Intrathecal Morphine vs Paravertebral Nerve Blocks for Analgesia After Breast Reconstruction With Abdominally Based Free Flaps

Matthew W. Swisher, MD, MS; Austin T. Nguyen, BS; Miriam Becker, MS; Jacklynn F. Sztain, MD; Wendy B. Abramson, MD; Paige S. Tsuda, MD; Brenton S. Alexander, MD; Chris M. Reid, MD; and Engy T. Said, MD

Aesthetic Surgery Journal
2025, Vol 45(6) 605–610
Editorial Decision date: March 12, 2025; online publish-ahead-of-print March 19, 2025.

https://doi.org/10.1093/asj/sjaf043
www.aestheticsurgeryjournal.com

Abstract

Background: Breast reconstruction with abdominally based free flaps can be associated with more significant acute pain and longer hospital stays than implant-based techniques. As new pain management strategies are developed, there have not been any studies conducted to analyze the analgesic effects of intrathecal morphine (ITM) for patients undergoing abdominally based free flap reconstruction.

Objectives: The primary outcome analyzed in this retrospective study was opioid consumption, which was measured from the postoperative anesthesia care unit (PACU) through postoperative day (POD) 2. Secondary outcomes of the study analyzed included factors such as pain scores, hospital length of stay (LOS), and adverse effects.

Methods: Fifty-one patients presented for breast reconstruction with abdominally based free flaps and received ITM for postoperative analgesia. Results obtained were compared with a cohort that included an equal number of patients who received paravertebral nerve blocks (PVBs).

Results: Results showed that patients who received ITM displayed a lower median consumption in the PACU (0 mg vs 12.5 mg MEQ; $P = .009$), from PACU to POD 1 (0 mg vs 7.5 mg MEQ; $P = .046$), and POD 1 to POD 2 (7.5 mg vs 30 mg MEQ; $P = .002$) when compared with those who received PVBs. Those who received ITM also had lower median pain scores in the PACU and from PACU to POD 1 and a decreased LOS. There were similar rates of adverse events.

Conclusions: ITM improves postoperative analgesia after abdominally based free flaps when compared to PVBs and may facilitate recovery and earlier discharge.

Level of Evidence: 3 (Therapeutic)

Breast reconstruction with abdominally based free flaps can be associated with more significant acute postoperative pain from the donor site and longer hospital stays given the complex nature of the procedure compared to nonautologous breast reconstruction techniques.[1] Although this reconstructive technique has consistently shown better long-term and patient-reported outcomes, significantly increased donor site pain, morbidity, and length of stay (LOS) may limit broader adoption as a surgical technique in addition to other factors.[2] Various enhanced recovery after surgery protocols have been developed at different institutions to improve pain control and LOS for this surgical population.

Commonly used perioperative analgesic options for abdominally based free flap reconstruction patients include multimodal analgesia with opioids and nonopioid adjuncts, local infiltration, peripheral nerve blocks (PVBs), and neuraxial blocks.[3,4] The most commonly

Drs Swisher, Sztain, Abramson, Tsuda, Alexander, and Said are anesthesiologists, Department of Anesthesiology, University of California San Diego, La Jolla, CA, USA. Mr Nguyen and Ms Becker are medical students, School of Medicine, University of California San Diego, La Jolla, CA, USA. Dr Reid is a plastic surgeon, Department of Surgery, Division of Plastic Surgery, University of California San Diego, La Jolla, CA, USA.

Corresponding Author:
Dr Matthew W. Swisher, Department of Anesthesiology, University of California San Diego, 9500 Gilman Drive MC 0898, La Jolla, CA 92093, USA.
E-mail: matthew.swisher@gmail.com

Presented at: 49th Annual Regional Anesthesiology and Acute Pain Medicine Meeting in San Diego, CA, in March 2024.

studied peripheral nerve blocks include transversus abdominis plane (TAP) blocks (for the donor site) and PVBs (for both recipient and donor sites). However, results are conflicting if peripheral nerve blocks result in reduced postoperative pain and LOS.[5,6] Because coverage of the requisite thoracic and abdominal surgical sites may be challenging with peripheral nerve blocks and epidural analgesia, a single injection of preoperative intrathecal morphine (ITM) has the potential to cover both sites and improve postoperative analgesia.

To date, there have not been any studies conducted to analyze the analgesic effects of implementing intrathecal morphine in abdominally based free flap breast reconstruction patients. At our institution, these patients were historically offered PVBs for postoperative analgesia before the initiation of ITM. This retrospective cohort study serves to further investigate the analgesic effects of ITM for this surgical population through a comparison with a cohort that received PVBs. In doing so, the study highlights a potential alternative to PVBs for those undergoing this particular surgery.

