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Edited by: Igor Spiroski Citation: Bakeer A, Abdelhamid K, Nabil D, Rawi M. Perioperative Analgesic Efficiency of Ultrasound-Guided Quadratus Lumborum Block versus Epidural Analgesia in BACKGROUND AND AIM: Multimodal analgesia is currently used for perioperative pain management after radical cystectomy (RC). This study aimed to compare quadratus lumborum block (QLB) and thoracic epidural block (TEA) in patients subjected to RC. METHODS: This prospective randomized controlled study included 34 patients with bladder cancer subjected to RC

under general anesthesia, divided into two groups. The Quadratus Group (n = 17) underwent bilateral ultrasoundguided continuous QLB, and the Epidural Group (n = 17) underwent continuous TEA. The primary outcome was pain intensity measured by visual analog scale score (VAS) score, and the secondary outcomes were total morphine consumption during the first 48 h after surgery, post-operative nausea score, and patient satisfaction

RESULTS: There were no differences between the two groups in post-operative VAS scores starting immediately after surgery up to 48 h. Reduction of VAS score after QLB was delayed compared to that after TEA. The two groups had a comparable number of patients requesting rescue analgesia (p = 0.271) and total post-operative morphine consumption (p = 0.976) in the remaining patients. The nausea score was significantly lower in the Quadratus Group than in the Epidural Group (p = 0.020). There was no significant difference between the two groups in the satisfaction score (p = 0.612). Few mild complications were detected in the two studied groups

CONCLUSION: QLB and TEA are safe and effective in managing postoperative pain after RC with similar analgesic profiles. QLB was more effective in reducing post-operative nausea and vomiting.

REGISTRATION: Clinical Trials.gov (ID NCT04133051)

Abstract

Bladder Cancer Patients Undergoing Radical Cystectomy. Open Access Maced J Med Sci. 2022 Oct 06; 10(B):2451n Access Maced J Med Sci. 2022 Oct 06; 10(B):2451-2456. https://doi.org/10.3889/oamjms.2022.10845 Keywords: Pain management; Cystectomy; Urinary bladder neoplasms; Analgesia; Ultrasonography; Interventional *Correspondence: Ahmed Bakeer, Department of Anesthesia and Pain Management, National Cancer Institute, Cairo University, Cairo, Egypt. E-mail: ahmed_bakir77@yahoo.com Received: 25-Aug-2022 Revised: 13-Sep-2022 Accepted: 27-Sep-2022 Copyright: © 2022 Ahmed Bakeer, Khaled Abdelhamid, Dina Nabil Mohamed Saved Funding: This research did not receive any financial npeting Interests: The authors have declared that no

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Introduction

Globally, bladder cancer is the 10th most common cancer [1]. In Egypt, it is a widespread type of cancer among males [2]. Radical cystectomy (RC) is considered the gold standard for managing bladder cancer [3]. RC has substantial morbidity and mortality. The complication rate ranges from 28% to 64% within 3 months [4]. The 90-day mortality rates range from 5% to 8% [5]. Despite improvements in surgical technique and perioperative care, complications in the immediate post-operative period remain significant [6]. The patients often experience significant post-operative pain and functional impairment and need 5-10 days to recover [7], [8].

Opioid analgesics are the conventional method of post-cystectomy pain management [9]. However, respiratory depression, excessive sedation, and post-operative ileus are common adverse effects of opioids. Moreover, physical dependence is observed in some patients requiring long-term use of opioids after surgery [6].

modern practice, perioperative pain management of patients undergoing RC tends toward multimodal analgesic protocols. Recent enhanced recovery after surgery (ERAS) guidelines recommend continuous thoracic epidural analgesia (CTEA) for 3 days for pain management [10]. CTEA is characterized by better functional results and pain relief in patients undergoing RC [11], [12], However, a recent large. population-based study did not show an advantage of epidural use in reducing perioperative complications or length of hospitalization [13].

A more recent type of regional analgesics is ultrasound-guided quadratus lumborum block (QLB). It is an interfascial plane block used successfully for pain relief in various abdominal procedures. In the anterior approach of this technique, the local anesthetic (LA) is injected anterior to the QL muscle with the potential to spread to the paravertebral space to block both somatic and visceral pain pathways of the abdominal wall and viscera [14]. QLB has been used for post-operative analgesia in some urological procedures [15], [16], but its efficacy in patients undergoing RC was not sufficiently studied in the literature.

B - Clinical Sciences Anesthsiology

Hence, in this prospective study, we investigated the efficacy and safety of QLB compared to the classical TEA in patients subjected to RC.

