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NAUSEA, VOMITING, SLEEP, AND RESTFULNESS AFTER DISCHARGE HOME FOLLOWING OUTPATIENT ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION WITH REGIONAL ANESTHESIA AND MULTIMODAL ANALGESIA-ANTIEMESIS

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Abstract

Background and objectives— We analyzed discharge outcome data after anterior cruciate ligament reconstruction (ACLR) under spinal anesthesia including a perineural femoral catheter and multimodal analgesia/antiemesis. The outcomes specifically addressed in this report are: nausea, vomiting, retching (NVR), and quality of sleep/difficulty falling asleep/daytime restfulness.

Methods— ACLR patients were randomized to saline or 0.25% levobupivacaine as a bolus and/or 50-hour infusion. Patients completed the Quality of Recovery 40-item (QoR-40) survey on postoperative days 1–4. We analyzed predictors of perfect responses (i.e., no nausea-vomiting-retching, and perfect sleep-restfulness) by pooling these specific QoR-40 items. Prospectively-collected QoR-40 data were analyzed retrospectively.

Results— Data from 233 participants were analyzed. The addition of the femoral nerve block or perineural catheter did not predict associated improvements in NVR or sleep/restfulness. Previous days' NVR was the most consistent predictor of subsequent NVR, while gender and opioid consumption were less consistent predictors. Smoking status was not predictive of NVR. Previous days' sleep-restfulness was a consistent predictor of subsequent sleep-restfulness, while the presence of any moderate pain was a less consistent predictor of sleep-restfulness.

Conclusions— NVR and quality of sleep-restfulness after the described regional anesthetic with multimodal analgesia and antiemesis is reported. Smoking status was not a predictor of NVR, and

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gender and opioid consumption were not consistently predictive of NVR. The addition of a femoral nerve block to the described multimodal technique was not associated with NVR or quality of sleep-restfulness.

Keywords

postoperative nausea and vomiting; sleep; anterior cruciate ligament reconstruction; continuous nerve block; femoral nerve block; spinal anesthesia; quality of life; perphenazine

INTRODUCTION

Recently, Ilfeld and Enneking (2005) provided an excellent outcomes review of continuous nerve block catheters at home.[1] This review included descriptions of sleep quality improvements with continuous perineural analgesia when compared with placebo and opioids, in patients who were commonly co-administered a general anesthetic for surgery. More recently, we reported on a very low (4%) rate of postoperative nausea and vomiting (PONV) after anterior cruciate ligament reconstruction (ACLR) using spinal anesthesia and multimodal analgesia and antiemesis.2 This latter report of low PONV is relevant in comparison to previous ACLR patients from our institution who had PONV rates ranging from 12% 3 to 39% 4, associated with the anesthetics, analgesics, and antiemetics used (or not used. These recent manuscripts call for additional reports of how patients' outcomes evolve after discharge home with perineural catheters in place.

The objective of the current study was to determine sleep quality and restfulness, and nausea/vomiting/retching (NVR) after same-day discharge home in our prospectively-studied outpatient ACLR population.2 To do so, we retrospectively analyzed prospectively-collected Quality of Recovery 40-item (QoR-40) scale data.5 Our goal was to determine if femoral nerve block use (versus placebo) was definitively associated with quality of sleep and daytime restfulness after outpatient ACLR, in the context of previous reports by Ilfeld et al. It is possible that quality of sleep and restfulness during the preceding day (not reported in the reports of Ilfeld et al.) may have been more predictive of a high-quality sleep-restfulness outcome, emphasizing the overall importance of creating analgesic and antiemetic conditions to allow early sleep and restfulness after discharge home (not specifically traceable to the perineural analgesic technique).

As a secondary aim, we used QoR-40 data to determine whether 3 of the generally-accepted PONV predictors (female, non-smoker, opioids) also predict NVR after discharge in the context of regional anesthesia and multimodal analgesia/antiemesis. We are not aware of any studies of these generally-accepted PONV predictors in contexts where regional anesthesia is used without general anesthesia.

METHODS

After achieving approval by the Institutional Review Board of the University of Pittsburgh Medical Center, and obtaining informed consent, ACLR patients (American Society of Anesthesiologists' Physical Status Classification of 1 or 2) underwent a standardized multimodal analgesia regimen (ketamine 0.2 mg/kg IV, plus intra-articular meperidine 100 mg with neostigmine 0.5 mg and ketorolac 15 mg) and anesthetic (ipsilateral hyperbaric spinal with bupivacaine) technique.[2] Oxycodone and rofecoxib were taken by patients postoperatively as daily analgesics, as previously described.2 In total, 270 patients were recruited, and exclusions after enrollment were not replaced. Other inclusion and exclusion criteria are also as previously described.2

Patients were randomized to one of the following femoral nerve block catheter treatment groups: (i) saline bolus (30 mL) plus saline infusion (270 mL at 5 mL/hr, group SbSi); (ii) levobupivacaine (0.25%) bolus with saline infusion (group LbSi), or (iii) levobupivacaine (0.25%) bolus plus levobupivacaine (0.25%) infusion (group LbLi), according to the method described previously.[2]

Patients were administered routine antiemetic prophylaxis with dexamethasone (4 mg IV at the start of surgery) and ondansetron (4 mg IV at the end of surgery). In addition, perphenazine was given (bioavailable dose range of 1.6 – 3.2 mg).

