



LIPOSOMAL BUPIVACAINE, PLAIN BUPIVACAINE, AND SALINE FOR TRANSVERSUS ABDOMINIS PLANE BLOCKS: THE CLEVELAND RANDOMIZED TRIAL

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Introduction

- ❖ Transversus abdominis plane (TAP) blocks are commonly used in Enhanced Recovery After Surgery pathways to reduce postoperative pain and opioid use after abdominal surgery.
- ❖ TAP blocks provide abdominal wall analgesia but do not treat visceral pain, so their clinical benefit remains uncertain.
- ❖ Liposomal bupivacaine may prolong analgesia after single-injection TAP blocks, but evidence compared with conventional bupivacaine is inconsistent.
- ❖ **Co-primary hypotheses:** opioid consumption during the first 24 postoperative hours would be greater with saline placebo than with liposomal or plain bupivacaine, and opioid consumption during 24–48 hours would be lower with liposomal bupivacaine than with saline or plain bupivacaine.
- ❖ **Secondary hypothesis:** liposomal bupivacaine TAP blocks would result in longer duration of local anesthetic effect, lower pain scores during the first 72 postoperative hours, and reduced opioid requirements between 48–72 hours compared with plain bupivacaine and saline.

Methods

- ❖ **Design:** Investigator-initiated, randomized, blinded clinical trial conducted at Cleveland Clinic.
- ❖ **Population:** Adults (18–85 yr) undergoing elective open or laparoscopic abdominal surgery.
- ❖ **Randomization:** (1:1:1):
 - ❖ Liposomal bupivacaine TAP block
 - ❖ Plain bupivacaine TAP block
 - ❖ Saline placebo TAP block.
- ❖ **Intervention:** Pre-incision bilateral four-quadrant ultrasound-guided TAP blocks; patients, clinicians, nurses, and investigators blinded to group assignment.
- ❖ **Outcomes:**
 - ❖ **Co-primary:** opioid consumption (MME) during 0–24 h and 24–48 h
 - ❖ **Secondary:** duration of sensory block, pain scores over 72 h, opioid use 48–72 h.

Figure 1. Opioid use, in milligram morphine equivalents (MME)

