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A comparison of the effects of hyperbaric and isobaric bupivacaine spinal anesthesia on hemodynamics and heart rate variability*

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Aim: To compare the effects of hyperbaric and isobaric bupivacaine spinal anesthesia on hemodynamics and heart rate variability (HRV) in nonobstetric surgery.

Materials and methods: Sixty patients were randomly allocated to 2 groups. Group I (n = 30) received 15 mg (3 mL) of hyperbaric bupivacaine and Group II (n = 30) received 15 mg (3 mL) of isobaric bupivacaine for spinal anesthesia. Hemodynamic parameters were recorded before and after spinal anesthesia over 30 min. Analyses of HRV were performed on the day of surgery, after volume loading, and 20 min after spinal injection. Low frequency (LF) values, high frequency (HF) values, and LF/HF ratios were recorded. The incidences of hypotension and alterations of HRV parameters in both groups were investigated.

Results: The incidence of hypotension was 26.6% and 23.3% in Groups I and II, respectively. There were no significant differences in the LF and HF values and LF/HF ratios between groups. In Group I, LF/HF ratios were significantly lower and HF values were significantly higher at 20 min after spinal anesthesia, in comparison to the baseline value ($P < 0.05$).

Conclusion: Hyperbaric bupivacaine caused a significantly greater decrease in LF/HF ratios and a significantly greater increase in HF values.

Key words: Spinal anesthesia, bupivacaine, heart rate variability, hypotension

1. Introduction

Spinal anesthesia is a form of regional anesthesia used frequently in various lower abdominal, orthopedic, and gynecologic operations, as well as cesarean sections (1–4). Its rapid onset and short duration of action, straightforward application, lower costs, and fewer side effects and complications constitute significant advantages for outpatient procedures (2).

The most significant complication of spinal anesthesia is hypotension, with a frequency ranging between 5% and 56%. Factors that increase the risk of hypotension include patient factors (advanced age, female sex, pregnancy, obesity, diabetes mellitus, hypertension, and anemia) and technical factors such as a block level at or above T5, use of opioids during premedication, and high local anesthetic dosages (5–8).

Heart rate variability (HRV) analysis is a noninvasive marker of sympathovagal balance and has been recently used to determine patients who carry a risk of hypotension after spinal anesthesia, especially in cesarean sections (9,10). Studies comparing hyperbaric and isobaric bupivacaine reported variable results on spinal anesthesia-induced hypotension (11–14). In addition to their role in predicting hypotension due to spinal anesthesia, HRV parameters also undergo significant changes following spinal anesthesia (9,10,15,16). However, there are no reports that have compared the effects of hyperbaric versus isobaric bupivacaine on HRV.

In this study we aimed to compare the effects of hyperbaric and isobaric bupivacaine spinal anesthesia on hemodynamics and HRV in operations other than cesarean sections.

2. Materials and methods

This study included 60 patients between the ages of 18 and 65 with American Society of Anesthesiologists (ASA) status of I or II, for whom lower abdominal, urologic, or lower extremity operations under spinal anesthesia were planned. The Haseki Training and Research Hospital Ethical Committee approved the study protocol. Informed

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consent in accordance with the Helsinki Declaration was obtained from the patients. Patients having contraindications to spinal anesthesia, a history of allergy to local anesthetics, hypertension, cardiovascular illness or diabetes mellitus, intraoperative bleeding that necessitated blood transfusion, operative periods of longer than 2 h, or use of β-blockers were excluded from study, as well as patients with body mass indexes of under 18 or over 25.