Data collection procedures

During the preoperative interview after informed consent for the study was obtained, additional demographic information was elicited (age, gender, ethnicity, height, weight, smoking status). The research coordinator called postoperative patients at a pre-determined phone number (home phone and/or cell phone) on each of the 4 postoperative days to (i) gather data regarding oxycodone consumption, and (ii) remind patients to complete the daily QoR-40 survey. The oxycodone consumption data were incorporated into the statistical models described below to determine the extent of opioid-induced NVR. Even though retching and vomiting involve the same physiologic response, and even though "post-discharge nausea and vomiting" is the generally accepted outcome terminology in our specialty, Myles et al. included a separate survey item addressing retching in the QoR-40.[5] As a result, we will use the "NVR" outcome terminology.

Postoperative course

After surgery, all patients were transferred to the postanesthesia care unit (PACU) for postoperative perineural femoral catheterization, the details of which having been previously described.[2] Neither the study investigators, research coordinator, nor patients were aware of the contents of the study boluses and infusions.

Patients completed the QoR-40 survey first as a preoperative baseline, then on postoperative days 1–4. This survey includes 8 items relevant to this current manuscript: NVR (3 separate items), moderate pain, severe pain, difficulty falling asleep, having had a good sleep, and feeling rested. All items were scored by patients on a 5-point Likert scale. For NVR through difficulty falling asleep, a score of 5 for an individual item indicated "none of the time," and a score of 1 indicated "all of the time." For "having had a good sleep" through "feeling rested," a score of 5 indicated "all of the time," and a score of 1 indicated "none of the time." Thus for all items, a higher score represented a more favorable outcome.

Statistics

Data were first explored to determine demographic equivalence between treatment groups. The demographic variables of gender, age, race (Caucasian versus other), body mass index (BMI), and smoking history, were analyzed for differences between treatment groups using one-way analysis of variance (for continuous variables) or the chi-square test (for categorical variables). Several intraoperative and immediate postoperative parameters were also recorded and analyzed: including immediate hydromorphone or oxycodone use for rescue analgesia, use of a surgical tourniquet, and surgical case duration. Oxycodone consumption on postoperative days 1–4 was analyzed using quartiles in order to facilitate logistic regression analysis when considering the opioid consumption variable in the described models below.

P-values less than or equal to 0.05 noted in the tables are considered statistically significant. Appropriate adjustments were made for multiple comparisons. All analyses were conducted

using the Statistical Package for the Social Sciences (SPSS for Windows, version 13.0, Chicago, IL).

Analysis of "Feeling Rested," "Had a Good Sleep," and "Difficulty Falling Asleep"—Scores for "Feeling Rested," "Had a Good Sleep," and "Difficulty Falling Asleep" based on QoR-40 responses, were converted from Likert scale responses per response (range 1–5) into a single dichotomous ("perfect" versus "less than perfect") variable. The "perfect" response was "all of the time" for "feeling rested" and "had a good sleep," and "none of the time" for "difficulty falling asleep;" all other responses were categorized as "less than perfect." Hereafter, we will term this outcome as "perfect sleep-restfulness."

Analysis of NVR—Similar to the method above, scores for the individual NVR variables were pooled first then converted into a dichotomous variable ("none of the time" versus "any more than none of the time"), in an effort to consider a "perfect" NVR outcome.

Regression analyses for Sleep-Restfulness and NVR—Logistic regression models were run for sleep-restfulness and NVR. Univariate regression models with each of the following variables were evaluated: study treatment group, surgical graft type ("single-bundle" allograft versus other); surgical duration, age, BMI (as continuous variables); thigh tourniquet use, race (Caucasian versus not), gender (as dichotomous variables); moderate postoperative pain, severe postoperative pain (dichotomized as "none" versus "any" from QoR-40 responses), and cumulative oxycodone consumption (as a dichotomous variable using the 25^{th} percentile as a "cut point"). NVR (dichotomized as above) was also evaluated as a variable in the analysis of sleep-restfulness. To keep each patient report relevant and time-appropriate, we ensured that survey responses from previous days were used to evaluate the outcome quality on the next day. For example, the presence of any moderate pain on day 2 was used to determine effects on sleep-restfulness as answered in the day 3 survey (since the day 3 survey asks about quality of sleep from the previous night).

