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# Intraperitoneal ropivacaine reduces early postoperative pain and improves post-surgical outcomes after laparoscopic herniorrhaphy in toddlers: a randomized clinical trial

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Clinical trial registration: www.ClinicalTrials.gov, NCT: 01997593

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**What is already known**

Intraperitoneal local anesthesia has been shown to significantly reduce postoperative pain and opioid use in adults after laparoscopic general surgical or gynecological procedures.

**What this article adds**

Intraperitoneal ropivacaine reduces early postoperative pain and improves recovery after laparoscopic herniorrhaphy in toddlers.

**Implications for translation**

Intraperitoneal local anesthesia might be considered an option to conventional techniques in laparoscopic surgery in children. Future studies should clarify possible benefits and safety profiles of this technique in different ages of children.

**Abstract**

**Background:** Postoperative pain can cause physiological distress, postoperative complications and extended lengths of hospitalized stay. In children, management of postoperative pain is still recognized as being inadequate.

**Objective:** To investigate the effects of intraperitoneal ropivacaine on postoperative pain, recovery of bowel function and emetic events after laparoscopic herniorrhaphy in toddlers.

**Methods:** 76 children aged from 9 months to 3 years were recruited between August 2013 and June 2014 at Tongji hospital and randomly assigned into 2 groups. One group received intraperitoneal ropivacaine right before surgery and the control group received intraperitoneal saline. A standard combined general anesthesia procedure was performed under regular monitoring. Postoperative pain assessed by the FLACC scale, post-operative analgesic consumption, time to flatus, time to first stool and postoperative emetic events were recorded and analyzed.

**Results:** When compared with the control group, children who received intraperitoneal ropivacaine experienced less pain 0-4h after surgery ($P < 0.001$, difference in median FLACC (95% CI) for 2h time point is 2.00(0.87-3.13), for 4h time point is 1.00(0.55-1.45) ). In addition, the number of toddlers who received analgesia 0-24h after surgery in the ropivacaine group was lower than that in the control group ($P < 0.001$, difference in proportions(95% CI) is 0.575( 0.3865~0.7638)). Compared with the control group, time to flatus in ropivacaine group was also much shorter (21.1 h *vs* 16.7 h, $P$=0.04, difference in

mean (95% CI) is 4.4(1.49~7.28) ), and the time to first stool after surgery was earlier in the ropivacaine group (30.7 h *vs* 25.6 h, *P*=0.003, difference in mean (95% CI) is 5.1(1.78~8.45)). Furthermore, the incidence of emetic events in the ropivacaine group was significantly lower than the control group (32.4% *vs* 11.1%, *P*=0.03, difference in proportions(95% CI) is 0.212 (0.0246~0.4002)).

**Conclusion:** The present results indicate that intraperitoneal ropivacaine reduces early postoperative pain and improves recovery after laparoscopic herniorrhaphy in toddlers. Therefore IPLA is a good stratagem for postoperative pain management after laparoscopic surgery in toddlers.

**Key words**: ropivacaine, postoperative pain, laparoscopic herniorrhaphy

## Introduction

Postoperative pain management in children has particularly become a big challenge in a hospital or clinical setting. However, during the last 20 years, there has been a rapid development of new drugs that relieve pain in pediatric patients. Unfortunately too many children still continue to experience intense pain (1, 2) especially in developing countries. Many factors that may contribute to their suboptimal postoperative pain relief include difficulties in quantifying pain in preverbal children, and fear of serious adverse drug effects.

Of the various procedures undergone by hospitalized children, inguinal hernia repair (IHR) is a very common elective operation. It is traditionally performed under general anesthesia and usually caudal block is used to minimize postoperative pain. Recently, a new rapidly-advancing minimally invasive technique called laparoendoscopic single-site surgery (LESS) has emerged, which is very popular for carrying out IHR. However, pediatric postoperative pain management in this kind of surgery is poorly researched. Intraperitoneal local anesthesia (IPLA) has become an important addition to modulate postoperative pain and literature suggests that IPLA significantly reduces postoperative pain and opioid use in adults after laparoscopic, general surgical or gynecological procedures (3-6). The aim of this study was to examine the preemptive analgesia effect of IPLA in toddlers undergoing laparoscopic inguinal hernia repair by evaluating the postoperative pain score, the need for rescue analgesic and some other postsurgical outcomes.

