PROTOCOL **NCT04254692**

Title: Randomized Controlled Trial Evaluating Liposomal Bupivacaine Following Abdominoplasty

Protocol:

- Version 2 – 04/09/2021

PI: Venkat Rao, MD, MBA[1]
Professor of Surgery, Division of Plastic Surgery

Affiliation:
Department of Surgery-Division of Plastic Surgery
University of Wisconsin School of Medicine and Public Health
G5/350 Clinical Sciences Center
600 Highland Ave
Madison, WI 53792

Project Summary

Postoperative pain, nausea, and vomiting can be frustrating sequelae of elective surgery. Poorly managed postoperative pain can lead to increased opioid use, increased postoperative nausea and vomiting (PONV), delayed return to work and usual activities, unplanned hospital admissions, surgical complications, and patient dissatisfaction. In light of the growing opioid epidemic in the United States, any intervention that potentially minimizes opioid use may have meaningful individual and societal impact. Despite the use of multiple techniques for managing postoperative pain in abdominoplasty patients, pain control continues to be a challenge for this patient population.

One technique commonly employed to improve pain control is the use of abdominal wall and incisional injection of local anesthetic agents to block the sensory nerves supplying the anterior abdominal wall and abdominal incisions in order to decrease sensation and pain in the abdomen in the setting of abdominoplasty surgery. Local anesthetic often used in this procedure is bupivacaine (Marcaine) ± epinephrine. However, in 2012, a liposomal bupivacaine suspension (Exparel; Pacira BioSciences, Inc, San Diego, California) was introduced as a longer-acting local anesthetic used for management of postoperative pain[1]. At the University of Wisconsin, patients undergoing abdominoplasty routinely receive intraoperative injection of local anesthetic to the abdominal wall and abdominal incisions, using bupivacaine as the local anesthetic, along with standard multimodal perioperative pain management including cool compresses, non-steroidal anti-inflammatories (NSAIDs), acetaminophen, and opioids.

The overall purpose of this study is to evaluate the analgesic efficacy of liposomal bupivacaine in optimizing pain control, minimizing the risk of PONV, and improving recovery after abdominoplasty. We will do this by comparing intraoperative abdominal wall and incisional injection of bupivacaine to bupivacaine plus liposomal bupivacaine in patients undergoing abdominoplasty. This will be studied using pain assessments, validated surveys, medication logs and review of medical records.

Background and Significance

Abdominoplasty is a routine plastic surgery procedure commonly performed on an outpatient basis, with more than 150,000 procedures performed in the US in 2018[2]. In this operation the abdominal muscles are tightened with sutures to improve the abdominal contour. This tightening of the muscles can increase muscle spasm and pain. Postoperative pain management in these patients can be challenging, resulting in decreased patient satisfaction, delayed recovery including delayed return to work and daily activities, increased opioid pain medication requirements and occasionally unplanned hospital admissions, surgical complications, and increased cost of care[1].

Abdominal wall and incisional injection of local anesthetics are commonly used as an adjunctive pain control technique for abdominoplasty and other surgeries involving the abdominal wall. Although local anesthetics are effective in treatment of postoperative pain, their relatively short duration of action (typically less than 8 hours) can make postoperative pain management challenging. This short duration of action is due to systemic absorption and subsequent elimination of the anesthetic limiting its time of contact with the local nerve endings[3]. Since its introduction in 2012, liposomal bupivacaine has been widely used as a local anesthetic in controlling postoperative pain. Liposomal bupivacaine is a dose-dependent slow-release formulation that consists of bupivacaine in an aqueous core enclosed inside a liposome. The liposomal preparation prevents the rapid systemic abruption of bupivacaine and allows it to remain at the injection site for a longer period as well as its gradual release overtime[4]. Liposomal bupivacaine demonstrates an initial peak analgesic effect immediately after injection, due to the presence of extra-liposomal bupivacaine in the solution, followed by a delayed peak occurring within 10-36 hours after administration. This is in contrast to non-liposomal bupivacaine that has a duration of up to 8 hours[3].