When any of these variables in the univariate regression were significant or showed a trend of predicting sleep-restfulness or NVR (i.e., $P<0.1$), then the variables were incorporated into a multivariable logistic regression. In addition, gender, opioid consumption, and smoking status were included in all multivariable analyses of NVR even if these factors were not significant in the "screening" univariate analysis. Finally, treatment group LbLi was evaluated as a variable in the multivariable models, regardless of univariate regression outcomes with the LbLi variable.

Additional analysis of Nausea/Vomiting/Retching—In our previous report,[2] PONV (as a dichotomous variable) was determined based any of the following occurrences: (i) the parenteral dosing of ondansetron either in the PACU or in the phase II recovery unit when intraoperative ondansetron had already been given per protocol; and/or (ii) the recording of the presence of nausea and/or vomiting in the narrative section of the PACU and/or phase II recovery nursing notes. This definition is presented here, since PONV was analyzed as a predictor of NVR at home.

Of note, we did not specifically query patients regarding previous PONV/motion siockness history. That said, preoperative PONV risk factors did not influence the multimodal antiemetic protocol used, based on our group practice (for outpatient orthopedic surgery) having a zero-tolerance position on PONV [6], again based on an unacceptably high PONV rate in this population of 12–40%.[3,4]

RESULTS

Recruitment began in July 2001, and study follow-ups were completed by January 2005. Two hundred seventy patients consented to participate in the study. Thirty-five of the 270 recruited patients were excluded before the end of the day of surgery, with the reasons for exclusions having been detailed previously.[2] Two hundred thirty three of the remaining 235 had retrievable QoR-40 data, while the other 2 participants had been lost to follow-up (and/or had missing QoR-40 data) beginning at postoperative day 1. The "perfect outcome" dichotomous variables for sleep-restfulness and NVR were determined only from participants who did not omit any of these items on the survey.

There were no significant differences between treatment groups with respect to gender, age, race/ethnicity, BMI, smoking history, baseline NVR (i.e., before surgery), length of surgery, tourniquet use, day-of-surgery postoperative opioid requirements, PONV in the PACU or phase 2 recovery unit, or "perfect" baseline sleep-restfulness (Table 1). As previously reported[2], oxycodone consumption was significantly higher on days 1–2 in saline control patients.

Raw Data for Sleep-Restfulness and NVR

On postoperative days 1–4, an increasing proportion of patients reported perfect sleep-restfulness per day (Days 2–4 individually better than postoperative day 1, $P \leq 0.01$ by the Chi square test, Table 2). Table 2 also lists the raw data as a benchmark for potential future study.

There were no day-to-day improvements in NVR (Table 3). Daily responses of "No NVR" ranged between 24% and 30% (24% on day 1, 30% on day 2, 26% on day 3, and 24% on day 4). Post-discharge nausea was reported as more common than "some of the time" in very few patients (5 on day 1, 14 on day 2, 13 on day 3, and 9 on day 4), with daily percentages being 2%, 6%, 6%, and 4% on days 1–4, respectively (Table 3). Daily rates of vomiting or retching did not exceed 4% on any given postoperative day. There were no statistically significant differences based on nerve block treatment group for NVR.

Raw data addressing presence of any moderate or severe pain based on nerve block treatment group

Severe pain (as queried on the QoR-40) was less likely in the LbLi treatment group on postoperative days 1–2, while moderate pain was less likely in the LbLi treatment group on postoperative days 1 and 4 (Table 4). These findings are reasonably consistent with our previous report of the same patients' numeric rating pain score outcomes based on nerve block treatment group.[2] These data are presented strictly for QoR-40 outcome benchmarking purposes, as well as for the reason of these QoR-40 pain reports being analyzed as variables in the described regression models to follow.

Regression analyses of sleep-restfulness

Having reported "perfect" sleep-restfulness on the previous night was a reliable associated predictor of similar reports of perfect sleep-restfulness on subsequent postoperative nights (Table 5). The presence of moderate pain on days 1 and 3 was associated with a lower likelihood of perfect sleep-restfulness on those same nights (as reflected on the next day's survey responses). Nerve block treatment group and oxycodone consumption were not predictors of sleep-restfulness in the multivariable regression models.

Regression analyses of PONV and NVR

Immediately postoperatively, opioid dosing for rescue analgesia before hospital discharge was the only predictor of PONV (i.e., gender, smoking status, and baseline NVR were not predictive). There were no other predictors of PONV (i.e., on the day of surgery), which is not surprising given the low (4%) incidence. Nerve block treatment group, smoking status, and moderate or severe pain were not predictors of PONV/NVR on any postoperative day.

