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Comparison of Methods of Providing Analgesia after Pancreas Transplant: IV Opioid Analgesia Versus Transversus Abdominus Plane Block with Liposomal Bupivacaine or Continuous Catheter Infusion

Running Title: Post pancreas transplant analgesia

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ABSTRACT

Background: Current practices emphasize a multimodal approach to perioperative analgesia due to higher efficacy and decreased opioid usage. Analgesia for pancreas transplant (PT) has traditionally been managed with intravenous (IV) opioids, and reports of transversus abdominis plane (TAP) blocks are limited in this population.

Methods: Three interventions were compared in adult PT patients, including IV opioids, TAP catheter, and TAP block with liposomal bupivacaine. Time to return of intestinal function and oral diet, postoperative pain scores, opioid usage, and length of stay were recorded.

Results: Study included 197 PT patients: 62 (32%) standard care, 90 (45%) TAP catheters with continuous 0.2% ropivacaine, and 45 (23%) single liposomal bupivacaine TAP block. Pain scores were lowest for the IV opioids group ($P < .001$). The liposomal bupivacaine group had lower pain scores on postoperative (POD) day 1-5 than the TAP catheter group. Opioid use during POD 1-5 was lower for both TAP block groups ($P = .03$). Time to bowel function was faster for the TAP block groups ($P < .05$).

Conclusions: Compared with IV opioid analgesia, TAP block interventions were associated with lower overall use of opioids and a faster time to intestinal function following pancreas transplant.

KEYWORDS: TAP block, regional analgesia, multimodal, ropivacaine, postoperative

INTRODUCTION

Abdominal organ transplants may cause a high level of postoperative pain, as the surgery involves a long incision through the abdominal wall. Uncontrolled postoperative pain may lead to complications causing increased morbidity and longer hospital stays. Recent analgesia practices emphasize a multimodal approach by targeting multiple areas in the pain pathway thus decreasing the use of opioids.[1] During abdominal procedures, a transversus abdominis plane (TAP) block may be used to help control the source of incisional pain.

The TAP block blunts neural afferents from T6 to L1 that supply the anterior abdominal wall, as local anesthetic is injected just deep to the fascial plane between the transversus abdominis and internal oblique muscles. The first TAP block technique (described by Rafi et al in 2001)[2] targeted the triangle of Petit bordered by the latissimus dorsi, external oblique, and iliac crest. Since then, ultrasound has been used to continuously visualize the needle tip and anatomical landmarks.[2,3] The TAP block has been shown to be an effective non-opioid method of pain control in abdominal surgeries,[4-9] leading to reduced postoperative opioid consumption and improved pain scores.[10] Such benefits have been documented specifically for renal transplant recipients.[11-14]

In December 2015, the United States Food & Drug Administration (FDA) approved liposomal bupivacaine for “local surgical infiltration”, thus expanding its use to TAP blocks. Bupivacaine has a long terminal half-life of 3.5 hours due to extensive protein binding. In a liposomal formulation, the internalized bupivacaine can be released in a delayed way as the multivesicular liposomes are biodegraded.[15] Patients given

liposomal bupivacaine TAP blocks in abdominal procedures have shown decreased length of stay (LOS) and opioid use, and improved pain scores as compared to only intravenous (IV) pain management.[16,17] Hutchins' study comparing bilateral subcostal TAP blocks with single administration of bupivacaine versus liposomal bupivacaine demonstrated decreased total opioid requirement for the first 72 hours following a robot assisted hysterectomy.[18] Another study compared liposomal bupivacaine to continuous epidural analgesia with plain bupivacaine and IV opioid management, finding similar postoperative pain scores and opioid use between the continuous epidural group and the liposomal bupivacaine group.[19]

