JOURNAL OF ENDOUROLOGY
Volume 29, Number 4, April 2015

Pp. 401–405
DOI: 10.1089/end.2014.0249

Retrograde Intrarenal Surgery with Combined Spinal-Epidural *vs* General Anesthesia: A Prospective Randomized Controlled Trial

Guohua Zeng, PhD,[1,*] Zhijian Zhao, MD,[1,*] Fengquan Yang, MD,[2,*] Wen Zhong, MD,[1] Wenqi Wu, PhD,[1] and Wenzhong Chen, MD[1]

Abstract

Objective: Retrograde intrarenal surgery (RIRS) involves a minimally invasive stone surgery, lending itself potential to combined spinal-epidural anesthesia (CSEA), although it is performed preferably under general anesthesia (GA). This prospective randomized study was undertaken to evaluate the feasibility and efficacy of CSEA for patients undergoing RIRS.

Patients and Methods: Seventy consecutive patients who were scheduled for RIRS were randomized to receive CSEA ($n=35$) or GA ($n=35$). Operative time, stone clearance rate, visual analog scale (VAS) of pain, complication rate, anesthetic cost, and hospital stay were compared between the two groups.

Results: A total of 65 patients randomized to CSEA (31) or GA (34) completed the study. In the CSEA group, each procedure was completed and there was no anesthetic conversion. Although based on the prospective randomized method, the GA group still had a little larger stone size ($p=0.059$) and more multiple caliceal stones ($p=0.037$). Overall, there were no statistically significant differences in operative time ($p=0.088$), stone fragmentation time ($p=0.074$), postoperative VAS pain score at 6 and 24 hours ($p=0.156$, 0.146), incidence of complications ($p=0.870$), stone-free rate ($p=0.804$), and hospital stays ($p=0.907$) between the two groups. The patients in the GA group experienced a higher mean hemoglobin drop (6.5 ± 3.2 *vs* 8.6 ± 2.7 g/L, $p=0.012$). In addition, the anesthetic cost was much cheaper in the CSEA group (183.8 ± 31.4 *vs* 391.9 ± 59.1 dollars, $p<0.001$).

Conclusion: RIRS with CSEA can be completed with no anesthetic conversions and with the same efficacy and safety compared with GA. When considering economical aspects, CSEA appears to be a preferable alternative to GA for the patient whose general health status permits it.

Introduction

Retrograde intrarenal surgery (RIRS) is one of the most common surgical procedures for stone treatment, especially for stone sizes less than 2 cm. This has been ascribed to the minimally invasive nature of the procedure, which is associated with less postoperative pain, shorter hospitalization time, and is also achieving a higher stone-free rate (SFR) than extracorporeal shockwave lithotripsy (ESWL) and lower morbidity than percutaneous nephrolithotomy (PCNL).[1] RIRS is normally performed preferably under general anesthesia (GA) to prevent aspiration and respiratory embarrassment. Traditionally, GA is associated with risk of pulmonary complications; an overview of randomized trials indicates that regional anesthesia (RA) helped to reduce postoperative discomfort and other serious problems and reduce anesthetic requirement, resulting in a shortened hospital stay.[2]

Technical advances in the field of RIRS have helped to revolutionize surgical procedures and reduce surgical trauma and discomfort,[3] and thus should influence the practice and techniques of anesthesia. For example, combined spinal-epidural anesthesia (CSEA) may be used in the RIRS procedures. However, there are no studies focusing on the CSEA in RIRS procedures. A minimally invasive procedure in combination with a less minimally invasive method of anesthesia, in theory, can improve the quality of surgery. Based on our previous experience in CSEA for rigid ureteroscopic lithotripsy and PCNL procedures, we designed the first prospective randomized trial to assess the feasibility and safety of RIRS in adult patients who are anesthetized with CSEA.

[1]Guangdong Key Laboratory of Urology, Department of Urology, Minimally Invasive Surgery Center, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China.
[2]Department of Anesthesiology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China.
*These authors have contributed equally to this work as cofirst authors.

We hypothesized that RIRS with CSEA could be performed safely and effectively with additional health benefits and less early postoperative pain compared with RIRS with GA.