The most reliable associated predictor of NVR was PONV or NVR on the previous day (Table 6). PONV (on the day of surgery) and NVR (on days 1–3) predicted NVR on days 1–4, respectively (odds ratios 10–16, $P \leq 0.001$ throughout). Baseline NVR (i.e., on the preoperative QoR-40 survey) was associated with more NVR on days 1 and 3 (Table 6). Patients in the lower quartile of cumulative oxycodone consumption had less associated NVR only on days 2 and 4 (odds ratios 0.3, $P \leq 0.02$, Table 6). Women had higher risk of NVR only on days 1 and 2 (P values ≤ 0.03, respectively, odds ratios 2.1 and 2.8, respectively, Table 6).

DISCUSSION

In this retrospective analysis of prospectively collected data, we have shown that a femoral nerve block superimposed upon a multimodal anesthetic/analgesic/antiemetic technique did not appear to improve associated patient outcomes of sleep-restfulness or post-discharge nausea and/or vomiting. It should be noted that this analysis used extremely stringent “zero tolerance” criteria based on “perfect” responses derived from a constellation of related symptoms queried on the QoR-40 outcome survey. These qualifications are addressed in the paragraphs below.

The data collected from these study patients have shown significantly reduced numeric-rating pain scores with movement, and oxycodone consumption based on use of a continuous perineural femoral catheter. We previously reported this finding, which was our specific aim of this study, as soon as these data became available.[2] We used the outcome survey data from the QoR-40 as a secondary aim of the originally proposed study, and this data did not become available to us until months after our original manuscript was accepted for publication. Therefore, we were forced to retrospectively analyze these prospectively collected data. The study was originally powered to determine pain score differences between treatment groups. No sample size calculations were based on QoR-40 outcomes, therefore we opted to conservatively present outcomes determined from this instrument.

By opting for a “zero tolerance” threshold for sleep-restfulness and NVR, we have transformed the QoR-40 data from ordinal/continuous data to dichotomous data. By doing so, we have also moved in a direction that our subspecialty could consider when studying outpatients (versus inpatients). It is possible that our findings of “no difference” based on nerve block treatment group may not be true in the context of less stringent statistical criteria, for example, applied to inpatients. In either case, it is important that the QoR-40 be introduced as a potentially meaningful outcome measure in the regional and ambulatory anesthesia patient populations. The QoR-40 survey may help to detect significant outcome differences when regional versus general anesthesia techniques are being compared, or when various multimodal analgesic-antiemetic strategies are being compared.

Restfulness and quality of sleep

To our knowledge, this is the first study that used the QoR-40 as a metric for the assessment of quality of sleep and patients’ descriptions of restfulness. However, this is not the first study to examine sleep quality in the context of outpatient continuous perineural analgesia. Ilfeld and Enneking (2005) provided an excellent review of continuous nerve block catheters

at home.[1] These authors evaluated insomnia by asking the question "Did you have difficulty sleeping last night because of pain?" 7–9 In contrast, we separately evaluated sleep quality and difficulty falling asleep, since these were two separate items in the QoR-40. Unlike our current study, reports by Ilfeld et al.[7–9] also addressed middle-of-the-night awakenings by asking the questions: "Did you awaken last night because of pain? If yes, then how many times?"

When Ilfeld and Enneking (2005)[1] reviewed quality-of-sleep outcomes comparing perineural analgesia with placebo and opioids, they concluded that: (i) 0–30% of patients receiving perineural ropivacaine reported insomnia as a result of pain, compared with 60%–70% of patients using only oral opioids; and (ii) patients receiving perineural ropivacaine awoke from sleep because of pain an average of 0.0–0.2 times on the first postoperative night, compared with 2.0 –2.3 times for patients receiving perineural saline.1 In earlier studies, the mepivacaine/clonidine bolus/saline infusion used by Ilfeld et al.7–9 had lower quality sleep outcomes when compared with patients receiving the same mepivacaine/clonidine bolus with ropivacaine infusion. These outcome differences make sense given the shorter-acting drug used for the perineural bolus in the studies by Ilfeld et al. 7–9 Interestingly, our patients who received a levobupivacaine bolus with or without a levobupivacaine infusion (i.e., treatment groups LbLi and LbSi) did not show an increased association of "perfect" sleep-restfulness outcomes, using the stringent criteria described.