Pancreas transplantation has the potential to render diabetic recipients euglycemic and is most commonly performed either as a simultaneous pancreas and kidney transplant (SPK) or as a pancreas after kidney (PAK) transplant. Less frequently, pancreas transplant alone (PTA) may be indicated in candidates with poor glycemic control--most commonly in diabetic patients with hypoglycemia unawareness. Postoperative analgesia is complicated in this population due to diabetic gastrointestinal motility disorders (particularly gastroparesis) which are exacerbated by IV opioids. Reports of TAP blocks in pancreas transplant recipients are limited, with the first application of bilateral TAP injections of local anesthetic documented in 2011.[20] Epidural catheters are typically avoided in these patients due to risk of spinal hematoma and/or infection. Traditionally, pancreas transplant recipients have been managed with IV analgesia,[21] and this was the standard at our hospital until 2013 when bilateral TAP blocks via continuous infusion of 0.2% ropivacaine were instituted. In June 2016, this was replaced by a single injection of liposomal bupivacaine, thus eliminating the need for bilateral pain catheters.

The primary objective of this study was to retrospectively compare postoperative pain scores and opioid use in pancreatic transplant patients who received either IV opioid pain management, continuous ropivacaine via TAP catheter, or liposomal bupivacaine. Secondary objectives included evaluation of hospital length of stay and return of postoperative bowel function in these 3 groups.

METHODS

Study design

This was a retrospective study of all pancreas transplants performed at a single center from 2009 to 2017. Recipient outcomes, demographic data, laboratory values, and survival data were collected from the comprehensive transplant recipient registry maintained at our center, as well as individual written and electronic medical records. Anesthetic and pain interventions were extracted from intraoperative documentation and from post-transplant pharmacy records.

Patient population

Recipient inclusion criteria included all adult pancreas transplant recipients (18 years and older) that received either SPK, PAK, or PTA. Exclusion criteria included: presence of major surgical complications (e.g., perioperative bowel or organ injury), requirement for re-laparotomy, contraindication to adjuvant anesthetic intervention (TAP block or liposomal bupivacaine), receipt of a pancreas allograft as part of a multi-visceral or modified multi-visceral transplant, active daily opioid use (≥ 30 mg oral morphine equivalent), diagnosed chronic pain syndrome, or known history of substance abuse within 3 months of surgery.

All recipients were listed for transplantation at Indiana University according to standard procedures and protocols as established by our own center and the United Network for Organ Sharing (UNOS). During the study period, in order to qualify for pancreas transplant listing at our institution, the potential recipient had to be insulin dependent with a fasting serum C-peptide level < 2 ng/ml.

Procedures and immunosuppression

Pancreas allografts were typically procured using an en-bloc technique following aortic flush with preservation solution and topical cooling with saline slush as previously described.[22,23] The recipient operation was performed through a midline incision. The pancreas was routinely positioned with the tail toward the pelvis and the head and duodenum oriented superiorly in order to facilitate the enteric anastomosis. Systemic venous drainage was performed to the vena cava or to the right common iliac vein. Arterial perfusion of the allograft was routinely established from the right common iliac artery, although rarely if this vessel was diseased or had been the site for arterial anastomosis for a prior transplant, the inflow was established either from the aorta or the left common iliac artery. All SPK transplants were performed with ipsilateral placement of both the kidney and the pancreas to the right iliac vessels as previously described.[24] Pulsatile perfusion was used routinely for the renal allograft portion of the SPK transplant regardless of the preservation solution used for organ procurement.[25,26] All pancreas allografts were drained enterically using a stapled technique as described elsewhere.[27]

All regional anesthesia procedures at our institution were performed under supervision by an Acute Pain Service attending physician. All TAP catheters were placed with ultrasound (US) visualization. After identifying the transversus abdominis plane, the anesthesiologist bilaterally injected 30ml of 0.2% ropivacaine onto each side of the TAP space. All patients then had an elastomeric pain relief ball (ON-Q, Halyard Health, Roswell, Georgia, USA) attached to the TAP catheter to provide continuous infusion. All TAP catheters were placed at the completion of the surgery. In cases where liposomal bupivacaine was used, a single dose of this anesthetic was injected bilaterally with US visualization into each TAP space. Originally, these procedures were performed at the completion of the transplant operation; however, later study patients had TAP injections before any surgical incision. The standard of care changed at our institution because it was apparent that visualization of the site was easier before the planes had been disrupted.