Methods

This prospective randomized controlled study included 34 patients with bladder cancer subjected to RC in the surgical department of the National Cancer Institute, Cairo University, from January 2021 to January 2022. Written informed consent was obtained from each patient before enrollment in the study. The study applied the principles of the Declaration of Helsinki (1964) and its subsequent revisions. The study was approved by the Institutional Review Board (approval no. AP1811–30103) and registered on Clinical Trials. gov (ID: NCT04133051).

The inclusion criteria were bladder cancer patients undergoing RC older than 18 years with ASA Class II or III. Patients with allergy to drugs used in the study, chronic pain, coagulopathies, local or intra-abdominal infections, and hemodynamic instability were excluded from the study.

The patients were divided into two equal groups according to the perioperative analgesic modality. The Quadratus Group (n = 17) underwent bilateral ultrasound-guided continuous QLB. The Epidural Group (n = 17) underwent continuous TEA, serving as a control group.

Pre-operative assessment

Routine pre-operative assessment was done on all patients, including evaluation of medical history, clinical examination, and laboratory investigations. All patients were trained to use the visual analog scale score (VAS), assigning (0) as no pain and (10) as the worst imaginable pain.

The patients were sedated with midazolam (0.02 mg/kg) intravenously. The standard monitoring was applied, including pulse oximetry, blood pressure monitoring, 5-lead ECG, and capnography (after intubation). The analgesic procedure was performed before catheter insertion, which was evaluated using 5 ml of lidocaine 5% before proceeding with regular anesthetic doses. Analgesia at the T6 level was considered satisfactory.

QLB

With the patient in the lateral decubitus position, the hip was abducted and laterally flexed towards the same side of the block. An ultrasound machine (Sonoscape P40) with a low-frequency

curved array transducer (2-6 MHz) was used with the orientation marker directed laterally. Starting posteriorly, the QL muscle was identified with its attachment to the lateral edge of the transverse process of the L4. With the psoas major muscle anteriorly, the erector spinae muscle posteriorly, and the QL muscle adherent to the apex of the transverse process, a well recognizable pattern of a shamrock with three leaves can be seen (shamrock sign), which was used to confirm the identification of QL muscle [17]. Under aseptic conditions, an 18-gauge Touhy's epidural needle (BBRAUN epidural set) was used. The needle was introduced using an in-plane approach in a lateral to the medial manner in relation to the US transducer using a posterior-to-anterior trajectory to pierce the QL muscle (anterior transmuscular approach) to reach the desired injection site between the fascial layers of the QL and psoas major muscles outside the anterior layer of the thoracolumbar fascia. Normal saline 5 mL was used to identify the plane then we inserted an epidural catheter through the needle after confirmation of the injection site. A 20 ml of 0.25% Bupivacaine bolus was injected in that plane just over QL muscle; this was followed by fixation of the epidural catheter to facilitate continuous infusion later on. A similar procedure was performed on the other side. A continuous infusion of 0.125% Bupivacaine at 10 ml/h was administered (10 micrograms of adrenaline were added to every 1 ml of the injectate to increase the safety profile of the injectate). The infusion was continued during and after the surgery.

TEA

The puncture site was identified with the patients in the sitting position at T10–11 intervertebral spaces. Under aseptic conditions, an 18G Tuohy epidural needle was used to insert an epidural catheter as appropriate. Induction of epidural analgesia started with a bolus dose of 10–15 ml bupivacaine 0.25% preoperatively, followed by continuous infusion at a rate of 5–7 ml/h using bupivacaine 0.25% till we achieved the analgesic level of T4 to L1. The infusion was continued during and after the surgery.

General anesthesia technique

Under standard monitoring, anesthesia was induced with fentanyl (1 μ g/kg), propofol (1.5–2.5 mg/kg), and cisatracurium 0.15 mg/kg IV boluses. Sevoflurane was delivered by face mask until deep anesthesia was achieved. An endotracheal tube was introduced, secured, and connected to mechanical ventilation (ventilation parameters were adjusted to maintain ETCO₂ at 35–40 mmHg). Paracetamol 1 gm IV infusion was administered. Anesthesia was maintained with sevoflurane (2%) and cisatracurium 0.03 mg/kg (starting 50 min after induction). Before the

end of the surgical procedure, inhalational anesthesia was discontinued. Muscle relaxation was reversed by neostigmine (0.04–0.08 mg/kg) and atropine sulfate (0.02 mg/kg).