METHODS

The University of California San Diego Institutional Review Board (protocol #200392) confirmed approval for this retrospective study. In addition, informed consent for the study was waived, given its retrospective nature. However, informed consent was obtained preoperatively for each intervention.

Between October 2022 and August 2023, 52 consecutive patients presented for breast reconstruction with an abdominally based free flap and were provided with the option of ITM as their form of postoperative analgesia preoperatively. No exclusion criteria were utilized. One patient's surgery was aborted after induction of anesthesia due to bronchospasm.

After informed consent for each intervention was obtained, patients were placed in the sitting position with accompanying standard monitors applied. Then, their lower lumbar region was prepared with 10% povidone-iodine solution and draped under sterile procedure. Skin penetration was performed with 1% lidocaine, and a 25-gauge Whitacre spinal needle (Becton Dickinson, Franklin Lakes, NJ) was used to proceed into the intrathecal space between the second and fifth lumbar vertebrae. Once confirmation of cerebrospinal fluid was made, 200 to 300 µg of preservative-free morphine was injected (43 patients received 300 µg, 7 patients received 250 µg, and 2 patients received 200 µg). Dosage was based on age, comorbidities, perceived sensitivity to analgesics, and expected degree of postoperative pain.

After the injection, patients were given general anesthesia in the operating room, and they were examined by our acute pain service to support pain management. All patients were administered a postoperative multimodal analgesia consisting of acetaminophen, opioids, gabapentinoids, and nonsteroidal anti-inflammatory drugs based on their age and comorbidities. ITM patients received postoperative respiratory monitoring consistent with the American Society of Anesthesiologists (ASA) guidelines.[7]

The historical comparison group included an equal number of 51 consecutive patients who presented for abdominally based free flap breast reconstruction between May 2021 and September 2022 and received preoperative PVBs, and similarly no exclusion criteria were used.

For the PVB group, blocks were performed similarly to previously described studies.[8,9] Target paravertebral spaces for the chest were T2, T3, or T4, and target spaces for the abdominal donor site were T8, T9, or T10. For the recipient upper chest site, 34 of the 51 patients received paravertebral catheters (with the other 17 receiving single injections only), of which 6 were removed on postoperative day (POD) 1, 21 on POD 2, and 7 on POD 3. Paravertebral nerve catheter infusions consisted of 0.2% ropivacaine at 8 mL/hour with patient-controlled boluses of 4 mL every 30 to 60 minutes depending on whether surgery was unilateral or bilateral. The abdominal donor sites were exclusively administered single-shot injections in 36 of the 51 patients. No paravertebral catheters were placed for the abdominal donor sites.

The primary outcome consisted of opioid consumption measured in oral morphine equivalents (MEQ) during the patient's time from the postoperative anesthesia care unit (PACU) until the morning of POD 2 in the 2 groups. Secondary outcomes included pain scores as expressed in a numeric rating scale (NRS; 0-10), LOS, and adverse events.

Statistical analysis was performed, comparing median values for each outcome with the Mann-Whitney test. Patient baseline characteristics were compared with independent *t* tests or chi-squared tests, as appropriate. The primary outcome was further evaluated with multivariate regression. Regression analysis examined postoperative opioid consumption as a function of analgesia type (ITM vs PVB), controlling for age, BMI, smoking status (former, current, never), diabetes diagnosis, surgery type, intraoperative opioid dose, presence of postoperative complications, and total pain score. Backward selection was applied with an inclusion threshold of 0.2 and α of .05. Analyses were conducted with R (R Core Team, 2024).[10]

A post hoc power analysis was conducted to evaluate the statistical power of the study. With an observed effect size of Cohen's d of −0.5, a total sample size of 102 (51 per group), and a significance level of $\alpha = .05$, power was estimated with GPower 3.1.[11] The analysis assessed the probability of detecting a true medium effect size within the study sample.

RESULTS

Fifty-two patients presented for abdominally based flap breast reconstruction and were offered ITM as their form of postoperative analgesia. One ITM patient experienced suspected bronchospasm after induction of general anesthesia, and the surgery was postponed and therefore was excluded from the final analysis. Table 1 highlights patient demographics and surgical characteristics of both groups. There were no statistically significant differences in baseline demographic characteristics (age, BMI, ASA classification, diabetes diagnosis, smoking status, or preoperative opioid use) between patients who received ITM vs PVB ($P > .05$). All patients were female (52 in both groups). Ages ranged from 32 to 67 in the ITM group (average 51) and 31 to 71 in the PVB group (average 50).