Patients in all 3 groups received postoperative intravenous opioids by patient-controlled analgesia for either primary pain control (standard care group) or breakthrough pain (TAP block groups). At the discretion of the attending surgeon, and after the first flatus, patients were transitioned to an oral narcotic (oxycodone/acetaminophen 5 mg/325mg per os q4-6 h as needed).This was typically on postoperative day 2-4.

The induction immunosuppression protocol consisted of 5 doses of rabbit antithymocyte globulin (rATG; 1 mg/kg/dose) and maintenance with tacrolimus (target trough blood concentration 6-8 ng/mL) and sirolimus (target trough blood concentration 3-6 ng/mL) for SPK and PAK transplants. Mycophenolate mofetil (MMF; 500 mg PO q12h) was added for pancreas transplant alone.[28,29] Steroids

were exclusively used as a premedication for rATG and were discontinued following induction in all recipients. All recipients received routine perioperative antibiotics, prophylaxis against cytomegalovirus (CMV) with oral valganciclovir, and prophylaxis against *Pneumocystis jiroveci* with trimethoprim and sulfamethoxazole, unless contraindicated. Systemic anticoagulation was not routinely used. Nasogastric tubes were usually removed at the time of extubation. All patients were given metoclopramide (10 mg IV q6h) unless contraindicated, and methylnaltrexone (12 mg SC q24h for the first 3 postoperative days). The metoclopramide was converted to oral administration prior to meals before discharge from the hospital and weaned whenever possible in the outpatient clinic. Urethral catheters were routinely removed on postoperative day 3 for all SPK transplants, and sooner, in some cases, for isolated pancreas transplants.

Data collection and analysis

The data obtained included pain intensity scores from postoperative day 0 to day of discharge, opioid usage, time to first flatus, time to first bowel movement, length of hospital stay, and occurrence of opioid-related side effects including nausea, vomiting, respiratory depression, pneumonia, and aspiration. Standard statistical testing was utilized for continuous and categorical variables, as indicated, including chi-squared analysis and analysis of variance (ANOVA). Statistical testing was performed on SPSS software (IBM SPSS Statistics Version 25, IBM Corporation, Armonk, New York, USA). This retrospective study was reviewed and approved by the Institutional Review Board of the Indiana University School of Medicine (#1011003619).

RESULTS

Overall, 197 patients were included, with 46 patients (23%) receiving TAP block with single shot liposomal bupivacaine, 89 (45%) receiving TAP catheters with continuous 0.2% ropivacaine, and 62 (32%) receiving no TAP block intervention (pain managed through IV opioids). Characteristics of transplant recipients and donors are shown in Table 1. The groups did not differ significantly in basic demographics or in type of pancreas transplant performed. The ropivacaine group was apparently under-represented by males (47%) compared to the other two groups (65% and 61%), although the difference was not significant ($P = .08$). The groups did differ for pancreas donor age ($P < .001$), although this factor was unlikely to substantially impact postoperative pain control.

Pain was assessed on a 0 to 10 scale by the nurse assigned to the patient (Table 2). Median pain scores in the post anesthesia care unit (PACU) were significantly lower for the standard care patients compared with both TAP groups (2.0 versus 5.6 and 4.6, $P < .001$). This was also true for the average daily postoperative pain scores (2.6 versus 4.1 and 3.3, $P < .001$). Opioid usage in the PACU was highest for the TAP catheter group, and it was significantly lower for the standard care and liposomal bupivacaine groups ($P = .02$). Total opioid usage, however, was markedly lower for both TAP groups as an average daily requirement ($P = .03$) and for the total required for the first 5 days post-transplant ($P = .03$). The liposomal bupivacaine group had the lowest average daily and total opioid usage.

