

## Randomized Trial

# Ultrasound-guided Techniques for Perioperative Analgesia in Pediatric Lower Abdominal Surgeries: Quadratus Lumborum Block with Bupivacaine versus Caudal Bupivacaine and Neostigmine

Tarek M. Ashoor, MD, Eman M. Zain, MBBCh, Mostafa K. Reyad, MD, Ahmad M. Hasseb, MD, and Ibrahim M. Esmat, MD

From: Department of Anesthesia, Intensive Care, and Pain Management, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

Address Correspondence: Ibrahim Mamdouh Esmat, MD  
Department of Anesthesia, Intensive Care, and Pain Management, Faculty of Medicine, Ain-Shams University  
29th Ahmed Fuad St., Saint-Fatima Square  
Heliopolis, Cairo, Egypt  
E-mail: ibrahim\_mamdouh@med.asu.edu.eg

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 08-16-2022

Revised manuscript received: 10-12-2022

Accepted for publication: 11-10-2022

Free full manuscript: [www.painphysicianjournal.com](http://www.painphysicianjournal.com)

**Background:** Ultrasound-guided regional anesthesia techniques for perioperative analgesia in pediatric patients scheduled for lower abdominal surgeries can be achieved either by quadratus lumborum block (QLB) or caudal block (CB). Neostigmine was co-administered with caudal bupivacaine to shorten the onset and extend the duration of analgesia.

**Objectives:** This study aimed to compare between 2 ultrasound-guided techniques used for perioperative analgesia (QLB with bupivacaine vs. CB with bupivacaine/neostigmine) regarding the total amount of rescue analgesic (acetaminophen mg/kg) used for pain relief at 24 hours postsurgery in pediatric patients undergoing lower abdominal surgeries in a developing country and to discuss existing barriers during the implementation of both techniques.

**Study Design:** A randomized, double-blind, prospective, single-center study.

**Setting:** Ain-Shams University Hospitals

**Methods:** Eighty pediatric patients scheduled for lower abdominal surgeries under general anesthesia were randomly allocated to receive either ultrasound-guided QLB using bupivacaine or ultrasound-guided CB using a bupivacaine/neostigmine mixture. The total amount of rescue analgesic (acetaminophen mg/kg) 24 hours postsurgery was considered as the primary outcome while the time to first rescue analgesia, pain score, postoperative nausea and vomiting, bradycardia, hypotension, and urinary retention were considered as secondary outcomes.

**Results:** In the QLB group, the time to first rescue analgesia was longer whereas the total analgesic dose (mg/kg) was lower than the CB group ( $P < 0.001$ ,  $P = 0.007$ , respectively). While, on the other hand, in CB group, the time to perform the block was shorter and Parents Satisfaction Score 24 h postsurgery was lower than the QLB group ( $P < 0.001$ ,  $P < 0.001$ , respectively). Side effects were infrequent and comparable between the study groups.

**Limitations:** First, the researchers did not assess the dermatomal level before or after the operation in either group. Second, the investigators should have noticed the first voiding time to demonstrate accurately the incidence of urine retention. Third, a cost-effectiveness analysis of perioperative costs (drugs, staff, resources being used) of these regional anesthesia techniques when applied in an ambulatory setting should have been done, which would be helpful for those in resource-limited settings.

**Conclusions:** Postoperative analgesia for pediatric patients undergoing lower abdominal surgeries can be safely and effectively achieved by QLB with bupivacaine and a CB with a bupivacaine/neostigmine mixture with priority given to CB, especially in resource-limited settings.

**Key words:** Quadratus lumborum, caudal, bupivacaine, neostigmine, ultrasound, pediatric, postoperative, pain

**Pain Physician 2023; 26:137-147**

**P**ostoperative pain remains the distressing consequence of surgery, especially in pediatric patients who lack appropriate expression of pain sensation (1). Added to the problem, the enhanced recovery after surgery protocol recommends a multidisciplinary approach to optimize perioperative analgesia by using nonopioid medications and regional anesthesia techniques, making pediatric postoperative pain control more challenging to be adjusted to desired clinical effects in resource-limited areas (2).

Quadratus lumborum block (QLB) is a block of the posterior abdominal wall that is only done with ultrasound (ULSD) guidance. A QLB allows the local anesthetic to spread between the posterior aspect of the quadratus muscle and the middle layer of the thoracolumbar fascia, which is close to the thoracic paravertebral space (3). Many studies performed on cadavers have shown that the injected contrast medium in a QLB can spread up to the thoracic portion (T4) of the sympathetic trunk cranially and lumbar nerve roots caudally. However, the volume of the drug application and individual anatomical variations can also influence the level of the block. Clinically, a QLB induces both somatic and visceral analgesia (4). Nevertheless, the widespread use of QLBs in pediatrics may be limited by the fear of local anesthetic toxicity (5) and the unavailability of an ULSD, specially in resource-limited countries.

Caudal epidural analgesia in pediatric patients is the commonest regional technique because it is a simple approach and it has a high success rate (1). However, pain relief with a single-shot caudal block (CB) is short-lasting. So additives like opioids, clonidine, and ketamine have been used to prolong CB's analgesic effect but with different degrees of undesirable effects (6). Neuraxial neostigmine induces analgesia in animals and patients with pain (7). It creates its effect by inhibiting the breakdown of the endogenous spinal acetylcholine that mediates its analgesic effect through its action on spinal M1 muscarinic acetylcholine receptors (8). Neostigmine use as an adjuvant to bupivacaine in CB was found to exert prolonged analgesia in pediatric patients (1).

This study aimed to compare between 2 ULSD-guided techniques used for perioperative analgesia (QLB vs caudal bupivacaine/neostigmine) regarding the total amount of rescue analgesic (acetaminophen mg/kg) used for pain relief during 24 hours postsurgery in pediatric patients undergoing lower abdominal surgeries in a developing country, and to discuss existing barriers during the implementation of both techniques.

## **METHODS**

### **Ethics**

After approval of the local ethical committee (FMASU MS 728/2020/2021), this study was prospectively registered at ClinicalTrials.gov (NCT04720287) (first posted on ClinicalTrials.gov on 22/1/2021), followed the regulations of the Helsinki Declaration-2013 and conducted from February 1, 2021 to April 30, 2021 at Ain-Shams University Hospitals. An informed written consent was obtained from the parents of every study patient.