With respect to the primary outcome, the patients who received ITM displayed a lower median opioid consumption in the PACU (0 mg vs 12.5 mg MEQ; $P = .009$), from PACU to morning of POD 1 (0 mg vs 7.5 mg MEQ; $P = .046$), and morning of POD 1 to morning of POD 2 (7.5 mg vs 30 mg MEQ; $P = .002$) than those who received PVBs. For secondary outcomes, the patients who received ITM also displayed lower median pain scores in the PACU (0 vs 2; $P = .015$) and PACU to morning of POD 1 (0.5 vs 3; $P = .001$). Both groups had similar pain scores from the morning of POD 1 to POD 2 (3 for ITM group vs 4 for PVB group; $P = .09$). Figures 1 and 2 show the distributions of opioid consumption and pain scores in the 2 groups. Table 2 summarizes the primary and secondary outcomes of the 2 groups. The range of follow-up was 1 to 3 days for the ITM group (average 1.5 days) and 1 to 6 days for the PVB group (average 2.3 days).

Interestingly, 11 of the 51 ITM patients (22%) required no opioids postoperatively compared to 3 of the 51 PVB patients (6%). Six of the ITM patients (12%) did not require an opioid prescription at the time of discharge, compared to 2 of the PVB patients (4%). Patient

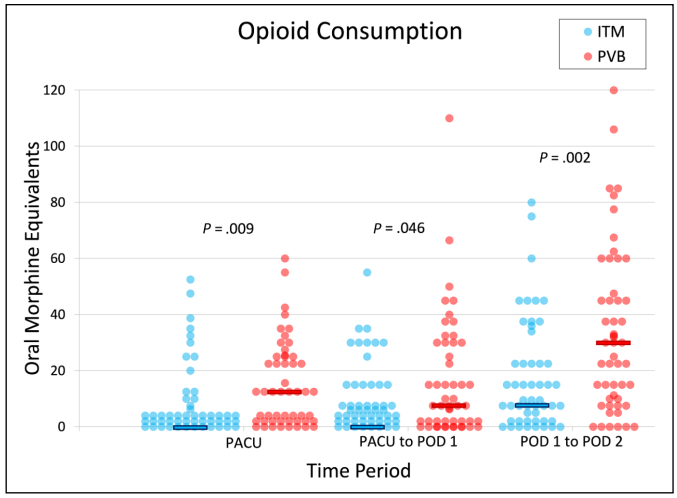

Figure 1. Median opioid consumption in oral morphine equivalents for the postoperative time periods of the 2 groups. Horizontal bars represent the overall median for that time period. ITM, intrathecal morphine; PACU, postoperative anesthesia care unit; POD, postoperative day; PVB, paravertebral block.

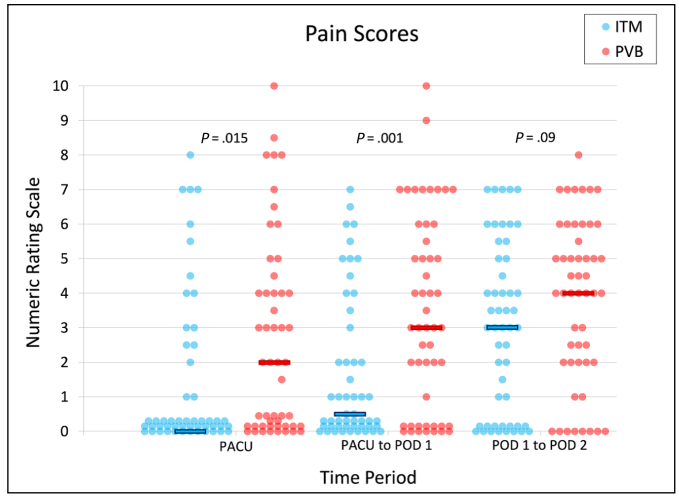

Figure 2. Median numeric rating scale pain scores (0-10) for the postoperative time periods of the 2 groups. Horizontal bars represent the overall median for that time period. ITM, intrathecal morphine; PACU, postoperative anesthesia care unit; POD, postoperative day; PVB, paravertebral block.

data were collected for the duration of their hospital stay (maximum stay was 6 days in 1 PVB case).

The increased opioid consumption observed in the PVB group at each time point (PACU, PACU through POD 1, POD 1 through POD 2, and overall) compared to the ITM group remained significant after adjusted analysis. Compared to ITM, PVB was associated with a 28.86-unit increase in total opioid consumption (95% CI, 12.52 to 45.19, $P < .001$). The only other significant covariate was age. Each additional year in patient age was significantly associated with a 1.21-unit decrease in postoperative opioid consumption (95% CI, −2.07 to −0.35, $P = .01$). The overall model was significant: $F(2,99) = 10.86$, adjusted $R^2 = 0.163$, $P < .001$.

