

A COMPARISON OF THE EFFECTS OF GENERAL ANESTHESIA VERSUS SPINAL ANESTHESIA ON CATHETER-RELATED BLADDER DISCOMFORT AFTER HoLEP: A PROSPECTIVE TRIAL

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Submitted: 9 February 2020. Accepted: 19 March 2020. Published: 20 May 2020.

ABSTRACT

Background and objective

Using an indwelling urinary catheter during lower urinary tract surgeries frequently leads to catheter-related bladder discomfort (CRBD) in the immediate postoperative period. The purpose of the present study was to compare the effectiveness of general and spinal anesthesia on CRBD in patients who underwent Holmium laser enucleation of the prostate (HoLEP).

Material and methods

This clinical trial included male patients who underwent HoLEP for benign prostatic hyperplasia. Forty-five participants were divided into two groups: general anesthesia and spinal anesthesia. The incidence and the severity of CRBD were assessed postoperatively for 24 h. The severity of CRBD was graded using an 11-point scale (0 = no CRBD, 10 = worst CRBD imaginable). Moderate to severe CRBD, having a score of ≥ 4 , was treated with 1 $\mu\text{g}/\text{kg}$ fentanyl incrementally every 5 min during immediate postoperative period, and the total consumption was compared between the two groups.

Results

The overall incidence of CRBD 24 h following HoLEP was 80% in the general anesthesia group, which was significantly higher than that of the spinal anesthesia group ($p = 0.017$). The severity of CRBD was

significantly lower in the spinal anesthesia group compared with the general anesthesia group postoperatively at 2 and 6 h ($p < 0.001$ and $p = 0.005$ respectively). Furthermore, opioid consumption was significantly higher in the general anesthesia group compared with the spinal anesthesia group ($p = 0.009$).

Conclusion

Spinal anesthesia has a CRBD-reductive effect compared with general anesthesia during the early postoperative hours following HoLEP.

Key Words: *benign prostatic hyperplasia; recovery; urinary catheter*

INTRODUCTION

Benign prostatic hypertrophy (BPH) is a highly prevalent disease in aging men. Although there are various treatment options, including watchful waiting and drug therapy with alpha-blockers and/or 5-alpha reductase inhibitors, for BPH with lower urinary tract symptoms (LUTS), surgical treatment is the most effective option in refractory cases. Over the years, various surgical techniques have evolved from open prostatectomy to transurethral prostate surgery (TUPS), including transurethral resection of prostate (TURP), holmium laser enucleation of the prostate (HoLEP), and other vaporization techniques. There are considerable advantages of performing TUPS such as lower invasiveness, lower mortality, and a shorter hospital stay compared to open surgery.¹⁻³ However, inserting an indwelling urinary catheter following TUPS poses a significant challenge to the patients postoperatively.

The catheter-related bladder discomfort (CRBD) to an indwelling urinary catheter is defined as painful urethral discomfort, that is, resistant to conventional opioid therapy, and this decreases the quality of postoperative recovery. The incidence of CRBD following endoscopic urologic surgery is reported to be 66.7~93.0%,^{4, 5} and it is most troublesome during the immediate recovery phase when the patients are awake following general anesthesia. Furthermore, severe CRBD may cause emergence agitation or postoperative delirium in the post-anesthesia care unit (PACU). Some studies have suggested that the type of anesthesia administered may affect

CRBD. Spinal anesthesia, which is available for lower urinary tract surgery, may be beneficial for CRBD due to its long-lasting analgesic effects.

The purpose of the present study was to compare the effectiveness of general and spinal anesthesia on postoperative recovery outcomes, such as the incidence and the severity of CRBD and opioid consumption after HoLEP. Furthermore, we investigated the patient-reported quality of postoperative recovery following the surgery.