The patients were taken to the preparation room without any premedication and an intravenous line was inserted. Next, 500 mL of 6% HES solution was infused in 15 min. The patients were randomly separated into 2 groups using closed envelopes. Spinal anesthesia was given with the patient sitting on the operating table, using a 25-gauge Quincke spinal needle inserted through the L3–L4 space. Patients in the first group were injected with 3 mL of 0.5% hyperbaric bupivacaine, and patients in the second group received 3 mL of 0.5% isobaric bupivacaine in 30 s. Immediately after the injections, the chest was brought into a 30° upward position in both groups. Sensory block was evaluated according to dermatomal distribution using a pinprick test, and motor block was assessed with a modified Bromage score, where 1 = ability to raise extended legs, 2 = ability to flex the knees, 3 = ability to move the feet, and 4 = no movement. Surgery was allowed when sensory block reached the T10 level.

Electrocardiography (ECG), noninvasive blood pressure, and peripheral oxygen saturation were monitored. Hemodynamic parameters including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR) were measured by an assistant and recorded in the following manner: basal value (the average of preoperative 3 consecutive measurements), T0; after fluid loading, T1; and 1, 3, 5, 10, 15, 20, 25, and 30 min after spinal injection, T2–T9. A decrease in SBP of greater than 20% compared to the basal value was accepted as hypotension. Patients with a decrease in SBP of between 20% and 30% received an additional rapid infusion of 500 mL of 6% HES. Patients who did not respond to additional fluid therapy or who had a decrease in SBP of more than 30% received 5 mg of ephedrine. A heart rate of lower than 50 beats/min was accepted as bradycardia and 0.5 mg of atropine was given.

In compliance with task force recommendations, HRV measurements were made at 3 periods: in the morning of the operation (T0), after fluid loading (T1), and at 20 min following spinal injection (T2) (17). A 5-min ECG recording was made with a Norav-800 Holter, then recorded onto an SD card and transferred to a computer. The data were analyzed based on frequency using a NH-300 processing system, and then the low frequency (LF) values, high frequency (HF) values, and LF/HF ratios were determined. During the measurements, the respiratory rate was kept at 12–14 breaths/min by having the patient breathe according to a metronome.

Statistical analysis of the data from the study was done with SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). All numeric data were evaluated for normal distribution using the Kolmogorov–Smirnov test. Differences between the groups were analyzed using Student's t-test for parametric data (SBP, DBP, MBP, and HR) and the Mann–Whitney U test for nonparametric data (LF, HF, and LF/HF ratio). Analysis of variance for repeated measures with Bonferroni correction was used for the sequential measurements of parametric data, and differences were determined by paired t-test. Friedman's analysis of variance was used for nonparametric data and the post hoc Wilcoxon test was applied for multiple comparisons. Categorical data were compared with the chi-square test and Fisher's exact chi-square tests. The value of the LF/HF ratio for the prediction of hypotension risk was investigated with receiver operator characteristic (ROC) curve analysis. The sensitivity and specificity of the threshold LF/HF of 2.5 were calculated. All parametric data are shown as mean ± standard deviation (SD) and nonparametric data are shown as median and range. Categorical values are shown as number of cases and percentages. $P < 0.05$ was accepted as the limit for statistical significance.

3. Results

The study included 60 patients, including 7 females and 53 males, with a mean age of 36.7 ± 13.1 years. There were no statistically significant differences between the groups with respect to age, height, weight, ASA score, sex, maximal sensorial block height, or the incidence of hypotension and bradycardia ($P > 0.05$; Table).

The results of the HRV analysis are shown in Figures 1–3.

There were no significant differences in the LF and HF values and LF/HF ratios between groups. In Group I, the LF/HF ratio was significantly lower and HF values were significantly higher 20 min after spinal anesthesia in comparison to the baseline value ($P < 0.05$). One out of the 8 patients with a LF/HF rate over 2.5, and 14 among 52 patients with rates below 2.5, developed hypotension. ROC analysis showed that the area under the curve was 0.507 ($P = 0.932$), and when the limit for the LF/HF ratio was taken as 2.5, the sensitivity and specificity were 0.13 and 0.89, respectively.

Intergroup comparison of SBP measurements taken 5 min after spinal injection (T4) showed that Group I had significantly higher values than Group II ($P < 0.05$). The difference between SBP values in these 2 groups was not significant in other time periods. SBP values were significantly higher in Group I at T2, and in Group II at T1 and T2, in comparison to the baseline value (P

Table. Demographic data, block height, and the frequency of hypotension and bradycardia.