As with any research construct, it likely will be helpful in the future to use the same assessment tool to evaluate outcomes such as sleep quality and restfulness, to make studies comparable with each other. In addition, it will be important in future studies (as we did in this current study) to incorporate baseline (preoperative) descriptions of restfulness and quality of sleep, as well as previous postoperative days' descriptions of the same in daily analysis. By using statistical techniques such as logistic regression used in the current study, one can incorporate multiple variables into the regression equation to determine whether the nerve block treatment group factor becomes insignificant in the context of other studied predictors. One can correct for patients' baseline tendencies more easily when recording a preoperative baseline, and integrating the preoperative and previous-day's reports into the reports of subsequent-days' outcomes. For example, the LbLi treatment group was predictive in the univariate analysis of patients having a perfect sleep-restfulness outcome on the second and third nights after surgery (Table 5), but the LbLi factor was deemed non-predictive when compared in multivariable regression with other significant variables discovered in the univariate logistic regression (e.g., baseline sleep-restfulness, and perfect sleep-restfulness the previous night).

PONV and NVR

We also demonstrated a daily NVR rate ranging from 24–30%; but this NVR report exceeded "some of the time" in no more than 6% of patients on any given postoperative day. In addition, daily rates of any vomiting or retching were no more than 4% on any given postoperative day. We believe that this is the first report of PONV and NVR in the context of a regional-only anesthesia plan combined with multimodal analgesics and antiemetics, using the QoR-40 survey to assess NVR incidence. However, it is difficult to make meaningful comparisons across studies from other institutions involving different patient populations and anesthesia protocols, since this is the first report using the QoR-40 as a metric.

PONV—In reviewing the incidence of PONV after regional anesthesia, Borgeat et al. (2003) stated that regional techniques without GA are historically considered to decrease the incidence of PONV. 10 The summarized incidences of PONV in this review were 34%

(62/180) whenever intravenous patient-controlled opioids were used postoperatively, 18% (15/85) whenever a general anesthetic with volatile agents was co-administered with a continuous peripheral nerve block, and 7.7% (10/130) when the continuous peripheral nerve block used for surgical anesthesia initially was co-administered with a propofol infusion or no sedation.10 The present study (with a notable sample size of 233 analyzed participants) shows much different PONV outcomes in the setting of the multimodal antiemetics and analgesics used. However, it was interesting that the placebo (SbSi) treatment group did not experience significantly more PONV (6% versus 3.1% in the LbSi-LbLi treatment groups). The overall low incidence in this study may require larger sample sizes to assess PONV when a multimodal antiemetic prophylaxis technique is used in addition to a non-triggering anesthetic. Our ACLR patients from historical controls had much higher reported PONV rates (12–40%) on the day of surgery.3–4

NVR—It appears that the use of oxycodone for anticipatory pain pending nerve block resolution led to NVR rates (24–30%) consistent with the rates of PONV described in patients receiving intravenous patient-controlled opioids (34%) by Borgeat et al.10 However, all of our study patients were advised to take oxycodone on a regular schedule (at the request of our institutional review board, based on the work of Reuben et al.)11 to mitigate placebo group concerns of untreated pain. This is relevant because two-thirds of our study patients had placebo femoral perineural infusions. In clinical practice, perineural catheter patients would have infusions of local anesthetics (as opposed to placebo saline); therefore, a more appropriate opioid analgesic plan would be to dose only on a symptomatic basis (as opposed to a regular dosing schedule), in which case NVR rates may be further reduced. The incidence of symptoms after discharge home, where the patients had been instructed to take prophylactic oxycodone in anticipation of potential pain, is a seed for future study. Would the incidence of symptoms be less in a group of patients discharged with instructions to take opioid-based analgesics only with pain scores above a certain minimum, versus a group instructed to consume "prophylactic" opioid analgesics? Such a study would help quantify opioid-induced NVR at home. This type of study would also suggest a useful role of regional analgesic techniques in reducing opioid consumption and related symptoms at home.

That said, in our study population, the incidence of NVR (based on QoR-40 responses) was not consistently based on opioid dose-response relationships. Specifically, our patients in the lower quartile of oxycodone consumption on days 2 and 4 had lower incidences of NVR, but this was not the case on days 1 and 3 after surgery. When we repeated the regression analyses using median and 75th percentile oxycodone consumption values as “cut points,” opioid consumption was not predictive of NVR. Therefore, the lower quartile oxycodone doses listed in Table 1 may prove to be a useful threshold not to exceed if NVR is to be avoided. In either case, the finding of Zhao et al. (2004)[12] remains relevant: every 3–4 mg increase of morphine equivalent per day will be associated with at least 1 additional clinically meaningful opioid-related symptom, and/or at least 1 additional patient-day with an opioid-related clinically meaningful event.

