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# A Small Prospective Randomized Double-Blind Placebo Controlled Trial Evaluating the Efficacy of Postoperative Use of Elastomeric Pain Pumps Following Laparoscopic Ventral Hernia Repair

**Francis J Deasis**, **Brittany Lapin**, **Matthew E Gitelis**, **John G Linn**, **Woody Denham**, **Stephen P Haggerty**, **Joann M Carbray and Michael B Ujiki***

*Department of Surgery, Section of Minimally Invasive Surgery, North Shore University Health System, United States*

***Corresponding author**: Michael B Ujiki, Department of Surgery, Section of Minimally Invasive Surgery, North Shore University Health System, 2650 Ridge Avenue Evanston, IL 60201, United States, Tel: 847-570-1700; Fax: 847-570-1330; E-mail: mujiki@northshore.org

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## Abstract

Objective: Laparoscopic Ventral Hernia Repair (LVHR) can result in significant postoperative pain. Elastomeric pain pump devices may reduce pain and narcotic medication use postoperatively. We present a prospective randomized double-blind placebo-controlled trial evaluating device efficacy in LVHR patients. Methods: Pumps were preperitoneally placed in LVHR patients, and a 4-day continuous bupivacaine or saline infusion (4 ml/hour) was given. Demographics, intra/postoperative information, and quality-of-life were compared between groups using chi-square test, t-test, and Mann-Whitney-U test. Quality-of-life consisted of pre/postoperative Short Form-36 surveys and 7-day self-reported pain and medication logs. Results: Twenty-nine LVHR patients received pumps: 17 (59%) with bupivacaine and 12 (41%) with saline. There was no difference in demographic and intraoperative variables. Mesh size was larger for saline patients compared to bupivacaine patients (median 429 vs 225 cm2, p=0.05). There was no difference in length-of-stay or complications. Discharge pain scores were worse for saline patients versus those receiving bupivacaine (median (q1,q3): 4 (2,5) vs 2 (0,3), p=0.064). Ketorolac use was higher in saline patients (p=0.01), and saline patients used pain medication longer (median (q1, q3) 9 (7,10) vs 6 (4,8), p=0.05). Other narcotic and non-narcotic use did not differ. Pain and medication logs showed significantly worse self-reported pain and pain management for the saline group versus the bupivacaine group on days 1-4 (p<0.05), with no differences reported after day 4. There were no differences in quality-of-life scores preoperatively or at 3 weeks postoperative. Conclusion: In this prospective randomized double-blind placebo-controlled trial, we found less pain at discharge, fewer days on pain medications, and less self-reported pain in patients receiving bupivacaine versus saline. However there was no significant reduction in most narcotic and non-narcotic medication use and no postoperative improvements in quality-of-life for LVHR patients using pumps. Larger studies investigating bupivacaine and other alternatives for reducing postoperative pain after LVHR are needed.

**Keywords:** Ventral hernia repair; Laparoscopic; Pain control; Randomized controlled trial; Bupivicaine; Quality of life; Hernia

## Introduction

Ventral Hernia (VH) is a common medical problem in the United States, with about 100,000-150,000 VH repairs performed annually. Over time, VH repair techniques have evolved, with a shift from open sutured repair to open mesh repair to laparoscopic mesh repair in an attempt to lower recurrence rates and improve recovery. Most open and laparoscopic techniques use mesh to bridge the defect and produce a tension-free repair [1-3]. Based upon the open underlay technique defined by Stoppa and Rives, LeBlanc introduced Laparoscopic Ventral Hernia Repair (LVHR) in 1993 [4-6]. Several large studies have shown improved overall outcomes, including recurrence rates, postoperative complications, length of stay and the time needed to return to daily activities [7-10]. However, postoperative pain remains a significant issue following LVHR.

In recent years, there has been a shift away from the search for the "perfect" analgesics towards combination techniques. In order to decrease the dose of narcotics or non-narcotic analgesics, investigators introduced local anaesthetics in the last few years in a single dose wound infiltration for acute pain management. The combined effect of local anaesthetics and opioids may offer advantages by decreasing the dose of narcotics, which theoretically leads to fewer side effects and better pain control. This technique has gained popularity in recent years because of the aforementioned advantages. Execution of this technique generally utilizes elastomeric pain devices to administer a continuous infusion of local anaesthetic in proximity to or within the surgical site. This method has yielded promising results in other surgical procedures, including open inguinal hernia repair, segmental or total colectomy, thoracotomy, and gynaecology oncologic surgery involving midline laparotomy [11-14]. For this prospective randomized double-blind placebo-controlled trial, we focused on the specific anatomical location of elastomeric pain pump implantation and the subsequent relief of postoperative pain. The primary objective was to investigate if a continuous, bilateral preperitoneal infusion of a local anaesthetic would reduce both postoperative pain and narcotic pain medication use following LVHR.

