Usefulness of non-invasive cardiac output monitoring in elderly patients undergoing monopolar transurethral resection of the prostate: a pilot study

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Abstract
Objective: To assess the impact of irrigating fluid on hemodynamic profiles using real-time non-invasive cardiac output monitoring (NICOM) in elderly patients undergoing monopolar transurethral resection of the prostate (TURP).
Methods: Twenty patients between 65 and 80 years of age who were scheduled for monopolar TURP and received spinal anesthesia up to T10 were enrolled. Irrigating fluid (2.7% sorbitol with 0.5% mannitol solution) was used. Hemodynamic profiles including cardiac index, and stroke volume variation (SVV) using NICOM were obtained. Estimated irrigating fluid absorption was indirectly calculated.
Results: The median amount of irrigating fluid used was 6000 mL. The median SVV was 11%, which increased to 12% at 10 minutes after initiating surgery. No significant changes in the cardiac index were observed. The estimated absorption of irrigating fluid was almost zero.
Conclusions: Although the estimated amount of irrigating fluid that was absorbed was negligible, the increase in SVV may indicate intravascular volume depletion with diuresis resulting from mannitol in the irrigating fluid early during irrigation. Therefore, even during short irrigating times, intensive hemodynamic monitoring should be performed to monitor the possibility of intravascular volume depletion as well as volume overload, especially immediately after large amounts of irrigating fluid are used.

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Keywords
Hemodynamic monitoring, irrigating fluid absorption, cardiac output, spinal anesthesia, transurethral resection of prostate, intravascular volume depletion, volume overload

Introduction
Transurethral resection of the prostate (TURP) is the gold standard treatment for benign prostate hyperplasia. During monopolar TURP, a solution containing 1.5% glycine or 2.7% sorbitol is commonly used for irrigation at a height of over 60 cm. In that context, excessive fluid absorption may occur through the exposed prostatic venous sinus. This may increase the intravascular volume and left ventricular end diastolic volume, which can impair cardiac function in patients with reduced cardiovascular reserve. Recent reports have shown a significant reduction in the prevalence of TURP syndrome, which is characterized by hypervolemia, dilutional hyponatremia, nausea, and mental confusion that are caused by excessive intravascular absorption of irrigating fluids. However, it is still a dangerous complication in some cases, especially in patients with multiple co-morbidities.

Most patients who undergo TURP are elderly, and they are afflicted with multiple diseases. Hypertension, diabetes, coronary artery disease, and pulmonary disease are the most common conditions. Additionally, the incidence of major acute cardiovascular events (MACE) after TURP was reported to be about 1%, and mortality was significant higher in patients with MACE. In these patients, a low spinal block is usually recommended to avoid significant hemodynamic changes and to allow for the easy detection of systemic fluid absorption. Proper hemodynamic monitoring is also necessary to reduce the incidence of MACE and mortality rates during TURP.

The amount of systemic irrigating fluid absorption may differ by anesthetic method. Gehring et al. showed that systemic absorption of irrigating fluid containing ethanol and a 2.7% sorbitol–0.5% mannitol solution was higher during spinal anesthesia compared with during general anesthesia, and this was traced by the blood ethanol concentration. However, the mean arterial pressure (MAP) was also significantly decreased at the time of peak intravascular absorption, and it did not return to the baseline value even when the patient was discharged from the recovery room. This suggested that the spinal block level may have been too high when Gehring et al. used 17.5 mg of bupivacaine. Therefore, investigation of hemodynamic profiles and fluid absorption during and after monopolar TURP with low-dose spinal anesthesia is required.

The non-invasive cardiac output monitoring (NICOM) device is based on a bio-reactance technique and analyzes the voltage shift that is driven from the pulsatile ejection of the left ventricle through frequency-modulation and phase-modulation. Cardiac output that is measured by NICOM is as accurate as that detected using thermodilutional pulmonary artery catheters. Additionally, indices that are obtained using the device including stroke volume variation (SVV) can be used for appropriate fluid and hemodynamic management. Therefore, NICOM may be useful for measuring cardiac output during TURP in awake patients.
The purpose of this study was to use real-time NICOM to assess the impact of irrigating fluid on hemodynamic profiles in elderly patients undergoing monopolar TURP with spinal anesthesia.