Regarding hospital LOS, the median LOS for the ITM group was 1 day vs 2 days for the PVB group ($P < .001$). Adverse events occurred in 20 out of 51 ITM patients. Seventeen patients demonstrated low blood pressure or orthostasis, 2 patients exhibited pruritis, 1 patient had nausea or vomiting, 1 patient had a suspected postdural puncture headache, and 1 patient experienced delayed awakening in the PACU. Neither the delayed awakening patient nor suspected postdural puncture headache patient required intervention. In the PVB group, 20 out of the 51 PVB patients experienced adverse events, which included low blood pressure or orthostasis in 14 patients, uncontrolled pain in 2 patients, hypoxia in 1 patient, upper extremity weakness in 1 patient, difficulty swallowing in 1 patient, a vasovagal code event in 1 patient, loss of consciousness or seizure event in 1 patient, swelling or pain at catheter site in 1 patient, and delayed catheter removal in 1 patient due to heparin administration. There were no recorded instances of apnea events or respiratory depression in the ITM group.

Post hoc power analysis indicated that, given the observed effect size ($d = -0.5$) and sample size ($n = 102$), the study had a power of 0.69. This suggests a 69% probability of detecting a true medium effect size at a significance level of .05.

DISCUSSION

In this retrospective cohort study, we demonstrated that the administration of preoperative ITM was associated with decreased consumption of opioids and pain scores following abdominally based flap breast reconstruction. Our results suggest that ITM produces improved postoperative analgesia compared to PVBs with a decreased hospital length of stay and a similar adverse event profile, regardless of patient BMI, diabetes diagnosis, age, smoking, and ASA status. Findings suggest that age may be a confounding variable, because increased age was associated with decreased opioid consumption. This trend has been observed in several previous studies and may be attributed to a range of causes, including differences in drug metabolism, polypharmacy, and increased sensitivity to adverse effects of opioids.[12-14] Opioid consumption was reduced at all time points (PACU, PACU to POD 1, and POD 1 to POD 2) for those receiving ITM. Interestingly, 22% of the ITM patients required no opioids postoperatively and 12% did not require an opioid prescription at time of discharge (compared to 6% and 4%, respectively, for the PVB group).

For implant-based breast reconstruction, peripheral nerve block techniques such as PVBs are commonly used in managing acute postoperative pain.[15-18] The literature has demonstrated that patients undergoing mastectomy who received a PVB, compared to patients who did not, require significantly less opioids intraoperatively and postoperatively, had lower pain scores postoperatively, and required less antiemetic medications perioperatively.[19] However, despite their analgesic potency, the pleural puncture and pneumothorax risks of PVBs may limit their widespread adoption at many institutions.[8] Newer regional anesthesia techniques have been developed to target the relevant peripheral nerves further away from the paravertebral space and pleura, however their efficacy may be decreased as a result.[8,20]

One such commonly studied regional analgesic technique for autologous breast reconstruction donor site pain is TAP block.[3-5,21,22] TAP blocks can be administered by surgical infiltration or, more precisely, with ultrasound guidance, similar to any peripheral nerve block. However, TAP blocks only provide analgesia to the donor abdominal site and will not cover the recipient thoracic area. A recent meta-analysis of 12 studies showed a reduction in postoperative opioid consumption and LOS but no difference in postoperative pain scores.[5] Another limitation of TAP blocks with plain local anesthetic such as bupivacaine is the limited duration of analgesia of 12 to 24 hours. More recent studies with liposomal bupivacaine TAP blocks have been performed in this surgical population with conflicting results.[23,24]

Given the presence of both donor and recipient sites in abdominally based free flap breast reconstruction, optimal postoperative pain can be

Table 1. Patient Demographics and Surgical Characteristics

	ITM group ($n = 51$)	PVB group ($n = 51$)
Age, years	52 (45-57)	49 (43-59)
BMI, kg/m^2	28 (18-39)	27 (19-38)
Gender identity, *n* (%)		
Female	51 (100)	51 (100)
Male	0	0
ASA classification, *n* (%)	0 (0)	1 (2)
1	29 (57)	27 (53)
2	22 (43)	22 (43)
3		
Patients with diabetes diagnosis, *n* (%)	5 (10)	8 (16)
Patient smoking status, *n* (%)		
Former	8 (16)	10 (20)
Current	2 (4)	0
Never	41 (80)	41 (80)
Patients taking preoperative opioids, *n* (%)	2 (4)	2 (4)

Values are reported as median (interquartile) or number (percentage of patients). ASA, American Society for Anesthesiologists; BMI, body mass index; ITM, intrathecal morphine; PVB, paravertebral block.

