JOURNAL of ANESTHESIA and PERIOPERATIVE MEDICINE

Original Article

# Transversus Abdominis Plane Block in Parturients Undergoing Intrapartum Cesarean Delivery

Yunping Li[1], Heather Ballard[2], Jessica L. Carani[3], Adrienne Kung[1], Anasuya Vasudevan[4], Kavita Kantak[5], and Philip E. Hess[1]

## ABSTRACT

**Background:** Transversus abdominis plane (TAP) block has been studied for pain control after elective cesarean delivery and has a limited role. The TAP block has not been studied after cesarean delivery for women who attempted to go through labor. We hypothesized that women have greater postoperative discomfort after prolonged labor and that a TAP block might improve analgesia.

**Methods:** In this single-blinded, randomized controlled trial, 40 women having a cesarean delivery following labor were randomized into a placebo or ultrasound-guided TAP block using 0.25% bupivacaine. We also enrolled 40 women undergoing elective cesarean delivery as the second comparator group to assess TAP block efficacy. A blinded investigator assessed the pain scores in the post anesthesia care unit (PACU) and at 2, 4, 8, and 24 h postoperatively and recorded analgesic use over the first 24 hours. The primary outcome measure was the time to first supplemental analgesic request, which was typically ketorolac.

**Results:** In women who underwent cesarean following labor, the median time to the first analgesic request was significantly longer in TAP cohort compared to placebo (75 (interquartile range [IQR], 50-142) min vs. 38 [IQR, 16-70] min, P = 0.02). The placebo group had higher pain scores at 2 hours, 8 hours, summary 24-hour pain scores, and were more likely to require fentanyl in the PACU (0% vs. 25%, P = 0.02). Among women undergoing elective cesarean, we found no difference in the time to first analgesic request (122 [IQR, 80-505] min vs. 100 [IQR, 75-172] min, P = 0.46) or need for fentanyl in PACU. Only pain scores at 4 hours were higher in the Placebo group (P < 0.01).

**Conclusion:** Women who undergo cesarean following labor may benefit from the addition of a TAP block to the standard neuraxial morphine. Women for scheduled cesarean may not receive benefit from routine use of a TAP block. (Funded by the Beth Israel Anesthesia Foundation, Boston, USA.)

From the [1]Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA; [2]Department of Anesthesia, Lurie Children's Hospital, Chicago, IL, USA; [3]Roper St. Francis Mount Pleasant Hospital, Mount Pleasant, SC, USA; [4]Geisinger Medical Center, Danville, PA, USA; [5]Franciscan Health, Indianapolis, IN, USA.

**Correspondence** to Dr. Philip E. Hess at phess@bidmc.harvard.edu.

**Citation: Yunping Li, Heather Ballard, Jessica L. Carani, Adrienne Kung, Anasuya Vasudevan, Kavita Kantak, Philip E. Hess. Transversus Abdominis Plane Block in Parturients Undergoing Intrapartum Cesarean Delivery. *J Anesth Perioper Med* 2019; 6 : x- xx.**

**doi: 10.24015/JAPM.2019.0004**

The transversus abdominis plane (TAP) block is an effective method of providing postoperative analgesia after surgery with lower abdominal wall incisions (1-3). In 2008, McDonnell demonstrated the effectiveness of the TAP block for reducing morphine requirements and pain scores after cesarean delivery (4). This finding was confirmed by other authors (5, 6). When compared to intrathecal morphine, however, a TAP block alone provided inferior pain relief following elective cesarean section(7, 8). Furthermore, a TAP block did not provide additional analgesic benefit when added to a regimen using intrathecal morphine following elective cesarean delivery (9-11). Thus, the TAP block is often reserved for patients who do not receive neuraxial morphine (e.g. general anesthesia) or as a rescue technique for treating breakthrough pain after cesarean delivery (12).

In clinical practice, not all women remain comfortable after cesarean delivery with neuraxial morphine. Our experience suggested that women who had a cesarean delivery after labor were more likely to experience pain in the recovery room, than those after scheduled surgery. Thus, our clinical practice evolved into performing a TAP block on these patients when needed. When reviewing the literature, we noted that all of the research on TAP block for cesarean pain relief has been conducted on patients undergoing scheduled surgery, and none on laboring patients – the patients that we find receive benefit from a TAP block. Thus, we conducted this study to determine whether a TAP block would benefit women undergoing non-elective cesarean delivery after labor.