## Methods

Ethical approval of was obtained from the local Institute's Ethical Committee (Huazhong University of Science and Technology, IRB ID: 20130801, 2013/08/02) and the study protocol registered with ClinicalTrials.gov (NCT: 01997593). After obtaining written informed consent from parents, 76 children were recruited to the study during a period of 9 months between October, 2013and June, 2014 at Tongji hospital (Figure1). The sample was formed of toddlers of both sex, aged between 9 months to 3 years who fulfilled the ASA I and II criteria and were scheduled for elective laparoscopic inguinal herniorraphy (LIH). Children were excluded from the study for the following reasons: allergy to anesthetics (propofol, atracurium, local anesthetics and opioid); if they had any neurological, cardiovascular, digestive system diseases, muscular diseases, history of abdominal surgery and obesity (defined as a body mass index 30 $kg\cdot m^{-2}$); those without written informed consent were also excluded.

## Grouped by randomization

Randomization was performed by using a computer- generated random web-based allocation system (Randomization.com) by Professor Hui Yang, who was not involved in the intervention or assessment. Those enrolled were assigned a subject number in sequential order of their enrollment into the trial. When the child arrived in the operation theater, the researcher received from the nurse identical sterile syringes with either ropivacaine or saline solution, labeled with the randomly assigned numbers. The nurse as well as other personnel (investigators, surgeon, staff and

participants) was unaware of the assigned intervention group of the child.

**Anesthetic regimen**

Premedication was administered in the waiting room in the presence of the parents. All children received 0.03 mg/kg midazolam and 0.06 mg·kg-1 scopolamine intramuscularly. A strict anesthesia protocol was applied as following: anesthesia was induced in all children with sevoflurane 8% in oxygen and then they were monitored. Once a sufficient depth of anesthesia (Guedel phase 3) was achieved, sevoflurane concentration was reduced to 4% and a venous catheter was inserted. Then fentanyl 3-4μg/kg, propofol 2-3mg/kg and atracurium 0.7 mg/kg were given intravenously before tracheal intubation. The trachea was intubated 3 min after the administration of atracurium. An end-tidal CO2 value (35 mmHg-45 mmHg) in the normal range was achieved with pressure controlled ventilation. Anesthesia was maintained by 2%–3% sevoflurane and a constant infusion rate of remifentanil 0.3μg·kg$^{-1}$·min$^{-1}$. At the end of surgery (when the surgeon took trocars out), the remifentanil and sevoflurane were discontinued. The trachea was extubated when in the head down left lateral position. All children were transferred to post anesthesia care unit (PACU) where standard monitoring was established and were observed for one hour. Both surgical time and anesthesia time were recorded.

**Intraperitoneal analgesia**

When periumbilical local ropivacaine (0.25%, 2ml) infiltration was done, the Veress needle or primary trocar was placed through a periumbilical incision. Intraperitoneal ropivacaine or saline nebulization was performed by using the Aeroneb Pro device, as

demonstrated by P. M. Ingelmo(3). Ropivacaine (1%, 0.3ml/kg) was nebulized in the abdominal cavity through the primary trocar outlet for about 5 minutes. Then the peritoneum was desufflated and reinsufflated with CO2 to remove the local anesthetic mist. After that, the standard surgical procedure of transumbilical single-port laparoscopic transabdominal preperitoneal repair of inguinal hernia was performed.

**Outcome measures**

The primary outcome measure was postoperative pain intensity which was evaluated using the Face Legs Activity Cry Consolability (FLACC) score. FLACC was first assessed 1 hour after the toddler arrived on the ward (2 hours after surgery) by a trained investigator blinded to the study groups. By that time, the children and parents had familiarized themselves to the ward surroundings and atmosphere. The follow-up was conducted 24 hours postoperatively. The secondary outcome was analgesic consumption within 24h after surgery. Paracetamol, the rescue analgesic was given (rectally 30 mg/kg) on the ward when the fixed pain score exceeded a critical value (FLACC score>3) and then 15 mg/kg every 6 hours. If there was still inadequate pain relief 2 hours after the first dose of paracetamol (FLACC score>3), tramadol was administered according to the dose of 2mg/kg. All the analgesic consumption was recorded. Emetic episodes, time to first flatus and stool passage during the first 24h postoperative period were reported by the child's guardian. An emetic episode was defined as a single vomit or retch or any number of continuous vomits or retches separated by the absence of both vomiting and retching for at least 3 min.

