

# Transversus Abdominis Plane Block with Liposomal Bupivacaine Reduces Post-Operative Opioid Requirements in Living Liver Donors

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## Abstract

Pain management with the current open surgical approach for LLDH and opioid epidemic is a substantial concern and should be addressed. Patients undergoing LLDH often anticipate that they will experience significant pain after surgery and although many report that their pain was not as severe as they anticipated, this pre-emptive anxiety could represent a potential barrier when advocating for living donation. With the weight of the opioid crisis looming over our healthcare system, how we balance the risks associated with opioid-based pain management in the living donor population should be underscored. Exposure to opioid medications in both donors and recipients can lead to significant adverse effects including constipation, somnolence, and an increased risk of physical dependence.

**Keywords:** Pain management; Opioid use; Post-surgical pain; Perioperative analgesia

epidemic is a substantial concern and should be addressed. Patients undergoing LLDH often anticipate that they will experience significant pain after surgery and although many report that their pain was not as severe as they anticipated, this preemptive anxiety could represent a potential barrier when advocating for living donation [3]. Therefore, acute post-surgical pain after open living donor hepatectomy is extremely relevant to the overall donor experience. Additionally, there are risks associated with post-operative opioids in an otherwise healthy patient and opioid use should be minimized in this patient population.

With the weight of the opioid crisis looming over our healthcare system, how we balance the risks associated with opioid-based pain management in the living donor population should be underscored. Exposure to opioid medications in both donors and recipients can lead to significant adverse effects including constipation, somnolence, and an increased risk of physical dependence [4]. The risk versus benefit of opioid-based pain regimens in patients undergoing LLDH is especially prudent given most are traditionally opioid naïve and would otherwise not be exposed to opioids outside of liver donation. This is even more pertinent especially when alternative methods of analgesic management after LLDH, have demonstrated success in avoiding opioid-related adverse effects [5]. Alternative methods of analgesic management may also allow the transplant community to expand the living donor pool and consider potential donors with a history of opioid abuse disorder in sustained remission. Due to the inherent risks associated with opioid use, opioid minimization strategies should be employed whenever possible, without sacrificing pain control, patient satisfaction, or overall patient experience.

Transverse Abdominis Plane (TAP) block, given as perioperative analgesia, could serve as a meaningful strategy to reduce opioid exposure in patients undergoing LLDH. TAP block is a perineural block affecting the anterior rami of T7-L1 spinal nerves, which innervate the anterolateral abdominal wall [6].

## Description

Living liver donation has progressively increased since the first living donor liver transplant was performed in 1989 [1]. This increase has substantially impacted the donor pool, with 523 living liver donor transplants being performed in 2019 alone [1]. Traditionally, patients undergoing Living Liver Donor Hepatectomy (LLDH) undergo open surgical resection. Following the movement toward minimally invasive techniques in living kidney donation, there has been an effort in LLDH toward laparoscopic and robotic approaches due to the potential for less morbidity, better pain management and quicker recovery times [2]. However, due to technical complexity and the steep learning curve, a full shift toward minimally invasive techniques in LLDH has not occurred [2]. Given this, pain management with the current open surgical approach for LLDH and opioid

Using local anesthesia such as liposomal bupivacaine as part of a TAP block provides regional anesthesia to the abdominal wall by blocking the initiation and conduction of nerve impulses through effects on the propagation of the nerve impulse and slowing of action potential [7].

Utilization of TAP block with liposomal bupivacaine could aid in reducing exposure to opioids in patients undergoing LLDH. A retrospective review was conducted with the aim to evaluate the efficacy and safety of TAP block with liposomal bupivacaine for opioid reduction, and pain control in patients undergoing LLDH.

## Methods

A single center, retrospective chart review was conducted on all adult patients >18 years old undergoing LLDH from October 2015 to January 2019 at Yale New Haven Hospital in New Haven, Connecticut. Demographic information including age, race, sex, dates of admission and discharge were collected. This study protocol was approved by the Institutional Review Board at Yale New Haven Hospital.

Between October 2015 and February 2017, patients undergoing LLDH received hydromorphone-based Patient-Controlled Analgesia (PCA) post-operatively. These patients were then transitioned to oral analgesics once they were able to tolerate oral medications. In March 2017, our transplant center shifted to using TAP block with liposomal bupivacaine as an alternative to hydromorphone PCA in LLDH patients. The study group consisted of LLDH patients receiving liposomal bupivacaine TAP block during the period of March 2017 to January 2019.

## Procedure

TAP block was administered by anesthesiologists specializing in regional anesthesia. An ultrasound guided 21-gauge needle was used to identify the transversus abdominis plane and administer liposomal bupivacaine. With the use of ultrasound imaging, appropriate dissemination of the medication was observed and recorded in real time. Patients received liposomal bupivacaine at the maximum dose of 266 mg (20 ml).

## Data collection and analysis

The primary endpoint was reduction in post-operative opioid use in Morphine Milligram Equivalents (MME) until discharge.

Secondary end points included: Total non-opioid analgesia, post-operative pain scores, length of hospital and Intensive Care Unit (ICU) stay, re-hospitalizations, and total doses of laxative agents administered. Pain scores were measured *via* a visual analog scale scoring system. A Fisher's exact test was performed for categorical data. A student t-test was used to compare continuous data, with a p-value of  $\leq 0.05$  considered to be statistically significant.