### **Study Population**

Eighty patients, aged from 1-5 years, with American Society of Anesthesiologists physical status I-II risk class scheduled for lower abdominal surgeries were recruited to the study. Children with anatomical abnormalities or infection at the site of the block; a history of neurological, heart, renal or coagulation abnormalities; and a history of a previous abdominal surgery or preoperative opioid administration were excluded. A parent's or legal guardian's refusal and known allergy to study medications were also considered as exclusion criteria.

### **Randomization and Blinding**

Patients were randomized using a computer-generated random allocation sequence into 2 groups (40 each): the QLB group or CB group. Patients' parents were blinded to the allocation group. After group assignment, a letter explaining standardized instructions for the study drug preparation was handed to a well experienced anesthesia consultant in both blocks who prepared the study solution then performed the block; this person did not share in any other part of the study. QLB patients received one mL/kg of 0.25% bupivacaine divided in 2 equal syringes (a syringe to perform one side of trunk nerve block); CB patients received 2 µg/kg neostigmine in one mL/kg of 0.25% bupivacaine. The neostigmine was in the form of 0.5 mg /1 mL neostigmine methylsulfate ampoule that was prepared by diluting the neostigmine ampule in 20 mL normal saline 0.9% syringe (concentration will be 25 µg/mL) and then the exact dose was calculated and was added to the bupivacaine.

### **Study Nondependent Protocol**

Premedication was not required. On arrival to the operating room, standard monitoring including electrocardiogram, pulse oximeter, and noninvasive blood

pressure was applied and baseline vital data were obtained.

Patients underwent inhaled induction of anesthesia using 8% sevoflurane in 50% oxygen and air administered via a face mask followed by establishing an intravenous (IV) access. One  $\mu\text{g}/\text{kg}$  fentanyl and 0.1 mg/kg cisatracurium were administered intravenously followed by tracheal intubation and mechanical ventilation. Anesthesia was maintained by sevoflurane in 50% oxygen and air and intermittent doses of a muscle relaxant if needed to provide adequate muscle relaxation during surgery. The IV fluid therapy was standardized for all patients as 6 mL/kg/h lactated Ringer's solution intraoperatively and 4 mL/kg/h 5% dextrose in the postoperative period. Patients were laterally positioned and the block was carried out.

Both blocks were performed prior to skin incision using an ULSD machine with high-frequency linear probe (Mindray code: 75L38EB freq.: 7.5 MHz, Probe band width: 5.0-10.0). Skin preparation was done to confirm aseptic injection techniques. Surgical incision was allowed 15 minutes after performing the block.

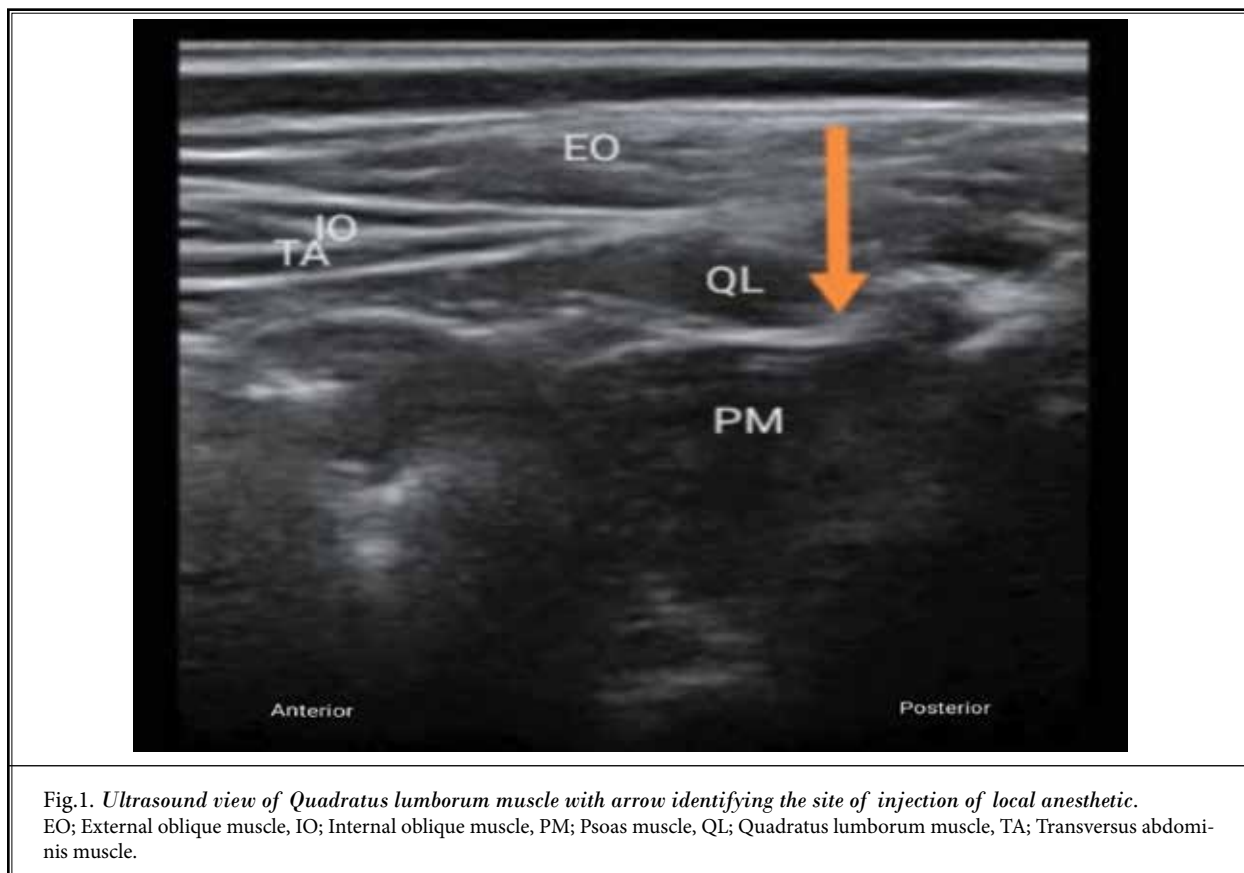
### Study Dependent Protocol

#### QLB (Posterior QLB) (QLB type 2)

The patient was placed in the lateral decubitus position with the ULSD probe (linear array ULSD probe transducer 7L4P; Mindray Z6) placed above the iliac crest at the midaxillary line. The probe was then moved posteriorly to identify the "shamrock sign" (quadratus lumborum muscle, psoas major muscle, erector spinae muscle, and L3 transverse process). An "in-plane" approach using an echogenic needle (22G, 100 mm) was performed targeting the middle thoracolumbar fascia layer between quadratus lumborum muscle and the psoas major muscle. The spread of local anesthetic between those 2 muscles was considered as a correct injection. The QLB was then performed on the contralateral side (9). (Fig. 1)