	Group I (n = 30)	Group II (n = 30)
Age (years)	36.8 ± 12.4	36.6 ± 14
Weight (kg)	78.1 ± 18.1	74.9 ± 15.3
Height (cm)	173.4 ± 7.6	173 ± 6.8
Sex, M/F	27/3	26/4
ASA I/II	24/6	25/5
Bradycardia (%)	2 (33.3%)	3 (36.7%)
Hypotension (%)	8 (26.6%)	7 (23.3%)
Maximal sensorial block height (dermatome)[a]	T_7 (T_4–T_{11})	T_8 (T_4–T_{12})

The data are given as mean ± SD, number of cases, percentages, and [a]median (maximum and minimum block height).

< 0.05). SBP values were significantly lower in Group I at T6, T7, and T9, and in Group II at T7, T8, and T9, in comparison to the baseline value (P < 0.05; Figure 4). The difference between DBP measurements in the 2 groups was insignificant at all time periods. DBP values were significantly lower in Group I at T5, T6, T7, and T8, and in

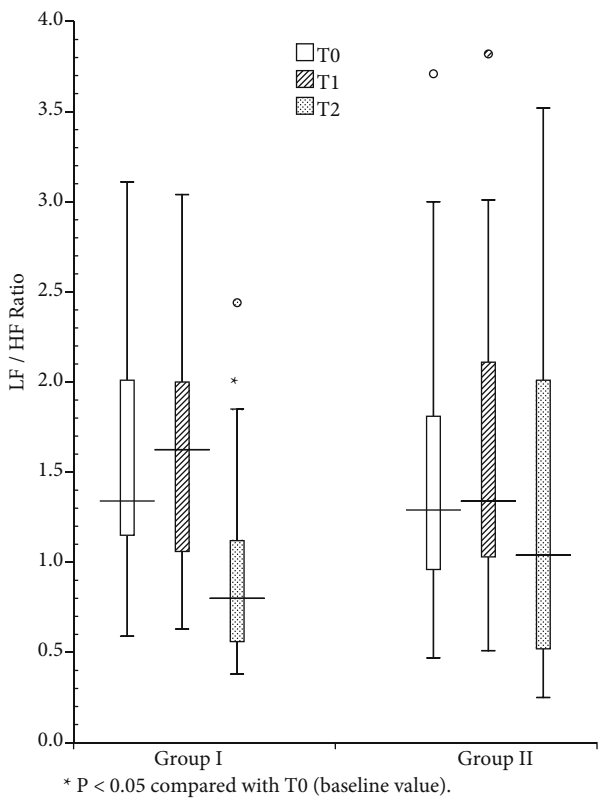

Figure 1. Boxplot distribution of the LF/HF ratios of Groups I and II at the T0, T1, and T2 time points. The horizontal lines from the bottom to the top represent the 10th, 25th, 50th (median), 75th, and 90th percentiles. Outlying values are represented by circles.