## METHODS

The study was conducted at Beth Israel Deaconess Medical Center, with Institutional Review Board approval and informed, written consent. Inclusion criteria included ASA I or II singleton pregnancy undergoing primary cesarean delivery either electively or after labor. Exclusion criteria included ASA ⩾ III; a history of alcohol or substance abuse; allergy to local anesthetics; a history of tolerance to narcotic pain medications; and inability to receive non-steroidal anti-inflammatory medications. We also excluded the patients who underwent repeat cesarean section as these patients might experience a different amount of pain due to the lysis of adhesions.

Our goal was to enroll a cohort of women undergoing intrapartum cesarean delivery after labor for non-fetal indications. Patients would be enrolled after the obstetric decision for cesarean delivery for failure to progress due to dystocia -- no emergent cesarean was to be included. All patients had an epidural in place for labor pain control using the standard institutional protocols. The second cohort of women undergoing elective cesarean delivery was enrolled at the same time as a comparison group to determine if the results of our study were due to the TAP block or due to laboring patients experiencing greater postoperative pain. Patients in both groups were randomized to receive a TAP block or placebo (sham block). Randomization was performed by computer generation in two blocks, to allow for mid-study assessment of harm or futility. Group assignment was maintained in sequentially numbered opaque envelops for each mode of delivery, and these envelopes were opened after enrollment.

For women undergoing cesarean delivery after labor, the epidural was dosed with fentanyl 100 μg, followed by lidocaine 2% wt/vol in 5 mL increment, titrating to T4 sensory blockage. Additional doses of lidocaine were administered by the clinical team to maintain a surgical level. Immediately after delivery of the neonate, 3 mg of morphine (0.5 mg/mL) was given through the epidural catheter. If the epidural could not provide adequate anesthesia during cesarean section, the patients received intravenous supplement of opioids, or a sedative at the discretion of the clinical team. Conversion to general anesthesia would result in elimination from further analysis, as the epidural catheter would be deemed a failure, and thus the neuraxial morphine ineffective. For scheduled cesarean delivery, all subjects received standard spinal anesthesia consisting of hyperbaric bupivacaine 11.25 mg, fentanyl 25 μg and preservative-free morphine 0.25 mg (total volume of 2.5 mL).

The ultrasound-guided bilateral TAP or placebo block was performed at the end of surgery with the patient still anesthetized. After the patient' s surgical dressing was applied, a clean,