Patients and Methods

Patients

The prospective, randomized pilot study protocol was approved by the Institutional Review Board, and then was undertaken. After receiving patients' written informed consent, 70 patients (18–75 years old) who were scheduled for RIRS were included in this study from October 2013 to December 2013. Patient selection for this RIRS intervention included previously failed SWL and residual stones after PCNL and the preference of patients and the surgeon regardless of the stone size and numbers. Patients were excluded if they had American Society of Anesthesiologists (ASA) $\geq$ grade III, a contraindication for RIRS surgery or CSEA, or were currently having chronic pain therapy. The following preoperative data were collected: age, sex, body–mass index (BMI), stone size, stone location, serum creatinine, hemoglobin, ASA status, and associated comorbidities.

Following preoperative evaluation, such as computed tomography (CT), serum biochemistry, urinalysis, urine cultures, and other biochemistry tests and accepting preparation for surgery, the enrolled patients were randomly assigned to have RIRS under CSEA ($n = 35$) or GA ($n = 35$) at a ratio of 1:1 using the sealed envelope technique, which was placed in the preoperative area and only opened at the time of the patient's arrival on the day of surgery. Anesthesia was administered and the operations were undertaken by the same team for all patients. All patients received 1 g of cephazoline 30 minutes before anesthesia. Patients with a urine culture positive for microorganisms were treated with a complete course of culture-specific antibiotics to confirm sterility.

Anesthesia management

Group 1 underwent GA. Fentanyl at 2 μg/kg and midazolam at 0.03 mg/kg were administered 2 minutes before induction, and after losing verbal contact, induction was initiated by injection of 2 mg/kg propofol and 0.5 mg/kg atracurium (relaxant agent), and finally laryngoscopy and tracheal intubation were at tempted. Propofol infusion during GA was adjusted according to the level of the cerebral status index; likewise, remifentanyl was administered during anesthesia according to the blood pressure changes.

Group 2 underwent CSEA. An epidural catheter is introduced through an 18-gauge needle in the intervertebral space at the T11 to T12 level; a test dose (xylocaine 2 mL with adrenaline 1: 200,000) is administered. Spinal anesthesia was administered using 2 mL of 0.5% ropivacaine and 25 mg of fentanyl through the L3 to L4 space, and then a catheter was inserted in the epidural area. An additional 4 mL of 2% lidocaine was administered using the epidural catheter when the operation lasted more than 80 minutes.

RIRS technique

All procedures were performed by two surgeons using an Olympus URF-P5 flexible ureteroscope (Olympus Corporation). Under the randomized anesthesia method, patients were placed in the lithotomy position. Semirigid 8F/9.8F ureteroscopy (Richard Wolf) was routinely performed before flexible ureteroscopy in all patients for dilation of the ureter and to place two 0.038 inch hydrophilic wires—one as the guidewire and another as the safety wire—into the renal pelvis. A 12/14F ureteral access sheath (UAS) (Cook Urological) was placed under C-arm fluoroscopic guidance and the flexible ureteroscope was passed through the UAS. The stones were fragmented with a 200 or 365 μm Holmium-YAG laser fiber until they were deemed small enough to pass spontaneously. Laser energy and pulse frequency were varied on the basis of stone size. Basket extraction was not routinely performed for stone dust; however, some residual fragments $\approx$3 mm were removed by a basket (NCircle® Tipless Stone extractor; Cook Medical, Inc.), as much as possible, for stone analysis. A pigtail Double-J stent was routinely placed in all patients and was removed at postoperative 2 weeks. On the first postoperative morning, radiography of the kidneys, ureters, and bladder (KUB) was performed for all the patients to assess the status of stone fragmentation and the location of the stents. A noncontrast spiral CT was performed at postoperative 4 weeks, allowing another 2 weeks for the spontaneous passage of stone fragments after removal of the Double-J stent, to evaluate the initial SFR. SFR was defined as complete stone clearance or residual fragments, 3 mm or smaller, at 1 month by the evaluation of the CT scan.[4] In patients with residual calculi, repeated RIRS and ESWL were considered as auxiliary treatment alternatives when indicated.

