

### ETHICAL APPROVAL:

The Ethics Committee of Aydin Adnan Menderes University, School of Medicine approved the study with protocol number 2021/139, dated 26 August 2021.

### PATIENTS' CONSENT:

The study was conducted on the medical records of patients who had provided informed consent.

### COMPETING INTEREST:

The authors declared no conflict of interest.

### AUTHORS' CONTRIBUTION:

EB, SY: Conceptualised the study and drafted the manuscript. EB: Took care of patients, provided samples, and revised the manuscript critically.

SY: Performed the statistical analysis and revised the manuscript critically.

Both authors approved the final version of the manuscript to be published.

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