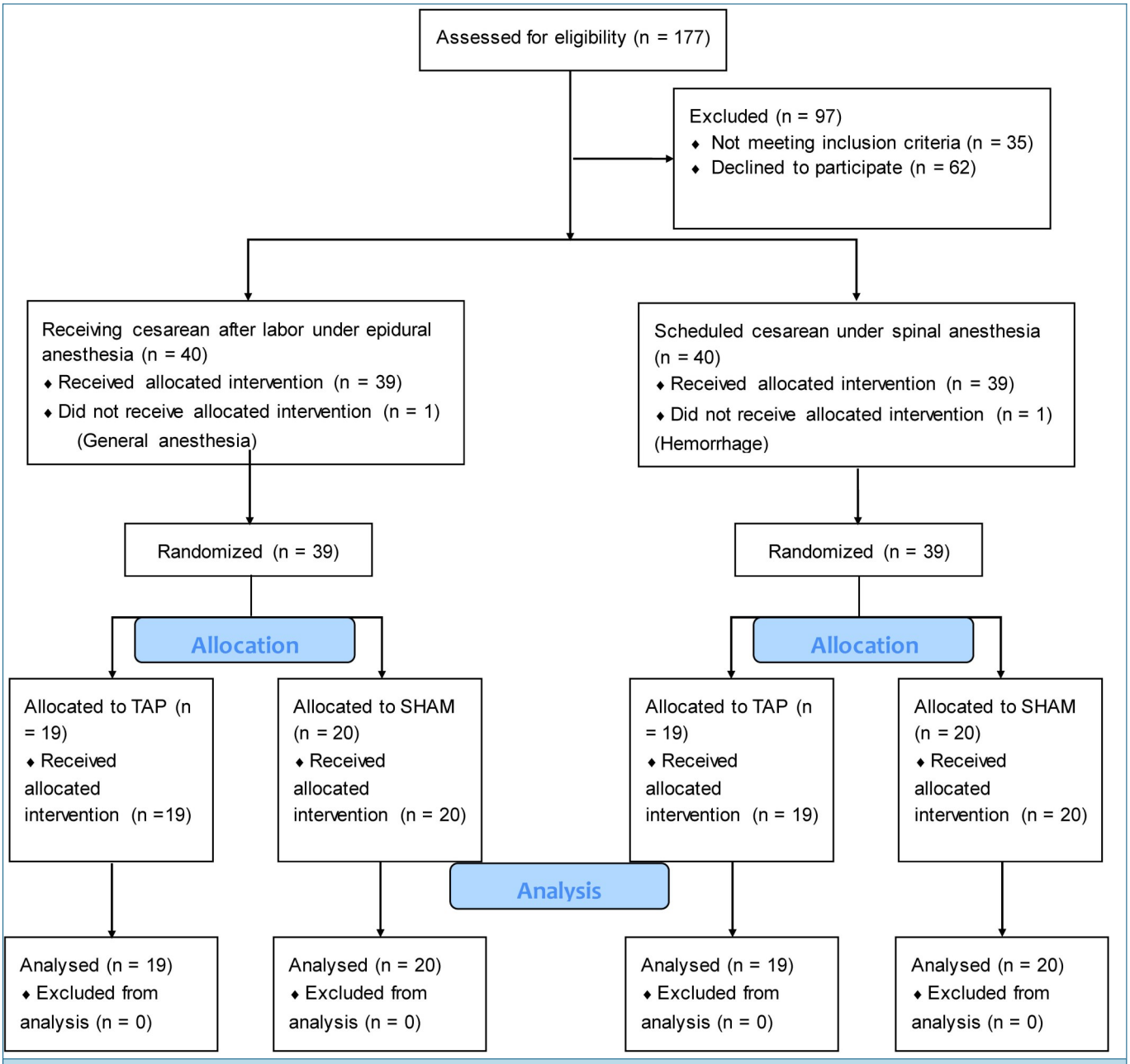


**Figure 1. Flowchart of Patient Enrollment, Randomization, and Study Completion.**

opaque surgical drape was used to prevent the patient from observing the procedure. The transversus plane was identified using a 12 MHz ultrasound probe. For the TAP blocks, 20 mL of 0.25% bupivacaine was injected bilaterally. Success required visualization of the separation of the internal oblique and transversus muscles with injection. For the sham blocks, no injection of fluid was performed. A bandage was placed on each side of injection or sham puncture. The patients and staff providing postoperative care were blinded to group assignment.

All participants were observed in the recovery room at least for 2 hours after procedure. They may receive 30 mg ketorolac as the first analgesic supplementation. If pain control was not adequate, patients may also receive supplemental opioids at the discretion of anesthesia providers.

**Table 1. Patient Characteristics and Clinical Data.**

| Characteristic | Elective Cesarean Delivery | | Intrapartum Cesarean Delivery | |
|---|---|---|---|---|
| | TAP (n = 19) | Placebo (n = 20) | TAP (n = 19) | Placebo (n = 20) |
| Age (yr) | 33 (31-39) | 33 (31-37) | 31 (27-35) | 31 (28-32) |
| BMI (kg/m$^2$) | 28 (26-32) | 29 (27-31) | 31 (29-36) | 32 (29-36) |
| Nulliparity (%) | 64% | 80% | 100% | 100% |
| Fetal Weight (g) | 3440 (3140-4050) | 3610 (3270-4820) | 3540 (3270-3830) | 3600 (3425-3800) |
| Duration of Epidural (min) | NA | NA | 720 (660-900) | 740 (585-980) |
| Surgical Time (min) | 78 (68-86) | 77 (73-84) | 81 (73-99) | 80 (68-94) |

BMI, body mass index. Data Presented as median (interquartile range), or incidence of group: percentage.
Duration of epidural determined by time of initiation of epidural labor analgesia until the initial entry into the operating room for cesarean delivery.

We assessed visual analogue scale (VAS) scores at arrival to the recovery room, and at 2 h, 4 h, 8 h, and 24 h after delivery. VAS consisted of a 10 cm line with "no pain" on the left and "worst possible pain" on the right. Total pain was the sum of all pain scores over 24 hours (area under the curve). We also assessed analgesic use over the 24 h after surgery, including the need for opioids. Participants were asked to rate the severity of nausea, vomiting, pruritus, and sedation on a four-point scale (none, mild, moderate, and severe). Any local complications of the TAP block were recorded.