Evaluation variables and statistical approach

The stone size was defined as the maximum length of the stone on preoperative radiologic investigation. In the case of multiple stones, the same was achieved by adding maximum length of the individual stones.[4] The stone locations were pointed as pelvis: lower, middle, upper calix. The operative time was defined as the time passed from insertion of a rigid ureteroscope to the completion of stent placement. Length of postoperative stay was the interval between the operative day and hospital discharge day.

Intraoperative incidents related to the anesthetic (renal pain, pruritus, shivering, nausea, hypotension, hypertension, tachycardia, bradycardia, and vomiting) were documented. Hypotension and hypertension were defined as blood pressures less than and greater than 20% of the baseline value, respectively; Tachycardia was defined as a heart rate of >100 beats/minute and bradycardia as a decrease in heart rate to $<$50 beats/minute and oxygen desaturation as a pulse oximetry reading of $<$90% for longer than 1 minute.[5]

Postoperatively, pain was assessed by using a 100 mm visual analog scale (VAS) from 1 to 100, with 100 being most severe. Patients were asked to mark a point over a line 100 mm long at 6 to 24 hours postoperatively to express the intensity of their pain experience. A doctor of our study group performed the post-treatment pain assessment and stone-free assessment. He was not blinded from the study, but the patients were. Postoperative complications were recorded according to the modified Clavien classification system. Fever should be defined when the temperature reading is above 38.5°.

The end point of this study was a comparison of the feasibility and safety of the two anesthesia regimens against perioperative complications. Power analysis identified a minimum of 65 patients (32 per group) as the total sample

size to detect 12% complication rates (12% was an average rate in other published articles, which reported a range of 6% to 15.6% of complication rates[4,6–8]) between the two groups with a maximum permissible error of 20% and a power of 80%, at a 5% significance level. With consideration of anticipated patient dropouts, we chose to randomize more patients. Analysis was performed using the chi-square test for categorical variables, and the Kruskal–Wallis and Wilcoxon and Mann–Whitney U tests for continuous variables. Statistical Package for the Social Sciences (SPSS), version 13.0, was used to perform statistical analysis. A p-value < 0.05 was considered statistically significant.

Results

Of the 70 randomized patients, 5 dropped out of the study leaving 65 who completed the study, including CSEA in 31 and GA in 34. Three patients from the CSEA group were lost to follow-up after treatment and were excluded from the study. One patient from the CSEA group was also excluded from the study in the operating room because he had an acute infundibulopelvic angle causing the inability to reach the stone and underwent the surgical conversions of PCNL. One patient from the GA group was excluded from the study because of the failure of UAS placement due to ureteral stricture of the patient who was converted to PCNL procedure.

There were no significant differences between the groups with regard to age, gender, BMI, distribution of stone location, stone burden, and the incidence of associated comorbidities, although the incidences of preoperative placement of ureteral stents and multiple caliceal stones were more common in the GA group (Table 1).

In the CSEA group, all procedures were completed under CSEA and there were no anesthetic conversions. Both the operative time and stone fragmentation time were similar between the two groups with a median time of 41.5 and 29.9 minutes for the CSEA group and 48.3 and 38.7 minutes for the GA group, respectively ($p = 0.088$ and 0.074). The mean serum creatinine increase was 5.1 ± 3.7 μM for the CSEA group and 3.6 ± 3.9 μM for the GA group, $p = 0.118$ (Table 2).

The VAS 100-mm line was used to assess and quantify pain at the postoperative 6 and 24 hours. Postoperative VAS pain score was 23.6 ± 6.2 *vs* 25.7 ± 5.6 at 6 hours ($p = 0.156$) and 19.3 ± 5.6 *vs* 17.4 ± 4.8 at 24 hours ($p = 0.146$) for CSEA *vs* GA, respectively. Analgesic requirement was needed to obtain pain relief in three patients of each group.

The median postoperatively hospital stay was 1.9 ± 1.9 days (range, 1–13 days). Overall, 45 of the 65 (69.2%) patients were stone free after the initial treatment, with no significant difference between the CSEA (67.7%, 21/31) and GA (70.6%, 24/34) groups. In addition, the anesthetic fee was much cheaper in the CSEA group (183.8 ± 31.4 *vs* 391.9 ± 59.1 dollars).