Return of intestinal function occurred more quickly for the TAP catheter and liposomal bupivacaine groups ($P < .05$), with times to first oral intake of 12 and 14 hours, versus 26 hours for the standard care group ($P < .001$). Gastrointestinal complications (e.g., prolonged ileus) were very rare, and postoperative reinsertion of a nasogastric tube was rarely required. No hematomas or other injection site complications were observed in any patients in the TAP block groups. The 3 groups did not differ in length of hospital stay or 90-day graft survival.

DISCUSSION

Integrating TAP blocks into a multimodal analgesic plan for post-operative pain control may allow for decreased opioid use and associated side effects. Studies have shown the efficacy of TAP blocks in achieving adequate pain control in a variety of surgeries. This study is the first comparing 3 modalities of pain control in post-pancreas transplant patients: IV opioid pain management, continuous ropivacaine infusion through TAP catheter, and single-shot liposomal bupivacaine into the TAP space. Patients who received either TAP block intervention required less postoperative opioids compared to patients receiving no TAP block. The average daily dose of opioids was almost halved in the liposomal bupivacaine group and decreased by about 20% in the TAP catheter group. This is a very important finding as we strive to limit opioid usage at a time when opioid addiction is being declared a national public health emergency. Using TAP blocks following pancreas transplant surgery has the potential to drastically decrease opioid usage during the hospital stay, and this might be integrated into an enhanced recovery after surgery (ERAS) pathway. Campsen et al. recently described one potential post-nephrectomy ERAS pathway for kidney transplant donors including ketorolac and

pregabalin.[30] We are working on ERAS pathway for pancreas transplant in our institution, so combining our data and current literature on ERAS pathway will be very helpful.

Unexpectedly, patients in the standard care group reported improved pain scores in the PACU and POD 1-5 when compared with either TAP block intervention. Interestingly, multiple studies have demonstrated similar if not lower pain scores when comparing TAP block to IV opioid use.[8,13,31] The lower pain scores for the standard care group in the PACU might be related to a tendency for anesthesiologists to administer more intraoperative opioids to patients not receiving nerve blocks. In addition, TAP blocks may have a lower effect on visceral pain as opposed to incisional somatic pain [32], and the visceral pain associated with pancreas transplants could potentially be greater than with many other abdominal procedures. The patients in the standard care group did receive significantly more postoperative opioids compared with the TAP block patients. The difference in median pain scores, although statistically significant, was rather small (2.6 for standard care group versus 3.4 for liposomal bupivacaine during POD 1-5), and the benefits of opioid reduction may outweigh the small difference in pain scores.

Our results support that liposomal bupivacaine provides superior analgesia compared to bilateral continuous TAP catheters, as the liposomal bupivacaine group showed significantly lower pain scores than the continuous TAP catheter group over postoperative days (POD) 1-5. The liposomal bupivacaine group also required less daily and total postoperative opioids compared to the TAP catheter group. This demonstrates the prolonged analgesic benefit with the single-shot liposomal

formulation of bupivacaine. An additional benefit of liposomal bupivacaine is the potentially lower risk of infection compared to implanted catheters, although infectious complications associated with regional anesthesia are incredibly rare events (on the order of 1 per 40,000-100,000 blocks).[33,34]

Our secondary endpoints for this study involved length of hospital stay and return of bowel function. We hypothesized that the use of TAP blocks in these patients would decrease opioid use, therefore lessening the complications associated with opioids such as ileus and longer hospital stay. Patients receiving continuous TAP infusions did indeed have a faster return of bowel function, and patients receiving either TAP intervention had shorter time to first oral intake compared to the standard care group. These findings may be explained by the significantly lower amount of average daily and total opioids that the TAP intervention groups received over postoperative days 1-5. There was no significant difference in length of stay, postoperative nausea and vomiting, or other opioid-related complications (aspiration, pneumonia, naloxone administration, and respiratory depression) between the 3 groups. The size and design of the study may have been suboptimal for detecting these endpoints, however, as there were only 2 aspiration events, 1 documented pneumonia, and 1 naloxone administration for all of the patients in the study.