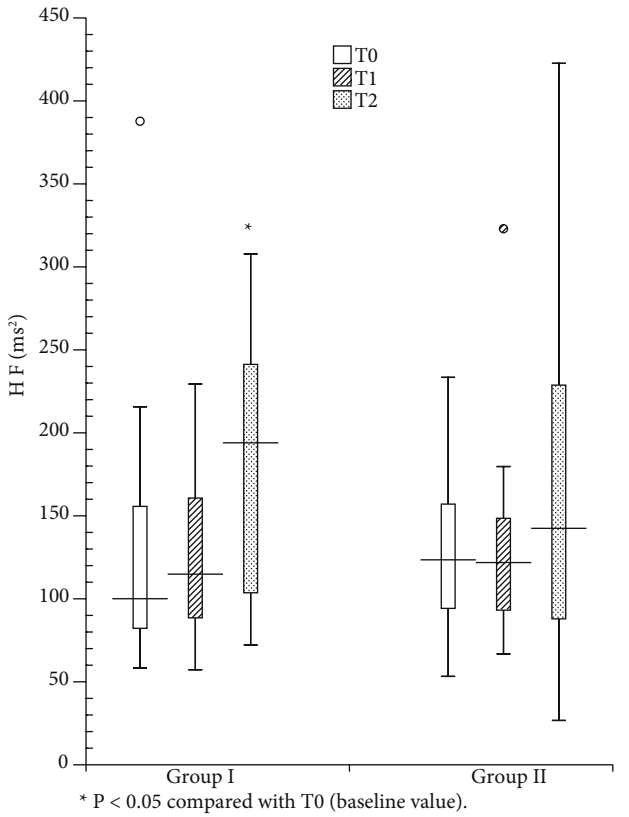

Figure 2. Boxplot distribution of the HF values of Groups I and II at the T0, T1, and T2 time points. The horizontal lines from the bottom to the top represent the 10th, 25th, 50th (median), 75th, and 90th percentiles. Outlying values are represented by circles.

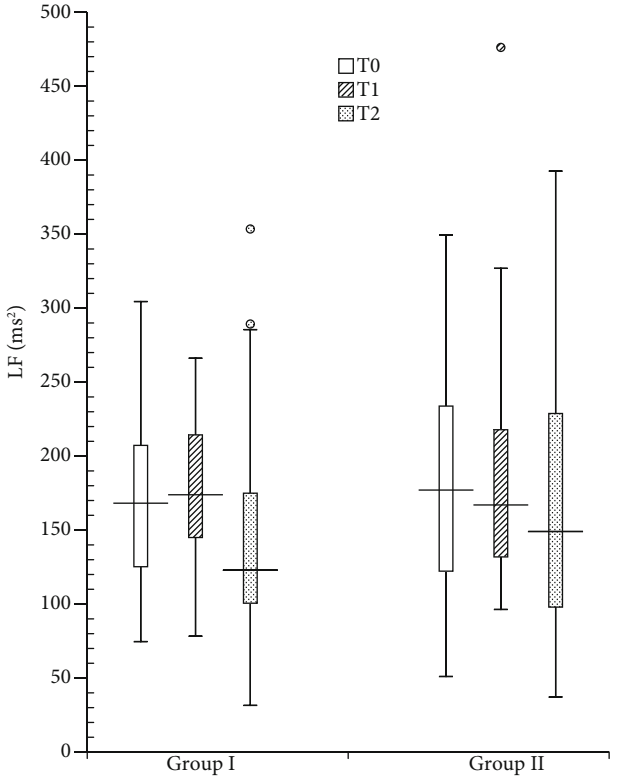

Figure 3. Boxplot distribution of the LF values of Groups I and II at the T0, T1, and T2 time points. The horizontal lines from the bottom to the top represent the 10th, 25th, 50th (median), 75th, and 90th percentiles. Outlying values are represented by circles.

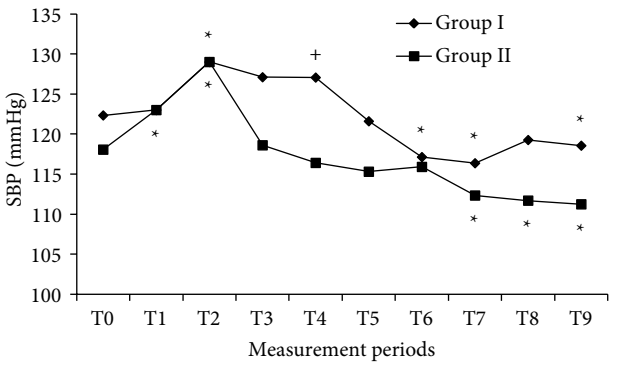

Figure 4. Systolic blood pressure (SBP). *: P < 0.05 compared with baseline value, +: P < 0.05 between Group I and Group II.