METHODS

This single-blinded, prospective cohort study was approved by the Institutional Review Board of Jeonbuk National University Hospital (IRB No. CUH 2018-05-029), and registered with the Clinical Research Information Service (CRIS, <http://cris.nih.go.kr>), number KCT0003530. After obtaining written informed consent, 50 male patients undergoing elective HoLEP due to BPH were enrolled in the study. Patients with literacy problems or language difficulties, having a history of psychotic disorder or drug abuse, with chronic opioid usage for over 3 months, having severe hepatic or renal impairment, and a coagulation abnormality were excluded from this study.

During pre-anesthetic visits, patients were sufficiently explained about the anesthetic plan, including type of anesthesia provided (general vs. spinal anesthesia) by an anesthesiology resident. Patients were then allocated to either the general or spinal anesthesia group, considering each patient's general medical condition and their preferred

anesthetic strategy without randomization. The patients with a previous history of spinal surgery, severe degenerative spine, or coagulation abnormality were allocated to general anesthesia group. The anesthetic techniques were standardized for both groups. In the general anesthesia group, anesthesia was induced with 1.5–2.5 mg/kg propofol and 0.3–0.8 mg/kg rocuronium, and effect-site concentration of 0.5–3.5 ng/mL remifentanyl was administered using a target-controlled infusion (TCI) pump. The patient's airway was secured with a supraglottic airway device (I-gel™, Intersurgical Ltd., UK). In order to maintain adequate general anesthesia, 1–4 vol% sevoflurane in 50% oxygen was adjusted to maintain a noninvasive arterial pressure within 20% of the pre-anesthetic value and a bispectral index (BIS) value between 40 and 65. At the end of surgery, the residual neuromuscular blockage was reversed with 50 µg/kg neostigmine and 10 µg/kg glycopyrrolate at the reappearance of the second twitch response by the train-of-four monitoring.

For anxiolysis, 1–2-mg Midazolam was given intravenously to all the patients of spinal anesthesia group. After usual sterilization, the spinal needle was inserted at L4/5 interspace. Once the cerebrospinal fluid (CSF) was obtained, 12-mg 0.5% hyperbaric bupivacaine (Marcain® Heavy, AstraZeneca, Sweden) was used to achieve spinal anesthesia. If systolic blood pressure decreased by more than 30% of the pre-anesthetic value or less than 90 mmHg, 5–10-mg ephedrine was administered intravenously. During the operation, 1-mg midazolam was incrementally administered intravenously when needed to achieve mild-to-moderate sedation. In both groups, hemodynamic parameters were monitored and recorded until the end of operation.

Surgery was performed by single surgeon experienced in HoLEP. HoLEP was performed using a 26-Fr resectoscopic sheath, 30° telescope. We used a 45-W holmium laser (Versapulse, Lumenis Ltd., Yokneam, Israel) with a power setting of 1.5 J at

30 Hz. At the end of surgery, a three-way, 30-cc balloon, 20-Fr urethral Foley catheter was inserted. After HoLEP, the patency of Foley catheter was closely checked by a medical team.

Assessment of Postoperative Recovery Outcomes

The primary outcome of the study was the incidence of postoperative CRBD for 24 h. Secondary outcomes, including the severity of CRBD, development of emergence agitation, analgesic consumption, and the incidence of postoperative nausea and vomiting (PONV), were also evaluated postoperatively for 24 h.

The development of CRBD was evaluated using a 3-point scale (1 = comfortable, 2 = uncomfortable but bearable, 3 = severely uncomfortable). Patients with a score of 2 or higher were considered to have experienced CRBD. The severity of CRBD was graded using an 11-point scale (0 = no CRBD, 10 = worst CRBD imaginable). Moderate to severe CRBD, with a score of 4 or higher, was treated with 1 µg/kg fentanyl incrementally every 5 min during stay in post-anesthesia care unit (PACU). Similarly, PONV ≥ 4 was treated with 4-mg ondansetron as the first-line and 10-mg metoclopramide as the second-line antiemetic rescue drug. Meanwhile, emergence agitation was evaluated using the Aono's 4-point scale (1 = calm, 2 = slightly agitated but consolable, 3 = moderately agitated and inconsolable, 4 = severely agitated and highly inconsolable),⁶ and the occurrence of the emergence of agitation was defined by Aono's score ≥ 2 . All the data were collected postoperatively at 2, 6, and 24 h.