Low rate of complications was observed in both groups. There were no grade IV and V Clavien complications and no blood transfusion was required in both groups (Table 3). The most common intraoperative adverse event was shivering, which was reported by three patients under CSEA. Three patients in the GA cohort experienced bradycardia and hypotension at the start of insufflations. In these cases, ephedrine 10 mg IV was administered and hemodynamics were stabilized. Vomiting occurred in one patient with CSEA. Two patients who were randomized to CSEA complained of occasionally mild and transient discomfort requiring propofol to strengthen the sedation. A Double-J stent was placed at the end of the procedure in all cases. Postoperative adverse events were assessed after operation until hospital discharge. None of the patients in either group experienced respiratory depression, pruritus, nausea, and vomiting. Only one (3.2%) and three (8.8%) patients had febrile urinary-tract infection ($p = 0.615$), all of who required antibiotic treatment in the CSEA group and GA group, respectively, and no urosepsis happened. Each group had one patient undergoing Steinstrasse, which was resolved by the rigid ureteroscope. The difference of the hemoglobin drop between both groups was statistically significant, with a mean drop of 6.5 ± 3.2 in the CSEA group

Table 1. Demographic and Clinical Preoperative Characteristics

Characteristics	*CSEA* (n = *31*)	*GA* (n = *34*)	p-*Value*
Mean ± SD age (year)	47.6 ± 11.6	49.3 ± 11.6	0.568
Male/female (*n*)	20/11	20/14	0.638
BMI (kg/m^2)	23.3 ± 2.9	23.4 ± 3.9	0.954
Side (right/left)	12/19	14/20	0.839
History of ipsilateral surgery (%, *n*)	16.1% (5)	29.4% (10)	0.204
ASA status			0.901
II	80.6% (25)	79.4% (27)	
III	19.4% (6)	20.6% (7)	
Mean stone size (mm)	1.9 ± 0.9	2.4 ± 1.3	0.059
Solitary kidney	19.4% (6)	20.6% (7)	0.901
Hounsfield unit values of stones (HU)	847.6 ± 295.2	811.8 ± 294.7	0.712
Comorbidities (%, *n*)	22.6% (7)	26.4% (9)	0.569
Multiple caliceal stones (%, *n*)	48.8% (15)	73.5% (25)	0.037
Low caliceal stones (%, *n*)	35.5% (11)	50% (17)	0.238
Positive preoperative urine culture (%, *n*)	12.9% (4)	14.7% (5)	0.834
Preoperative stent placement (%, *n*)	48.4% (15)	76.5% (26)	0.019
Preoperative serum creatinine (μM)	132.4 ± 14.6	135.6 ± 15.2	0.391

ASA = American Society of Anesthesiologists; BMI = body–mass index; CSEA = combined spinal-epidural anesthesia; GA = general anesthesia; SD = standard deviation.

Table 2. Outcome of Retrograde Intrarenal Surgery Between Two Groups Under Different Anesthesia

Outcomes	*CSEA* (n = *31*)	*GA* (n = *34*)	p-*Value*
Operative time (minutes)	41.5 ± 13.8	48.3 ± 17.4	0.088
Stone fragmentation time (minutes)	29.9 ± 14.4	38.7 ± 23.3	0.074
Hemoglobin drop (g/L)	6.5 ± 3.2	8.6 ± 2.7	0.012
Postoperative serum creatinine (μM)	137.5 ± 15.1	139.2 ± 16.6	0.668
Serum creatinine increase (μM)	5.1 ± 3.7	3.6 ± 3.9	0.118
SFR after initial treatment (%, *n*)	67.7% (21)	70.6% (24)	0.804
VAS at postoperative 6 hours	23.6 ± 6.2	25.7 ± 5.6	0.156
VAS at postoperative 24 hours	19.3 ± 5.6	17.4 ± 4.8	0.146
Postoperative hospital stay (day)	1.9 ± 2.4 (1–13)	1.9 ± 1.3 (1–6)	0.907
Anesthetic cost (dollars)	183.8 ± 31.4	391.9 ± 59.1	< 0.001
Stone composition (%, *n*):			0.435
Struvite stones	9.7% (3)	20.6% (7)	
Urate stones	9.7% (3)	5.9% (2)	
Calcium-based stones	80.6% (25)	73.5% (25)	

SFR = stone-free rate; VAS = visual analog scale.

and a mean of 8.6 ± 2.7 in the GA group ($p = 0.012$). However, the difference did not have clinical significance because no patients received blood transfusions in both groups.