Group II at T3, T5, T7, T8, and T9, in comparison to the baseline value (P < 0.05; Figure 5). The difference in MBP values between the 2 groups was insignificant at all time periods. MBP values were significantly lower in Group I at T6 and T7, and in Group II at T5, T7, T8, and T9, in

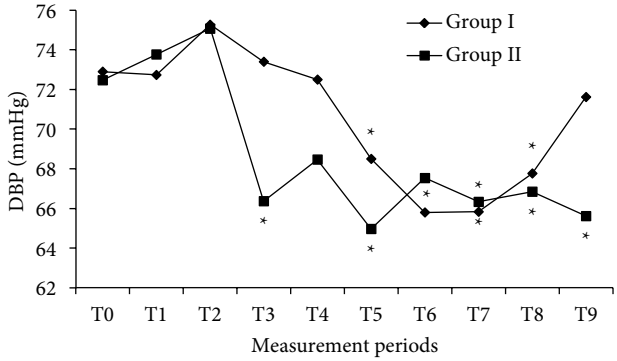

Figure 5. Diastolic blood pressure (DBP). *: P < 0.05 compared with baseline value.

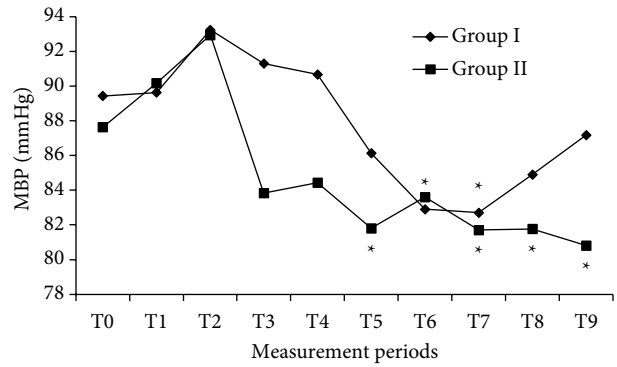

Figure 6. Mean blood pressure (MBP). *: P < 0.05 compared with baseline value.

comparison to the baseline value (P < 0.05; Figure 6). There were no significant differences in HR values between the 2 groups in all periods. In the intragroup comparison, when compared to the baseline values, Group I and Group II had significant increases at T2, T3, and T4 (P < 0.05; Figure 7).

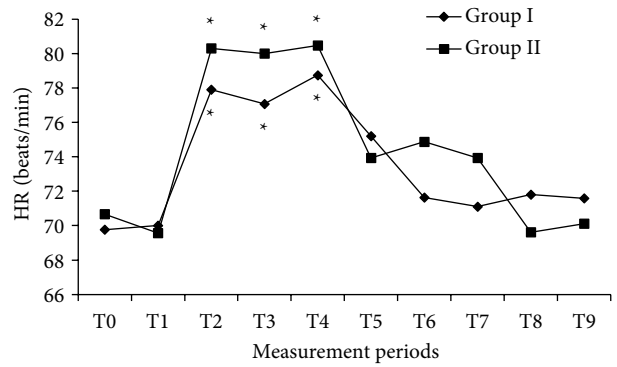

Figure 7. Heart rate (HR). *: P < 0.05 compared with baseline value.

4. Discussion

In our study, 15 patients (25%) developed hypotension that resolved shortly after fluid replacement or ephedrine treatment, with 8 (26.6%) in the hyperbaric bupivacaine group and 7 (23.3%) in the isobaric bupivacaine group. The difference between the 2 groups was not significant with respect to the frequency of hypotension (Table). The reported rates of spinal anesthesia-induced hypotension in various studies range between 5% and 60%. This wide range is due to the description of hypotension, the time interval when blood pressure measurements are made, age, sex, type of operation, presence of hypertension or diabetes, and the techniques used to collect data (5–8).