## Materials and Methods

### Study population and characteristics

Upon approval from the Institutional Review Board, eligible patients older than 18 years undergoing elective LVHR between August 2012 and April 2015 at our institution were recruited and informed consent was obtained. Patients were excluded if there was

any of the following: American Society of Anaesthesiologists (ASA) Class greater than IV, emergent case, history of drug abuse, allergy or dependency to morphine, meperidine, hydromorphone, fentanyl, bupivacaine, lidocaine, or ropivacaine, and history of any gastrointestinal, hepatic, renal, or other condition that could interfere with absorption, distribution, metabolism, or excretion of any drug utilized during the study. Before surgery, patients were randomized in a simple double-blind fashion into either the bupivacaine group or the saline group using the website randomizer.org. Additionally, patients were educated preoperatively regarding the pump.

### Operative characteristics

Four experienced laparoscopic surgeons performed each procedure in a standardized fashion. Mesh type was chosen by the surgeon and was fixated with spiral tacks every 1 cm in a double crown fashion and by transfacial sutures every 5 cm. For pain pump (Halyard Health; Alpharetta, GA) placement, bilateral catheters were tunnelled between the parietal peritoneum and the transversalis fascia under direct vision through an introducer needle inferior to the costrochondral margin. Care was taken to ensure that the needle did not pierce the peritoneum. Depending on the group, patients either received 400 ml of saline or 0.5% bupivacaine, infused at 4 ml per hour over a 4 day period through the fixed flow rate pumps with 19-gauge (1.1 mm) catheters. Hospital pharmacists filled each pump to the exact specifications and measurements stated by the manufacturer, and the contents were stored at room temperature. Given the design both the surgeon and the scrub nurse were blinded to the contents of the pump and the group of the patient.

### Postoperative course

Postoperatively, patients were given a standard course of 800 mg ibuprofen and 5 mg hydrocodone/325 mg acetaminophen as needed. If admitted to the hospital, patients were also given ketorolac every 6 hours, if needed. To maintain a constant flow rate, it was emphasized to patients that they should always keep the pump and connectors at waist level. Prior to discharge, patients were also instructed on how to remove the pain pump catheters at home once the medication infusion was complete. They were given specific discharge instructions to call our nurse or emergency medical services if they experienced any toxicity symptoms (e.g. dizziness, tinnitus, numbness or tingling).

### Quality of life metrics

Patients were also sent home with 7 day pain surveys and medication logs. For the pain surveys, patients were instructed to evaluate their frequency and level of pain once in the morning and once at night. For level of pain, patients were given 4 options: 1: Severe, 2: Moderate, 3: Minimal and 4: None. For frequency of pain, patients were given 3 options: 1: Constant, 2: On movement, and 3: None. Patients were also asked to evaluate their satisfaction with their pain management, and this was evaluated on a scale of 1 (not satisfied at all) to 10 (completely satisfied). For the medication logs, patients were asked to record the amount of hydrocodone-acetaminophen and ibuprofen used each day. These logs were collected during the 3 weeks follow up appointment. Patients were also given the Short Form 36 Health Survey Version 2 (SF-36v2) pre and postoperatively at week 3 to evaluate quality of life. The survey is comprised of 36 questions that are used to generate eight different scores corresponding to health: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health. These scores are then converted into values from 0 (poor health) to 100 (best health).

### Data collection and statistical analysis

Collected data points included demographics, preoperative clinic visit data, perioperative data, postoperative data, follow-up clinic visit data, pre and postoperative quality of life surveys, and postoperative medication and pain logs. The primary endpoints of our study were postoperative pain and narcotic analgesic medication use, examining whether patients receiving local anaesthetic through the pump reported lower pain and medication use postoperatively in comparison to patients receiving only saline. A sample sizes of 34 (17 per group) achieve 80% power to detect a mean difference of 2.0 points on a pain scale assuming a standard deviation of 2.0. Patient demographics, preoperative, intraoperative, and postoperative characteristics, pain management, and quality of life were compared by group. Categorical variables were compared using chi-square test or Fisher's exact test (for small cell size). Continuous variables were compared using t-test or Mann-Whitney U test (nonparametric). Significance was established at a p-value less than 0.05. Statistical analysis was performed by a biostatistician using SAS version 9.3 (SAS Institute Inc., Cary, NC).