## Results

Data was collected on 24 total patients, including 12 in the study cohort who received liposomal bupivacaine TAP block (TAP block) and 12 historical control patients (control) who received a hydromorphone PCA. Patients were well-matched for baseline demographics such as race, age, and BMI in **Table 1** and there were no significant differences between the two groups

	Control (n=12)	TAP block (n=12)
Age (years), mean $\pm$ SD	43.17 $\pm$ 11	40.67 $\pm$ 11
Male, n (%)	9(75)	5(42)
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	28 $\pm$ 3	26 $\pm$ 3
Weight (kg), mean $\pm$ SD	85 $\pm$ 12	75 $\pm$ 13
Race, n (%)		
White	11(92)	10(83)
Black	0(0)	1(8)
Hispanic	1(8)	1(8)
TAP=Transverse Abdominis Plane, p=not significant		

**Table 1:** Baseline Demographics.

The primary end point of mean total post-operative opioid use in MME was statistically significantly lower in the TAP block cohort with liposomal bupivacaine (183.58 MME control vs. 40.42 TAP block,  $p=0.0094$ ). This reflects a difference of about 143 MME between groups. Mean total doses of additional analgesia used, including acetaminophen, ketorolac, tramadol, were not significantly different between the two groups (**Table 2**). Furthermore, there were no significant differences in mean pain scores between the two groups starting from Post-Operative Day (POD) 0 to 3.

Mean dose (mg)	Control (n=12)	TAP Block (n=12)
Mean ketorolac dose	185	150
Mean tramadol dose	479.17	300
Mean acetaminophen dose	1408.33	2843.75
p=not significant		

**Table 2:** Pain management and differences in mean pain scores.

There was no significant difference in hospital length of stay, however in the TAP block group, length of stay was shorter ( $4.67 \pm 1.2$  days vs.  $5.83 \pm 1.6$  days,  $p=0.0527$ ). No significant differences were detected regarding ICU length of stay (**Table 3**). Only one patient from each group was re-hospitalized in the month following LLDH, one for pneumonia in the control group and another for a wound repair in the TAP block group. Additionally, there were no significant differences in the total mean doses (mg) of bowel regimen medications including polyethylene glycol, senna, bisacodyl or docusate between the

two groups (**Table 3**). TAP block with liposomal bupivacaine was not associated with any adverse events with the drug or the procedure itself.

	Control (n=12)	TAP Block (n=12)
Mean Length of Hospital Stay, days	6 ± 1.6	5 ± 1.1
Mean Length of ICU Stay, days	1.3 ± 0.5	1.1 ± 0.3
Mean Length of Foley Catheter, days*	1.5 ± 0.7	0.9 ± 0.3
Mean doses of bowel regimen medications, mg		
Docusate	575 ± 346.7	533.3 ± 210.3
Polyethylene Glycol	66.6 ± 33.6	38.3 ± 31.7
Senna	32.3 ± 36.3	31.5 ± 18.5
Bisacodyl	10 ± 9.5	10 ± 7.4
TAP=Transverse Abdominis Plane; ICU=Intensive Care unit, p= <0.05		

**Table 3:** Secondary end points.

## Discussion

In this retrospective, single center review, use of TAP block with liposomal bupivacaine in patients undergoing LLDH resulted in a significant reduction in total post-operative opioid MME. Simultaneously, these patients had similar daily mean pain scores and similar use of non-opioid analgesia, indicating that pain control was not sacrificed when utilizing TAP block. These results demonstrate that TAP block with liposomal bupivacaine is a safe and efficacious strategy for opioid-minimization in LLDH patients.

Curbing the duration and use of acute post-operative pain control with opioids for living donors may assist with deterring the transition to long term opioid use. Whether perioperative nerve blocks reduce long-term opioid requirements or persistent post-operative pain remains unclear [8]. However, there are several published trials in various surgical procedures supporting the use of TAP block with liposomal bupivacaine in reducing acute, post-operative opioid requirements [9-13]. There are few studies in the living liver donor population evaluating the use of TAP block with liposomal bupivacaine. One randomized control trial in 50 living liver donors determined that TAP block using bupivacaine diluted with saline reduced morphine consumption up to 24 hours post-surgery, while also reducing pain scores [9]. Another retrospective review in 77 patients undergoing LLDH and TAP block with liposomal bupivacaine found that opioid use with significantly decreased with TAP block on POD 0 and POD 1, but not after that [10]. However, time to full diet and bowel activity was significantly decreased with TAP block, thus representing further positive outcomes known to contribute to better patient experience and recovery [10]. When utilized in living kidney donors, patients receiving TAP block with liposomal bupivacaine also experienced significant reductions in post-operative opioid use compared to those receiving a

hydromorphone PCA, without significant differences in pain scores between the groups [13]. Our retrospective review further contributes to this body of literature supporting the use of TAP block in adult patients undergoing LLDH and one of the few evaluating TAP block with liposomal bupivacaine. To our knowledge, ours is the only study in LLDH patients revealing a significant mean reduction of 143 MME between groups across the patient's entire hospitalization, without a significant change in daily post-operative pain scores or utilization of non-opioid analgesia. This suggests that pain control with TAP block with liposomal bupivacaine resulted in more stable and consistent analgesia

Given the retrospective nature of this study, there are a few limitations to this study. Retrospective reviews inherently make it difficult to control for differences in pain management, including the impact of each individual non-opioid analgesic used. Additionally, although we had a well-matched study and control groups we had a smaller cohort compared to other studies

## Conclusion

In conclusion, use of TAP block with the aid of liposomal bupivacaine in LLDH patients significantly reduced post-operative opioid requirements without the compromise of analgesic coverage. Therefore, this may be a valuable tactic in the effort to minimize opioid exposure in an otherwise healthy living donor patient population undergoing LLDH. Based on our positive experience we believe that prospective and randomized control studies may help further solidify the findings of our study in improving patient experience and outcomes.

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