Survey of the Patient-Reported Quality of Postoperative Recovery

The quality of postoperative recovery was evaluated with a validated Korean version of the Quality of Recovery-40 (QoR-40K) questionnaire.⁷ QoR-40K includes 40 items of five domains associated with physical comfort, emotional status, physical independence, psychological support, and pain. All the items are rated on a 5-point Likert

scale (1 = none of the time, 2 = some of the time, 3 = usually, 4 = most of the time, and 5 = all of the time), and, consequently, the global score ranges from 40 to 200. The patients were requested to complete the QoR-40K questionnaire for three times in the ward: the day before surgery (baseline), 24 h after the end of surgery, and 3 days after surgery. The evaluation was performed by an investigator blinded to the group allocation of patients.

Statistical Analysis

The sample size was predetermined by the proportions sample size calculation using SigmaPlot version 13.0 (Systat Software Inc. USA) based on the assumption that the incidence of CRBD would be 70% in the general group and 25% in the spinal group. A sample size of 23 patients in each group was estimated to achieve 80% power for the two groups. Considering the dropout rate of 15%, the sample size was enlarged to 50 patients. All

data were expressed as the mean value and standard deviation (SD), median and interquartile range (IQR), or the number of patients (percentage). Patient demographics were analyzed with a Student’s *t*-test or Mann–Whitney rank-sum test after the Shapiro–Wilk test, and the categorical variables, including the incidence of CRBD, opioid usage, or the incidence of PONV, were analyzed by a Chi-square test or Fisher’s exact test. The QoR-40K score of both groups were analyzed with two-way repeated measures of ANOVA (RM ANOVA) and Bonferroni *t*-test for the post hoc test. A p-value of less than 0.05 ($p < 0.05$) was considered significant.

RESULTS

The Consort diagram is shown in Figure 1. Among the 50 patients who were enrolled, 45 patients (20 in the general anesthesia group and

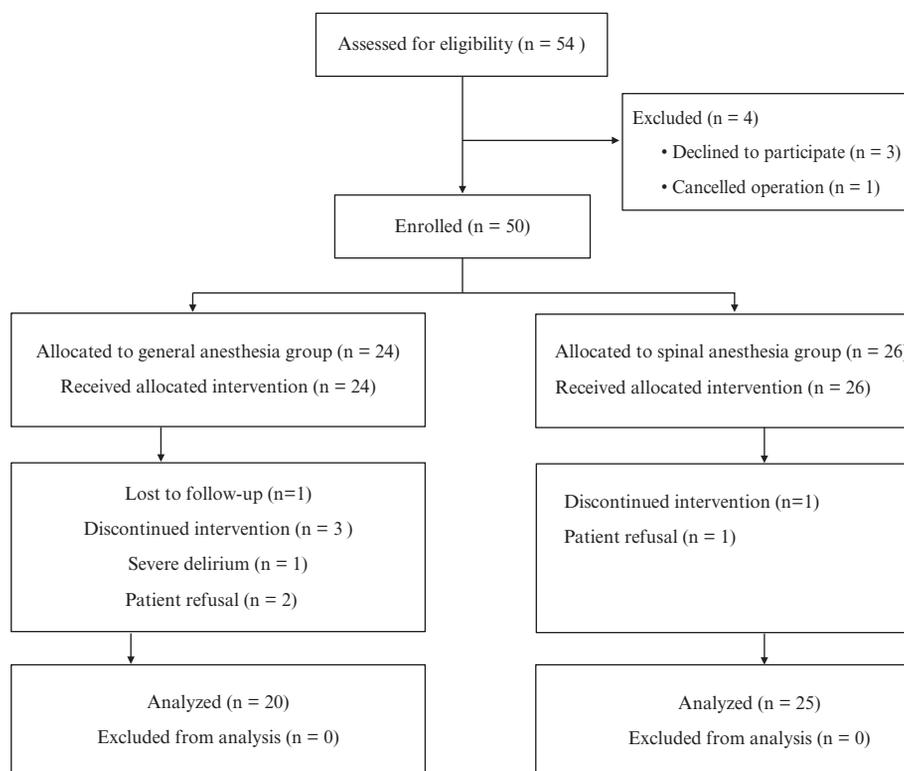


FIG. 1 The consort diagram.