## Results

Between August 2012 and April 2015, 30 patients consented to this prospective randomized double-blind placebo-controlled trial. After randomization, 17 patients received bupivacaine and 13 patients received saline. However, 1 patient in the saline group was dropped for noncompliance.

There was no change to the study methods or outcomes after trial commencement. Recruitment for the study was ended early due to difficulty in consenting patients to participate. Preoperatively, there was no difference in age, gender, BMI, smoking history, ASA class, or prior hernia repair between groups (Table 1).

Preoperatively, there was also no difference in hernia types, operative time, transfascial sutures, use of tacks, or hernia size. Mesh size was higher in the saline group but was not significantly larger than the bupivacaine group (median (q1, q3): 429 (190, 500) $cm^2$ vs 225 (144, 300) $cm^2$, p=0.07. There were no perioperative complications in either group.

| Characteristics | Total | Bupivacaine | Saline | P-Value |
|---|---|---|---|---|
| | N (%) | N (%) | N (%) | |
| Total no. of Patients | 29 | 17 (58.6) | 12 (41.4) | |
| **Patient demographics** | | | | |
| Age (years)-Mean ± SD | 60.4 ± 10.9 | 60.1 ± 12.2 | 60.9 ± 9.1 | 0.85 |
| BMI ($kg/m^2$)-Mean ± SD | 33.4 ± 6.4 | 33.8 ± 6.3 | 32.8 ± 6.7 | 0.66 |
| Obese | 19 (65.5) | 12 (70.6) | 7 (58.3) | 0.69 |
| Female Gender | 18 (62.1) | 11 (64.7) | 7 (58.3) | 0.99 |
| Former Smoker (vs Never) | 12 (41.4) | 6 (35.3) | 6 (50.0) | 0.47 |
| ASA Class 3 (vs 2) | 6 (20.7) | 3 (17.7) | 3 (25.0) | 0.67 |
| Previous Hernia Repair | 8 (27.6) | 4 (23.5) | 4 (33.3) | 0.68 |

| **Procedure characteristics** | | | | |
|---|---|---|---|---|
| OR Time (min)-Median (Q1, Q3) | 80 (55, 103) | 75 (55, 90) | 95 (59, 129) | 0.25 |
| Transfascial Sutures-Mean ± SD | 5.1 ± 1.7 | 4.8 ± 1.6 | 5.5 ± 1.9 | 0.3 |
| Tacks (# of patients) | 28 (96.6) | 17 (100.0) | 11 (91.7) | 0.41 |
| Mesh Size ($cm^2$)-Median (Q1, Q3) | 225 (148, 400) | 225 (144, 300) | 429 (190, 500) | 0.05 |
| Hernia Size ($cm^2$)-Median (Q1, Q3) | 20 (9, 42) | 15 (9, 29) | 44 (15, 161) | 0.13 |
| Hernia Type | | | | 0.19 |
| Incisional | 16 (55.2) | 7 (41.2) | 9 (75.0) | |
| Ventral | 8 (27.6) | 6 (35.3) | 2 (16.7) | |
| Other | 5 (17.2) | 4 (23.5) | 1 (8.3) | |

**Table 1**: Patient characteristics by group (n=29).

Postoperatively, there was no difference in length of stay or complications (Table 2). There were five postoperative complications in the cohort. Three patients in the bupivacaine group developed a seroma. In the saline group, 1 patient developed a seroma and 1 patient had urinary retention. These complications resolved without issue.

Although medication use was higher in the saline group, there was no significant difference between groups for in-hospital usage of hydromorphone, fentanyl, morphine, hydrocodone, acetaminophen, or ibuprofen. In-hospital ketorolac usage was significantly higher for saline patients (p=0.01).