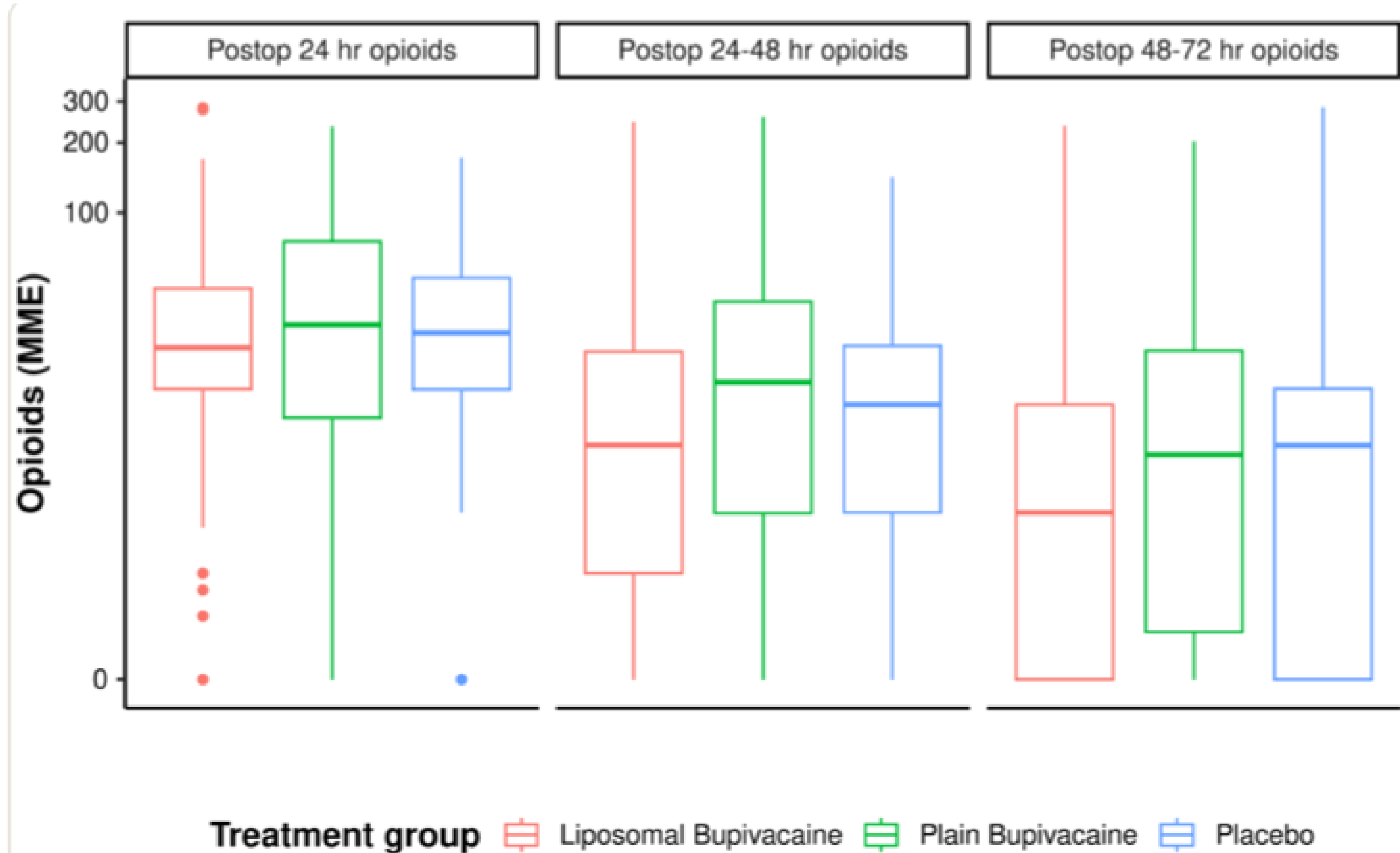


Table 1. Primary Analysis Results, Modified Intention-to-treat Population

Outcome	Liposomal Bupivacaine [A]	Plain Bupivacaine [B]	Placebo [C]	Treatment effect: A vs. C	Treatment effect: B vs. C
Primary outcomes*					
Total opioids, during postoperative 24 h, MME†	26 [18, 48] (n = 89)	33 [13, 75] (n = 84)	31 [17, 53] (n = 88)	Ratio of geometric means 0.86 (97.7% CI, 0.60 to 1.24; P value = 0.355) (n = 259)	Ratio of geometric means 0.91 (97.7% CI, 0.63 to 1.32; P value = 0.578) (n = 259)
Total opioids, during postoperative 24–48 h, MME†	10 [2, 25] (n = 89)	19 [5, 42] (n = 84)	15 [5, 27] (n = 88)	N/A*	N/A*
Secondary outcomes‡					
Time to sensation return, days§	0 (95% CI: 0, 0) (n = 79)	0 (95% CI: 0, 0) (n = 73)	0 (95% CI: 0, 0) (n = 83)	Hazard ratio 0.63 (95% CI, 0.29 to 1.37; P value = 0.248) (n = 233)	Hazard ratio 1.65 (95% CI, 0.64 to 4.23; P value = 0.297) (n = 233)
Pain scores during postoperative 72 h	4 [3, 6] (n = 89)	5 [3, 6] (n = 83)	4 [3, 5] (n = 88)	Mean difference −0.08 (99.2% CI, −0.87 to 0.71; P value = 0.796) (n = 1,422)	Mean difference 0.26 (99.2% CI, −0.55 to 1.07; P value = 0.399) (n = 1,422)
Total opioids, during postoperative 48–72 h, MME†	5 [0, 15] (n = 89)	9 [1, 26] (n = 84)	10 [0, 18] (n = 88)	Ratio of geometric means 0.72 (99.2% CI, 0.39 to 1.32; P value = 0.152) (n = 259)	Ratio of geometric means 1.18 (99.2% CI, 0.63 to 2.18; P value = 0.482) (n = 259)
Tertiary/exploratory outcomes					
Opioid related side effects#	62 of 88 (70%)	57 of 81 (70%)	70 of 87 (80%)	Odds ratio 0.52 (97.5% CI, 0.23 to 1.18; P value = 0.078)	Odds ratio 0.54 (97.5% CI, 0.23 to 1.23; P value = 0.097)
Patient pain management satisfaction scores**	9 [8, 10] (n = 69)	8 [6, 9] (n = 60)	8 [7, 10] (n = 69)	Mean difference 0.56 (97.5% CI, −0.19 to 1.30; P value = 0.096) (n = 196)	Mean difference −0.28 (97.5% CI, −1.07 to 0.51; P value = 0.423) (n = 196)
Pain score after leg-raise test	5 [4, 7] (n = 89)	6 [4, 7] (n = 83)	5 [4, 7] (n = 88)	Mean difference −0.19 (97.5% CI, −0.91 to 0.52; P value = 0.548) (n = 1,385)	Mean difference 0.05 (97.5% CI, −0.68 to 0.78; P value = 0.875) (n = 1,385)

Results

- ❖ 261 patients analyzed after randomization of 285 patients: liposomal bupivacaine (n=89), plain bupivacaine (n=84), placebo (n=88).
- ❖ **Co-primary outcomes:** postoperative opioid consumption during 0–24 h was similar across groups, with no significant differences between liposomal bupivacaine or plain bupivacaine compared with placebo.
- ❖ **Secondary outcomes:** no significant differences were observed in:
 - ❖ Pain scores during the first 72 h,
 - ❖ Time to sensory recovery, or
 - ❖ Opioid consumption during 48–72 h.
- ❖ Overall interpretation: TAP blocks performed with liposomal or plain bupivacaine did not improve postoperative analgesic outcomes compared with saline placebo.

Discussion

- ❖ These findings suggest limited analgesic benefit of TAP blocks in mixed abdominal surgical populations, likely because TAP blocks primarily treat somatic abdominal wall pain rather than visceral pain.
- ❖ Because the block itself did not demonstrate benefit compared with placebo, relative advantages of liposomal versus conventional bupivacaine could not be meaningfully assessed.

Limitations and Conclusion

- ❖ Immediate block success was not fully confirmed, as formal sensory reassessment occurred later postoperatively.
- ❖ Normal saline injections into fascial planes may have antinociceptive effects, potentially reducing observed differences between groups.
- ❖ Heterogeneous abdominal procedures may dilute procedure-specific analgesic effects.
- ❖ Results may not apply to catheter techniques or other regional approaches.
- ❖ **Conclusion:** Single-shot TAP blocks using liposomal or plain bupivacaine did not improve postoperative opioid consumption or pain scores compared with saline placebo in mixed abdominal surgical populations.