**Methods**

**Study design and inclusion and exclusion criteria**

This prospective observational study was conducted at the Severance Hospital, Yonsei University Health System, Seoul, Korea, and the study protocol was approved by the institutional review board (IRB number, 4-2015-0362) and registered at www.ClinicalTrials.gov (identified: NCT02483819). The study protocol conformed to the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained from all patients before patient enrollment.

Twenty patients between 65 and 80 years of age who were scheduled to undergo elective monopolar TURP under spinal anesthesia were consecutively enrolled. Patients with contraindications to spinal anesthesia including bleeding diathesis, infections at the puncture site, hypersensitivity to any local anesthetics, or pre-existing neurologic disease were excluded. Patients with a height less than 150 cm, history of coronary artery bypass surgery, dementia, or difficulty understanding during the informed consent process were also excluded.

**Anesthetic management and data collection**

To prevent hypotension, all patients received intravenous pre-hydration, which consisted of 5 mL/kg lactated Ringer’s solution before spinal anesthesia. No premedication was given. In addition to routine standard monitoring including non-invasive arterial blood pressure, electrocardiogram, and pulse oximetry (SpO2), a NICOM™ monitoring device (Cheetah Medical, Portland, OR, USA) was used to continuously monitor the cardiac index and stroke volume. Mean blood pressure (MBP), heart rate (HR), SpO2, cardiac index, SVV, and total peripheral resistance (TPR) were continuously monitored throughout the surgery.

After hemodynamic parameters were measured, patients were placed in the lateral position, and then spinal block was performed with a 0.5% hyperbaric bupivacaine (6 mg) using a 25-gauge Quincke needle (Hakko Co. Ltd., Chikuma, Japan) at the L3–4 or L4–5 intervertebral space. Spinal anesthesia was induced by an anesthesiologist who was not involved in the study. Patients were immediately placed in the supine position, and the block level was adjusted to reach the level of T10. The peak sensory block level was defined when the same level persisted over four consecutive pin-prick tests every 2 minutes. Hemodynamic parameters were recorded before spinal anesthesia (T0), immediately after the peak sensory level was reached (T1), 10 minutes after the start of surgery (T2), 20 minutes after the start of surgery (T3), 30 minutes after the start of surgery (T4), and at the end of the surgery (T5).

Patients received monopolar TURP in the lithotomy position with the irrigating fluid (2.7% sorbitol with 0.5% mannitol solution) at a level of 60 cm above the operating table. Intravenous fluid (0.9% NaCl) was maintained at a rate of 2 mL/kg/hour during surgery. When hypotension (MBP <65 mmHg or decreased to MBP <20% of baseline) or bradycardia occurred, the patient was treated with additional fluid including 10 mL/kg of lactated Ringer’s solution, intravenous ephedrine, or intravenous atropine depending on SVV (>12) and HR (<45 bpm).

Preoperative (before spinal anesthesia) and postoperative (1 hour after surgery)
levels of serum sodium, hemoglobin, and hematocrit were also measured. The estimated absorption of irrigating fluid was indirectly calculated using the following formula: extracellular fluid (ECF) excess = % decrease in sodium \times ECF (0.2 \times body weight).^{16}

Additionally, intraoperative fluid intake (lactated Ringer’s solution) and the amount of irrigating fluid used were also recorded. Additionally, use of vasopressors, analgesic requirements, incidence of TURP syndrome, resected prostate volume, and side effects related to spinal anesthesia (e.g., nausea, vomiting, pruritus, or post-dural puncture headache) were also evaluated.

### Statistical analysis

This study was designed to observe changes in the cardiac index and hemodynamic data in patients during TURP with spinal anesthesia. We defined a decrease in cardiac index that was greater than 15% after 30 minutes of surgery compared with the baseline value to be significant for the primary end point analysis.^{16} Given a type-1 error of 0.05 and a power of 0.8, it was determined that 16 patients were required for statistical significance. Considering a 10% drop-out rate, 20 patients were included in this study.