Table 2. Primary and Secondary Outcomes

	ITM group ($n = 51$)	PVB group ($n = 51$)	*P* value
Opioid consumption, MEQ			
PACU	0 (0-8.8)	12.5 (0-25)	.009
PACU to POD 1	0 (0-15)	7.5 (0-30)	.046
POD 1 to POD 2	7.5 (0-22.5)	30 (10-46.3)	.002
Pain scores, 0-10			
PACU	0 (0-2)	2 (0-4)	.015
PACU to POD 1	0.5 (0-2.5)	3 (0-6)	.001
POD 1 to POD 2	3 (0-5)	4 (2-6)	.09
Length of stay, days	1 (1-2)	2 (2-3)	<.001
Adverse events, *n* (%)	20 (39)	20 (39)	

Values are reported as median (interquartile) or number (percentage of patients). ITM, intrathecal morphine; MEQ, oral morphine equivalents; PACU, postanesthetic care unit; POD, postoperative day; PVB, paravertebral block.

more challenging to obtain with any combination of peripheral nerve blocks and multimodal analgesia, given the degree of postoperative pain as well as the sheer number of dermatomes needed to achieve effective anesthesia. The need to cover both the upper thoracic and lower abdominal surgical sites increases the challenge of providing optimal postoperative analgesia with peripheral nerve blocks.

Given the challenge of providing optimal analgesia in these patients, neuraxial analgesia with a single administration and injection site could theoretically cover both donor and recipient sites and facilitate recovery and discharge. For neuraxial analgesia, the options for postoperative analgesia include epidural and intrathecal single injections or continuous techniques with local anesthetic. Continuous techniques with local anesthetic are limiting for this type of surgery given the motor block that would inhibit postoperative ambulation as well as inability to cover both sites adequately with 1 catheter. Neuraxial opioids provide extensive analgesia for both thoracic and abdominal surgery with a relatively long duration of 20 to 48 hours (especially if a hydrophilic opioid such as morphine is given in the intrathecal space).[25-30] Therefore neuraxial morphine injected into the lumbar intrathecal space represents a promising option for this surgical population, because a single injection of ITM can theoretically cover both surgical sites with dense analgesia for up to 48 hours and facilitate postoperative ambulation and recovery. To date, there have been no previous studies examining the effects of ITM in the abdominally based free flap breast reconstruction surgical population.

Our results indicate that ITM provides improved postoperative analgesia after abdominally based free flap breast reconstruction upon comparison with PVBs. In this retrospective study, there was a decrease in opioid consumption through POD 2. The difference in opioid consumption was most pronounced between POD 1 and 2 in the 2 groups. This would be expected because the analgesia from ITM can last upward of 48 hours in comparison to the duration of PVBs, which is usually less than 24 hours. The ITM group had median pain scores close to zero or near-zero from PACU to POD 1 and then started to have mild pain scores from POD 1 to 2. In comparison, the PVB group had mostly mild pain in the PACU and PACU to POD 1 and moderate pain POD 1 to 2. There was no significant difference seen in pain scores from POD 1 to 2 between the 2 groups, because the ITM was likely starting to wear off in most patients.

One of the interesting findings in our study has been the ability to discharge these patients on POD 1 with ITM, presumably given the improved pain control. Enhanced recovery after surgery (ERAS) pathways have been increasingly utilized for autologous breast reconstruction patients.[1,3] Our institution previously started an interdisciplinary recovery pathway for these patients and compared our results to nonautologous breast reconstruction patients, showing decreased opioid consumption with comparable LOS.[31] With the addition of ITM (rather than PVBs), we are now able to routinely discharge patients on POD 1. In comparison, other recent ERAS studies on similar surgical patients showed an LOS of 3 to 5 days.[1,3,32,33] Although many factors may ultimately determine a patient's LOS, we believe that optimal analgesia with ITM improves the ability to safely discharge earlier. Notable also is the lack of adverse events seen by discharging in an expedited fashion. No flap losses were encountered in any patients. Furthermore, discharging patients on POD 1 is a significant stride in attaining equivalent pain and recovery for implant and autologous reconstruction.