### Statistical analysis

We performed a sample size calculation based on an observational pilot which showed that our patients received ketorolac 45 ± 15 minutes after arrival in the post anesthesia care unit (PACU). Using a two-tailed alpha of 0.05, and a power of 0.80, we estimated we would require 17 patients per group for a 30% prolongation of this time. We increased the enrollment to 20 per group to account for potential losses.

We compared the TAP and Placebo groups within each mode of delivery to assess the effect of the block on postoperative analgesia. In addition, we assessed the effectiveness of analgesia between the delivery groups to assess the effectiveness of neuraxial analgesia, with or without a TAP block. Comparisons between two groups (e. g. elective TAP vs. elective placebo) were made using the Mann-Whitney or Fisher's exact tests.

The primary outcome was time to first analgesic request assessed by Kaplan Meier survival curve analyzed with log-rank analysis. The starting time to calculate the time to first analgesic was defined as the time of arrival in the PACU, and the end time was administration of ketorolac. Secondary outcomes included pain scores, requirements for opioids for pain, and side effects such as nausea and pruritis. The data are presented as median (interquartile range, IQR) or incidence, as appropriate. Outcome incidence presented with 95% confidence interval, where appropriate. $P \leqslant 0.05$ was considered statistically significant difference. Analysis was done using the SPSS software, version 18.0 (IBM).

## RESULTS

Eighty patients were recruited to participate in this study, 40 with an elective cesarean delivery and 40 with an intrapartum cesarean delivery (Figure 1). One participant in the elective cohort was excluded from the final analysis because she had significant blood loss and was converted to general anesthesia. One participant in the intrapartum cohort was excluded from the analysis due to conversion to general anesthesia for a failed epidural catheter. The demographic and obstetric characteristics are detailed in Table 1. Of note, all of the cesarean deliveries in the intrapartum cohort were nulliparous.

### Intrapartum Cesarean Cohort

The primary outcome, time to first analgesic supplementation, is shown in Figure 2. Women