A decrease in venous return and systemic vascular resistance caused by sympathetic nervous system block are the primary causes of spinal anesthesia-induced hypotension. Additionally, extension of the sensory block beyond the T4 level will lead to blockage of cardioaccelerator fibers, with subsequent decrease in the heart rate and cardiac output (18). A close correlation between peak block height and the amount of systolic pressure decrease and incidence of hypotension was shown (19). Sensory blocks at or above T6 increased hypotension risk by 2.4 times (7,20), which increased to 3.8 in sensory blocks at or above T5 (19).

The baricity of a local anesthetic used in spinal anesthesia influences the block level and, as a result, the severity and frequency of changes in blood pressure. Hyperbaric bupivacaine has a greater tendency for cephalic spread than isobaric bupivacaine; therefore, it has a greater peak sensory block height and, as a result, a greater incidence of hypotension and blood pressure drops in patients undergoing nonobstetric surgery (11,12,21,22).

On the other hand, our results showed that peak sensory block height and incidence of hypotension were similar in hyperbaric and isobaric bupivacaine (Table). This may be related to the slight elevation of the torso after spinal injection. Similarly, Kooger Infante et al. (23) observed that following spinal anesthesia with 3 mL (15 mg) of hyperbaric bupivacaine, patients who had 30° torso elevation had a lower sensory block height and incidence of hypotension compared to those in the horizontal position. The most significant difference between our study and the designs of the studies that showed that hyperbaric bupivacaine caused higher sensory block heights and blood pressure decreases is supine positioning after subarachnoid injections (11,21,22). In our study, we applied torso elevation to all patients after spinal anesthesia. Although we did not have a supine patient group for a control, we believe that the torso-elevated position possibly limited the block height resulting from hyperbaric bupivacaine and the hypotension caused by spinal anesthesia.

Short-term regulation of arterial blood pressure is under control of the autonomous nervous system (24). HRV is a noninvasive and straightforward test that shows the balance between sympathetic and parasympathetic systems at the sinoatrial node level (25). There is general agreement in the literature that the HF component (0.15–0.4 Hz) derived from the spectral analysis of HRV reflects cardiovagal activity and is influenced by respiratory frequency and tidal volume (17,25,26). Although there are studies reporting that the LF component (0.04–0.15 Hz) reflects both the parasympathetic and sympathetic efferent activity, more recent studies show that the LF is principally affected by sympathetic activity (9,10,15,17,27). The LF/HF ratio represents sympathovagal balance and recent studies state that it may be useful in determining patients at risk for hypotension after spinal anesthesia (9,10,15,27).

Our results showed that spinal anesthesia altered the HRV. Spinal anesthesia with hyperbaric bupivacaine resulted in a significant decrease in LF/HF ratio, but the decrease in LF/HF ratios with isobaric bupivacaine was not statistically significant (Figure 1). HF values increased in both groups after subarachnoid injection, but only the increase seen with hyperbaric bupivacaine was statistically significant (Figure 2). LF values decreased after spinal anesthesia in both groups; however, these were not significant (Figure 3).

High basal LF/HF ratios were shown to be associated with marked decreases in LF/HF ratios and LF after subarachnoid block. In elderly patients undergoing prostate surgery, Hanss et al. found that spinal anesthesia with isobaric bupivacaine caused a decrease in LF/HF and LF, along with an increase in HF (27). Their findings showed that the most important factors affecting changes in HRV were basal values. Mean values were 1.2 ± 0.8 in patients with LF/HF of <2.5 before spinal anesthesia, whereas in patients with LF/HF of >2.5, mean values were 5.5 ± 2.5. Fifteen minutes after spinal anesthesia, these values decreased to 0.8 ± 0.6 and 2.2 ± 1.9, respectively. In another study, the authors found that in patients undergoing cesarean sections, HRV measurements taken 15 min after spinal anesthesia revealed similar decreases in LF and LF/HF ratios, the latter associated with HF increase (15). Although these changes in HRV after spinal anesthesia were similar to our results, they were at lower levels in our study. Lower mean basal values in our study may be one cause. Additionally, more patients in our study required vasopressor treatment, which could have affected HRV results. The lack of standardization between vasopressor treatment times and HRV measurements, and also the inability to leave severely hypotensive patients without any vasopressor treatment, makes interpretation of results difficult. In our study, hypotension requiring ephedrine treatment was seen in only one patient who received hyperbaric bupivacaine.