Although ITM provides significant analgesia for this surgical population, it is important to understand the limitations, side effects, and adverse events that may be associated with neuraxial opioid administration. As a potent analgesic, neuraxial opioids may be associated with oversedation, delayed emergence, and respiratory depression if combined with other systemic opioids, sedatives, or hypnotics. Patients require a higher level of care for respiratory monitoring postoperatively according to the ASA guidelines on neuraxial opioid administration.[7] Notably, this does not require any significant change in burden of care, given that breast flap patients are monitored every hour as a standard of care. For hydrophilic opioids such as morphine,

these guidelines require patients to be checked hourly for adequacy of ventilation, oxygenation, and level of sedation for the first 12 hours after administration and then every other hour for the subsequent 12 hours. Because ITM is administered preoperatively, many of the hourly checks occur while the patient is under general anesthesia during the procedure, decreasing the duration postoperatively for the nursing staff. The dosage of ITM used in this study is considered a "high dose" (greater than 150 µg based on the literature), therefore care must be taken intraoperatively and postoperatively to limit systemic opioids and sedatives to prevent delayed emergence and oversedation.[34] Of note, in our study, there were no instances of respiratory depression in the ITM group, but there was 1 case of delayed awakening in the PACU that did not require intervention.

In addition to oversedation and respiratory depression, other side effects and adverse events related to ITM include the risk of postdural puncture headache (PDPH), nausea, vomiting, and pruritus.[34] The risk of PDPH after ITM for thoracic and abdominal surgery is not definitively known compared to more commonly studied obstetric patients receiving spinal anesthesia in addition to morphine. In our study, there was 1 case of suspected PDPH in the ITM group, but no intervention such as an epidural blood patch or sphenopalatine ganglion block was required. One patient in the ITM group experienced nausea or vomiting and 2 patients had significant pruritus managed with medications.

Because this was a retrospective study, there are several limitations to mention. The association between ITM administration and improved pain control may be a result of other factors not accounted for in our analysis, such as differing multimodal analgesic regimens between the 2 groups. Although both groups had their multimodal analgesia ordered by our acute pain service, it is possible that regimens changed during the course of this study. Another caveat for the PVB group is that the abdominal site was not uniformly covered in every case with nerve blocks. In addition, the data we collected depended on the accuracy and frequency of pain scores reported by nursing and the electronic medical record system. Other outcomes such as the incidence of delayed emergence, for example, could be missing in the record collection. To address these limitations, a prospective, randomized study could be performed to further assess and confirm causality between ITM administration and improved pain control. This type of study would standardize the analgesic protocols between both groups to account for any external factors previously not controlled. However, due to the recent implementation of ITM as part of standard of care, this type of prospective, randomized study may not be feasible because of the recognized clinical benefits.

Last, another limitation we did not investigate in this study was the individual response to different opioids with respect to pharmacogenomics. It is possible that individual patients may respond differently to neuraxial morphine based on their genetic predispositions. Pharmacogenomic testing was not performed on the patients in our study. To our knowledge, pharmacogenomics has not been studied for neuraxial morphine and may form the basis for a future study.

Additional studies of ITM for autologous breast reconstruction patients are necessary. Future prospective trials should report outcomes in a standard way to aid in data analysis and comparison to results of previous studies. Studies should report, at minimum, length of stay, opioid consumption, pain scores, and adverse events. Studies should also discuss and highlight any barriers and limitations faced so that different institutions can adapt their protocols accordingly.

CONCLUSIONS

Administering ITM as a form of postoperative analgesia for patients undergoing abdominally based free flap breast reconstruction can be considered a safe and potent analgesic modality. It is believed that this retrospective cohort study is the first to describe the effects of ITM administration for this particular surgical group. For patients undergoing abdominally based free flap breast reconstruction, ITM administration contributes to decreased opioid consumption and pain scores postoperatively and a decreased LOS. Adoption of this technique is an important and effective means in working to achieve equivalency when patients choose between implant and autologous reconstruction.

Disclosures

The University of California San Diego has received funding or product from the following companies for other research studies performed by Dr Swisher and Dr Said: Epimed International (Farmers Branch, TX), SPR Therapeutics (Cleveland, OH), Infutronix (Natick, MA), and Avanos Medical (Irvine, CA). Dr Swisher is a paid consultant for Vertex Pharmaceuticals (Boston, MA). The remaining authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

Funding

The authors received no financial support for the research, authorship, and publication of this article.