#### Caudal Block (CB)

With the patient in the lateral decubitus position, a linear transducer was transversely placed in the middle of the sacral hiatus targeting the view of



the hyperechoic sacrococcygeal ligament in between 2 sacral cornua and the deeper sacral bone. The probe was then turned 90° for the longitudinal axis so that the echogenic needle (22G, 100 mm) could be inserted “in-plane” into the sacral hiatus (maximum 5 mm). The spread of local anesthetic between the sacrococcygeal ligament and the deeper sacral bone was considered as a correct injection (10). (Fig. 2)

### Parameters and Outcomes

The heart rate and the mean arterial pressure were recorded before induction (baseline reading, T0), 5 minutes after intubation and before performing the block (T1), 20 minutes after performing the block (T2); the mean intraoperative values were measured every 5 minutes until the end of the surgery (T3) and 30 min after extubation (T4). Block failure was defined as an increase in heart rate or mean arterial pressure within 15 minutes of skin incision and a bolus dose of 0.5 µg/kg fentanyl was given intravenously. Hypotension was defined as a 25% decrease in mean arterial pressure compared with the baseline value and was managed by an intravenous fluid bolus (10 mL/kg) only or in addition to intravenous boluses of ephedrine as appropriate. Bradycardia was defined as a heart rate lower than 60 beats per minute and was managed using an intravenous 0.02 mg/kg atropine bolus.

Postoperative pain was assessed using Face, Legs, Activity, Cry, Consolability (FLACC) scores (11) at the immediate postoperative period, at 30 minutes, and at 2, 4, 6, 12, and 24 hours postsurgery. A FLACC score of  $\geq 4$  was managed by 15 mg/kg slowly administered intravenous acetaminophen which could be repeated

once after 15 minutes if pain persisted. The time to first rescue analgesia, the need for analgesia, and the total analgesic dose (mg/kg) required in a 24-hour period were recorded. All measurements were recorded by anesthesia residents who were blinded to the study intervention allocation.

The length of time required to perform the block (time from ULSD orientation of the area to be blocked until the end of the injection and needle withdrawal) and the incidence of block failure were recorded. Any adverse events, including postoperative nausea and vomiting (PONV), postoperative urinary retention (no voiding of urine for 6 hours postoperatively), hypotension, and bradycardia were also recorded and treated in both groups. Hospital stay duration and parental satisfaction regarding the postoperative pain management protocol at 30 minutes after extubation and 24 hours postsurgery using a parent satisfaction score (12) were documented.

The total amount of rescue analgesic (acetaminophen) (mg/kg) 24 hours postsurgery was considered as a primary outcome, while the time to first rescue analgesia, pain score, PONV, bradycardia, hypotension, and urinary retention were considered as secondary outcomes.

### Statistical Analysis

#### Power of the Study

Setting the power = 0.80,  $\alpha = 0.05$ , using PASS 11.0 (NCSS Statistical Software) (13) and based on an earlier pilot study (14), a sample size of 23 patients in each group was required to keep a statistically significant

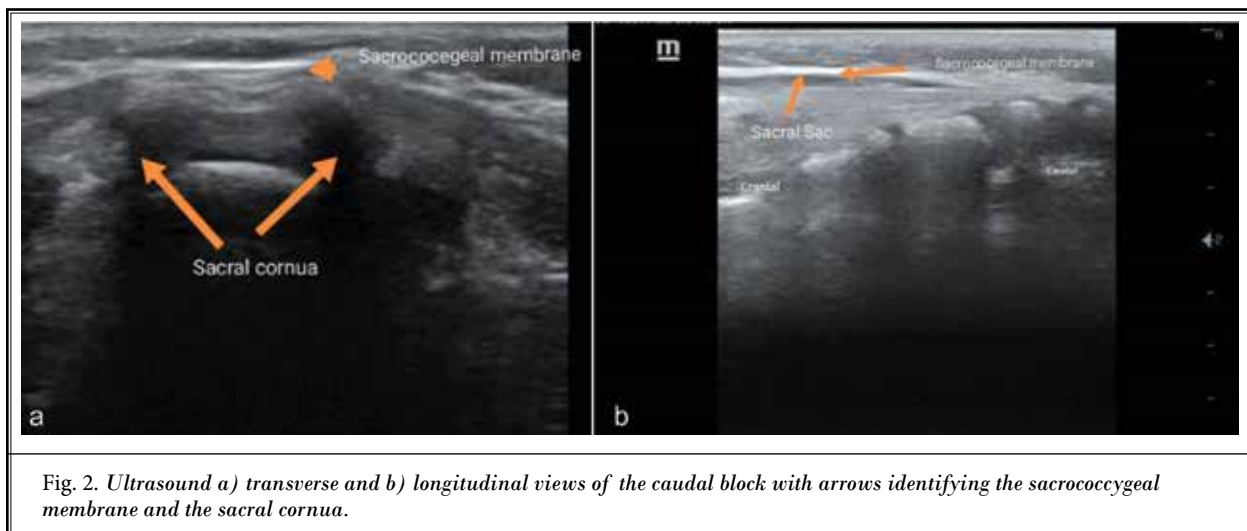


Fig. 2. Ultrasound a) transverse and b) longitudinal views of the caudal block with arrows identifying the sacrococcygeal membrane and the sacral cornua.

difference for postoperative rescue analgesia during the first 24 hours between the QLB group ( $0.8 \pm 1.6$ ) and the CB group ( $3.8 \pm 4.6$ ). This sample was raised up to 40 patients in each group for possible attrition and block failure.

### Data Analysis

IBM Statistical Package for Social Sciences (SPSS) version 22.0, (IBM Corp.) was used for data management and analysis. Quantitative data were checked for normality using the Shapiro-Wilk test, then were described as mean  $\pm$  standard deviation and minimum and maximum of the range and finally were compared using independent t test for 2 independent groups and paired t test for paired variables. Qualitative data were described as number and percentage, then compared using the  $\chi^2$  test and Fisher's exact test. The level of significance was taken at  $P < 0.050$ .