To date, there have been several studies looking at the use of bupivacaine as the local anesthetic in these techniques in abdominoplasty patients. However, no prospective, randomized, blinded study has been performed to evaluate the analgesic efficacy of liposomal bupivacaine in the same setting. Sforza et al.[5] performed a double-blinded, randomized controlled trial to assess the analgesic efficacy of TAP block using 0.25% bupivacaine versus standard of care in 28 women undergoing elective abdominoplasty. In this study, the TAP block cohort demonstrated significantly lower pain scores, lower morphine requirements in the first 12 postoperative hours, and also exhibited early ambulation compared to the control group. In a retrospective chart review of 64 female patients undergoing abdominoplasty with abdominal field block injections, using liposomal bupivacaine as local anesthetic, Morales et al.[1] reported reduced postoperative pain, lower postoperative opioid requirements, and earlier resumption of normal activity and ambulation compared to studies using other anesthetics for nerve blocks.

Thus, the overarching goal of this study is to prospectively evaluate the safety and efficacy of intraoperative abdominal wall and incisional injection of bupivacaine plus liposomal bupivacaine, compared to standard bupivacaine alone in abdominoplasty patients. We are conducting this study because, to our knowledge, no previous study has prospectively evaluated postoperative pain optimization in abdominoplasty patients using abdominal wall and incisional injection of bupivacaine plus liposomal bupivacaine as local anesthetic. We hypothesize that the use of bupivacaine plus liposomal bupivacaine will improve postoperative pain, minimize the risk of PONV and improve patient experience in abdominoplasty surgery beyond standard of care.

Experimental Design

This study will assess safety and efficacy of intraoperative abdominal wall and incisional injection of liposomal bupivacaine suspension in abdominoplasty patients. We hope that results from this study will help guide clinical decision-making with respect to postoperative pain management and overall optimization of recovery in elective plastic surgery.

The primary aim in this study is to evaluate postoperative total opioid use, measured via morphine equivalent (ME) dose, on postoperative day 1 (POD 1) in patients receiving either bupivacaine and epinephrine or bupivacaine plus liposomal bupivacaine and epinephrine injections intraoperatively during abdominoplasty. Additional outcomes include quality of recovery scores on POD1, pain scores on POD1, pain score at 1 week post op, total opioids (ME) at 1 week post op, use of antiemetic medication, development of PONV, time to discharge, patients' assessment of quality of recovery as determined by a validated survey and overall patient satisfaction.

Research Design and Methods

<u>Target population</u>

i. Male or female patients undergoing abdominoplasty by Dr. Venkat Rao, Dr. Ahmed Afifi or Dr. John Siebert, at Madison Surgery Center (MSC).

<u>Inclusion criteria</u>

i. Age equal to and greater than 18 years.
ii. Medically cleared to undergo elective surgery (including associated anesthesia) at Madison Surgery Center.

<u>Exclusion criteria</u>

i. Minors or under the age of 18
ii. Pregnant or breast-feeding women

iii. Incarcerated women or men
iv. Individuals unable to give consent due to another condition such as impaired decision-making capacity.
v. Men or women who take opioid pain medications on a regular basis prior to surgery.
vi. Men or women with a history of opioid abuse and/or dependence.
vii. Patients with a history of bleeding disorders precluding safe abdominoplasty
viii. Patients with renal and hepatic impairment
ix. Patients on anticoagulation therapy who have not held their anticoagulation as recommended by their surgeon or anesthesiologist.
x. Patients not medically cleared for surgery at Madison Surgery Center. This would include patients with sepsis/bacteremia, significant valvular disorders or heart conditions.

Recruitment and Group Selection:

Patients seeking abdominoplasty who are seen by one of the participating attending physicians and meet all inclusion and exclusion criteria will be approached to participate in this study. Participation in this study is voluntary. Patients interested in participation in this study who meet all inclusion and exclusion criteria will be approached to participate in this study. Those patients interested in participation in this study will be consented for participation per IRB approved process. The consent process will only be completed by study personnel who have completed the necessary training to do so.