**Quality control**

Researchers were trained before conducting the study; the FLACC score was assessed by one researcher who was blind to the treatment groups; the height and weight of children with their ward clothes on was measured without shoes at fasting; and only one group of surgeons were involved in this study and responsible for both groups.

**Statistical analysis**

SPSS statistical software version 19.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Sample size estimation was based on the assumption that there is a difference in the first FLACC scores between the two groups. We computed the sample size needed for a Student's two-sample t-Test and then adjusted the sample size based on the ARE of the Mann-Whitney U relative to the t-test. Based on our preliminary clinical experience, a true difference of 2.0 in mean FLACC scores is anticipated. A sample size of at least 29 participants in each group was deemed to be sufficient to give us a power of 0.90 with 95% confidence (one tailed). Since the A.R.E. for the Mann-Whitney U is never less than 0.864, in practice we adjusted the final sample size to 34(29 divided by 0.864). Measurement data were expressed as mean± standard deviation (SD) and were analyzed by Student's *t* test. Nominal and dichotomous data such as sex were expressed as percentage and comparison was made by $\chi 2$ test. Difference in proportions were calculated by an online applets (http://www.math.hope.edu/isi/applets.html). Difference in medians were calculated by an applets which downloaded from online (http://www.gmw.rug.nl/~huisman/spssmanual ). Ordinal data such as FLACC scale were expressed as median (range) and were analyzed using Mann–Whitney *U* test.

$P<0.05$ was considered statistically significant.

## Results

### Groups' equivalence

Out of a total of 76 children assessed for eligibility, four were excluded because their operation changed to laparotomy and two due to an asthmatic attack in PACU. Seventy were therefore enrolled onto the study and subsequently randomized to the two groups: Control group (n=34) or Ropivacaine group (n=36) using computer generated random numbers and sealed envelopes. Participant characteristics are illustrated in Table 1. The two randomized groups were well matched for age, gender, and weight. No significant differences were observed between the two groups for either the mean operation time, or anesthesia time.

TABLE 1 about here

### Intraperitoneal analgesia can reduce postoperative pain

During the time period 0 to 2h, only 7 children in the ropivacaine group had a FLACC score >3 and received paracetamol rectally. However, in the control group there were 29 children who needed analgesic administration. Similarly, 0-24h after surgery, the number of children in the ropivacaine group who required analgesic administration was lower than that in the control group ($P<0.01$)(Table 2). Furthermore, there were 4 toddlers in the control group that were administered tramadol in comparison to only one in the ropivacaine group (not statistically differen, Table 2). These results indicate

that analgesic consumption in the ropivacaine group was notably lower than that in the control group.

Postoperative pain intensity was evaluated by the FLACC scale and the results are shown in Table 3. 2h after operation, the FLACC score in the ropivacaine group was significantly reduced than that in the control group ($P$<0.001). Even 4 hours after surgery, the FLACC score in ropivacaine group remained markedly lower than the control group ($P$<0.001). During 4 to 24 h, no further significant differences were found between the two groups. These results demonstrate that during 0-4h, the children in the ropivacaine group experienced less postoperative pain than the control group.

TABLE 2 about here

TABLE 3 about here

**Intraperitoneal analgesia can shorten the postoperative recovery time of gastrointestinal function.**

Variables evaluating recovery of bowel function are summarized in Table 4. Compared with the control group, time to flatus in the ropivacaine group was much shorter ($P$<0.05). The time to first stool after surgery occurred earlier in the ropivacaine group ($P$<0.01). Furthermore, the incidence of emetic events in the

ropivacaine group was significantly lower than in the control group ($P<0.05$). These results illustrate that the intraperitoneal ropivacaine administration significantly benefits recovery of gastrointestinal function and reduces postoperative emetic events.