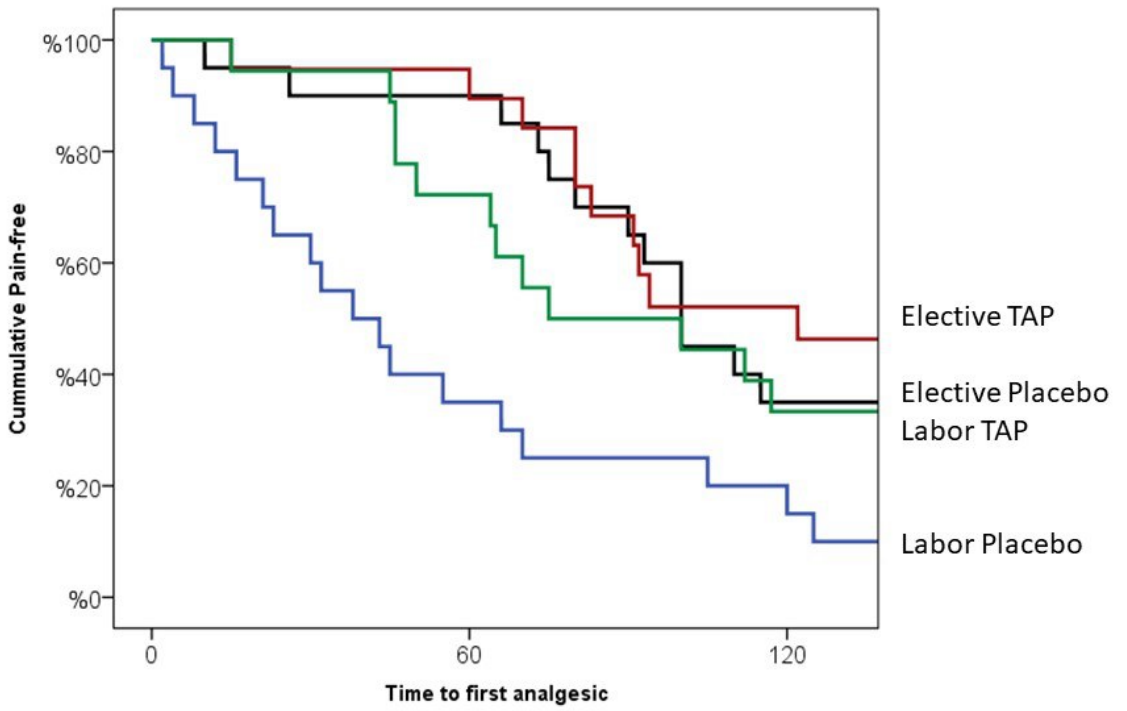


**Figure 2. Kaplan-Meier Survival Curves of the Four Study Groups.**
The curves represent the cumulative pain-free survival of patient until time to first request for analgesia (ketorolac). Comparisons were performed using log-rank analysis between the TAP and placebo groups of each delivery cohort. The Labor group consisted of intrapartum cesarean under epidural anesthesia. The TAP group had a significantly greater pain-free median survival compared to the Placebo group (P = 0.02). There was no difference in median times between the TAP and Placebo of the Elective group.

who underwent intrapartum cesarean delivery had a significantly shorter median time to first request in the placebo group, compared to who had TAP block 38 (IQR, 16 - 70) min vs. 75 (IQR, 50 - 412) min, P = 0.02. In addition, the Placebo group pain scores at 2 hours and 8 hours were higher, and they were more likely to require fentanyl in the PACU (Table 2). There was no difference in the pain scores at 24 hours, or in the oral medication required over 24 hours. The Total pain scores in 24 hours were significantly lower in the TAP group than placebo group (7.75 [IQR, 5-13.25] min vs. 13 [IQR, 9.25-18.75] min, P < 0.03).

### Elective Cesarean Cohort

We found no difference in the median time to first analgesic among women undergoing scheduled cesarean delivery comparing the TAP and Placebo groups (122 [IQR, 80 - 505] min vs. 100 [IQR, 75 - 172] min, P = 0.46). Furthermore, there was no difference in the need for fentanyl in PACU or for oral medication over 24 hours. Pain scores and Total pain score were similar between groups, with the exception of pain scores at 4 hours which were higher in the Placebo group (P < 0.01, Table 2).

### Elective vs. Intrapartum Cesarean Delivery

To evaluate our hypothesis that patients who have an intrapartum cesarean have greater analgesic requirements than elective cesarean patients, we examined the patients who in either delivery cohort by the treatment group. Women with an intrapartum cesarean who received a sham block had higher pain scores, earlier first analgesic, required intraoperative supplementation, and received fentanyl in the PACU than

**Table 2. Pain Scores and Medications.**

| | Elective Cesarean Delivery | | | Intrapartum Cesarean Delivery | | |
|---|---|---|---|---|---|---|
| | TAP (n=19) | Placebo (n=20) | P value | TAP (n=19) | Placebo (n=20) | P value |
| Pain Scores | | | | | | |
| PACU | 0 | 0 | 0.56 | 1 (0-2) | 1.5 (0-4) | 0.50 |
| 2-hour | 0 (0-2) | 1.75 (0-4) | 0.08 | 1 (0.5-2) | 3.25 (1.5-5) | 0.02 |
| 4-hour | 0 (0-1) | 1.25 (0.5-3) | 0.005 | 1 (0-2) | 2 (1-3.75) | 0.11 |
| 8-hour | 1 (0-2) | 1 (1-2.25) | 0.31 | 2 (0-3.25) | 3 (1.25-4.75) | 0.05 |
| 24-hour | 3 (1-5) | 3 (1-4) | 0.79 | 3 (1-4) | 3 (1.25-5) | 0.36 |
| Total pain | 6.5 (2.75-8.75) | 7.5 (3.75-11) | 0.28 | 7.75 (5-13.25) | 13 (9.25-18.75) | 0.03 |
| Pain Medications | | | | | | |
| Time to first analgesic (min) | 122 (80-505) | 100 (75-172) | 0.46 | 75 (50-412) | 38 (16-70) | 0.02 |
| Fentanyl in PACU | 1 (5%) | 0 (0%) | 0.23 | 0 (0%) | 5 (25%) | 0.05 |
| Oxycodone-acetaminophen | 9 (47%) | 12 (60%) | 0.53 | 10 (53%) | 12 (60%) | 0.75 |
| Ketorolac 30 mg | 3 (2-3) | 3 (2-4) | 0.59 | 3 (2-4) | 3 (2-4) | 0.18 |