All patients, regardless of study group / treatment arm, will undergo routine preoperative workup and management that all patients undergoing abdominoplasty with the attending physicians routinely undergo.

Study Outcome Measures

To prospectively determine the safety and efficacy of intraoperative abdominal wall and incisional injection of liposomal bupivacaine on perioperative pain and postoperative recovery following abdominoplasty, we will use total opioid use (ME) on POD 1 to evaluate our primary endpoint. To determine the safety and efficacy of intraoperative injection of liposomal bupivacaine on secondary endpoints of this study (quality of recovery POD1, pain score POD1, pain score 1 week post op, total opioid 1 week post op [ME], total antiemetic medication use POD 1, total antiemetic medication use 1 week post op), we will use Quality of Recovery assessments (QOR-40)[6–8], as well as perform chart review and collect patient surveys that gather this information. To gather descriptive data, (including demographic information, average time [minutes] spent in the PACU, average time [minutes] spent in Phase 2, total time [minutes] between the end of the operation and discharge to home, and evaluate the occurrence of unplanned hospital admission, PONV) we will perform review of medical records, surveys, and postoperative diaries.

The primary outcome is total opioid use (ME) on POD 1. Secondary outcomes include QOR-40 score on POD 1, pain score on POD1, pain score 1 week post op, total opioids (ME) 1 week post op, total antiemetic medication use POD 1, total antiemetic medication use 1 week post op.

Group Descriptions

Patients electing to undergo abdominoplasty will be invited to participate in the study at their preoperative visit. All patients choosing to take part in the study will be consented prior to their procedure. The study participants will consist of Dr. Venkat Rao, Dr. Ahmed Afifi and Dr. John Siebert's patients. The study participants will be randomized to one of two groups using block randomization. Block randomization will be performed using a computer-generated number list and an Excel spreadsheet

template; this will ensure equal numbers of subjects in each group. The subject will be randomized to receive either (a) intraoperative abdominal wall and incisional bupivacaine and epinephrine injection or (b) intraoperative abdominal wall and incisional bupivacaine plus liposomal bupivacaine and epinephrine injection. Intraoperative abdominal wall and incisional injection will be performed by the attending surgeon or appropriately trained surgical resident, using small aliquots, targeting sensory nerves in the abdominal wall and the abdominal incision. Surgery will take place in the usual fashion and participants will receive standard of care for pain control. Standard postoperative pain control includes: acetaminophen (Tylenol) 650-1000mg every 6 hours (obtained over the counter); Ibuprofen 600-800mg every 8 hours (obtained over the counter); Oxycodone 5-10mg every 4-6 hours as needed- 25 tablets total prescribed.

Following surgery, patients will be assessed for quality of recovery, postoperative pain, nausea and vomiting. Assessment of quality of pain will consist of a validated VAS score. VAS will also be administered prior to transfer to phase II postoperatively and at their one-week postoperative visit. Assessment of postoperative quality of recovery will consist of a validated QOR-40 score on POD 1. Participants will also be asked to record, using a postoperative diary/log, when they take postoperative analgesics and antiemetics, which medications are taken, and quantity of medication taken. This will also be reviewed both in the medical record and upon discussion with the participant at the postoperative visits. Assessment of the time spent in the recovery room, time spent in Phase 2 of recovery, will be obtained via review of the medical record. At the first postoperative visit, participants will undergo a routine interview that includes discussion of their pain control, analgesic and antiemetic use, recovery process, and overall satisfaction. The medical record will be reviewed for any unplanned postoperative hospital readmissions related to the surgery and for any referral placed for pain medication management after completion of peri-operative care.