25 in the spinal anesthesia group) completed the study, and their data were analyzed. Among the five patients who were excluded from the study, one patient, in the general anesthesia group, had received haloperidol due to the severe emergence agitation and delirium in PACU. There were no significant differences in patient characteristics between the two groups except the duration of anesthesia (see Table 1).

The spinal anesthesia group exhibited a better postoperative recovery profile than the general anesthesia group (see Table 2). The overall incidence of CRBD for 24 h following HoLEP was 80% in the general anesthesia group, which was significantly higher than in the spinal anesthesia group ($p = 0.017$). The severity of CRBD was also significantly lower in the spinal anesthesia group compared with the general anesthesia group at postoperative 2 h and 6 h ($p < 0.001$ and $p = 0.005$ respectively). The incidence of emergence agitation during the immediate recovery phase (at 0–2 h) was significantly higher in the

general anesthesia group compared with the spinal anesthesia group ($p = 0.013$).

In the general anesthesia group, five patients (25%) received opioid analgesics in PACU, while none of the patients received opioid analgesics in the regional anesthesia group ($p = 0.013$) (see Table 3). Furthermore, the cumulative consumption of fentanyl significantly differed between the two groups ($p = 0.009$). Meanwhile, the incidence of PONV did not significantly differ between the two groups at 2 h, 6 h, and 24 h.

The patients-centered quality of postoperative recovery evaluated by QoR-40K questionnaire showed that there was no significant difference between the two groups by independent comparison of the two samples. The global QoR-40K scores did not significantly differ between the two groups at baseline on the postoperative day 1 and 3 despite the scores on the dimension of physical comfort and emotional status being significantly different between the two groups at postoperative day 3 ($p = 0.044$ and $p = 0.037$ respectively) (see Table 4).

TABLE 1 Patient Demographics and Clinical Features

	General	Spinal	p
Number of patients	20	25	
ASA PS (I/II)	2/18	3/22	1.000
Age (years)	70.8 ± 7.3	68.9 ± 6.4	0.373
BMI (kg/m ²)	24.1 ± 3.4	24.6 ± 2.9	0.574
Prostate-specific antigen (ng/mL)	3.6 ± 2.8	2.9 ± 2.3	0.093
Prostate volume (mL)	50.3 ± 23.4	47.3 ± 20.2	0.182
Hemoglobin (mg/dL)			
Preoperative	13.9 ± 1.3	14.0 ± 1.2	0.548
At postoperative 1st day	13.1 ± 1.3	13.1 ± 1.5	0.624
Surgery time (min)	45.0 (32.0–59.8)	37.0 (26.5–53.5)	0.134
Anesthesia time (min)	75.0 (65.0–87.3)	60.0 (52.5–81.0)	0.044*
Duration of PACU stay (min)	66.5 (60.0–88.8)	60.0 (60.0–79.0)	0.405
Duration of urinary catheterization (day)	3.0 (2.0–5.0)	3.0 (2.0–5.0)	0.416
Duration of hospital stay (days)	3.0 (2.0–5.0)	3.0 (2.0–5.0)	0.437

Values are expressed as numbers, mean ± SD or median (25th–75th percentile).

*Mann–Whitney rank-sum test.