Statistical analysis was performed using SPSS version 20 (SPSS, IBM, Armonk, NY, USA). The results were expressed as the median (interquartile range) or as the number of patients (percentage). The Wilcoxon signed-rank test was used to determine any significant differences before and after spinal anesthesia. To account for the time effect on changes in the cardiac index in the same patient, a linear-mixed effects model was applied. $P$ values less than 0.05 after the Bonferroni correction were considered to be statistically significant.

### Results

Between July 2015 and February 2016, 20 male patients were included. There were no patients with a height less than 150 cm. No patients dropped out of the study.

### Patient demographics and perioperative parameters

The patients’ demographic data are shown in Table 1. Seventeen of 20 patients (85%)

| Table 1. Demographic data. | All patients (n = 20) |
|---------------------------|----------------------|
| Characteristic            | Age (years) 72 [67–76] |
|                          | Height (cm) 165 [162–169] |
|                          | Weight (kg) 64 [60–74] |
|                          | Body mass index (kg/m²) 24.2 [21.9–26.5] |
| Comorbidities             | Hypertension (n) 11 (55%) |
|                          | Diabetes (n) 3 (15%) |
|                          | Stroke (n) 5 (25%) |
|                          | Coronary artery occlusive disease (n) 2 (10%) |
|                          | Chronic obstructive pulmonary disease (n) 1 (5%) |
|                          | Others (tumor, thyroid disorder, arrhythmia) (n) 7 (35%) |
|                          | Estimated prostate volume on ultrasound (g) 49 [30–79] |

Values indicate median [interquartile range] or number (%).

All patients were male.
had more than one co-existing disease. Surgery was completed without additional analgesics or anesthetics. The median time from the spinal anesthesia to peak sensory level was 15 minutes. The duration of surgery was 29 (22–43) minutes. The median amount of irrigating fluid used was 6000 mL, and the intraoperative intravenous fluid intake was approximately 600 mL. Additionally, the postoperative serum sodium level was 142 mmol/L, which was similar to the preoperative level (141 mmol/L). The hematocrit level decreased slightly from 41% to 39%, although it was not statistically significant. The estimated ECF excess was almost zero (Table 2).

**Hemodynamic profiles**

Hemodynamic profiles are presented in Figure 1. The median MBP before spinal anesthesia was 111 mmHg. At 10 minutes after the start of surgery, the MBP significantly decreased to 104 mmHg and remained significantly decreased until 30 minutes after the start of surgery (P < 0.05 compared with T0). The MBP then returned to the baseline level at the end of surgery. The median HR was 66 beats/minute before spinal anesthesia and began to decrease significantly at 10 minutes after the start of surgery (P < 0.05 compared with T0). It remained significantly low, decreased to 59 beats/minute at the end of the surgery (P < 0.05 compared with T0). The median SVV was 11% and it increased to 12% at 10 minutes after the start of surgery (T2; P < 0.05 compared with T0). At the end of surgery (T5), SVV was decreased to 10% (P < 0.05 compared with T0). No significant changes in the cardiac index and TPR were observed throughout the surgery. Linear mixed model analysis showed that changes in the cardiac index over time were not statistically significant. There were no episodes of hypotension or bradycardia. No one showed headache, nausea or vomiting, hypotension or hypertension, and electrolyte disturbance during the postoperative period. There were no intraoperative and postoperative complications or adverse events throughout the study period.

| Characteristic                          | All patients (n = 20) |
|----------------------------------------|-----------------------|
| Peak sensory block level              | 9 [8–10]              |
| Time to peak sensory level (minutes)   | 15 [10–20]            |
| Anesthetic time (minutes)              | 70 [60–85]            |
| Surgical time (minutes)               | 29 [22–43]            |
| Resected prostate (g)                 | 28 [16–44]            |
| Fluid intake                           |                       |
| Preoperative hydration (mL)            | 300 [300–350]         |
| Intraoperative crystalloid (mL)        | 300 [250–388]         |
| Amount of irrigating fluid used (mL)  | 6000 [5000–11500]     |
| Hematocrit (%)                        |                       |
| Preoperative                          | 41 [39–44]            |
| Postoperative                         | 39 [37–43]            |
| Sodium (mmol/L)                       |                       |
| Preoperative                          | 141 [140–143]         |
| Postoperative                         | 142 [141–144]         |
| Estimated extracellular fluid excess (mL) | −7 [−21–9]          |