Study Procedures

Abdominoplasty will be performed in the standard fashion, and all patients will receive routine management as deemed appropriate by the surgeon and anesthesiologist regardless of treatment arm. Postoperatively, all patients will proceed to the recovery room/PACU, where they will receive routine postoperative cares, including standard ASA monitoring, and availability of analgesics and antiemetics. Prior to transfer from PACU to Phase II, all patients will be asked to assess their pain, including rate their pain on a 0 to 10 numeric rating scale (where 10 is associated with the “worst pain ever” and 0 is associated with no pain).

Each participant will be transferred from PACU to Phase 2 when he or she meets standard requirements for transfer. Patient will be discharged when all discharge criteria have been met. All other postoperative patient care will be routine for all patients undergoing abdominoplasty.

Per our routine care for patients undergoing abdominoplasty, post-operative medications for all patients, regardless of study group, will include 5-10mg oxycodone every 4-6 hours as needed, 600-800mg ibuprofen every 8 hours and 650-1000mg acetaminophen every 6 hours. Patients are typically prescribed 25 tablets of oxycodone, and are encourage to take acetaminophen and ibuprofen scheduled as above for the first 5 days post-operatively, and then on an as-needed basis.

Data collection will occur intra-operatively, in PACU, on POD1 and POD 7. Medical record review will be performed to collect intra-operative and PACU data. Patients will be asked to fill out 3 surveys on POD 1- VAS, QOR-40 and POD 1 survey. They will also be asked to complete a medication log and pain diary until POD 7. These surveys will be collected at their 1 week post-operative visits.

Intraoperative local anesthetic injection

Regional analgesia techniques are routinely performed at Madison Surgery Center; all members of the perioperative team (nursing staff, anesthesiologists, and surgery team) understand the risks of local anesthetics and the facility is equipped and prepared to address potential complications.

The injection of local anesthesia to the abdominal wall will be performed intraoperatively. The patient will be positioned supine on the surgical table during the procedure. The patient, the anesthesiologist and the postoperative nursing staff will not be informed regarding whether bupivacaine and epinephrine or bupivacaine plus liposomal bupivacaine and epinephrine is being used as the local anesthetic. The surgical attending and resident assisting will be the only team members informed regarding which local anesthetic is being injected. All intraoperative local anesthetic injections will be performed by the attending surgeon or resident appropriately trained in the injection technique. Patients will undergo initial abdominoplasty procedure in the standard fashion. Prior to closure of abdomen, either bupivacaine and epinephrine or bupivacaine plus liposomal bupivacaine and epinephrine will be injected into the abdominal wall, targeting the plane between the transversus abdominus and internal oblique muscles, and the incision line.

A 25 gauge 50 or 80 mm needle will be used for the injection of local anesthetic. A 20-30 mL syringe of either 0.25% bupivacaine with 2.5 mcg/mL of epinephrine or 0.25% bupivacaine mixed with liposomal bupivacaine with 2.5 mcg/mL of epinephrine, depending on the study group, will be connected to the needle and used for injection. Local anesthetic will be injected bilaterally. Patients weighing at least 40kg will either receive approximately 80mL of 0.25% bupivacaine with 2.5mcg/mL epinephrine or 80mL of bupivacaine plus liposomal bupivacaine (20mL containing 266mg of liposomal bupivacaine mixed with 60mL of 0.25% bupivacaine containing 150mg of bupivacaine) with 2.5 mcg/mL of epinephrine. This will be divided into 2 separate injections of approximately 40mL, divided equally in multiple small aliquots on each side. The injections will also performed along the surgical abdominal incision.

A list of liposomal bupivacaine side effects can be found under the Data and Safety Monitoring section of the protocol. Any adverse event related to local anesthetic will be handled in the same manner that is standard clinical practice at Madison Surgery Center. Local anesthetics are used frequently at Madison Surgery Center. Local anesthetic toxicity may occur if the dose of bupivacaine or liposomal bupivacaine is miscalculated. In the event of any emergency, patient will be treated in the same clinical practice standards that are applied to all patients undergoing surgery at Madison Surgery Center.