To summarize, the combination of regional anesthesia and multimodal analgesia/antiemesis after ACLR led to a rare (4%) incidence of PONV, to the extent that considering triple-therapy with these agents and combining with regional anesthesia (along with the avoidance of volatile agents and minimizing of opioids) may allow our subspecialty to consider a “zero-tolerance” approach for prevention of PONV in outpatients. Smoking status influenced neither PONV nor PDNVR in our study. Neither female gender nor baseline nausea/vomiting/retching predicted PONV in our study. Gender (women) and opioid consumption were inconsistent predictors of NVR. Risk factors or PONV and NVR may

need to be rigorously re-evaluated when general anesthesia with airway devices are avoided, and when multimodal analgesia/antiemesis and regional anesthesia are employed.

Potential value of individual QoR-40 items in addressing outcomes in a homogeneous study sample—The patient responses to the myriad outcomes addressed on the QoR-40 seem to make it a potentially useful research tool to evaluate a constellation of patient concerns in the effort to achieve the highest recovery quality possible, and to determine which anesthetic factors are contributors to such outcomes, and for how long these factors contribute to such outcomes after surgery. To find patient outcome benefits after single-injection and continuous nerve block analgesia (for quality indicators other than the commonly-studied nausea, vomiting, and pain) helps to further solidify the justification for routine use of such techniques for invasive outpatient orthopedic surgery, when performed by sufficiently skilled practitioners.

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Table 1

Demographic data based on Femoral Nerve Block Catheter Treatment Group

Variable	Placebo group: Saline bolus and infusion	Levobupivacaine bolus with saline infusion	Levobupivacaine bolus and infusion	Total
N	78	79	76	233
Age, mean (95% CI)	28 (26, 31)	28 (25, 30)	27 (24, 30)	28 (26, 29)
Female (% within categories)	36 (46%)	28 (35%)	32 (42%)	96 (41%)
Not Caucasian (including African-American, Asian, Hispanic, and from India)	7 (9%)	13 (16%)	7 (9%)	27 (12%)
Smoker	4 (5%)	4 (5%)	9 (12%)	17 (7%)
Body Mass Index, mean (95% CI)	26 (25, 27)	26 (25, 27)	26 (25, 27)	26 (25, 27)
Preop QoR-40 Report of no NVR, n (%)	68 (88%)	65 (83%)	69 (92%)	202 (88%)
Preop QoR-40 Report of perfect sleep-restfulness n (%)	24 (31%)	27 (34%)	26 (35%)	77 (33%)
Tourniquet used, n (%)	41 (53%)	36 (47%)	40 (53%)	117 (50%)
Length of surgery, min (95% CI)	103 (95, 112)	114 (107,122)	111 (103, 119)	110 (105, 114)
Any hydromorphone and/or oxycodone used postoperatively on day of surgery, n (%)	21 (27%)	17 (22%)	13 (17%)	51 (22%)
PONV (in PACU or phase 2 recovery), n (%)	5 (6%)	3 (4%)	2 (3%)	10 (4%)
*Day 1 oxycodone consumption (mg), median (interquartile range)	40 (30, 55)	30 (20, 40)	30 (20, 40)	30 (20, 45)
† Day 1–2 oxycodone consumption (mg), median (interquartile range)	65 (40, 98)	55 (40, 78)	50 (40, 65)	55 (40, 80)
Day 1–3 oxycodone consumption (mg), median (interquartile range)	83 (54, 125)	75 (60, 99)	70 (53, 90)	75 (55, 100)
Day 1–4 oxycodone consumption (mg), median (interquartile range)	93 (60, 136)	90 (70, 110)	80 (64, 110)	90 (65, 120)

Preop: preoperative; QoR: Quality of Recovery 40-item scale

ASA/PS: American Society of Anesthesiologists' Physical Status classification;

95% CI: 95% confidence interval

PONV: postoperative nausea and/or vomiting; PACU: post-anesthesia care unit

NVR: nausea, vomiting, and/or retching, as reported on the Quality of Recovery 40-item Anesthesia Recovery Scale

There were no significant demographic differences among treatment groups except

*P=0.001 and

†P=0.028 by Kruskal-Wallis test.

Table 2

Patient Reponses Addressing Sleep Quality, Difficulty Falling Asleep, and Feeling Rested Preoperatively and on the first 4 Postoperative Days