Values indicate median [interquartile range] or number (%).
Discussion

In this pilot study, we hypothesized that the changes in hemodynamic profiles, including cardiac output, would approximately reflect the level of systemic fluid absorption during monopolar TURP. However, we did not find hemodynamic changes that reflected the intravascular fluid absorption level during the 30-minute surgical period. Instead, MBP and HR were decreased and SVV was significantly increased compared with the baseline values during irrigation, although the cardiac index was not reduced significantly. This may have indicated intravascular volume depletion with diuresis because of the mannitol in the irrigating fluid during the early irrigation period.

In this current study, we measured the amount of irrigating fluid absorption using a formula that included preoperative and postoperative serum sodium concentrations, and the estimated amount of irrigating fluid absorbed was negligible.

Figure 1. Median values for hemodynamic variables. (a) Mean blood pressure, (b) heart rate, (c) cardiac index, (d) stroke volume variation, and (e) total peripheral resistance. T0, before spinal anesthesia; T1, immediately after the peak sensory level; T2–4, 10 minutes, 20 minutes, and 30 minutes after the initiation of surgery; and T5, at the end of the surgery. *P value < 0.05 compared with the baseline value after Bonferroni correction.

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There were three possible reasons for this, as follows: 1) low-pressure irrigation; 2) short surgical time; and 3) the use of a sorbitol–mannitol solution. Use of low-pressure irrigation with the fluid bag placed 60 cm above the operating table might reduce the extent of fluid absorption via the exposed prostatic vein. Systemic fluid absorption has been shown to increase as the extent of the prostate resection and the exposure time to the irrigating fluid increases. In this present study, the median values of the surgical time and the resected prostate volume were 29 minutes and 28 g, respectively, and the median amount of irrigating fluid used was 6000 mL. Therefore, a shorter surgical time might be associated with less exposure of the irrigating fluid to the open prostatic vein. Finally, using a 2.7% sorbitol solution containing 0.5% mannitol may induce diuresis, and this could affect the intravascular volume. However, the results should be interpreted with caution because irrigating fluid absorption was indirectly estimated using a serum sodium measurement. Because the serum sodium concentration only reflects the major fluid shift within the initial 10 minutes of the procedure, estimation of fluid absorption using the serum sodium concentration that was measured at postoperative 1 hour might be inappropriate.

In this study, hemodynamic profiles including cardiac output were unchanged after the spinal block level reached T10. However, MBP and HR were significantly reduced at 10, 20, and 30 minutes after the start of surgery. Additionally, SVV was significantly increased at 10 minutes after initiation of surgery. However, the cardiac index and TPR were maintained within acceptable ranges (Figure 1). MBP recovered to the pre-anesthetic values by the end of surgery. Postoperative hematocrit levels were slightly decreased, but serum sodium concentrations were almost unchanged. These results suggest that intravascular volume is decreased early in the surgery using irrigation fluid, which was caused by surgical bleeding or mannitol-induced diuresis. By the end of surgery, the intravascular volume would have been replenished to some extent with irrigating fluid absorption. Thus, there may be a risk of early fluid depletion when using a sorbitol–mannitol solution as an irrigating fluid, based on MBP, HR, and SVV. These results suggest that fluid depletion occurred immediately after using the irrigation fluid and that it recovered at the end of the surgery. This also suggests that intensive hemodynamic monitoring is necessary from the beginning of irrigation to maintain the hemodynamic stability during monopolar TURP, because detailed information on volume status or systemic vascular resistance is difficult to obtain using routine perioperative monitoring, even if the irrigation time is less than 1 hour. When HR or MBP are decreased, clinicians often administer cardiovascular drugs such as atropine or ephedrine to optimize cardiac output, if only routine monitoring is used. However, these drugs may put a strain on the cardiovascular system, and they may not represent the appropriate management if it is the volume depletion that causes hypotension. Moreover, volume depletion is difficult to diagnose during the perioperative period with routine hemodynamic monitoring. Therefore, if NICOM is used, monitoring the cardiac index, SVV, and TPR might provide optimal management of cardiac output, especially in elderly patients who are vulnerable to volume status.