TABLE 2 Postoperative Recovery Outcomes

	General (n = 20)	Spinal (n = 25)	P
CRBD [n (%)]			
0–2 h	12 (60%)	1 (4%)	<0.001*
2–6 h	8 (40%)	9 (36%)	0.973
6–24 h	5 (25%)	5 (20%)	0.731
0–24 h	16 (80%)	10 (40%)	0.017*
Severity of CRBD (0–10)			
0–2 h	3.0 (1.3–4.0)	0.0 (0.0–0.0)	<0.001†
2–6 h	1.0 (0.0–2.0)	0.0 (0.0–1.0)	0.005‡
6–24 h	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.393
Emergence agitation [n (%)]			
0–2 h	5 (25%)	0 (0%)	0.013‡
2–6 h	4 (20%)	6 (24%)	1.000
6–24 h	1 (5%)	2 (8%)	1.000
0–24 h	5 (25%)	6 (24%)	1.000

CRBD = catheter-related bladder discomfort.

Values are expressed as median (25th–75th percentile) or numbers (percentage).

*Chi-square test.

†Mann–Whitney rank-sum test.

‡Fisher’s Exact test.

TABLE 3 Opioid Usage and the Development of PONV in PACU

	General	Spinal	p
Opioid usage [n(%)]	5 (25%)	0 (0%)	0.013*
Cumulative fentanyl consumption (µg)	0.0 (0.0–75.0)	0.0 (0.0–0.0)	0.009
PONV [n (%)]			
0–2 h	1 (5%)	1 (4%)	1.000
2–6 h	2 (10%)	1 (4%)	0.577
6–24 h	2 (10%)	2 (8%)	1.000

PONV = postoperative nausea and vomiting; PACU = post-anesthesia care unit.

*Fisher’s Exact test.

In the two-way RM ANOVA and Bonferroni post hoc analysis, the global QoR-40K score on postoperative day 3 was significantly lower than that of the preoperative baseline score in the general anesthesia group ($p = 0.004$) (see Figure 2); however, there was no significant difference

between the two groups. In the two-way RM ANOVA of each dimension, the emotional status score on the postoperative day 3 and postoperative day 1 was significantly lower than that of the preoperative baseline score in the general anesthesia group ($p = 0.014$) (see Figure 3a).

TABLE 4 Quality of Postoperative Recovery by QoR-40K

	Range	General	Spinal	p
Preoperative				
Global QoR-40K	40–200	181.5 (174.3–190.8)	181.0 (165.0–193.0)	0.615
Physical comfort	12–60	57.0 (52.3–60.0)	57.0 (52.0–58.5)	0.636
Emotional status	9–45	41.0 (37.0–43.0)	39.0 (36.0–42.0)	0.232
Physical independence	5–25	21.0 (19.3–24.0)	23.0 (18.0–25.0)	0.853
Psychological support	7–35	29.0 (28.0–33.8)	29.0 (24.5–33.5)	0.558
Pain	7–35	35.0 (33.0–35.0)	35.0 (32.5–35.0)	0.940
Postoperative day 1				
Global QoR-40K	40–200	172.0 ± 15.9	170.2 ± 20.4	0.743
Physical comfort	12–60	55.5 (49.3–57.0)	53.0 (50.0–58.5)	0.900
Emotional status	9–45	39.5 ± 4.0	37.4 ± 5.4	0.169
Physical independence	5–25	18.2 ± 3.8	18.4 ± 4.9	0.828
Psychological support	7–35	29.0 (28.0–32.5)	29.0 (24.5–33.5)	0.954
Pain	7–35	33.0 (30.0–35.0)	33.0 (31.0–34.5)	0.754
Postoperative day 3				
Global QoR-40K	40–200	162.6 ± 20.3	172.3 ± 18.3	0.101
Physical comfort	12–60	51.8 ± 6.3	55.0 ± 3.9	0.044*
Emotional status	9–45	36.6 ± 4.8	39.4 ± 4.0	0.037*
Physical independence	5–25	17.9 ± 4.0	19.2 ± 5.1	0.374
Psychological support	7–35	27.0 (21.3–29.8)	29.0 (22.0–33.5)	0.378
Pain	7–35	32.5 (30.3–35.0)	33.0 (31.5–34.5)	0.693

QoR-40K = Korean version of Quality of Recovery-40 questionnaire.