A potential strength of this study is the standardization of the transplant team (all procedures were performed by a team of 2 transplant surgeons that performed the majority of transplants together), operative technique, immunosuppression strategy and postoperative management. Limitations include lack of study blinding and randomization, as these were not possible in a retrospective study. We were also

unable to control for other factors such as changes over time to institutional standards, postoperative nursing care, and/or data entry.

One anesthesia protocol factor that changed during this study was the timing of liposomal bupivacaine injection (originally performed at the completion of the transplant but later performed prior to incision). Later TAP blocks would potentially be more successful due to improved visualization afforded by preoperative injections. The exact transition date from post-surgery to preoperative TAP blocks was not noted; therefore, we were unable to compare these procedural differences.

Another factor that may have changed over time was the widespread institutional drive to initiate oral diets sooner due to beliefs regarding opioid minimization. This might have impacted the study outcome on time to first oral diet, as attending physicians might be increasingly skewed over time to allow earlier oral intake. The effect should be minimal in our study since there was a consistent attending surgeon using an objective criterion (time to first flatus) before allowing an oral diet.

Since return of bowel function was a study endpoint, our protocol to reduce opioid-induced bowel dysfunction should be noted as it may have impacted factors such as time to first flatus, time to first oral intake, and time to first stool output. The protocol includes removal of nasogastric tubes at the completion of the procedure with early introduction of oral intake, liberal use of intravenous metoclopramide as a prokinetic agent, and subcutaneous methylnaltrexone (peripheral μ-opioid antagonist). Patients in all groups received the same care; therefore, this should not have impacted the comparison of groups.

The significantly lower 90-day readmission rate for the TAP catheter group was an unexpected finding in this study. This finding is most likely an era-related phenomenon reflecting practice patterns and an institutional drive to lower hospital readmissions. It is unlikely that a specific perioperative analgesic protocol alone could have such an impact on the need for hospital readmission at 3 months postoperative. No other overt factors in the study groups were identified to account for the differences in readmission rates.

In conclusion, TAP block techniques may be opioid-sparing in the postoperative period following pancreatic transplant. A single dose of liposomal bupivacaine by TAP block provided better analgesia in this study compared with ropivacaine by implanted TAP catheters.

REFERENCES

1. Song K, Melroy MJ, Whipple OC. Optimizing multimodal analgesia with intravenous acetaminophen and opioids in postoperative bariatric patients. *Pharmacotherapy.* 2014;34 Suppl 1:14s-21s.
2. Rafi AN. Abdominal field block: a new approach via the lumbar triangle. *Anaesthesia.* 2001;56(10):1024-1026.
3. Lissauer J, Mancuso K, Merritt C, Prabhakar A, Kaye AD, Urman RD. Evolution of the transversus abdominis plane block and its role in postoperative analgesia. *Best practice & research Clinical anaesthesiology.* 2014;28(2):117-126.
4. El-Dawlatly AA, Turkistani A, Kettner SC, et al. Ultrasound-guided transversus abdominis plane block: description of a new technique and comparison with conventional systemic analgesia during laparoscopic cholecystectomy. *British journal of anaesthesia.* 2009;102(6):763-767.
5. Hosgood SA, Thiyagarajan UM, Nicholson HF, Jeyapalan I, Nicholson ML. Randomized clinical trial of transversus abdominis plane block versus placebo control in live-donor nephrectomy. *Transplantation.* 2012;94(5):520-525.
6. Maeda A, Shibata SC, Wada H, et al. The efficacy of continuous subcostal transversus abdominis plane block for analgesia after living liver donation: a retrospective study. *Journal of anesthesia.* 2016;30(1):39-46.
7. McDonnell JG, O'Donnell B, Curley G, Heffernan A, Power C, Laffey JG. The analgesic efficacy of transversus abdominis plane block after abdominal surgery: a prospective randomized controlled trial. *Anesthesia and analgesia.* 2007;104(1):193-197.