Arakawa et al. (28) found that low epidural anesthesia (T10) was associated with an activation in peripheral sympathetic vasomotor activity, as demonstrated by an increased LF/HF ratio. This activation was eliminated in high block (T5). In patients who underwent spinal anesthesia with isobaric bupivacaine, Fujiwara et al. (29) showed that the height of low block was associated with a significant rise in LF/HF ratios. Therefore, in patients with central neuraxial blocks, the resultant compensatory increase of sympathetic activity in areas above the sympathetic blockade may be another reason why HRV parameter changes related to block height are at lower magnitudes.

The transition from a decubitus position to a sitting position causes sympathetic stimulation, an increase in LF, and a decrease in HF (30–32). In contrast to the studies above, we immediately placed the patients into a slight sitting position after subarachnoid block. We believe that sympathetic stimulation caused by positional change may have contributed to the lower decrease of LF in our study. The significant increase in heart rates compared with control values during the first 5 min after conversion to the sitting position supports this hypothesis.

Tetzlaff et al. (12) found that spinal anesthesia with isobaric bupivacaine caused a decrease in LF and LF/HF without a change in HF. In another study, they found that in patients who were converted to a prone position after a supine position, spinal anesthesia had better preservation of sympathetic activity and hemodynamics when compared to general anesthesia (33). Our results support these studies, which found that in sensory block levels lower than T8, sympathetic stimulation may limit the changes in HRV parameters.

Our literature search did not reveal any studies that compared the effects of hyperbaric versus isobaric bupivacaine on HRV. Sympathetic preganglionic fibers are more sensitive towards the effects of local anesthetics because of small fiber diameters, and sympathetic blocks are a few segments above sensory blocks (34). Cephalic progression of spinal block causes a quantitative decrease in HRV in parallel with block height (16). Although the median sensory block height was only one segment higher in the hyperbaric group, we thought that it could be the reason for the difference in LF/HF ratios.

In contrast to previous studies, we found that the LF/HF ratio was not useful in determining the risk of hypotension due to spinal anesthesia. In the literature, the LF/HF ratio related to hypotension is >2.5. It is reported that there is a strong correlation between LF/HF ratio and the decrease in SBP with spinal anesthesia in elderly patients undergoing surgery or in pregnant females undergoing cesarean sections (9,10,15,27). Patients with LF/HF of >2.5 are also reported to have a higher incidence of hypotension and vasopressor requirements. We suggest that a lower mean LF/HF ratio and a low number of patients with LF/DF of >2.5 in our study was the reason for the difference from other studies. Our findings were similar to those of Meyhoff et al. (35), who found no difference in the incidence of spinal anesthesia-induced hypotension in patients with LF/HF above or below 2.5 (6 patients among 9 and 9 patients among 15, respectively). The principal goal of this study was to evaluate the effect of spinal anesthesia on HRV, not to use HRV as a prognostic tool.

In conclusion, our findings support that LF and LF/HF are indirect markers of sympathetic activity. We found that there was no difference between hyperbaric and isobaric bupivacaine with respect to maximal sensory block height and frequency of hypotension and bradycardia when patients were placed in a 30° sitting position after spinal injection. We observed similar hemodynamic effects with isobaric and hyperbaric bupivacaine. However, we found that hyperbaric bupivacaine caused a significant decrease in LF/HF ratios and a significant increase in HF values. Although we observed that analysis of HRV was inadequate for the prediction of hypotension due to spinal anesthesia, this may be due to the limited number of patients with high basal sympathetic activity, and therefore we think that further studies are needed.

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