Discussion

This study demonstrates, for the first time, that RIRS can be completed with CSEA as it is as feasible and safe as that performed under GA. CSEA yielded an operative time, early postoperative pain, SFR, and complication rate similar to that of GA, but with the advantages of less anesthetic cost. The pain score was also lesser in the CSEA group, although this finding was not significant.

Table 3. Complications by Modified Clavien Classification Under Different Anesthesia

Complications	*CSEA* (n = *31*)	*GA* (n = *34*)	p-*Value*
No. of kidneys with complications	6 (19.3%)	7 (20.6%)	0.901
No. of total complications[a]	11	9	
Intraoperative complications (%, *n*)	6 (19.3%)	3 (8.8%)	
Postoperative complications (%, *n*)	5 (16.1%)	6 (17.6%)	
% Grade I			
Postoperative pain (VAS score > 30)	1	1	
Postoperative fever	2	1	
Intraoperative vomit	1	0	
Intraoperative discomfort	2	0	
Intraoperative shiver	3	0	
Intraoperative bradycardia and hypotension	0	3	
% Grade II			
Infection needed antibiotic	1	3	
% Grade III			
Steinstrasse	1	1	

[a]Some cases experienced one or more complications.

Traditionally, RIRS procedures are performed under GA.[1,4,6–8] The reason for this is unclear, and in our opinion, it may be that the perceived risk of patients under CSEA may appear as a larger tidal volume resulting in greater diaphragm and renal movement, and thus causing instability to reach stones, which is not thought to be well tolerated by surgeons during the stone fragmentation by the Holmium:YAG laser fiber. As we know, the breathing rate and tidal volume can be controlled in patients with GA. In fact, there was no influence on the manipulation in the group patients with CSEA in the present study. In addition, no patients underwent mucosal injury (stabbing and thermal) by the holmium laser due to renal mobility. Introducing the idea to combine a minimally invasive surgical procedure with minimally invasive anesthesia, and based on considering economical aspects, we try to assess the feasibility and safety of RIRS performed under CSEA.

What is important is the fact that the results obtained with CSEA must not be worse than those obtained by using GA. Our overall success rate of anesthesia was 100%, with nobody in the CSEA group needing the conversion to GA. We also believe in the necessity of GA during RIRS. However, because of our patients' economic conditions in China, we also believe that any patient who can tolerate the rigid ureteroscopic lithotripsy in the ureter and PCNL with holmium laser lithotripsy in the kidney under CSEA can also tolerate RIRS, thus decreasing the medical cost. Keeping in mind that RIRS procedures are sufficiently safe and that there is a very low morbidity rate, we prefer and advise that under similar clinical and economic conditions RIRS can be performed under CSEA in any patient, if the general health status permits it. In a patient who would not accept the procedure under CSEA, the procedure can be performed or continued with GA.

For the RIRS procedure in the treatment of kidney stones, previous studies assessed some parameters that might influence the surgical outcomes, such as stone burden, BMI, stone location, stone composition, number of stones, and lower pole infundibulopelvic angle, but the real impact of the type of anesthesia on RIRS outcomes has not been clarified precisely.[6–8]

In the present study, when we compared these homogeneous groups, there were no significant differences between groups among operative times, advent events of anesthesia, hemoglobin drop, and SFRs. This situation might signify that

RA did not negatively affect RIRS and its success rate. As we know, febrile urinary-tract infections and even urosepsis were common complications postoperatively. Thus, the timely detection of infection during the operation was a positive effect of the CSEA technique according to shiver manifestation of patients, which would decrease the postoperative infection complications or their severity by timely intraoperative anti-infection treatment.

The postoperative hospital stay of these groups was similar, although it was expected to be shorter in the RA group. This might be explained by the application of KUB and routine blood biochemistry to all patients routinely on the second post-operative day, and hospital stay was rounded to the nearest whole day and is not a precise calculation to hours.

Several studies report lower levels of postoperative pain for PCNL procedures undertaken with spinal or epidural anesthesia compared with GA.[9–11] However, in RIRS, pain assessed at multiple postoperative time points was not significantly different in patients who had CSEA compared with patients who had GA. The reason may be explained by the minimally invasive nature of the RIRS procedure, which itself is associated with slight postoperative pain.