TAP, transversus abdominis plane; PACU, post anesthesia care unit.
Data Presented as median (interquartile range), or incidence of group: N (percentage).
Pain scores determined on an 11-point scale. Medications were compared for incidence of use of fentanyl (in PACU), oxycodone-acetaminophen doses used during the first 24 hours, or number of intravenous ketorolac doses.
Comparisons were performed using Mann-Whitney test, or Fisher's exact, as appropriate. $P \leq 0.05$ considered significant.

sham elective cesarean patients (Table 2). There were no statistically significantly different among the subjects who had an elective or intrapartum delivery if they received a TAP block.

## DISCUSSION

In this randomized, single-blind, placebo-controlled trial, we demonstrated that a TAP block improved the quality of early postoperative pain control in the women who underwent intrapartum cesarean delivery. This was evidenced by lower initial PACU and total pain scores, and a lower requirement for supplemental fentanyl in the PACU. This finding was true only for those patients that underwent a cesarean after undergoing labor under epidural anesthesia with epidural morphine, and not those who had a scheduled surgery under spinal anesthesia with intrathecal morphine. Previous research demonstrated that a TAP block provides minimal additional benefits to either intrathecal morphine (9, 10) or diamorphine (13). However, those studies only recruited women underwent elective cesarean delivery with spinal anesthesia. Because our results in patients who had elective cesarean delivery were consistent with these previous findings, this suggests that the improvement in the intrapartum cohort may represent a new and important finding.

The hypothesis for this present study was based on our clinical observation that patients undergoing an intrapartum cesarean have greater pain in the PACU and required more medications for postoperative pain control. To assess whether the foundation of this hypothesis was true, we compared the patients who had no additional medication for pain relief beyond our standard of care – those who had a sham block. We found that patients who had an intrapartum cesarean had significantly greater pain and analgesic requirements than those who had an elective cesarean delivery. Interestingly, patients who received a TAP block had pain control that appeared similar to patients with an elective cesarean delivery without a TAP block (Figure 2), but this was not the primary intent of our study and further research should examine this outcome.

Post-cesarean delivery analgesia can be influenced by several factors. In two studies, parturients in early labor without neuraxial pain relief appeared to have reduced morphine requirements in the first 24-hours after surgery (14, 15). This was hypothesized that endogenous spinal noradrenergic activation may increase pain threshold in parturients experienced pain in early labor. In contrast, the patients in our study un-

derwent many hours of labor followed by a median of 12 hours of epidural analgesia. During this long period of time, parturients might experience central sensitization, local anesthetic tachyphylaxis, or tolerance to opioids (16, 17). In a retrospective study, Carvalho et al. found no differences in postoperative pain scores and analgesic consumption between scheduled and unplanned cesarean deliveries over the first five days after surgery (18). We note a few differences between their study and ours: their population received lower intrathecal morphine (0.2 mg) and higher epidural morphine (4 mg) doses than in our present study. Secondly, our study focused only the first day, and our difference in analgesic requirement occurred in the first few hours after surgery. As in their findings, our 24-hour pain scores were similar between groups. Finally, our study was prospective, which allowed us to collect our pain scores on a precise timetable, as opposed to nursing documentation of pain scores which may be obtained after pain medication was administered.

Another possibility for the difference between scheduled cesarean and labor cesarean postoperative pain control is that women who had intrapartum cesarean delivery received epidural morphine while women who had elective cesarean delivery received spinal administration. Calculating the precise equivalent morphine dose between epidural and spinal administration is very difficult, if not impossible. In a well-designed dose-response study, Palmer, et al. found that analgesia improved with the dose of epidural morphine up to 3.75 mg – increasing the dose further to 5 mg did not improve analgesia (19). In a retrospective study of 4880 parturients, the optimal dose of epidural morphine for post-Caesarean pain was 3 mg (20). The optimal spinal morphine dose remains yet to be defined. Although one study found that 75 μg of intrathecal morphine was the lowest effective dose, augmentation with systemic opioids was often needed (21). A national survey of perioperative and postoperative anesthetic practices for cesarean delivery found that the morphine median range dose was 200 μg (50 - 400 μg) (22). Thus, while the morphine doses used in this study were within the norm of obstetric anesthesia practice, it is not clear whether 3 mg of epidural morphine is perfectly equivalent to 0.25 mg of spinal administration. For example, a slower onset time of epidural morphine might contribute to the differences between analgesia in the PACU but not over 24 hours. A final possibility in the difference in pain control between women receiving spinal bupivacaine and epidural lidocaine is that the later medication has a shorter duration of analgesia. thus, the lidocaine may regress more rapidly in the PACU, resulting in higher pain scores at 2 hours. However, epidural bupivacaine, which has a longer duration of action, is considerably more toxic in pregnancy, and is infrequently used during cesarean delivery. Our goal, however, was not to compare the analgesia between modes of delivery, but to determine if a TAP block would benefit women who went through labor.