### RESULTS

Among the 94 patients who were assessed for eligibility, 80 patients were enrolled and randomly allocated into either the QLB group or the CB group (40 each). Owing to block failure, 32 patients in the QLB group and 39 patients in the CB group completed the study and were subjected to statistical analysis (Fig. 3).

The demographic and surgical characteristics were comparable between study groups ( $P > 0.05$ , Table 1). Group members didn't show any significant differences in heart rate or mean arterial pressure during the study.

In the QLB group, the time to perform the block was longer, whereas the need for analgesia was lower than the CB group ( $P < 0.001$ ,  $P < 0.001$ , respectively, Table 2). In the QLB group, the time to first rescue analgesia was longer and the total analgesic dose (mg/kg) was lower than the CB group ( $P < 0.001$ ,  $P = 0.007$ , respectively, Table 2).

The 12 and 24 hours postoperative FLACC scores were higher in the CB group compared to the QLB group ( $P < 0.001$ ,  $P < 0.001$ , respectively, Fig. 4) while the rest of the time points the FLACC scores were comparable between study groups (Fig. 4). The amount of rescue analgesia required was lower in the QLB group compared to the CB group ( $P < 0.001$ , Fig. 5).

In the CB group, the incidence of block failure was lower, whereas the incidence of PONV was higher than the QLB group ( $P = 0.029$ ,  $P = 0.125$ , respectively, Table 3). Only one patient in the QLB group showed bradycardia while 3 patients (2 in the QLB group and one in the CB group) developed hypotension (Table 3). More patients in the QLB group complained of postoperative urine retention and postoperative hematoma

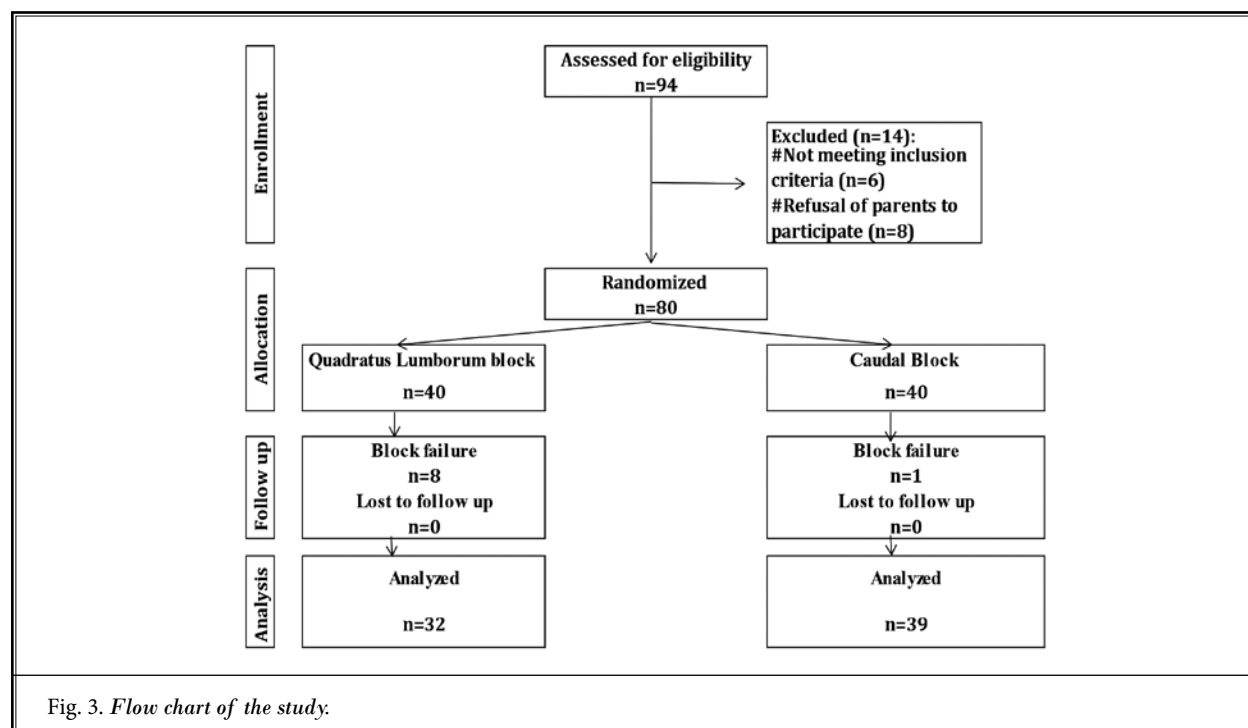


Fig. 3. Flow chart of the study.

Table 1. Demographic and surgical characteristics between the study groups.

Variables		Quadratus Lumborum Block (QLB) Group (n = 32)	Caudal Block (CB) Group (n = 39)	P value
Age (years)	Mean ± SD	3.3±1.1	3.1±1.1	^0.392
	Range	2.0-5.0	2.0-5.0	
Gender, (n, %)	Boys	27 (84.4%)	31 (79.5%)	#0.596
	Girls	5 (15.6%)	8 (20.5%)	
Weight (kg)	Mean ± SD	15.1±2.1	14.8±2.0	^0.585
	Range	11.1-18.6	11.3-18.9	
ASA, (n, %)	I	28 (87.5%)	34 (87.2%)	§0.999
	II	4 (12.5%)	5 (12.8%)	
Type of Operation, (n, %)	Inguinal hernia repair	20 (62.5%)	23 (59.0%)	#0.762
	Orchiopexy	12 (37.5%)	16 (41.0%)	
Duration of Surgery (minutes)	Mean ± SD	52.9±2.3	52.4±2.0	^0.276
	Range	49.0-58.0	47.0-56.0	

Data are presented as mean ±SD or number and (%). ^Independent t test. #χ<sup>2</sup> test. §Fisher's Exact test. ASA: American Society of Anesthesiologists.

Table 2. Time to perform the block and rescue analgesia (need, time, and dose) between the study groups.