TABLE 4 about here

**Discussion**

The results of this study confirm that the technique of IPLA relieved postoperative pain considerably and improved postsurgical outcome in those toddlers who received laparoendoscopic single-site inguinal herniorraphy. Nowadays, postoperative pain in children is still often undertreated (7), especially in developing countries. There are several reasons for this suboptimal alleviation of pain in children: difficulties in quantifying pain in preverbal children (8), parental behavior and misconceptions regarding pain medications, including fear of opioid addiction and serious adverse analgesic effects, inter-patient variability in pain perception and analgesic requirements (9), differences in pharmacodynamics and pharmacokinetics (10), and so on. Here, by investigating ropivacaine, we found that the technique of IPLA could provide an ideal way for postoperative pain management after laparoendoscopic surgery in toddlers. This way, other analgesic consumption such as opioids and NSAIDS could be significantly reduced.

Ropivacaine is the preferred local anesthetic in adults because of its long duration, reduced CNS toxicity and cardiotoxic potential compared to bupivacaine (11). Some

studies have shown that intraperitoneal ropivacaine (the maximum safe dose is 3 to 4 mg/kg) is safe with a similar pharmacokinetic profile to that of extravascular administration (12, 13). In Callesen's study, a total dose about 4mg/kg of ropivacaine was used for combined field block and i.p. instillation and no signs of local anaesthetic toxicity were found(14). Ropivacaine is a highly bound toα1-acid glycoprotein (AAG), which means that the concentration of AAG in plasma may markedly affect the free drug concentration of ropivacaine. AAG concentrations are very low at birth but progressively increase to adult level in the next 9-12 months. Thus, in toddlers, the risk of low levels of AAG causing increased free drug in plasma is rare. In this study, for safety, the dosage of IP ropivacaine (<3mg/kg) is at a relatively low dose when compared with the adult dose (3-4 mg/kg). In practice, we did not notice systemic side effects of ropivacaine in any children, but patients were under general anesthesia when ropivacaine administrated and could not describe minor central nerve system toxic symptoms such as visual and hearing disturbance, tingling, perioral numbness, and so on. Ropivacaine has been shown to have duration of about 4 hours in many previous studies (15-18). In this study, 79.5% of children in the ropivacaine group did not receive any rescue analgesic during the first 24 hours ,which may suggest that the duration of ropivacaine may be longer than 4 hours in toddlers, which is in agreement with findings of other studies (11, 19).

The pain experience (including occurrence rate, location and character) after laparoscopic surgery in toddlers is not well documented. In adults, abdominal and shoulder pain following laparoscopy is common. In this study, 2 hours after

surgery, there were about 85% children in the control group who had a FLACC score over 3 and needed analgesic administration. This indicates that post laparoscopic surgery pain in toddlers is also prevalent. Both surgical manipulations and complex neural dissection contribute to post laparoscopic surgery pain: pneumoperitoneum resulting in peritoneal stretching, diaphragmatic irritation, changes in intra-abdominal pH, and retention of the insufflated gas in the abdominal cavity after surgery. Two neural afferents are also stimulated after laparoscopic surgery: the peripheral somatic nervous system is activated as a result of direct insult to the abdominal wall. The second pathway arises from visceral neural irritation and most of its sensory fibers appear to converge via the celiac plexus and subdiaphragmatic vagus nerve, bypassing the spinal cord.

Intraperitoneal delivery of ropivacaine has also been reported to reduce postoperative pain and opioid analgesic requirements (20, 21) and our results are in agreement with this finding: as toddlers who received IPLA with ropivacaine, their FLACC score was significantly lower than of those in the control group 0-4h after surgery. Intraperitoneal ropivacaine probably works through several pathways. Firstly, it inhibits action potentials and the neural transmission of local nerve fibers at high concentration. Secondly it can modulate pain pathways at low plasma concentrations achieving a systemic effect (22, 23). Systemic effects involve direct interaction of the local anesthetic with neuronal tissue (24, 25) as well as indirect mechanisms via a reduction of circulating pro-inflammatory cytokines (26, 27). Recently published data concluded that ropivacaine may be useful in suppressing inflammation, mechanical

and visceral hypersensitivity (28, 29) and can even be used to treat chronic pain states in the same way(30).