No procedure is without risk. Complications of TAP block such as liver and bowel injury have been documented and concern has been raised about the potential for high plasma concentrations of local anesthetic after TAP blocks (23, 24). This is of particular relevance in obstetric patients, given the previous exposure to the local anesthetic. We believe that the risk of organ or intraperitoneal injury is minimal when using ultrasound. Further research should be performed to determine 1) the minimum volume required for a TAP block to be successful, and 2) whether direct nerve blocks with minimal volumes would be effective. Our study was not large enough or designed to assess safety, but there were no instances of toxicity, nor intra-abdominal organ injury.

There are a number of limitations to this study. We can only claim that the study was single-blinded due to the TAP block procedure. The operators and the operating room nurse could not be effectively blinded. We did attempt to maintain blinding with the assessor and the postpartum nurses who provided care. Second, we did not assess the success rate of the block or the extent of abdominal wall sensory blockade. This was done as an attempt to preserve the blinding of the assessor. It is possible that some of the TAP blocks were unsuccessful; however, this would only serve to increase the benefit of this procedure.

All of the patients in the intrapartum cohort

were nulliparous, but only 70% among those having an elective delivery. This finding is consistent with a much higher rate of cesarean deliveries in nulliparous patients and especially primary cesareans. All of the subjects in this study had primary cesarean deliveries as there might be differences in postoperative pain with successive cesarean surgeries. We do not believe that the parity would affect immediate postoperative pain, but this must be considered.

We conclude that patients who undergo cesarean delivery after labor and receive epidural morphine often have higher pain scores in the PACU and require supplemental pain control. A TAP block improves pain control in these patients. A TAP block does not provide benefit to patients who undergo a routine, scheduled cesarean delivery.

This study was supported by a grant from the Beth Israel Anesthesia Foundation (internal departmental funding), Boston, USA.

The authors have no other potential conflicts of interest for this work.