REFERENCES

1. Gort N, van Gaal BGI, Tielemans HJP, Ulrich DJO, Hummelink S. Positive effects of the enhanced recovery after surgery (ERAS) protocol in DIEP flap breast reconstruction. *Breast*. 2021;60:53-57. doi: 10.1016/j.breast.2021.08.010
2. Santosa KB, Qi J, Kim HM, Hamill JB, Wilkins EG, Pusic AL. Long-term patient-reported outcomes in postmastectomy breast reconstruction. *JAMA Surg*. 2018;153:891-899. doi: 10.1001/jamasurg.2018.1677
3. Araya S, Webster TK, Egleston B, et al. Significant reduction in length of stay in deep inferior epigastric perforator flap breast reconstruction with implementation of multimodal ERAS protocol. *Ann Plast Surg*. 2023;91:90-95. doi: 10.1097/SAP.0000000000003578
4. Hivelin M, Wyniecki A, Plaud B, Marty J, Lantieri L. Ultrasound-guided bilateral transversus abdominis plane block for postoperative analgesia after breast reconstruction by DIEP flap. *Plast Reconstr Surg*. 2011;128:44-55. doi: 10.1097/PRS.0b013e3182174090
5. Chi D, Chen AD, Ha AY, Yaeger LH, Lee BT. Comparative effectiveness of transversus abdominis plane blocks in abdominally based autologous breast reconstruction: a systematic review and meta-analysis. *Ann Plast Surg*. 2020;85:e76-e83. doi: 10.1097/SAP.0000000000002376
6. Parikh RP, Sharma K, Guffey R, Myckatyn TM. Preoperative paravertebral block improves postoperative pain control and reduces hospital length of stay in patients undergoing autologous breast reconstruction after mastectomy for breast cancer. *Ann Surg Oncol*. 2016;23:4262-4269. doi: 10.1245/s10434-016-5471-1
7. Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration: an updated report by the American society of anesthesiologists task force on neuraxial opioids and the American society of regional anesthesia and pain medicine. *Anesthesiology*. 2016;124:535-552. doi: 10.1097/ALN.0000000000000975
8. Swisher MW, Wallace AM, Sztain JF, et al. Erector spinae plane versus paravertebral nerve blocks for postoperative analgesia after breast surgery: a randomized clinical trial. *Reg Anesth Pain Med*. 2020;45:260-266. doi: 10.1136/rapm-2019-101013
9. Ilfeld BM, Madison SJ, Suresh PJ, et al. Treatment of postmastectomy pain with ambulatory continuous paravertebral nerve blocks: a randomized, triple-masked, placebo-controlled study. *Reg Anesth Pain Med*. 2014;39:89-96. doi: 10.1097/AAP.0000000000000035
10. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing; 2024. Accessed February 2025. https://www.R-project.org/
11. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41:1149-1160. doi: 10.3758/BRM.41.4.1149
12. Dagenais-Beaulé V, Tourigny JF, Papillon-Ferland L. Opioid use and pain control in the elderly after elective or urgent orthopaedic surgery: a retrospective cohort study. *Clin Drug Investig*. 2019;39:301-308. doi: 10.1007/s40261-018-00744-7