8. Niraj G, Searle A, Mathews M, et al. Analgesic efficacy of ultrasound-guided transversus abdominis plane block in patients undergoing open appendicectomy. *British journal of anaesthesia.* 2009;103(4):601-605.
9. Choi YM, Byeon GJ, Park SJ, Ok YM, Shin SW, Yang K. Postoperative analgesic efficacy of single-shot and continuous transversus abdominis plane block after laparoscopic cholecystectomy: A randomized controlled clinical trial. *Journal of clinical anesthesia.* 2017;39:146-151.
10. Petersen PL, Mathiesen O, Torup H, Dahl JB. The transversus abdominis plane block: a valuable option for postoperative analgesia? A topical review. *Acta anaesthesiologica Scandinavica.* 2010;54(5):529-535.
11. Guner Can M, Goz R, Berber I, Kaspar C, Cakir U. Ultrasound/Laparoscopic Camera-Guided Transversus Abdominis Plane Block for Renal Transplant Donors: A Randomized Controlled Trial. *Annals of transplantation.* 2015;20:418-423.
12. Parikh BK, Waghmare V, Shah VR, et al. The analgesic efficacy of continuous transversus abdominis plane block in renal transplant recipients. *Journal of anaesthesiology, clinical pharmacology.* 2015;31(4):531-534.
13. Singh PM, Borle A, Makkar JK, Trisha A, Sinha A. Evaluation of transversus abdominis plane block for renal transplant recipients - A meta-analysis and trial sequential analysis of published studies. *Saudi journal of anaesthesia.* 2018;12(2):261-271.
14. Soltani Mohammadi S, Dabir A, Shoeibi G. Efficacy of transversus abdominis plane block for acute postoperative pain relief in kidney recipients: a double-blinded clinical trial. *Pain medicine (Malden, Mass).* 2014;15(3):460-464.
15. Malik O, Kaye AD, Kaye A, Belani K, Urman RD. Emerging roles of liposomal bupivacaine in anesthesia practice. *Journal of anaesthesiology, clinical pharmacology.* 2017;33(2):151-156.
16. Fayezizadeh M, Majumder A, Neupane R, Elliott HL, Novitsky YW. Efficacy of transversus abdominis plane block with liposomal bupivacaine during open abdominal wall reconstruction. *American journal of surgery.* 2016;212(3):399-405.
17. Oppenheimer AJ, Fiala TGS, Oppenheimer DC. Direct Transversus Abdominis Plane Blocks With Exparel During Abdominoplasty. *Annals of plastic surgery.* 2016;77(5):499-500.
18. Hutchins J, Delaney D, Vogel RI, et al. Ultrasound guided subcostal transversus abdominis plane (TAP) infiltration with liposomal bupivacaine for patients undergoing robotic assisted hysterectomy: A prospective randomized controlled study. *Gynecologic oncology.* 2015;138(3):609-613.
19. Ayad S, Babazade R, Elsharkawy H, et al. Comparison of Transversus Abdominis Plane Infiltration with Liposomal Bupivacaine versus Continuous Epidural Analgesia versus Intravenous Opioid Analgesia. *PloS one.* 2016;11(4):e0153675.
20. Aniskevich S, Clendenen SR, Torp KD. Bilateral transversus abdominis plane block for managing pain after a pancreas transplant. *Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation.* 2011;9(4):277-278.
21. Troppmann C. Complications after pancreas transplantation. *Current opinion in organ transplantation.* 2010;15(1):112-118.
22. Fridell JA, Mangus RS, Powelson JA. Histidine-Tryptophan-Ketoglutarate for Pancreas Allograft Preservation: The Indiana University Experience. *Am J Transplant.*
23. Fridell JA, Powelson JA, Kubal CA, et al. Retrieval of the pancreas allograft for whole-organ transplantation. *Clinical transplantation.* 2014;28(12):1313-1330.
24. Fridell JA, Shah A, Milgrom ML, Goggins WC, Leapman SB, Pescovitz MD. Ipsilateral placement of simultaneous pancreas and kidney allografts. *Transplantation.* 2004;78(7):1074-1076.
25. Agarwal A, Goggins WC, Pescovitz MD, Milgrom ML, Murdock P, Fridell JA. Comparison of histidine-tryptophan ketoglutarate and University of Wisconsin