## References

1. Carney J, McDonnell JG, Ochana A, Bhinder R, Laffey JG. The transversus abdominis plane block provides effective postoperative analgesia in patients undergoing total abdominal hysterectomy. *Anesth Analg* 2008;107(6):2056-60.
2. Favuzza J, Brady K, Delaney CP. Transversus abdominis plane blocks and enhanced recovery pathways: making the 23-h hospital stay a realistic goal after laparoscopic colorectal surgery. *Surg Endosc* 2013; 27(7):2481-6.
3. O'Donnell BD, McDonnell JG, McShane AJ. The transversus abdominis plane (TAP) block in open retropubic prostatectomy. *Reg Anesth Pain Med* 2006;31:91.
4. McDonnell JG, Curley G, Carney J, Benton A, Costello J, Maharaj CH, et al. The analgesic efficacy of transversus abdominis plane block after cesarean delivery: a randomized controlled trial. *Anesth Analg* 2008;106(1):186-91.
5. Belavy D, Cowlishaw PJ, Howes M, Phillips F. Ultrasound-guided transversus abdominis plane block for analgesia after Caesarean delivery. *Br J Anaesth* 2009;103(5):726-30.
6. Baaj JM, Alsatli RA, Majaj HA, Babay ZA, Thallaj AK. Efficacy of ultrasound-guided transversus abdominis plane (TAP) block for postcesarean section delivery analgesia--a double-blind, placebo-controlled, randomized study. *Middle East J Anaesthesiol* 2010; 20 (6):821-6.
7. Kanazi GE, Aouad MT, Abdallah FW, Khatib MI, Adham AM, Harfoush DW, et al. The analgesic efficacy of subarachnoid morphine in comparison with ultrasound-guided transversus abdominis plane block after cesarean delivery: a randomized controlled trial. *Anesth Analg* 2010;111(2):475-81.
8. Loane H, Preston R, Douglas MJ, Massey S, Papsdorf M, Tyler J. A randomized controlled trial comparing intrathecal morphine with transversus abdominis plane block for post-cesarean delivery analgesia. *Int J Obstet Anesth* 2012;21(2):112-8.
9. McMorrow RC, Ni Mhuircheartaigh RJ, Ahmed KA, Aslani A, Ng SC, Conrick-Martin I, et al. Comparison of transversus abdominis plane block vs spinal morphine for pain relief after Caesarean section. *Br J Anaesth* 2011;106(5):706-12.
10. Costello JF, Moore AR, Wieczorek PM, Macarthur AJ, Balki M, Carvalho JC. The transversus abdominis plane block, when used as part of a multimodal regimen inclusive of intrathecal morphine, does not improve analgesia after cesarean delivery. *Reg Anesth Pain Med* 2009;34(6):586-9.
11. Singh S, Dhir S, Marmai K, Rehou S, Silva M, Bradbury C. Efficacy of ultrasound-guided transversus abdominis plane blocks for post-cesarean delivery analgesia: a double-blind, dose-comparison, placebo-controlled randomized trial. *Int J Obstet Anesth* 2013;22(3):188-93.
12. Mirza F, Carvalho B. Transversus abdominis plane blocks for rescue analgesia following Cesarean delivery: a case series. *Can J Anaesth* 2013;60:299-303.
13. Puddy E, Edwards B, Wrench I, Roberts F. Does the transversus abdominis plane (TAP) block improve analgesia following subarachnoid anaesthesia with intrathecal diamorphine? A randomised double blinded control trial. *Anaesthesia* 2010;65:95.
14. Eisenach JC, Dobson CE 2nd, Inturrisi CE, Hood DD, Agner PB. Effect of pregnancy and pain on cerebrospinal fluid immunoreactive enkephalins and norepinephrine in healthy humans. *Pain* 1990;43:149-54.
15. Yoo KY, Jeong CW, Kang MW, Kim SJ, Chung ST, Shin MH, et al. Bispectral index values during sevoflurane-nitrous oxide general anesthesia in women undergoing cesarean delivery: a comparison between women with and without prior labor. *Anesth Analg* 2008;106(6):1827-32.
16. Ravalia A, Browne D, Robinson PN. Tachyphylaxis and epidural anaesthesia. *Anaesthesia* 1989; 44(6): 529.
17. Wang C, Sholas MG, Berde CB, DiCanzio J, Zurakowski D, Wilder RT. Evidence that spinal segmental nitric oxide mediates tachyphylaxis to peripheral local anesthetic nerve block. *Acta Anaesthesiol Scand* 2001;45(8):945-53.
18. Carvalho B, Coleman L, Saxena A, Fuller AJ, Riley ET. Analgesic requirements and postoperative recovery after scheduled compared to unplanned cesarean delivery: a retrospective chart review. *Int J Obstet Anesth* 2010;19(1):10-5.
19. Palmer CM, Nogami WM, Van Maren G, Alves DM. Postcesarean epidural morphine: a dose-response study. *Anesth Analg* 2000;90(4):887-91.
20. Fuller JG, McMorland GH, Douglas MJ, Palmer L. Epidural morphine for analgesia after caesarean section: a report of 4880 patients. *Can J Anaesth* 1990;37(6):636-40.
21. Palmer CM, Emerson S, Volgoropolous D, Alves D. Dose-response relationship of intrathecal morphine for postcesarean analgesia. *Anesthesiology* 1999;90(2):437-44.
22. Aiono-Le Tagaloa L, Butwick AJ, Carvalho B. A survey of perioperative and postoperative anesthetic practices for cesarean delivery. *Anesthesiol Res Pract* 2009;2009:510642.
23. Corvetto MA, Echevarria GC, De La Fuente N, Mosqueira L, Solari S, Altermatt FR. Comparison of plasma concentrations of levobupivacaine with and without epinephrine for transversus abdominis plane block. *Reg Anesth Pain Med* 2012;37(6):633-7.
24. Griffiths JD, Barron FA, Grant S, Bjorksten AR, Hebbard P, Royse CF. Plasma ropivacaine concentrations after ultrasound-guided transversus abdominis plane block. *Br J Anaesth* 2010;105(6):853-6.