Statistical Methods

Our primary outcome of interest is total opioid use (ME) on POD 1 between the two study groups; Patient receiving local anesthetic injection using bupivacaine as local anesthetic and patient receiving local anesthetic injection using bupivacaine plus liposomal bupivacaine as local anesthetic. Outcome metrics are the same between the 2 groups.

We reviewed previously published studies prior to performing a power calculation to identify a sample size. Data on the use of total opioid use (ME) in abdominoplasty was limited, however, we found data published by Fiala et al.[9] in 2015 most similar to our study design. In that study, the treatment group received intraoperative TAP block and their total hydromorphone use was compared to the control group. Based on 16 subjects per group, they found averages of 4.31mg and 2.63mg in control and treatment groups respectively and a resulting p-value of 0.024. This means the pooled standard deviation of the groups must have been around 2. Using a two-tailed, two sample t-test, performed at a significance level

of 0.05, we would need 23 subjects per group in order to have at least 80% power for finding a similar effect as significant. Power calculation was performed with the assistance of a biostatistician.

Our primary outcome of interest is total opioid use (ME) on POD 1. Additional outcomes of interest include QOR-40 score, pain score POD1, pain score 1 week post op, total opioid (ME) 1 week post op, total antiemetic medication use POD 1, total antiemetic medication use 1 week post op.

There will be 46 patients enrolled in the study (23 in each group, with 2 total groups) and therefore the medical record for 46 patients will be accessed to determine basic demographic information, analgesic use, time spent in PACU, time spent in phase 2, total time from end of surgery to discharge from surgery center, and postoperative complications.

	Outcome	Statistical Descriptor	Statistical Test
Primary outcome:	Total opioid at 24 hours (ME)	Average	t-test
Secondary outcomes:	QOR- 40 Score POD 1	Average	t-test
	Pain score POD 1	Average	t-test
	Pain score at 1 week	Average	t-test
	Total opioid at 1 week (morphine equivalents)	Average	t-test
	Total antiemetic mediation used at 24 hours	Average	t-test
	Total antiemetic mediation used at 1 week	Average	t-test
	PONV	Percentage	Fisher's exact test
	Complications	Percentage	Fisher's exact test

Data and Safety Monitoring Plan

1. Summary of the Protocol: Please see the beginning of this protocol document for study design and procedures, as well as primary and secondary outcome measures.
2. Roles and Responsibilities
    a. The principal investigator, Dr. Venkat Rao, will be responsible for monitoring the trial. Dr. Rao is a Professor of Surgery and the study is taking place under his supervision. Any adverse events will be reviewed promptly and reported to the IRB per current guidelines.
    b. Resident Physicians &/or future study team members who may assume a study coordinator role in the Department of Plastic Surgery, will be responsible for monitoring data collection, adverse events, and protocol deviations. Reportable events will be submitted per current guidelines.
3. Data and events to be captured
    a. Study members will be collecting basic demographic information via chart review on all patients enrolled in this study. This will include patient age, BMI, medical comorbidities, smoking status, history of PONV.
    b. Study members will also be collecting data during the peri-operative period that is pertinent to the study. This will include time in each phase of care, total opioid use in PACU, survey results from PACU, POD 1 and POD 7.

c. All adverse events, complications related to the procedure(s) performed as part of the study, deviations from the protocol will also be collected.