Post-operative care

Monitorina was continued Post-Anesthesia Care Unit (PACU) for 30 min to ensure hemodynamic stability. Then they were discharged from PACU according to the modified Aldrete's scoring system (9-10 points for safe discharge). Patients' pain evaluation was continued and recorded for 48 h at 6, 24, and 48 h using the VAS score. Nausea score was assessed on a scale from 0 to 3 (none = 0, mild = 1, moderate = 2, and vomiting = 3) at the same time points. When the VAS score was ≥4, intravenous morphine 3 mg was administered as rescue analgesia. The time of first morphine requirement and the total 48 h morphine consumption were recorded in all patients. When the nausea score reached 2 or more, intravenous Ondansetron 8 mg was administered and recorded. Patient satisfaction was assessed at the end of the study on a scale from 1 to 4 (poor = 1, fair = 2, good = 3, and excellent = 4). Heart rate, blood pressure, respiratory rate, nausea, sedation, and adverse effects were measured and documented.

The primary outcome was pain intensity measured by VAS score (0 no pain; 10 cm, worst pain imaginable) at 6, 24, and 48 h after surgery. The secondary outcomes were total morphine consumption during the first 48 h after surgery and patient satisfaction.

Sample size estimation

As there are no similar studies in the literature, thus, based on a previous study, a large effect size of approximately 1.13 is expected regarding the difference in VAS scores. A total sample size of 28 patients is required with a power of 80% and a significance level of 5%. This number was increased to 34 patients (17 patients in each group) to account for the possibility of using non-parametric tests. The sample size was calculated using the G*Power program (University of Düsseldorf, Düsseldorf, Germany) 17, 20, 21.

Statistical methods

Statistical analysis was made using IBM SPSS Statistics ver. 26 (IBM© Corp., Armonk, NY, USA). Numerical data were presented as mean and standard deviation or median and range as appropriate and categorical data were presented as frequency and percentage. Chi-square test (Fisher's exact test) was used to examine the relationship between

qualitative variables. Comparison between two groups of quantitative data was made using an independent sample t-test or Mann–Whitney test. Comparison of repeated measures was made using Friedman test followed by Wilcoxon signed-ranks test. p < 0.05 was considered significant.

Results

The two studied groups were comparable in age and sex (Table 1).

Table 1: Demographic characteristics in the two studied groups

Variable	Quadratus Group (n = 17)	Epidural Group (n = 17)	р		
Age (years)	63.8 ± 7.5	61.6 ± 7.8	0.414		
Sex (male/female)	15/2	16/1	0.656		
Data are expressed as mean ± SD, or n (%). SD: Standard deviation.					

There were no differences between the two groups in postoperative VAS scores starting immediately after surgery up to 48 h. In the Quadratus Group, VAS did not change significantly after 6 h. However, the VAS score decreased significantly after 24 and 48 h compared to immediate postoperative reading. In the Epidural Group, VAS score decreased significantly after 6, 24, and 48 h compared to immediate postoperative reading (Table 2).

Table 2: The post-operative analgesic profile, nausea score, and satisfaction score in the two studied groups

Quadratus	Epidural	p*
Group (n = 17)	Group (n = 17)	
3.0 (2.0-5.0)	3.0 (2.0-6.0)	0.610
3.0 (2.0-4.0)	3.0 (2.0-5.0)	0.394
0.210	0.009	
2.0 (2.0-3.0)	2.0 (1.0-4.0)	0.812
0.006	0.006	
2.0 (1.0-3.0)	2.0 (1.0-4.0)	1.000
0.003	< 0.001	
7 (41.2)	4 (23.5)	0.271
4.5 (3.0-12.0)	4.0 (2.0-20.0)	0.976
0 (0-1)	1 (0-3)	0.020
3.4 ± 1.1	3.2 ± 1.0	0.612
	Group (n = 17) 3.0 (2.0–5.0) 3.0 (2.0–4.0) 0.210 2.0 (2.0–3.0) 0.006 2.0 (1.0–3.0) 0.003 7 (41.2) 4.5 (3.0–12.0) 0 (0–1)	Group (n = 17) Group (n = 17) 3.0 (2.0-5.0) 3.0 (2.0-6.0) 3.0 (2.0-5.0) 0.210 0.009 2.0 (2.0-3.0) 2.0 (1.0-4.0) 0.006 2.0 (1.0-3.0) 2.0 (1.0-4.0) 0.003 < 0.001 7 (41.2) 4 (23.5) 4.5 (3.0-12.0) 4.0 (2.0-20.0) 0.00-1

⁶Within those who required morphine, *p-value for between groups difference, *p-value for within groups difference. Data are expressed as median (range), or n (%). VAS: Visual analog scale.

Seven patients of the Quadratus Group and four of the Epidural Group did not request morphine rescue analgesia during the postoperative period (p = 0.271). There was no significant difference between the two groups in the total post-operative morphine consumption (p = 0.976) in the remaining patients. The nausea score was significantly lower in the Quadratus Group than in the Epidural Group (Table 2). There was no significant difference between the two groups in the satisfaction score (Table 2). Few mild complications were detected in the two studied groups (Table 3).