In conclusion, although our observations on this small cohort of patients need to be verified by a randomized trial with more cases, we are the first to conclude that RIRS with CSEA was completed with no anesthetic conversions and with the same efficacy and safety compared with GA. When considering economical aspects, CSEA appears to be a preferable alternative to GA for patients undergoing RIRS. One important caveat is that although the postoperative pain has shown no difference between the two groups, it was probably more related to the minimal procedure itself and stenting. However, we had no data on the intraoperative pain experience by the CSEA group; it would be some important information for the choice of the anesthetic approach.

Acknowledgments

This work was financed by a grant from the National Natural Science Foundation, China (No. 81370804), colleges and universities in the Guangzhou Yangcheng scholars research project (No. 12A017S), and the Science and Technology project in Guangzhou (the people's livelihood special major science and technology) (No. 201300000096).

Disclosure Statement

No competing financial interests exist.

References

1. Resorlu B, Unsal A, Ziypak T, et al. Comparison of retrograde intrarenal surgery, shockwave lithotripsy, and percutaneous nephrolithotomy for treatment of medium-sized radiolucent renal stones. World J Urol 2013;31:1581–1586.
2. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: Results from overview of randomised trials. BMJ 2000;321:1493–1505.
3. Buscarini M, Conlin M. Update on flexible ureteroscopy. Urol Int 2008;80:1–7.
4. Lim SH, Jeong BC, Seo SI, et al. Treatment outcomes of retrograde intrarenal surgery for renal stones and predictive factors of stone-free. Korean J Urol 2010;51:777–782.
5. D'Ambrosio A, Spadaro S, Mirabella L, et al. The anaesthetic and recovery profile of two concentrations (0.25% and 0.50%), of intrathecal isobaric Levobupivacaine for combined spinal-epidural (CSE) anaesthesia in patients undergoing modified Stark method caesarean delivery: A double blinded randomized trial. Eur Rev Med Pharmacol Sci 2013;17:3229–3236.
6. Resorlu B, Unsal A, Gulec H, et al. A new scoring system for predicting stone-free rate after retrograde intrarenal surgery: The ''resorlu-unsal stone score.'' Urology 2012;80:512–518.
7. Martin F, Hoarau N, Lebdai S, et al. Impact of lower pole calculi in patients undergoing retrograde intrarenal surgery. J Endourol 2014;28:141–145.
8. Caskurlu T, Atis G, Arikan O, et al. The impact of body mass index on the outcomes of retrograde intrarenal stone surgery. Urology 2013;81:517–521.
9. Kuzgunbay B, Turunc T, Akin S, et al. Percutaneous nephrolithotomy under general versus combined spinal-epidural anesthesia. J Endourol 2009;23:1835–1838.
10. Singh V, Sinha RJ, Sankhwar SN, et al. A prospective randomized study comparing percutaneous nephrolithotomy under combined spinal-epidural anesthesia with percutaneous nephrolithotomy under general anesthesia. Urol Int 2011;87:293–298.
11. Nouralizadeh A, Ziaee SA, Hosseini Sharifi SH, et al. Comparison of percutaneous nephrolithotomy under spinal versus general anesthesia: A randomized clinical trial. J Endourol 2013;27:974–978.

Address correspondence to:
Guohua Zeng, PhD
Guangdong Key Laboratory of Urology
Department of Urology
Minimally Invasive Surgery Center
The First Affiliated Hospital of Guangzhou
Medical University
1# Kangda Road
Haizhu District
Guangzhou 510230
China

E-mail: gzgyzgh@vip.tom.com

Abbreviations Used

ASA = American Society of Anesthesiologists
BMI = body–mass index
CSEA = combined spinal-epidural anesthesia
CT = computed tomography
ESWL = extracorporeal shockwave lithotripsy
GA = general anesthesia
KUB = kidneys, ureters, and bladder
PCNL = percutaneous nephrolithotomy
RA = regional anesthesia
RIRS = retrograde intrarenal surgery
SFR = stone-free rate
UAS = ureteral access sheath
VAS = visual analog scale