Variables	Quadratus Lumborum Block (QLB) Group (n = 32)	Caudal Block (CB) Group (n = 39)	P value	Relative Effect	
				Mean ± SE	95% CI
Time to perform the block (min)	13.3 ± 0.9	6.6 ± 1.1	^ < 0.001*	6.6 ± 0.2	6.2 – 7.1
Need for analgesia (n, %)	12 (37.5%)	34 (87.2%)	# < 0.001*	RR: 0.43	0.27– 0.68
Time to first rescue analgesia (h)	10.9 ± 2.5	8.3 ± 1.2	^ < 0.001*	2.6 ± 0.5	1.5 – 3.7
Total acetaminophen dose (mg/kg)	20.4 ± 4.2	25.1 ± 5.1	^ 0.007*	- 4.6 ± 1.6	-7.9 – -1.3

Data are presented as Mean ± SD or number and (%). #χ<sup>2</sup> test. ^Independent t-test. RR: Relative risk. Relative effect: Effect of quadratus lumborum block relative to caudal block. CI: Confidence interval. \*Significant.

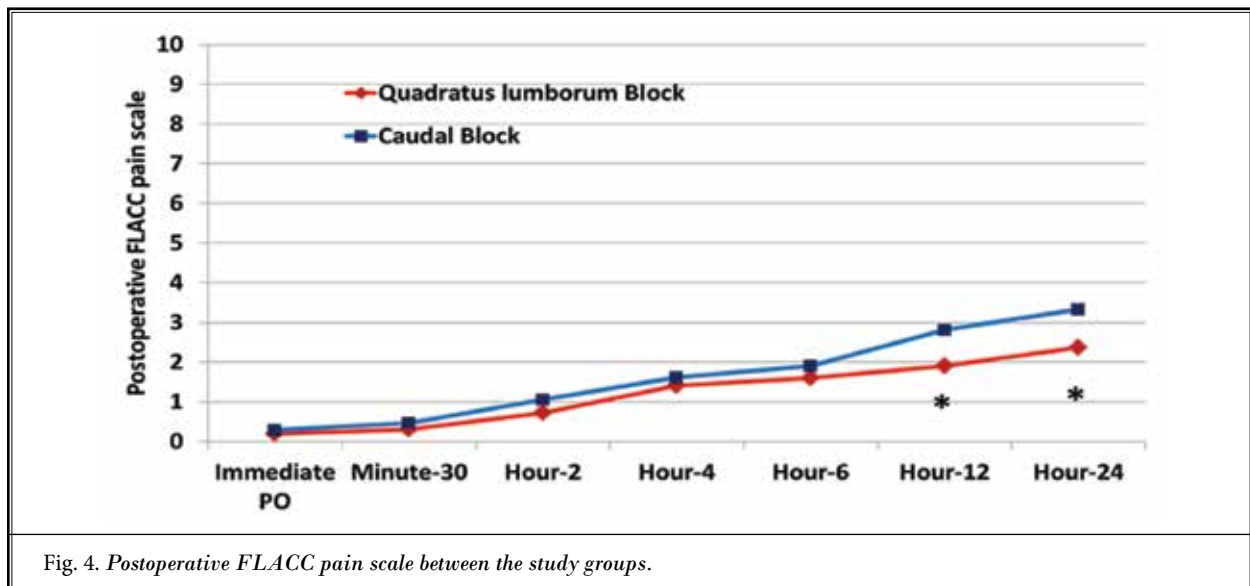


Fig. 4. Postoperative FLACC pain scale between the study groups.

compared to the CB group ( $P = 0.454$ ,  $P = 0.087$ , respectively, Table 3). The hospital stay was comparable between study groups ( $P = 0.181$ ). The 24 hours postoperative Parents Satisfaction Score (P2) was higher in the QLB group in comparison to the CB group ( $P < 0.001$ , Table 3) while the 30 minutes after extubation Parents Satisfaction Score (P1) was comparable between study groups ( $P = 0.075$ , Table 3).

### DISCUSSION

As far as the authors know, this is the first randomized controlled study comparing a caudal bupivacaine/neostigmine mixture, which is a relatively old and simple technique, with the recently adopted technique of QLB to achieve postoperative analgesia in pediatric patients scheduled for lower abdominal surgeries. The results of our study show that a bilateral QLB with plain bupivacaine and a CB with bupivacaine/neostigmine were equally effective in the first 12 hours postoperatively regarding the requirement for rescue analgesics, but a QLB was superior to a CB in the rest of the 24-hours postsurgery.

Regional anesthesia in the pediatric population provides a high-quality assurance of postoperative pain relief. In addition, regional anesthesia has been improved due to advances in ULSD technology. Moreover,

the benefits of using ULSD technology include reduced postoperative pain scores, reduced opioid consumption, a reduced incidence of PONV, and a reduced incidence of respiratory complications (15). Regional blocks were used clinically for the last 40 years as a part of perioperative analgesia for lower abdominal surgeries (4), starting with the ilioinguinal–iliohypogastric block (16) and the

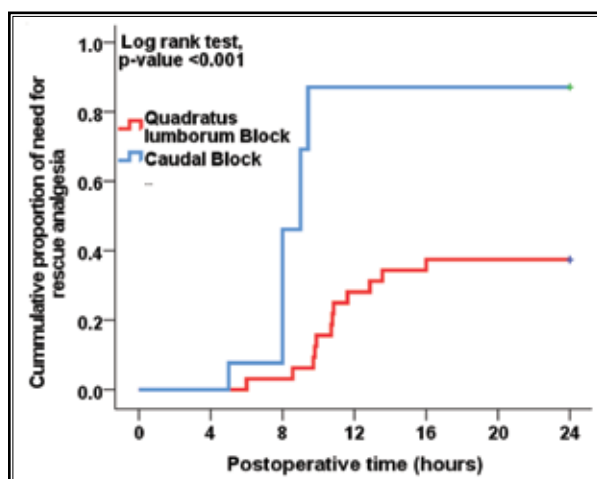


Fig. 5. Kaplan-Meier survival curves for rescue analgesia need between the study groups.

Table 3. Postoperative complications, hospital stay and Parents Satisfaction Score between the study groups.