| **Characteristics** | **Total** | **Bupivacaine** | **Saline** | **P-Value** |
|---|---|---|---|---|
| | N (%) | N (%) | N (%) | |
| Total no. of patients | 29 | 17 (58.6) | 12 (41.4) | |
| LOS (Days)-Median (Q1, Q3) | 0 (0, 2) | 0 (0, 1) | 1 (0, 2) | 0.14 |
| Complications, N (%) | 5 (17.2) | 3 (17.7) | 2 (16.7) | 0.99 |
| Pain score at discharge-Median (Q1, Q3) | 2.67 ± 2.04 | 2.0 (0.0, 3.0) | 4.0 (2.0, 5.0) | 0.06 |
| **Hospital Pain Management (mg) -Median (Q1, Q3)** | | | | |
| Dilaudid/Fentanyl/Morphine Use* (n=29) | 12 (6.5, 30) | 11 (7, 18) | 22 (7, 40) | 0.29 |
| Ketorolac Use (n=27) | 30 (30, 45) | 30 (15, 30) | 53 (30, 142) | 0.01 |
| Hydrocodone Use (n=11) | 55 (5, 70) | 35 (5, 68) | 55 (5, 75) | 0.5 |
| Acetaminophen Use (n=25) | 1000 (1000, 1975) | 1000 (1000, 1500) | 1325 (1000, 4950) | 0.09 |
| Ibuprofen Use (n=2) | 800 mg, 1600 mg | - | 800 mg, 1600 mg | - |
| Narcotics, (POD Stopped)-Median (Q1, Q3) (n=21) | 2 (1, 7) | 1 (1, 4) | 7 (1, 15) | 0.12 |
| Return to ADL (Days)-Median (Q1, Q3) (n=20) | 8 (7, 14) | 7 (7, 10) | 12 (7, 21) | 0.24 |
| Return to Work (Days)-Median (Q1, Q3) (n=10) | 12 (4, 15) | 14 (4, 14) | 10 (7, 21) | 0.53 |
| Pain Med Used (Days)-Median (Q1, Q3) (n=23) | 7 (5, 9) | 6 (4, 8) | 9 (7, 10) | 0.05 |
| Total Hydrocodone Use (n=14) | 110 (10, 130) | 80 (10, 120) | 130 (100, 145) | 0.24 |
| Total Acetaminophen Use (n=16) | 2950 (1038, 6256) | 2950 (750, 7800) | 3113 (1325, 4713) | 0.83 |
| Total Ibuprofen Use (n=17) | 7600 (5600, 9600) | 7400 (2400, 9800) | 8800 (6400, 9600) | 0.49 |

**Table 2**: Postoperative outcomes and pain management by group (n=29).

Pain scores at discharge were higher for saline patients compared to patients receiving bupivacaine (median (q1,q3): 4 (2,5) vs 2 (0,3), p=0.064).

Saline patients used pain medication for more days after discharge than patients in the bupivacaine group, although this difference did not reach conventional statistical significance (median (q1, q3): 9 (7,10) vs 6 (4,8), p=0.054). There were no differences in the length of time before returning to work or activities of daily living.

There were also no group differences in SF-36 quality of life scores preoperatively or at 3 weeks postoperatively (data not shown). The pain diary and medication log showed significantly worse self-reported pain, pain frequency, and pain management for the saline group compared to the bupivacaine group on postoperative days 1-4 (p<0.05), with no differences reported after day 4 (Figure 1).

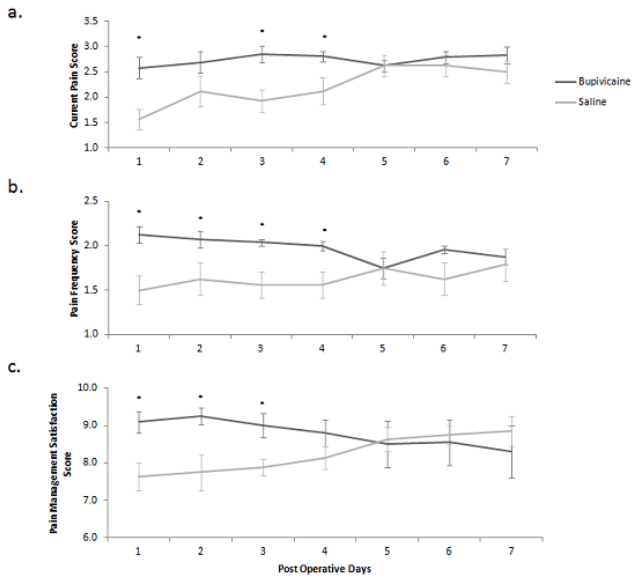


**Figure 1**: (a) Average self-reported current pain scores (an average of AM and PM scores) (b) pain frequency (an average of AM and PM scores) and (c) satisfaction with pain management are presented on postoperative days 1-7 by group. Higher scores indicate less pain. Vertical lines represent standard errors. Asterisks indicate statistically significant group differences by Mann-Whitney U test at $p<0.05$.