Good post-surgery analgesia management is beneficial for the outcome of surgery. Some studies have reported that effective postoperative analgesia improves patients' post-surgery outcomes such as early ambulation, decrease in side effects and so on (31-33). In contrast, poor pain control has been known to alter body metabolic response that can lead to delayed recovery, increased morbidity, prolonged hospital stay and the development of chronic pain state. In this study we showed that intraperitoneal ropivacaine could promote the recovery of gastrointestinal function and decrease post-surgical emetic events in toddlers. Nonetheless, previous reports have illustrated that the administration of intra- and postoperative epidural local anesthesia leads to improved bowel motility (19). Intraoperative instillation of ropivacaine might provide better outcomes related to postoperative bowel recovery in a similar fashion.

**Limitation**

Our results should be interpreted with caution because of some limitations. Firstly, the study sample; the relatively limited number of pediatric patients involved could be the reason why no complications or adverse reactions to ropivacaine occurred. It also remains unclear whether the lack of significant differences in tramadol consumption between the groups after surgery was due to the small sample size. Secondly, the sex ratio (male/female) was unequal in this study (10～15:1). However, currently there is no evidence showing that there is a significant

difference in post-surgery pain between boys and girls. In future, further studies may be needed to provide answers to these questions.

## Conclusion

This study suggests that intraperitoneal ropivacaine could relieve postoperative pain in toddlers, who undergo laparoscopic inguinal herniorraphy (LIH), as demonstrated by the lower pain scores and decreased use of rescue analgesic. This technique may also contribute to the recovery of gastrointestinal function and reduction of post-surgical emetic events.

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## Competing Interests

The authors declare no competing interests.

## Reference

1 Stanko D, Bergesio R, Davies K*, et al.* Postoperative pain, nausea and vomiting following adeno-tonsillectomy - a long-term follow-up. *Paediatr Anaesth* 2013; **23**: 690-696.

2 Segerdahl M, Warren-Stomberg M, Rawal N*, et al.* Children in day surgery: clinical practice and routines. The results from a nation-wide survey. *Acta Anaesthesiol Scand* 2008; **52**: 821-828.

3 Ingelmo PM, Bucciero M, Somaini M*, et al.* Intraperitoneal nebulization of ropivacaine for pain control after laparoscopic cholecystectomy: a double-blind, randomized, placebo-controlled trial. *Br J Anaesth* 2013; **110**: 800-806.

4 Futier E, Petit A, Pezet D. Randomized clinical trial of combined preincisional infiltration and

intraperitoneal instillation of levobupivacaine for postoperative pain after laparoscopic cholecystectomy (Br J Surg 2011; 98: 784-789). *Br J Surg* 2011; **98**: 1179; author reply 1179-1180.

5 Bucciero M, Ingelmo PM, Fumagalli R*, et al.* Intraperitoneal ropivacaine nebulization for pain management after laparoscopic cholecystectomy: a comparison with intraperitoneal instillation. *Anesth Analg* 2011; **113**: 1266-1271.

6 Sripada S, Roy S, Mathur M*, et al.* A prospective double-blind randomised controlled trial of intraoperative pelvic instillation with bupivacaine for management of pain following laparoscopy and dye. *BJOG* 2006; **113**: 835-838.

7 Taylor EM, Boyer K, Campbell FA. Pain in hospitalized children: a prospective cross-sectional survey of pain prevalence, intensity, assessment and management in a Canadian pediatric teaching hospital. *Pain Res Manag* 2008; **13**: 25-32.

8 Russell P, von Ungern-Sternberg BS, Schug SA. Perioperative analgesia in pediatric surgery. *Current opinion in anaesthesiology* 2013; **26**: 420-427.

9 Mohammed BS, Engelhardt T, Cameron GA*, et al.* Population pharmacokinetics of single-dose intravenous paracetamol in children. *Br J Anaesth* 2012; **108**: 823-829.

10 Kart T, Christrup LL, Rasmussen M. Recommended use of morphine in neonates, infants and children based on a literature review: Part 1--Pharmacokinetics. *Paediatr Anaesth* 1997; **7**: 5-11.

11 Ecoffey C. Local anesthetics in pediatric anesthesia: an update. *Minerva anestesiologica* 2005; **71**: 357-360.

12 Labaille T, Mazoit JX, Paqueron X*, et al.* The clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. *Anesth Analg* 2002; **94**: 100-105, table of contents.