Complications (n, %)	Quadratus Lumborum Block (QLB) Group (n = 32)	Caudal Block (CB) Group (n = 39)	P value	Relative effect Relative Risk (95% CI)
Nausea and vomiting	3 (9.4%)	9 (23.1%)	#0.125	0.41 (0.12–1.38)
Bradycardia	1 (3.1%)	0 (0.0%)	\$0.451	NA
Hypotension	2 (6.3%)	1 (2.6%)	\$0.585	2.44 (0.23–25.67)
Urine retention	5 (15.6%)	3 (7.7%)	\$0.454	2.03 (0.53–7.86)
Hematoma	3 (9.4%)	0 (0.0%)	\$0.087	NA
				Mean ± SE 95% CI
Hospital stay (days), Mean±SD	1.4 ± 0.2	1.5 ± 0.2	^0.181	- 0.1 ± 0.1 - 0.2–0.1
Parents Satisfaction Score, Mean±SD				
30 minutes after extubation (P1)	8.5 ± 0.6	8.2 ± 0.7	0.075	0.3 ± 0.2 0.0–0.6
24 hours after surgery (P2)	8.1 ± 0.9	6.5 ± 0.6	< 0.001*	1.6 ± 0.2 1.2–2.0

Data are presented as Mean ± SD or number and (%). ^Independent t test. \$Fisher's Exact test. Relative effect: Effect of quadratus lumborum block relative to caudal block. NA: Not applicable. CI: Confidence interval. \*Significant.

rectus sheath block (17), which are commonly used in pediatric anesthesia. A few years later, the transversus abdominis plane block was introduced which provides a much better field of postoperative analgesia (18).

The QLB is a newly defined procedure to achieve adequate analgesia for lower and upper abdominal surgeries (12). Blanco et al (19) described different approaches to perform a QLB. They suggested that the QLB type 2, where the local anesthetic is injected between the posterior edge of the QL muscle and the middle layer of the thoracolumbar fascia, which is connected with the thoracic paravertebral space, may provide a safe, effective, and relatively long-lasting postoperative pain relief through the spread of the local anesthetic to the paravertebral space (19). A QLB provides adequate analgesic coverage from T4-L1 (somatic and visceral block) and maintains postoperative analgesia for 24-48 hours (20).

A QLB has a favorable analgesic profile with minimal side effects compared to using conventional opioid analgesics in pediatric patients (21). In agreement with our results, the patients who received a QLB had lower pain scores at 24 hours postoperatively; a smaller number of patients required analgesia postoperatively and less rescue analgesics compared to the patients who received a transversus abdominis plane block (22). In addition, QLB provided superior analgesia than a CB using plain bupivacaine in pediatric patients scheduled for inguinal hernia repair and orchiopexy surgeries (3). However, both blocks were found to have an equal analgesic efficacy, especially in the immediate postoperative period in children undergoing appendectomy (23). Furthermore, Zhao et al (24) documented that a QLB was the most efficient technique to provide postoperative analgesia for pediatric patients undergoing lower abdominal surgeries. In addition, a QLB has a safe profile with minimal complications and/or side effects. Being a strictly ULSD-guided block, inadvertent injury to blood vessel or bowel is limited and the efficiency of the technique is increased. Also, there are no reports of nerve injury or local anesthetic toxicity (4). However, the lack of adequate training in ULSD-guided regional anesthesia techniques is believed to be one of the factors that limits ULSD use in pediatric practice (15). Also, a lack of resources (anesthesia provider training, equipment, and drugs), poor adaptive leadership and support, especially in rural hospitals in low-resource countries, are considered barriers to implementing new techniques to improve the management of postoperative pain (25).

A CB is the most frequently performed regional anesthesia technique in pediatric patients (26). In addition, a CB is a relatively simple and safe regional anesthesia technique with a high success rate and a low incidence of complications or adverse events (27). Apart from the relative merits of a CB, a single-shot CB may have a relatively short duration of action (10) while the placement of a catheter in the caudal region adds an infection risk and prevents early mobilization (27).

Additives to local anesthetics have been used to prolong the analgesic duration of a single-shot CB. The use of opioids in a CB in children has recently been questioned (28). In spite of the long-lasting analgesia provided by caudal morphine, it has common adverse reactions, e.g. nausea, pruritus, urinary retention, and respiratory depression. In addition, fentanyl is a lipophilic opioid which has the same side effects profile and a short duration of analgesia (29). Also, clonidine prolongs the duration of analgesia of caudal bupivacaine but the significant side effects, especially with higher doses, e.g. prolonged sedation, hypotension, and bradycardia limit its use in clinical practice (29). Furthermore, adding ketamine to caudal bupivacaine will prolong the duration of analgesia but its potential neurotoxicity limits its clinical use (30).

The neuraxial administration of neostigmine produces analgesic effects by inhibiting the breakdown of spinal cholinesterase, resulting in an increase of the endogenous spinal dorsal horn acetylcholine (31). Batra et al (7) concluded that caudally administered neostigmine is safe and efficient in pediatric patients with dose-dependent analgesia ranging from 20-50  $\mu\text{g}/\text{kg}$ . There was a higher incidence of PONV if the caudal neostigmine dose exceeded 30  $\mu\text{g}/\text{kg}$  (7). The research team added neostigmine (2  $\mu\text{g}/\text{kg}$ ) to caudal 0.25% bupivacaine in a volume of one mL/kg. In agreement with the results of this research, Abdulatif et al (32) proved that co-administered caudal neostigmine (2  $\mu\text{g}/\text{kg}$ ) with 0.25% bupivacaine (1 mL/kg) prolonged postoperative analgesia with a reduced incidence of PONV.

Congruent with our results, Mahajan et al (33) found that adding neostigmine in doses of 2, 3, or 4  $\mu\text{g}/\text{kg}$  to caudal 0.25% bupivacaine (0.5 mL/kg) prolonged the duration of postoperative analgesia ( $\geq 16.6 \pm 4.9$  hour) with a comparable incidence of PONV in all 4 groups of children undergoing hypospadias repair surgery (33). Similarly, adding neostigmine 2  $\mu\text{g}/\text{kg}$  to caudal 0.2% ropivacaine (0.5 mL/kg) provided an extended duration of postoperative analgesia ( $19.2 \pm 5.5$  hours) with a comparable incidence of PONV in the



2 groups of children undergoing inguinal hernia and hypospadias surgery (27). Also, Karaaslan et al (34) recommended neostigmine at 2 µg/kg to be added to caudal levobupivacaine as an optimal dose to achieve extended postoperative analgesia with minimal side effects in children scheduled for inguinal hernia, hypospadias surgery and/or orchidopexy (34).