13. Mohanty S, Rosenthal RA, Russell MM, Neuman MD, Ko CY, Esnaola NF. Optimal perioperative management of the geriatric patient: a best practices guideline from the American college of surgeons NSQIP and the American geriatrics society. *J Am Coll Surg*. 2016;222:930-947. doi: 10.1016/j.jamcollsurg.2015.12.026
14. Melucci AD, Lynch OF, Wright MJ, et al. Evaluating age as a predictor of postoperative opioid use and prescribing habits in older adults with cancer. *J Am Med Dir Assoc*. 2022;23:678-683.e1. doi: 10.1016/j.jamda.2022.01.081
15. Stein MJ, Waltho D, Ramsey T, Wong P, Arnaout A, Zhang J. Paravertebral blocks in immediate breast reconstruction following mastectomy. *Breast J*. 2019;25:631-637. doi: 10.1111/tbj.13295
16. Shamsunder MG, Chu JJ, Taylor E, et al. Paravertebral blocks in tissue expander breast reconstruction: propensity-matched analysis of opioid consumption and patient outcomes. *Plast Reconstr Surg*. 2023;151:542e-551e. doi: 10.1097/PRS.0000000000009981
17. Tokita HK, Polanco TO, Shamsunder MG, et al. Non-narcotic perioperative pain management in prosthetic breast reconstruction during an opioid crisis: a systematic review of paravertebral blocks. *Plast Reconstr Surg Glob Open*. 2019;7:e2299. doi: 10.1097/GOX.0000000000002299
18. Coopey SB, Specht MC, Warren L, Smith BL, Winograd JM, Fleischmann K. Use of preoperative paravertebral block decreases length of stay in patients undergoing mastectomy plus immediate reconstruction. *Ann Surg Oncol*. 2013;20:1282-1286. doi: 10.1245/s10434-012-2678-7
19. Fahy AS, Jakub JW, Dy BM, et al. Paravertebral blocks in patients undergoing mastectomy with or without immediate reconstruction provides improved pain control and decreased postoperative nausea and vomiting. *Ann Surg Oncol*. 2014;21:3284-3289. doi: 10.1245/s10434-014-3923-z
20. Gabriel RA, Swisher MW, Sztain JF, et al. Serratus anterior plane versus paravertebral nerve blocks for postoperative analgesia after non-mastectomy breast surgery: a randomized controlled non-inferiority trial. *Reg Anesth Pain Med*. 2021;46:773-778. doi: 10.1136/rapm-2021-102785
21. Afonso A, Oskar S, Tan KS, et al. Is enhanced recovery the new standard of care in microsurgical breast reconstruction? *Plast Reconstr Surg*. 2017;139:1053-1061. doi: 10.1097/PRS.0000000000003235
22. Lombana NF, Falola RA, Zolfaghari K, Roth C, Abraham JT, Saint-Cyr MH. Comparison of liposomal bupivacaine to a local analgesic cocktail for transversus abdominis plane blocks in abdominally based microvascular breast reconstruction. *Plast Reconstr Surg*. 2022;150:506e-515e. doi: 10.1097/PRS.0000000000009398
23. Ha AY, Keane G, Parikh R, et al. The analgesic effects of liposomal bupivacaine versus bupivacaine hydrochloride administered as a transversus abdominis plane block after abdominally based autologous microvascular breast reconstruction: a prospective, single-blind, randomized, controlled trial. *Plast Reconstr Surg*. 2019;144:35-44. doi: 10.1097/PRS.0000000000005698
24. Gatherwright J, Knackstedt RW, Ghaznavi AM, et al. Prospective, randomized, controlled comparison of bupivacaine versus liposomal bupivacaine for pain management after unilateral delayed deep inferior epigastric perforator free flap reconstruction. *Plast Reconstr Surg*. 2018;141:1327-1330. doi: 10.1097/PRS.0000000000004360
25. Mugabure Bujedo B. A clinical approach to neuraxial morphine for the treatment of postoperative pain. *Pain Res Treat*. 2012;2012:612145. doi: 10.1155/2012/612145
26. Rawal N. Intrathecal opioids for the management of post-operative pain. *Best Pract Res Clin Anaesthesiol*. 2023;37:123-132. doi: 10.1016/j.bpa.2023.01.001
27. Swisher MW, Dolendo IM, Sztain JF, et al. Intrathecal morphine injection for postoperative analgesia following gender-affirming pelvic surgery: a retrospective case-control study. *Cureus*. 2023;15:e36748. doi: 10.7759/cureus.36748
28. Meineke MN, Losli MV, Sztain JF, et al. Robot-assisted laparoscopic nephrectomy: early outcome measures with the implementation of multimodal analgesia and intrathecal morphine via the acute pain service. *World J Urol*. 2024;42:117. doi: 10.1007/s00345-024-04801-z
29. Dhawan R, Daubenspeck D, Wroblewski KE, et al. Intrathecal morphine for analgesia in minimally invasive cardiac surgery: a randomized, placebo-controlled, double-blinded clinical trial. *Anesthesiology*. 2021;135:864-876. doi: 10.1097/ALN.0000000000003963
30. Meylan N, Elia N, Lysakowski C, Tramèr MR. Benefit and risk of intrathecal morphine without local anaesthetic in patients undergoing major surgery: meta-analysis of randomized trials. *Br J Anaesth*. 2009;102:156-167. doi: 10.1093/bja/aen368
31. Clark RC, Segal R, Kordahi A, et al. An interdisciplinary, comprehensive recovery pathway improves microsurgical breast reconstruction delivery. *Ann Plast Surg*. 2024;92:549-556. doi: 10.1097/SAP.0000000000003833
32. Linder S, Walle L, Loucas M, Loucas R, Frerichs O, Fansa H. Enhanced Recovery after Surgery (ERAS) in DIEP-flap breast reconstructions-a comparison of two reconstructive centers with and without ERAS-protocol. *J Pers Med*. 2022;12:347. doi: 10.3390/jpm12030347
33. Salibian AA, Frey JD, Thanik VD, Karp NS, Choi M. Transversus abdominis plane blocks in microsurgical breast reconstruction: analysis of pain, narcotic consumption, length of stay, and cost. *Plast Reconstr Surg*. 2018;142:252e-263e. doi: 10.1097/PRS.0000000000004632
34. Sultan P, Carvalho B. Evidence-based guidance for use of intrathecal morphine as an alternative to diamorphine for Caesarean delivery analgesia. *Br J Anaesth*. 2021;127:501-505. doi: 10.1016/j.bja.2021.06.023