## Discussion

The evolution of ventral hernia repair from an open to laparoscopic technique has significantly improved outcomes with recurrence rates becoming lower and recovery time being shorter [7,15]. Even so, chronic postoperative pain remains an issue. Over the years, more understanding of the significance of postoperative pain control has led to several methods and combination techniques for management of postoperative pain. These include:

- Systemic opioids via Intramuscular Route (IM) or Intravenous Route (IV) and for the last 15 years via the Patient Control Analgesia (PCA) which has revolutionized pain management
- Intrathecal or epidural opioids: single dose or continuous administration of opioids via these routes
- Non-steroidal anti-inflammatory agents
- Combination techniques

However, all these modalities of pain control have many side effects such as nausea and vomiting which, although common, can aggravate the patient's postoperative condition and lead to prolonged hospitalization, morbidity as well as increased costs. More serious side effects such as respiratory depression, hypotension, and altered mental states are possible, especially in the elderly population. Non-steroidal analgesics can cause bleeding, especially when used for prolonged periods of time [9,16,17]. Our study yielded similar results as prior studies, as patients receiving bupivacaine reported significantly lower and less frequent postoperative pain, fewer days using pain medication, and higher overall satisfaction with their pain management [12,14]. This contrasts to a prior randomized controlled trial with LVHR patients that showed no difference in outcomes between bupivacaine and saline patients [10]. We think that our findings are primarily because we chose a different technique to insert the pain pumps, as we used them preperitoneally and bilaterally as opposed to directly into the hernia sac. Our rationale was based on findings by Beaussier and colleagues who found that preperitoneal infusion of 0.2% ropivacaine resulted in reduced morphine use and lower postoperative pain in patients following open colorectal resection by midline incision [18]. Additionally, we also chose to insert catheters bilaterally so that we could blockade as many nociceptive afferent receptors in the parietal peritoneum as possible.

We also acknowledge our technique is like a Trans Abdominal Plane (TAP) block, wherein local anaesthetic is injected between the internal abdominal oblique and the transversus abdominus with ultrasound guidance. The reason we chose a preperitoneal approach is because we found it an easier plane to work with under direct vision. In addition, a TAP block is primarily utilized for the initial postoperative period (i.e. within the first 24 hours) [19]. With the pain pumps, as our study has found, we are able to provide significant relief beyond the initial postoperative period because medication can be continuously infused as needed. However, we still agree that a TAP block is an excellent modality of postoperative analgesia and should certainly be considered as an option.

A concern of utilizing percutaneous devices near mesh prostheses is the risk of infection. However, our cohort did not experience any instances of mesh infection. A study conducted by Johnson et al. indicated that local anaesthetics may have antimicrobial properties, and this may explain our results [20]. As such, location of catheter placement is indeed something that surgeons need to consider in order to minimize infection risk. A limitation to our study is our relatively small sample size, which is likely why we did not see significant differences in both narcotic and non-narcotic pain medication use. Recruitment for our study ended before we could enroll adequate sample size, due to difficulty in consenting patients into the study. We think the primary reason was because many patients feared their pain would not be adequately managed if they were to receive the placebo and preferred to receive medication. Regardless, we believe the clinical implications from this study are important and could improve pain management following LVHR procedures.

## Conclusion

In this prospective randomized double-blind placebo-controlled trial, we found a significant difference in outcomes between LVHR receiving either bupivacaine or saline via elastomeric pain pumps. Patients receiving a continuous, bilateral infusion of bupivacaine from these devices experienced significantly less frequent self-reported pain. However, there was no significant reduction in most narcotic and non-narcotic medication use and there were no differences in quality of life for LVHR patients using elastomeric pain pumps post-surgery. A well-powered study investigating the continuous, bilateral infusion of bupivacaine after LVHR is needed to verify our results.

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## Declaration of Conflicts of Interest

FD, BL, MG, WD, SH, JC declare no conflict of interest and JL declares conflict of interest not directly related to the submitted work (speaker and consultant for Covidien and a speaker for GORE) MU declares conflict of interest not directly related to the submitted work (consultant for Covidien and a speaker and lecturer for GORE).

## Author Contributions

- FD: Acquisition of data, analysis and interpretation of data, drafting of manuscript, and critical review
- BL: Analysis and interpretation of data, drafting of manuscript, and critical review
- MG: Acquisition of data, analysis and interpretation of data, drafting of manuscript, and critical review
- JL: Study conception and design and critical review
- WD: Study conception and design and critical review
- SH: Study conception and design and critical review
- JC: Acquisition of data and critical review
- MU: Study conception, drafting of manuscript, and critical review

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