	Preop baseline			Day 1			Day 2			Day 3			Day 4		
	GS	**DFA**	**FR**	**GS**	**DFA**	**FR**	**GS**	**DFA**	**FR**	**GS**	**DFA**	**FR**	**GS**	**DFA**	**FR**
None of the time (%)	3 (1%)	156 (67%)	2 (<1%)	17 (8%)	115 (51%)	8 (4%)	12 (5%)	121 (54%)	6 (3%)	7 (3%)	131 (58%)	3 (1%)	4 (2%)	139 (65%)	3 (1%)
Some of the time	18 (8%)	54 (23%)	16 (7%)	48 (21%)	75 (34%)	30 (13%)	51 (23%)	65 (29%)	40 (18%)	27 (12%)	72 (32%)	29 (13%)	26 (12%)	55 (26%)	19 (9%)
Usually	31 (13%)	11 (5%)	27 (12%)	42 (19%)	14 (6%)	57 (25%)	35 (16%)	19 (8%)	49 (22%)	31 (14%)	12 (5%)	46 (20%)	30 (14%)	12 (6%)	30 (14%)
Most of the time	80 (34%)	8 (4%)	77 (33%)	79 (35%)	15 (7%)	85 (38%)	76 (34%)	14 (6%)	70 (31%)	84 (38%)	6 (3%)	69 (31%)	73 (34%)	6 (3%)	77 (36%)
All of the time	101 (43%)	2 (<1%)	111 (48%)	39 (17%)	5 (2%)	44 (20%)	51 23%	6 (3%)	60 (27%)	75 (34%)	4 (2%)	78 (35%)	83 (38%)	3 (1%)	86 (40%)
Respondents	231			223			225			224			213		
Patients with Perfect Responses (%)	77 (33%)			19 (9%)			35 (15%)			51 (22%)			60 (26%)		

Preop: preoperative; GS: had a Good Sleep; DFA: Difficulty Falling Asleep; FR: Feeling Rested

“Respondents” indicates the number of study participants per day with complete survey data available to calculate “Perfect Responses”

“Perfect Responses” consist of GS and FR “all of the time,” and DFA “none of the time.”

There were no significant demographic differences between respondents and non-respondents

There were no significant differences among nerve block treatment groups

Table 3

Patient Reponses Addressing Nausea, Vomiting, and Retching Preoperatively and on the first 4 Postoperative Days

	Preop baseline			Day 1			Day 2			Day 3			Day 4		
	N	**V**	**R**	**N**	**V**	**R**	**N**	**V**	**R**	**N**	**V**	**R**	**N**	**V**	**R**
None of the time (%)	207 (90%)	220 (95%)	217 (94%)	174 (78%)	222 (99%)	215 (97%)	160 (71%)	219 (97%)	215 (96%)	173 (77%)	220 (98%)	214 (96%)	166 (77%)	210 (98%)	205 (98%)
Some of the time	21	10	12	44	2	6	51	4	9	36	5	8	40	3	5
Usually	2	0	0	4	0	1	3	1	0	3	0	1	3	1	2
Most of the time	1	1	1	1	0	0	10	0	0	7	0	0	4	1	1
All of the time	0	0	0	0	0	0	1	1	0	3	0	0	2	0	0
Respondents	231			223			225			224			215		
Patients with Any Positive Responses (%)	28 (12%)			53 (24%)			67 (30%)			57 (26%)			52 (24%)		

Preop: preoperative; N: nausea; V: vomiting; R: retching (dry)

There were no significant demographic differences between respondents and non-respondents

There were no significant differences among nerve block treatment groups

Table 4

Treatment Group Differences/Trends in the Daily Incidence of Any Moderate Pain and Any Severe Pain as measured by the QoR-40

	Day 1	Day 2	Day 3	Day 4
Any Moderate Pain Overall	179/223 (80%)	185/223 (83%)	170/224 (76%)	156/215 (73%)
SbSi	64/73 (88%)	62/74 (84%)	57/73 (78%)	56/70 (80%)
LbSi	62/77 (80%)	64/77 (83%)	59/78 (76%)	55/75 (73%)
LbLi	53/73 (73%)	59/72 (82%)	54/73 (74%)	45/70 (64%)
P values	SbSi > LbLi, P=0.023	NS	NS	SbSi > LbLi, P=0.038
Any Severe Pain Overall	68/223 (30%)	845/225 (37%)	74/224 (33%)	60/215 (28%)
SbSi	30/73 (41%)	33/74 (45%)	28/73 (38%)	24/70 (34%)
LbSi	24/77 (31%)	32/78 (41%)	28/78 (36%)	17/75 (23%)
LbLi	14/73 (19%)	19/73 (26%)	18/73 (25%)	19/70 (27%)
P value	SbSi > LbLi, P=0.004 (LbSi > LbLi, P=0.09)	LbSi > LbLi, P=0.05 SbSi > LbLi, P=0.019	NS (SbSi > LbLi, P=0.075)	NS

QoR-40: Quality of Recovery 40-item scale

There were no significant demographic differences between respondents and non-respondents.

SbSi: placebo perineural femoral catheter treatment group that received saline bolus and infusion.

LbSi: perineural femoral catheter treatment group that received levobupivacaine bolus and saline infusion.

LbLi: perineural femoral catheter treatment group that received levobupivacaine bolus and levobupivacaine infusion.