4. Data Management, Analysis, and Quality Assurance:
    a. Identification of data sources (e.g., questionnaires, medical records, biospecimen collections, audio/video recordings)
        i. Data sources for this study include:
            1. Medical record review
            2. Questionnaires
            3. Postoperative diaries
    b. Frequency of Data Analysis
        i. For each group studied, study members will evaluate for complications due to study participation approximately every 15 patients that complete the study. This will allow for evaluation of safety while the study is taking place.
    c. Description of the security measures in place to protect data sources including how the data will be labeled and stored.
        i. To protect against and minimize potential risks to confidentiality, all the information collected in this study will be coded and data will be kept in a locked office on a secure password-protected Department of Surgery server backed up by Surgery's internal IT team at the University of Wisconsin Hospital and Clinics Clinical Science Center. Hard copies of the consent forms will be stored in a filing cabinet in a locked office at the University of Wisconsin Hospital and Clinics Clinical Science Center. The information will only be made available to the study team members directly involved in the study. Confidentiality will be maintained by assigning a number to all subjects. The research subject log linking the name and subject number will be stored separately from the data and only authorized personnel will have access to the subject log. The PI and study staff will be alert for any breach of confidentiality.
5. Trial Safety:
    a. Description of any specific events that would preclude a participant from continuing the intervention
        i. All subjects will be given the opportunity to discontinue their participation in the study at any time.
        ii. Peri-operatively, all subjects will be monitored using the same clinical practice standards that are applied to all patients undergoing surgery at Madison Surgery Center. This includes monitoring for signs of local anesthetic toxicity, as well as complications of regional blocks.
    b. Description of the consent/assent procedures (e.g., by whom, how and under what conditions will a subject be consented).
        i. Once deemed eligible to participate in the study by the physician, if a patient expresses interest in participating in the trial, a study team member will review the ICF and obtain written informed consent prior to enrollment for participation in the study.
        ii. On the day of surgery, a study team member will ensure written informed consent was obtained and reviewed prior to procedure and participation in the study.
    c. Description of the mechanisms in place to protect subject privacy.
        i. Patient confidentiality will be ensured throughout the duration of this study. Discussing the protocol with the subject in a private room will help protect the subject's privacy. The collection of sensitive information will be limited to the amount necessary to achieve the aims of the research. The hard copies of the consent forms will be stored in a locked filing cabinet at the University of

Wisconsin Hospital and Clinics Clinical Science Center. Confidentiality will be maintained by assigning a subject number to all subjects. The research subject log linking the name and subject number will stored separately from the data, and only authorized personnel will have access to the subject log.

d. Description of the process for the disclosure of any conflicts of interest that may potentially challenge participant safety or bias the data and how the conflict will be managed.
    i. If any conflicts of interest arise that may challenge safety or bias the data, they will be immediately brought to the attention of the PI. If it is the PI with the conflict of interest, the study will be discontinued.
e. Description of the data security in place to protect the confidentiality of the data (e.g., password protected encrypted electronic records) and any limits to confidentiality.
    i. To protect against and minimize potential risks to confidentiality, all the information collected in this study will be coded and data will be kept in a locked office on a secure password-protected Department of Surgery server backed up by Surgery's internal IT team at the University of Wisconsin Hospital and Clinics Clinical Science Center. Hard copies of the consent forms will be stored in a locked filing cabinet in a locked office at the University of Wisconsin Hospital and Clinics Clinical Science Center. The information will only be made available to the study team members directly involved in the study. Confidentiality will be maintained by assigning a number to all subjects, and all data will be coded. The research subject log linking the name and subject number will be stored separately from the data and only authorized personnel will have access to the subject log. The PI and study staff will monitor closely for any breach of confidentiality.

6. Reportable Events:
    a. Description of the process and timelines (e.g., hours, days) for collecting and reporting Adverse Events (AEs), Serious Adverse Events (SAEs), and Unanticipated Problems Involving Risks to Subjects or Others to appropriate monitoring and regulatory entities
        i. Adverse Events, Serious Adverse Events, and Unanticipated Problems will be brought to the attention of the PI via email or telephone call (with plan for telephone call if no confirmed response to email) when study members become aware. SAEs will be monitored for up to 30 days following initial procedure date, per current guidelines.
            1. There are few rare side effects of local anesthetic injection into abdominal wall and if they occur, an adverse event would be reported.
                a. These side effects are rare:
                    i. Visceral damage due to inadvertent peritoneal puncture
                    ii. Seizure
                    iii. Ventricular arrhythmia
                    iv. Transient femoral palsy
                    v. Bleeding and infection at the site of injection
                    vi. Hypotension
                    vii. Injecting local anesthesia into the wrong area including a blood vessel, and/or the space around the lungs.
                    viii. Nerve damage
                    ix. Cardiac arrest
                b. Rare side effects associated with liposomal bupivacaine
                    i. Methemoglobinemia
                    ii. Temporary prolonged loss of sensation
            2. Regional anesthesia is commonly used modality for adjunctive analgesia