*Student's *t*-test.

However, physical comfort scores did not significantly differ (see Figure 3b).

DISCUSSION

The results of the present study suggest that spinal anesthesia can reduce the incidence of CRBD by 50% for 24 h following HoLEP, compared with general anesthesia. In spite of various treatment strategies, including opioids and other analgesics or anesthetics, and interventions such as peripheral nerve block to reduce the incidence and severity of CRBD,^{4,6–8} the reported incidence of CRBD is as high as 66.7~93.0%.^{4,5} In a systemic review and meta-analysis, ketamine and anticholinergic drugs have demonstrated great

effectiveness in the relief of CRBD.⁸ However, there have been a few studies suggesting that the type of anesthesia administered also affects CRBD. To the best of our knowledge, this is the first investigation to demonstrate that spinal anesthesia has a CRBD-reductive effect during the early postoperative hours compared with general anesthesia. Consequently, the authors believe that spinal anesthesia could be a better alternative for TUPS in patients who have a high risk of CRBD. The results of this and the future studies could help to establish practice guidelines for the prevention and management of CRBD.

Emergence agitation following anesthesia is very difficult to control and could lead to safety

issues for both patient and staff; unexpected postoperative complications such as wound dehiscence or postoperative bleeding increase resource utilization and potential risk of postoperative

delirium.^{9,10} Urinary catheterization has been shown to increase the risk of emergence agitation among the several risk factors.⁹ In the current study, we also compared the incidence of emergence agitation between general and spinal anesthesia groups. As expected, we found that the long-lasting analgesic effect following spinal anesthesia also reduced the development of emergence agitation during the immediate recovery phase compared with the general anesthesia.

The quality of recovery is a postoperative outcome of complex entity involving physical, physiological, functional, and emotive aspects, and this is an important factor in terms of patient experience during the perioperative period. Traditionally, emphasis on postoperative recovery has been placed on provider-focused outcomes such as postoperative complications, survival rate, and morbidity and mortality rates. However, perioperative care has been recently centered on patient-focused quality of recovery. QoR-40 questionnaire has been a useful tool to assess the quality of postoperative recovery in patients undergoing surgery and anesthesia. More specifically, the Korean version of QoR-40 (QoR-40K) has been recently

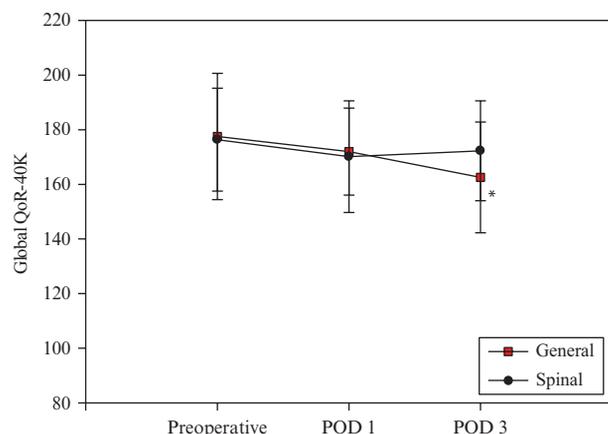


FIG. 2 Global QoR-40K scores between two groups. There were no significant differences between the two groups by two-way RM ANOVA and Bonferroni post-hoc analysis. *In general anesthesia group, global QoR-40K on the postoperative 3rd day was significantly lower than that of preoperative baseline in the general anesthesia group ($p = 0.004$).