Contradictory to our results, Bhardwaj et al (35) added neostigmine at a dose of 2, 3, or 4 µg/kg and Memis et al (36) added neostigmine at a dose of 1 µg/kg to caudal bupivacaine; they both found no extended duration of postoperative analgesia which might be attributed to the concentration of bupivacaine (1.875 mg/kg) in a volume of 0.75 mL/kg injected by Bhardwaj et al which affected the efficacy of the caudal adjuvant drug and the suboptimal neostigmine dose (1 µg/kg) by Memis et al. A recent meta-analysis study also concluded that adding neostigmine to bupivacaine is not recommended due to PONV, however, this could be argued by the fact that the authors put in their analysis studies testing high doses that add to the risk of PONV without extending the duration of analgesia (37).

The neostigmine preparation used in this research was neostigmine methylsulfate. Methyl- and propylparabens as preservatives present in most neostigmine preparations have no associated neurological side effects if administered intrathecally or caudally (32,34). In spite of the analgesic effectiveness of neuraxial neostigmine, it has a limited acceptance as an analgesic modality due to the frequent incidence of PONV. In this research, the incidence of PONV in the QLB group and CB group was 9.4% and 23.1%, respectively ( $P > 0.05$ ). With the use of the caudal epidural route and a dose of 2 µg/kg of neostigmine, the research team's efforts were successful in reducing the incidence of PONV in the CB group. PONV in the study groups were self-limited and patients required no special management. The results of Abdulatif et al (32) and Karaaslan et al (34) were in concordance with our recent findings concerning the comparable incidence of PONV in the caudal neostigmine group in comparison to the other intervention groups.

Patients in our study showed a safe hemodynamic profile. Only one patient in the QLB group had bradycardia while 3 patients (2 in the QLB group and one in the CB group) developed hypotension, which was effectively managed with a fluid bolus compared to regularly seen cases of bradycardia and hypotension associated with higher doses of caudal clonidine (29).

Neuraxial neostigmine has a favorable hemodynamic profile (32) and an ULSD-guided block allows visualization of the local anesthetic spread and a reduction in the local anesthetic volume (34). Urine retention was observed in 8 patients (5 in the QLB group and 3 in the CB group) ( $P > 0.05$ ). Patients did not require catheterization and all cases were self-limited.

In the QLB group, 3 patients developed bruising at the puncture site that didn't require any intervention. More boys than girls were included in this study in both groups. This was because nearly 40% of our study's patients underwent orchiopexy and the incidence of inguinal hernia is higher among boys (38). However, the research team did not think boy/girl discrepancy had any bearing on the outcomes of this study.

Our study has some limitations. First, the researchers did not assess the pain dermatome level before or after the operation in either group because this research was conducted in pediatric patients and the blocks were performed under general anesthesia. Second, the investigators should have noticed the first voiding time to demonstrate accurately the incidence of urine retention. Our definition of urine retention could have resulted in overestimation of it in the QLB group (no bladder distension) and an underestimation in the CB group (dribbling). Third, a cost-effectiveness analysis of perioperative costs (drugs, staff, resources being used) of the regional anesthesia technique applied to the ambulatory setting is necessary, especially in resource-limited settings.

An ULSD-guided peripheral trunk nerve block is no longer the icing on the cake in combined anesthesia, but an indispensable part of anesthesia administration and is gradually stepping onto the stage of clinical anesthesia. Expanding the use of an ULSD-guided peripheral trunk nerve blocks has potential safety, access, and cost benefits.

However, "Old wood best to burn . . . old friends to trust, and old authors to read." wrote Francis Bacon. True to this, a relatively old anesthetic technique (caudal bupivacaine/neostigmine) is in high demand in low-resource countries compared to a new anesthetic technique (ULSD-guided QLB). No matter how progressive we become with time, what's ancient and authentic will always remain the same and it will always be a fact that old is gold (39).

## CONCLUSIONS

A CB using bupivacaine/neostigmine provides a comparable analgesic effect compared to bilateral QLB

with plain bupivacaine for pediatric patients undergoing lower abdominal surgeries within the first 12 hours postsurgery. A CB using bupivacaine/neostigmine is a nonopioid pharmacological pain management option

suitable for postoperative pain control in low-resource countries where the suitable advanced equipment and trained staff may not be available in all hospitals treating pediatric patients.