13 McDermott AM, Chang KH, Mieske K*, et al.* Total systemic ropivacaine concentrations following aerosolized intraperitoneal delivery using the AeroSurge. *J Clin Anesth* 2014; **26**: 18-24.

14 Callesen T, Hjort D, Mogensen T*, et al.* Combined field block and i.p. instillation of ropivacaine for pain management after laparoscopic sterilization. *Br J Anaesth* 1999; **82**: 586-590.

15 Dingeman RS, Barus LM, Chung HK*, et al.* Ultrasonography-guided bilateral rectus sheath block vs local anesthetic infiltration after pediatric umbilical hernia repair: a prospective randomized clinical trial. *JAMA surgery* 2013; **148**: 707-713.

16 Bamigboye AA, Justus HG. Ropivacaine abdominal wound infiltration and peritoneal spraying at cesarean delivery for preemptive analgesia. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics* 2008; **102**: 160-164.

17 Kellogg KM, Fairbanks RJ, O'Connor AB*, et al.* Association of pain score documentation and analgesic use in a pediatric emergency department. *Pediatric emergency care* 2012; **28**: 1287-1292.

18 Rony RY, Fortier MA, Chorney JM*, et al.* Parental postoperative pain management: attitudes, assessment, and management. *Pediatrics* 2010; **125**: e1372-1378.

19 Thompson JS. The role of epidural analgesia and anesthesia in surgical outcomes. *Advances in surgery* 2002; **36**: 297-307.

20 Kahokehr A, Sammour T, Zargar Shoshtari K*, et al.* Intraperitoneal local anesthetic improves recovery after colon resection: a double-blinded randomized controlled trial. *Ann Surg* 2011; **254**: 28-38.

21 McDermott AM, Chang KH, Mieske K*, et al.* Aerosolized Intraperitoneal Local Anesthetic for Laparoscopic Surgery: A Randomized, Double-Blinded, Placebo-Controlled Trial. *World J Surg* 2015.

22 Haller Y, Gantenbein AR, Willimann P*, et al.* Systemic ropivacaine diminishes pain sensitization

processes: a randomized, double-blinded, placebo-controlled, crossover study in healthy volunteers. *Pain Ther* 2014; **3**: 45-58.

23 Koppert W, Brueckl V, Weidner C*, et al.* Mechanically induced axon reflex and hyperalgesia in human UV-B burn are reduced by systemic lidocaine. *Eur J Pain* 2004; **8**: 237-244.

24 Abram SE, Yaksh TL. Systemic lidocaine blocks nerve injury-induced hyperalgesia and nociceptor-driven spinal sensitization in the rat. *Anesthesiology* 1994; **80**: 383-391; discussion 325A.

25 Koppert W, Ostermeier N, Sittl R*, et al.* Low-dose lidocaine reduces secondary hyperalgesia by a central mode of action. *Pain* 2000; **85**: 217-224.

26 Kuo CP, Jao SW, Chen KM*, et al.* Comparison of the effects of thoracic epidural analgesia and i.v. infusion with lidocaine on cytokine response, postoperative pain and bowel function in patients undergoing colonic surgery. *Br J Anaesth* 2006; **97**: 640-646.

27 Herroeder S, Pecher S, Schonherr ME*, et al.* Systemic lidocaine shortens length of hospital stay after colorectal surgery: a double-blinded, randomized, placebo-controlled trial. *Ann Surg* 2007; **246**: 192-200.

28 Kfoury T, Mazoit JX, Schumacher M*, et al.* A comparison of different dosages of a continuous preperitoneal infusion and systemic administration of ropivacaine after laparotomy in rats. *Anesth Analg* 2011; **113**: 617-625.

29 Dias MP, Newton DJ, McLeod GA*, et al.* The inhibitory effects of local anaesthetics on the vascular flare responses to bradykinin and substance P in human skin. *Anaesthesia* 2008; **63**: 151-155.

30 Sato C, Sakai A, Ikeda Y*, et al.* The prolonged analgesic effect of epidural ropivacaine in a rat model of neuropathic pain. *Anesth Analg* 2008; **106**: 313-320, table of contents.