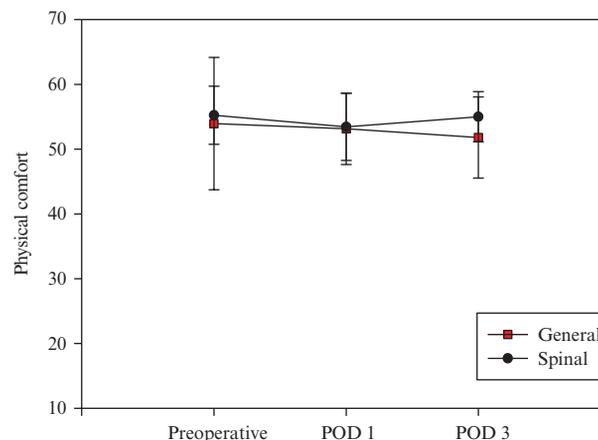
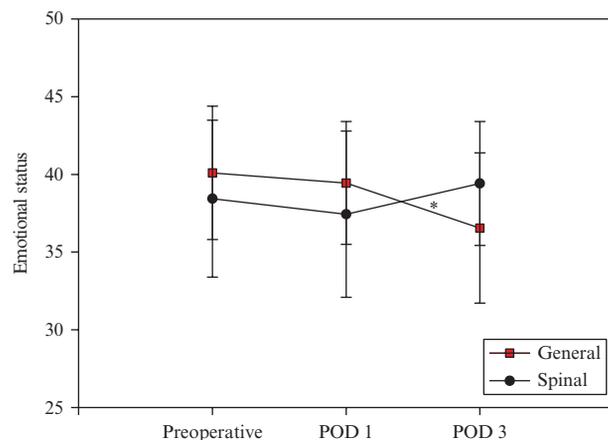


FIG. 3 Emotional status and physical comfort score. (a) Emotional status. *Emotional status score on the postoperative 3rd day was significantly lower than that of preoperative baseline and postoperative 1st day in the general anesthesia group ($p = 0.014$). (b) Physical comfort. There was no significant difference between two groups by two-way RM ANOVA.

reported to be a valid, reliable, and feasible tool to be used to evaluate Korean surgical patients.⁷ In the current study, the scores on the dimensions of physical comfort and emotional state in the spinal anesthesia group were significantly higher than that of the general anesthesia group. These results suggest that spinal anesthesia may improve the quality of postoperative recovery in a certain way despite no differences in global scores between the two groups.

The effects of anesthesia (general vs. neuraxial anesthesia) on postoperative recovery are still inconclusive. Possible advantages of neuraxial anesthesia include better postoperative analgesia, reduced opioid requirement, improved pulmonary function, and preservation of cognitive function postoperatively compared to general anesthesia.¹¹⁻¹³ Moreover, a few studies have suggested that neuraxial anesthesia was associated with reduced mortality in high-risk patients and reduced medical resource utilization.¹¹⁻¹⁴ On the other hand, several studies have refuted the benefits of neuraxial anesthesia as there was no significant difference in postoperative outcomes, including morbidity and mortality or functional recovery between general and neuraxial anesthesia in various surgical settings.^{15,16} The other factors affecting postoperative recovery after TUPS, which include overall assessment of provider- and patient-centered quality of recovery, could be investigated in the future studies.^{17,18} Furthermore, evidence-based consensus recommendations for the choice of type of anesthesia to reduce CRBD could be determined through the future investigations.

There are limitations to our study. First, the current study was a prospective cohort study without randomization. Generally, patients tend to have a strong preference for either general or spinal anesthesia due to preconceptions or previous experience associated with anesthesia. The authors assumed that patient-centered quality of recovery could be influenced by the discrepancy between the patient's expectation and the actual anesthesia

provided. Second, we evaluated the quality of postoperative recovery only during the early recovery phase. The long-term effects of anesthesia depending on the type provided for HoLEP should be investigated in the future studies. Third, the current study is limited by a small sample size.

CONCLUSION

The results of the current study suggest that spinal anesthesia appears to have a CRBD-reductive effect during the early postoperative hours compared to general anesthesia in patients who are undergoing HoLEP.

FUNDING

This study was supported by funds from the Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, South Korea.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

ETHICAL STATEMENT

The present study protocol was reviewed and approved by the institutional review board of Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, and was registered at the Clinical Research Information Service (CRIS, <http://cris.nih.go.kr>), number KCT0003530. Informed consent was submitted by all patients at the time of enrolment.

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