## REFERENCES

- Mekonnen S, Ali Y. Efficacy of caudal neostigmine for postoperative pain relief: A systemic review and meta-analysis. *Curr Pediatr Res* 2017; 21:403-409.
- Rove KO, Edney JC, Brockel MA. Enhanced recovery after surgery in children: Promising, evidence-based multidisciplinary care. *Paediatr Anaesth* 2018; 28:482-492.
- Öksüz G, Arslan M, Urfalloğlu A et al. Comparison of quadratus lumborum block and caudal block for postoperative analgesia in pediatric patients undergoing inguinal hernia repair and orchiopexy surgeries: A randomized controlled trial. *Reg Anesth Pain Med* 2020; 45:187-191.
- Akerman M, Pejčić N, Veličković I. A review of the quadratus lumborum block and ERAS. *Front Med (Lausanne)* 2018; 5:44.
- Elsharkawy H, El-Boghdady K, Barrington M. Quadratus lumborum block: Anatomical concepts, mechanisms, and techniques. *Anesthesiology* 2018; 130:322-335.
- Wiegele M, Marhofer P, Lönnqvist PA. Caudal epidural blocks in paediatric patients: A review and practical considerations. *Br J Anaesth* 2019; 122:509-517.
- Batra YK, Arya VK, Mahajan R, Chari P. Dose response study of caudal neostigmine for postoperative analgesia in paediatric patients undergoing genitourinary surgery. *Paediatr Anaesth* 2003; 13:515-521.
- Hood DD, Eisenach JC, Tuttle R. Phase I safety assessment of intrathecal neostigmine methylsulfate in humans. *Anesthesiology* 1995; 82:331-343.
- Huang C, Zhang X, Dong C, Lian C, Li J, Yu L. Postoperative analgesic effects of the quadratus lumborum block III and transversalis fascia plane block in paediatric patients with developmental dysplasia of the hip undergoing open reduction surgeries: A double-blinded randomised controlled trial. *BMJ Open* 2021; 11:e038992.
- Kao SC, Lin CS. Caudal Epidural Block: An updated review of anatomy and techniques. *BioMed Res Int* 2017; 2017:9217145.
- Nilsson S, Finnström B, Kokinsky E. The FLACC behavioral scale for procedural pain assessment in children aged 5-16 years. *Pediatr Anaesth* 2008; 18:767-774.
- Öksüz G, Bilal B, Gürkan Y, et al. Quadratus lumborum block versus transversus abdominis plane block in children undergoing low abdominal surgery: A randomized controlled trial. *Reg Anesth Pain Med* 2017; 42:674-679.
- Hintze J. *PASS (Power Analysis and Sample Size System) Quick Start Manual*. 2011.
- Sato M. Ultrasound - guided quadratus lumborum block compared to caudal ropivacaine/morphine in children undergoing surgery for vesicoureteric reflex. *Pediatr Anaesth* 2019; 29:738-743.
- Merella F, Canchi-Murali N, Mossetti V. General principles of regional anaesthesia in children. *BJA Educ* 2019; 19:342-348.
- Hannallah RS, Broadman LM, Belman AB, Abramowitz MD, Epstein BS. Comparison of caudal and ilioinguinal/iliohypogastric nerve blocks for control of post-orchiopey pain in pediatric ambulatory surgery. *Anesthesiology* 1987; 66:832-834.
- Smith BE, Suchak M, Siggins D, Challands J. Rectus sheath block for diagnostic laparoscopy. *Anaesthesia* 1988; 43:947-948.
- O'Donnell BD, McDonnell JG, McShane AJ. The transversus abdominis plane (TAP) block in open retropubic prostatectomy. *Reg Anesth Pain Med* 2006; 31:91.
- Blanco R, Ansari T, Riad W, Shetty N. Quadratus lumborum block versus transversus abdominis plane block for postoperative pain after cesarean delivery. *Reg Anesth Pain Med* 2016; 41:757-762.
- Anggraeni R, Kurniyanta P. Effectivity of quadratus lumborum block in pediatric patient undergoing abdominal surgery at Sanglah General Hospital: A case series. *Int J Res Rev* 2022; 9:123-127.
- Moralari DG, Cekmecelioglu BT, Aslan M, Hergünel GO. Effect of quadratus lumborum block on postoperative analgesic requirements in pediatric patients: A randomized controlled double-blinded study. *Minerva Anesthesiol* 2020; 86:150-156.
- Wang Y, Wang X, Zhang K. Effects of transversus abdominis plane block versus quadratus lumborum block on postoperative analgesia: A meta-analysis of randomized controlled trials. *BMC Anesthesiol* 2020; 20:103.
- Dmytriiev D, Glazov E, Zaletskyi B, Dmytriieva K. Ultrasound-guided Quadratus Lumborum Block versus caudal block for postoperative analgesia in children undergoing acute appendicitis: A comparative study. *Pain Medicine (Malden Mass)* 2020; 5:23-29.
- Zhao WL, Li SD, Wu B, Zhou ZF. Quadratus lumborum block is an effective postoperative analgesic technique in pediatric patients undergoing lower abdominal surgery: A meta-analysis. *Pain Physician* 2021; 24:E555-E563.
- Dohlman LE, Kwikiriza A, Ehie O. Benefits and barriers to increasing regional anesthesia in resource-limited settings. *Local Reg Anesth* 2020; 13:147-158.
- Silvani P, Camporesi A, Agostino MR, Salvo I. Caudal anesthesia in pediatrics: An update. *Minerva Anesthesiol* 2006; 72:453-459.
- Turan A, Memiş D, Başaran UN, Karamanlioğlu B, Süt N. Caudal ropivacaine and neostigmine in pediatric surgery. *Anesthesiology* 2003; 98:719-722.
- Lönnqvist PA, Ivani G, Moriarty T. Use of caudal-epidural opioids in children: Still state of the art or the beginning of the end? *Paediatr Anaesth* 2002; 12:747-749.

29. Jöhr M, Berger TM. Caudal blocks. *Paediatr Anaesth* 2012; 22:44-50.
30. Schnabel A, Poepping DM, Kranke P, Zahn PK, Pogatzki-Zahn EM. Efficacy and adverse effects of ketamine as an additive for paediatric caudal anaesthesia: A quantitative systematic review of randomized controlled trials. *Br J Anaesth* 2011; 107:601-611.
31. Naguib M, Yaksh TL. Antinociceptive effects of spinal cholinesterase inhibition and isobolographic analysis of the interaction with mu and alpha 2 receptor systems. *Anesthesiology* 1994; 80:1338-1348.
32. Abdulatif M, El-Sanabary M. Caudal neostigmine, bupivacaine, and their combination for postoperative pain management after hypospadias surgery in children. *Anesth Analg* 2002; 95:1215-1218.
33. Mahajan R, Grover VK, Chari P. Caudal neostigmine with bupivacaine produces a dose-independent analgesic effect in children. *Can J Anesth* 2004; 51:702-706.
34. Karaaslan K, Gulcu N, Ozturk H, Sarpkaya A, Colak C, Kocoglu H. Two different doses of caudal neostigmine co-administered with levobupivacaine produces analgesia in children. *Pediatr Anaesth* 2009; 19:487-493.
35. Bhardwaj N, Yaddanapudi S, Ghai B, Wig J. Neostigmine does not prolong the duration of analgesia produced by caudal bupivacaine in children undergoing urethroplasty. *J Postgrad Med* 2007; 53:161-165.
36. Memiş D, Turan A, Karamanlioğlu B, Kaya G, Süt N, Pamukçu Z. Caudal neostigmine for postoperative analgesia in paediatric surgery. *Paediatr Anaesth* 2003; 13:324-328.
37. Xiong C, Han C, Lv H, et al. Comparison of adjuvant pharmaceuticals for caudal block in pediatric lower abdominal and urological surgeries: A network meta-analysis. *J Clin Anesth* 2022; 81:110907.
38. Burcharth J, Pedersen M, Bisgaard T, Pedersen C, Rosenberg J. Nationwide prevalence of groin hernia repair. *PLoS One* 2013; 8:e54367.
39. Sakor A, Mulang IO, Singh K, Shekarpour S, Vidal MS, Lehmann J, Auer S. Old is gold: Linguistic driven approach for entity and relation linking of short text. In: Proceedings of the 2019 conference of the North American Chapter of the Association for Computational Linguistics: Human language technologies. *Association for Computational Linguistics* 2019; 1 (Long and Short Papers):2336-2346.