31 Liu SS, Wu CL. Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence. *Anesth Analg* 2007; **104**: 689-702.

32 Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. *Br J Anaesth* 2001; **87**: 62-72.

33 Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. *Anesthesiology* 2000; **93**: 1123-1133.

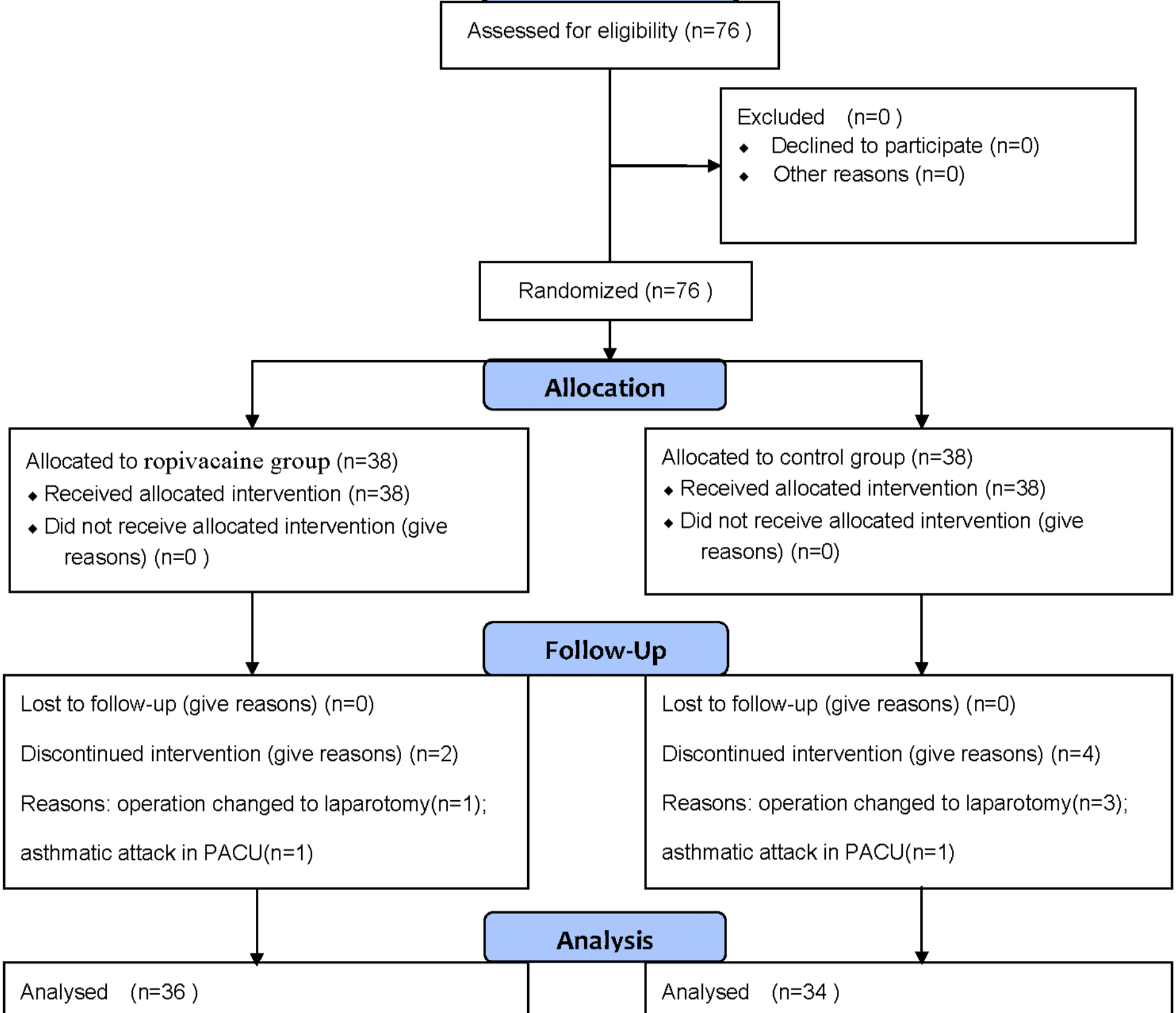
Assessed for eligibility (n=76 )
Excluded (n=0 )
Declined to participate (n=0)
Other reasons (n=0)
Randomized (n=76 )
Allocation
Allocated to ropivacaine group (n=38)
Received allocated intervention (n=38)
Did not receive allocated intervention (give reasons) (n=0 )
Allocated to control group (n=38)
Received allocated intervention (n=38)
Did not receive allocated intervention (give reasons) (n=0)
Follow-Up
Lost to follow-up (give reasons) (n=0)
Discontinued intervention (give reasons) (n=2)
Reasons: operation changed to laparotomy(n=1);
asthmatic attack in PACU(n=1)
Lost to follow-up (give reasons) (n=0)
Discontinued intervention (give reasons) (n=4)
Reasons: operation changed to laparotomy(n=3);
asthmatic attack in PACU(n=1)
Analysis
Analysed (n=36 )
Analysed (n=34 )