and anesthesia in elective abdominoplasty surgery, and is commonly performed at Madison Surgery Center. The risks of local anesthetic injection and regional anesthesia are not unique to Madison Surgery Center all providers performing regional anesthesia have been specifically trained to do so.

3. As injection of local anesthesia is commonly performed in abdominoplasty cases, any risks attributable to injection of the anesthesia alone are not unique to this study, as patients undergoing the same procedure outside the study would have the same risks.
    a. The act of randomization may cause a patient to receive a less beneficial pain management or recovery protocol. However since surgery is currently performed with and without local anesthetic, as well as with and without bupivacaine or liposomal bupivacaine, the risks are well within the standard risks of elective abdominoplasty surgery.

7. Stopping Rules
    a. Upon evaluation of patient data as described above, if any statistically significant increase in morbidity or mortality (including hospital admission or ER evaluation for complications related to respiratory depression) is identified, study members will re-evaluate all results. If it is determined that a statistically significant increase in morbidity or mortality is attributable to patient participation in either group, all patient recruitment will be halted and the IRB will be contacted via ARROW. The safety of continuing with the study will be further evaluated, and procession of study activities will be halted until IRB approval.

Protocol References

1. Morales R, Mentz H, Newall G, Patronella C, Masters O. Use of abdominal field block injections with liposomal bupivicaine to control postoperative pain after abdominoplasty. *Aesthetic Surg J*. 2013;33(8):1148-1153. doi:10.1177/1090820X13510720
2. The American Society for Aesthetic Plastic Surgery. *Cosmetic (Aesthetic) Surgery National Data Bank: Statistics 2018*.
3. Hu D, Onel E, Singla N, Kramer WG, Hadzic A. Pharmacokinetic profile of liposome bupivacaine injection following a single administration at the surgical site. *Clin Drug Investig*. 2013;33(2):109-115. doi:10.1007/s40261-012-0043-z
4. Grant GJ, Barenholz Y, Bolotin EM, et al. A novel liposomal bupivacaine formulation to produce ultralong-acting analgesia. *Anesthesiology*. 2004;101(1):133-137. doi:10.1097/00000542-200407000-00021
5. Sforza M, Andjelkov K, Zaccheddu R, Nagi H, Colic M. Transversus abdominis plane block anesthesia in abdominoplasties. *Plast Reconstr Surg*. 2011;128(2):529-535. doi:10.1097/PRS.0b013e31821e6f51
6. Myles PS. Measuring quality of recovery in perioperative clinical trials. *Curr Opin Anaesthesiol*. 2018;31(4):396-401. doi:10.1097/ACO.0000000000000612
7. Gornall BF, Myles PS, Smith CL, et al. Measurement of quality of recovery using the QoR-40: a quantitative systematic review. *Br J Anaesth*. 2013;111(2):161-169. doi:10.1093/bja/aet014
8. Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: The QoR-40. *Br J Anaesth*. 2000;84(1):11-15. doi:10.1093/oxfordjournals.bja.a013366
9. Fiala T. Tranversus abdominis plane block during abdominoplasty to improve postoperative patient comfort. *Aesthetic Surg J*. 2015;35(1):72-80. doi:10.1093/asj/sju019
10. Myles PS, Myles DB, Galagher W, Chew C, Macdonald N, Dennis A. Minimal Clinically

Important Difference for Three Quality of Recovery Scales. *Anesthesiology*. 2016;125(1):39-45. doi:10.1097/ALN.0000000000001158