solutions as primary preservation in renal allografts undergoing pulsatile perfusion. *Transplantation proceedings.* 2005;37(5):2016-2019.
26. Shah AP, Milgrom DP, Mangus RS, Powelson JA, Goggins WC, Milgrom ML. Comparison of pulsatile perfusion and cold storage for paired kidney allografts. *Transplantation.* 2008;86(7):1006-1009.
27. Fridell JA, Milgrom ML, Henson S, Pescovitz MD. Use of the end-to-end anastomotic circular stapler for creation of the duodenoenterostomy for enteric drainage of the pancreas allograft [corrected]. *Journal of the American College of Surgeons.* 2004;198(3):495-497.
28. Fridell JA, Agarwal A, Powelson JA, et al. Steroid withdrawal for pancreas after kidney transplantation in recipients on maintenance prednisone immunosuppression. *Transplantation.* 2006;82(3):389-392.
29. Fridell JA, Mangus RS, Chen JM, et al. Steroid-free three-drug maintenance regimen for pancreas transplant alone: Comparison of induction with rabbit antithymocyte globulin +/- rituximab. *Am J Transplant.* 2018.
30. Campsen J, Call T, Allen CM, et al. Prospective, double-blind, randomized clinical trial comparing an ERAS pathway with ketorolac and pregabalin versus standard of care plus placebo during live donor nephrectomy for kidney transplant. *Am J Transplant.* 2018.
31. Johns N, O'Neill S, Ventham NT, Barron F, Brady RR, Daniel T. Clinical effectiveness of transversus abdominis plane (TAP) block in abdominal surgery: a systematic review and meta-analysis. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland.* 2012;14(10):e635-642.
32. Findlay JM, Ashraf SQ, Congahan P. Transversus abdominis plane (TAP) blocks-a review. *The surgeon : journal of the Royal Colleges of Surgeons of Edinburgh and Ireland.* 2012;10(6):361-367.
33. Hebl JR, Niesen AD. Infectious complications of regional anesthesia. *Current opinion in anaesthesiology.* 2011;24(5):573-580.
34. Gronwald C, Vowinkel T, Hahnenkamp K. Regional anesthetic procedures in immunosuppressed patients: risk of infection. *Current opinion in anaesthesiology.* 2011;24(6):698-704.

TABLES

Table 1. Analysis of pancreas transplant recipients and donors with stratification by anesthesia intervention

	Total	*Anesthesia intervention*			
		Standard care	**TAP catheters**	**Liposomal bupivacaine**	***P* value**
Number of patients	197	62 (32%)	89 (45%)	46 (23%)	
Transplant recipients					
Age (years)	44 (18-66)	46 (28-65)	43 (18-63)	44 (27-66)	.23
Gender: Male	56%	65%	47%	61%	.08
Race: White	90%	95%	88%	87%	.18
Body mass index (kg/m^2)	25.7 (17.6-39.2)	25.2 (17.6-39.2)	25.7 (18.8-38.2)	25.8 (18.6-32.4)	.30
Transplant type					
Pancreas and kidney	115 (58%)	60%	54%	65%	.24
Pancreas after previous kidney	24 (12%)	18%	10%	9%	
Pancreas transplant alone	58 (29%)	22%	36%	26%	
Pancreas donors					
Age (years)	24 (7-49)	26 (19-49)	22 (7-38)	25 (11-48)	.001
Gender: Male	61%	61%	61%	62%	1.00
Race: White	80%	85%	75%	85%	.05
Body mass index (kg/m^2)	23.6 (13.0-39.5)	24.0 (13.8-39.5)	23.5 (13.0-33.9)	23.4 (16.8-39.5)	.75
Cause of donor death					