Table1. Demographic and clinical characteristics of the two groups

| | Control group (n=34) | Ropivacaine group(n=36) |
|---|---|---|
| Age(m) | 21.6 ± 8.4 | 19.7 ± 6.0 |
| Sex ratio(M/F) | 31/3 | 34/2 |
| Weight(kg) | 12. 3 ± 2.6 | 11.8 ± 2.6 |
| Operative time(min) | 55.9 ± 13.3 | 51.5 ± 11.4 |
| Anesthesia time(min) | 73.7 ± 13.6 | 71.6 ± 14.7 |

Data are presented as mean (SD), or frequency，

Table 2 Postoperative analgesic consumption in the two groups

| | Control group (n=34) | Ropivacaine group (n=36) | *P* value | Difference in proportions (95% CI) |
|---|---|---|---|---|
| NSAID (0–24 h) [n (%)] | 29(85.3%) | 10(27.7%) | 0.000 | 0.575( 0.3865~0.7638) |
| NSAID (0-2h) [n (%)] | 29(85.3%) | 7(19.4%) | 0.000 | 0.658(0.4827~0.8342) |
| NSAID (2-4h) [n (%)] | 0 | 3(8.3%) | 0.258 | 0.083 (-0.0070~0.1736) |
| NSAID (4-24h) [n (%)] | 0 | 0 | - | - |
| Tramadol (0-24h) [n (%)] | 4(11.8%) | 1(2.78%) | 0.320 | 0.090(-0.0310~0.2107) |

All data are shown as number of patients n (%) for NSAIDs or tramadol.

Table 3 Postoperative pain intensity after laparoscopic herniorrhaphy

| | Control group (n=34) | Ropivacaine group (n=36) | *P* value | Difference in median (95% CI) |
|---|---|---|---|---|
| FLACC 2h | 5.00(3.97-6.03) | 3.00(2.55-3.45) | 0.000 | 2.00(0.87-3.13) |
| FLACC 4h | 3.00(3.00-3.00) | 2.00(1.55-2.45) | 0.000 | 1.00(0.55-1.45) |
| FLACC6h | 2.00(2.00-2.00) | 1.50(1.05-1.95) | 0.183 | 0.50(0.05-0.95) |
| FLACC 8h | 1.50(0.98-2.02) | 1.00(0.55-1.45) | 0.303 | 0.50(-0.18-1.18) |
| FLACC 12h | 1.00(0.48-1.52) | 1.00(1.00-1.00) | 0.108 | 0.00(-0.52-0.52) |
| FLACC 24h | 1.00(1.00-1.00) | 1.00(0.55-1.45) | 0.703 | 0.00(-0.45-0.45) |

Data are expressed as median (95% confidence interval)

Table 4. Comparison of bowel function recovery time and postoperative emetic events

| | Control group (n=34) | Ropivacaine group (n=36) | *P value* | Difference in mean or proportions (95% CI) |
|---|---|---|---|---|
| Time to first flatus(h) | 21.1±6.8 | 16.7±5.3 | 0.004 | 4.4(1.49~7.28) |
| Time to first stool(h) | 30.7±7.4 | 25.6±6.5 | 0.003 | 5.1(1.78~8.45) |
| Patients with emetic events | 11(32.4%) | 4(11.1%) | 0.030 | 0.212 (0.0246~0.4002) |

Data are expressed as mean (SD) or number of patients n (%).