Theoretically, all patients undergoing TURP using irrigation fluid would benefit from NICOM. Specifically, it would be more beneficial for patients with cardiovascular disease or diseases such as cardiomyopathy, coronary artery obstructive disease, heart failure, chronic kidney disease, or pulmonary disease, who require careful
intravascular volume control and cardiovascular drug administration. In addition, there is a possibility that the replenishment volume at the end of surgery might be small because the median surgical time in our patients was about 30 minutes. Therefore, the longer the surgical time, the more fluid absorption that may occur, which may affect hemodynamic profiles. Thus, considering that patients undergoing TURP had various preoperative comorbidities and considering the results of this current study on early volume depletion and late volume replenishment, intensive hemodynamic monitoring using non-invasive NICOM might help to reduce the incidence of MACE and mortality rates by maintaining appropriate volume status and proper cardiovascular management.

As the number of elderly patients with various comorbidities continues to increase, the demand for anesthetic techniques that can minimize hemodynamic changes has also been increased. Low spinal anesthesia is the preferred anesthetic strategy compared with general anesthesia because of its hemodynamic benefits and the ability to detect fluid absorption at an early stage in elderly patients who are undergoing monopolar TURP. In the current study, we obtained a spinal block level of T10 using 6 mg of bupivacaine, and the hemodynamic status was stable until the beginning of irrigation. Gehring et al. reported that intravascular fluid absorption with TURP occurs more markedly with spinal anesthesia compared with general anesthesia. They suggested that the large fluid absorption was likely related to the central venous pressure of spontaneous breathing patients with spinal anesthesia. However, there was an additional possibility that large fluid absorption occurred after a high level of spinal block using 17.5 mg of bupivacaine, which is too high to use for TURP. After a high level of spinal block, the driving pressure of the irrigating fluid increased because of the reduced blood pressure, which may have caused large fluid absorption. In their study, MAPs and HRs were significantly lower compared with pre-irrigation values, and blood ethanol concentrations indicated that fluid absorption was highest at that time. Therefore, it is recommended to limit the spinal block level so that it does not reach to a level that is too high.

Hypotension is common after spinal anesthesia and perioperative hypotension is related to postoperative mortality and morbidity. In the previous study, hemodynamic fluctuation was less common and the duration of hemodynamic stability was longer with continuous non-invasive blood pressure monitoring compared with intermittent blood pressure monitoring. Therefore, continuous hemodynamic monitoring through NICOM during monopolar TURP under spinal anesthesia can provide hemodynamic stability and improved postoperative outcomes by reducing postoperative complications such as MACE.

This study has several limitations. First, we estimated the amount of irrigating fluid that was absorbed using an indirect method that used the serum sodium concentration. Second, because the sorbitol–mannitol solution was used for irrigation in this study, this result may not apply to other kinds of irrigating fluid. Additionally, although the statistically calculated sample size was applied in this study, the sample size was too small to use to draw a conclusion based on these results. However, intensive hemodynamic monitoring including NICOM is necessary to avoid cardiovascular impairment in elderly patients who are undergoing monopolar TURP, even if the procedure takes only a short time.

In conclusion, spinal anesthesia with 6 mg of bupivacaine was effective for elderly patients undergoing monopolar TURP. Although the estimated amount of irrigating fluid that was absorbed was negligible,
the increase in stroke volume variation may have indicated intravascular volume depletion with diuresis, which resulted from mannitol in the irrigating fluid during the early irrigation period. Therefore, even during short irrigating times, intensive hemodynamic monitoring should be performed with the possibility of intravascular volume depletion as well as volume overload, especially immediately after a large amount of irrigating fluid is used.

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