There were no significant differences between the two groups in heart rate and mean arterial pressure at the baseline and postoperatively up to 48 h. Heart rate and MAP showed statistically significant B - Clinical Sciences Anesthsiology

Table 3: Number of patients affected by different post-operative complications in the two studied groups

Variable	Quadratus	Epidural Group
	Group $(n = 17)$	(n = 17)
Hypotension	1	3
Insufficient analgesia	2	2
Nausea	0	3
Vomiting	0	2
Hypertension	2	1
Temporary LL motor weakness	2	1
Agitation	1	0
Unilateral pain	1	0
Tachycardia	0	1

changes during the postoperative period. However, all changes were within the clinically accepted ranges (Figures 1 and 2).

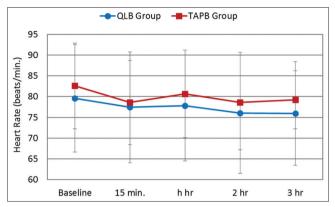


Figure 1: Changes in heart rate during the postoperative period in the two studied groups

iscussion

This study demonstrated a similar analgesic profile of QLB and TEA regarding morphine consumption and pain scores. The two groups were comparable in the VAS scores during the postoperative 48 h. The only difference was delayed reduction of VAS score after QLB, as VAS scores did not change significantly after 6 h. However, the VAS score decreased significantly after 24 and 48 h compared to immediate postoperative reading. On the other hand, the VAS score decreased significantly starting from 6 h compared to immediate postoperative reading in the TEA group. Both techniques were hemodynamically safe. Likewise, patient satisfaction was similar in the two groups. The main advantage of QLB was a significantly lower nausea score.

At present, studies examining continuous transmuscular QL technique for postoperative analgesia after major open abdominal surgery in adults are scarce. To the best of our knowledge, this study appears to be one of the first attempts to investigate QLB in patients subjected to RC to treat bladder cancer.

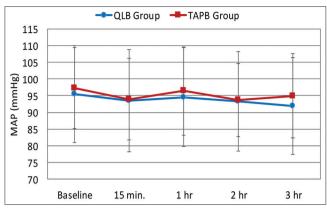


Figure 2: Changes in mean arterial pressure during the post-operative period in the two studied groups

We have chosen TEA as the conventional approach in the current study based on recommendations for ERAS guidelines [10]. However, neuraxial analgesia is associated with the risk of major complications, including neuraxial hematoma, pneumothorax, and respiratory depression [18]. Interfascial plane blocks have been introduced as an alternative to neuraxial blocks for post-operative analgesia to avoid these possible complications. QLB was recently introduced as a variant of the TAP block in 2007; then, four approaches were described afterward. In this study, we used the transmuscular approach, where the LA is injected in the plane between QL and psoas major muscles [19].

The similarity of QLB to TEA can be attributed to the mechanism of action of anterior QLB. It is supposed that the LA spreads along the thoracolumbar fascia (TLF) and endothoracic fascia into the paravertebral space to block the somatic nerves and the thoracic sympathetic trunk of the lower thoracic levels [20]. Two cadaveric studies support this notion. Dam et al. documented thoracic paravertebral spread involving somatic nerves and sympathetic trunk to the T9-T10 level [21]. In the subcostal anterior QL approach at the L1-2 level, cranial spread involved T7-12 level [22]. The TLF incorporates a high-density network of sympathetic fibers and pain receptors [23]. QLB can partially reduce somatic and visceral pain by blocking these receptors [24]. Therefore, QLB appears to be a good alternative analgesic modality in cases of RC to avoid the possible complications of neuraxial block like TEA.

The previous studies have demonstrated the effectiveness of QLB in different types of abdominal operations, including cesarean section [25], [26], laparoscopic gynecological surgery [27], total abdominal hysterectomy [28], and other abdominal surgeries [29], [30]. A meta-analysis showed that QLB provides better pain management with less opioid consumption after abdominal surgery compared with TAP block [31]. Transmuscular QLB was associated with reduced postoperative sufentanil consumption hours and nausea and vomiting compared to the control group in patients undergoing laparoscopic nephrectomy [32].

Similar findings were reported in patients undergoing percutaneous nephrolithotomy [33], [34].

There were some limitations of this study. It was conducted in a single center and was single-blind. Furthermore, the sample is rather small. We did not find a similar previous study and resorted to expecting a large effect size for the difference between groups.

Conclusion

Quadratus lumborum plane block QLB and TEA are safe and effective techniques for post-operative pain management after RC for bladder cancer with similar analgesic profiles. Both modalities effectively reduce postoperative morphine consumption and pain intensity. TEA achieved more rapid analgesia starting from 6 to 48 h. QLB was more effective in reducing post-operative nausea and vomiting.

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B - Clinical Sciences Anesthsiology

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