Stroke	9%	12%	8%	5%	.38
Trauma	59%	54%	65%	53%	
Anoxic brain injury	32%	34%	27%	42%	
Transplant procedure					
Length of surgery (minutes)	280 (105-537)	267 (124-475)	275 (105-409)	306 (120-537)	.09
Average blood loss (mL)	250 (0-1500)	300 (50-1500)	250 (20-1000)	250 (0-1000)	.26

mL = milliliters; TAP = transversus abdominis plane
Continuous variables are reported as median with range

Table 2. Summary of daily pain scores and opioid use in pancreas transplant recipients by anesthetic intervention

		Anesthesia intervention			
	Overall	Standard care	TAP catheters	Liposomal bupivacaine	*P* value
Number of patients	197	62 (32%)	89 (45%)	46 (23%)	
Pain scores (0-10 scale)					
PACU					< .001
Mean (SE)	3.9 (0.21)	2.7 (0.33)	4.7 (0.31)	4.1 (0.45)	
Median (range)	3.8 (0-10)	2.0 (0-10)	5.6 (0-10)	4.6 (0-10)	
Postop day 0					.81
Mean (SE)	3.8 (0.17)	3.6 (0.31)	3.9 (0.26)	3.8 (0.32)	
Median (range)	4.0 (0-10)	3.1 (0-10)	4.1 (0-10)	4.2 (0-8)	
Postop days 1-5 (average daily score)					< .001
Mean (SE)	3.5 (0.12)	2.9 (0.19)	3.9 (0.17)	3.4 (0.23)	
Median (range)	3.4 (0-7)	2.6 (0-7)	4.1 (0-7)	3.4 (0-7)	
Opioid use (calculated mg morphine equivalent)					
PACU					.02
Mean (SE)	13 (1.4)	9 (2.0)	17 (2.4)	11 (2.0)	
Median (range)	8 (0-124)	0 (0-80)	12 (0-124)	8 (0-60)	
Postop day 0					.29
Mean (SE)	57 (9.0)	70 (19.0)	61 (14.7)	32 (5.2)	
Median (range)	24 (0-936)	26 (0-936)	28 (0-936)	24 (0-140)	
Postop days 1-5 (daily requirement)					.03
Mean (SE)	91 (7.1)	113 (18.6)	90 (7.5)	63 (6.8)	
Median (range)	62 (5-919)	78 (13-919)	68 (5-383)	50 (8-236)	

Postop days 1-5 (total)					.03
Mean (SE)	682 (53.9)	846 (142.4)	680 (58.0)	465 (49.8)	
Median (range)	465 (36-7354)	529 (102-7354)	484 (36-3064)	349 (65-1655)	
Clinical outcomes (median, range)					
Time to first flatus (hours)	53 (2-145)	55 (2-145)	50 (9-100)	53 (3-130)	.22
Time to first stool output (hours)	65 (1-170)	71 (3-170)	60 (12-160)	68 (1-125)	.04
Time to first oral intake (hours)	15 (1-126)	26 (4-96)	12 (1-62)	14 (1-126)	< .001
Length of hospital stay (days)	7 (3-117)	7 (3-15)	7 (4-117)	6 (5-30)	.44
90-day graft survival	99%	98%	100%	100%	.34
90-day readmission	47%	60%	30%	61%	< .001

mg = milligrams; PACU = postanesthesia care unit; postop = postoperative; SE = standard error; TAP = transversus abdominis plane