Table 5

Predictors of Perfect Responses addressing Sleep/Restfulness (from Table 3) as reported on the QoR-40 Anesthesia Outcome Survey, using Logistic Regression

Day of Assessment	Day 1	Day 2	Day 3	Day 4
Univariate predictors with P≤0.1	• Perfect Sleep/ Restfulness response baseline • Smoker	• Perfect Sleep/ Restfulness response baseline • Perfect Sleep/ Restfulness response Day 1 • Any NVR on Day 1 • Any Moderate Pain on Day 1 • Lower Quartile of Oxycodone Consumption on Day 1 • LbLi	• Perfect Sleep/ Restfulness response baseline • Perfect Sleep/ Restfulness response Day 1 • Perfect Sleep/ Restfulness response Day 2 • Smoker • Any NVR on Day 2 • Any Moderate Pain on Day 2 • Lower Quartile of Cumulative Oxycodone Consumption on Day 1–2 • LbLi	• Perfect Sleep/ Restfulness response baseline • Perfect Sleep/ Restfulness response Day 1 • Perfect Sleep/ Restfulness response Day 2 • Perfect Sleep/ Restfulness response Day 3 • Female • Smoker • Any Moderate Pain on Day 3 • Any NVR on Day 3 • Lower Quartile of Cumulative Oxycodone Consumption on Day 1–3
Multivariable Predictor 1	**Perfect Baseline Sleep/Restfulness**	**Perfect Baseline Sleep/Restfulness**	**Perfect Sleep/ Restfulness on Day 2**	**Perfect Sleep/ Restfulness on Day 2**
Odds Ratio (95% CI)	3.8 (1.4, 10)	6.3 (2.3, 17)	21 (7.9, 54)	5.3 (1.5, 18)
Significance	<0.001	<0.001	<0.001	<0.001
Multivariable Predictor 2	**None**	**Perfect Sleep/Restfulness on Day 1**	**Any Moderate Pain on Day 2**	**Perfect Sleep/ Restfulness on Day 3**
Odds Ratio(95% CI)		17 (4.0, 72)	0.4 (0.2, 1.1)	13 (5.1, 36)
Significance		<0.001	0.092	<0.001
Multivariable Predictor 3	**None**	**Any Moderate Pain on Day 1**	**None**	**Any Moderate Pain on Day 3**
Odds ratio (95% CI)		0.4 (0.1, 1.0)		0.38 (0.14, 0.98)
Significance		0.05		0.045
Multivariable Predictor 4	**None**	**Any NVR on Day 1**	**None**	**None**
Odds ratio (95% CI)		0.11 (0.01, 0.9)		
Significance		0.043		

Day: postoperative day; CI: confidence interval; NVR: nausea/vomiting/retching

LbLi: perineural femoral catheter treatment group that received levobupivacaine bolus and levobupivacaine infusion

All univariate predictors (other than age, gender, nerve block treatment group, or based on oxycodone consumption) were based on patient responses to the Quality of Recovery 40-item survey. “Baseline” indicates survey response before surgery.

Perfect Sleep/Restfulness indicates “Had a Good Sleep all of the time” and “Feeling Rested all of the time,” and “Difficulty Falling Asleep none of the time” as the responses on the QoR-40 for the stated day.

“Any Moderate Pain,” or “Any NVR” indicated patient responses that were recorded as anything other than “None of the Time.”

Table 6

Predictors of any PONV on the Day of Surgery, or of Daily Reports of NVR, as reported on the QoR-40 Anesthesia Outcome Survey, using Logistic Regression

Day of Assessment	PONV on DOS	NVR Day 1	NVR Day 2	NVR Day 3	NVR Day 4
Univariate predictors with P≤0.1	• Oxycodone or hydromorphone given before discharge home	• Female • PONV on DOS • Baseline NVR	• Female • Lower quartile of oxycodone consumption(days 1–2) • Day 1 NVR • Baseline NVR	• Female • Lower quartile of oxycodone consumption(days 1–3) • Day 2 NVR • Baseline NVR	• Female • Lower quartile of oxycodone consumption(days 1–4) • Day 3 NVR • Baseline NVR
Multivariable Predictor 1	**As above**	**PONV on DOS**	**NVR on Day 1**	**NVR on Day 2**	**NVR on Day 3**
Odds Ratio (95% CI)	3.8 (1.1, 14)	16 (3.1, 81)	14 (6.5, 31)	9.8 (4.8, 20)	14 (6.4, 31)
Significance	0.041	0.001	<0.001	<0.001	<0.001
Multivariable Predictor 2	**None**	**Baseline NVR**	**Lower quartile of cumulative oxycodone consumption**	**Baseline NVR**	**Lower quartile of cumulative oxycodone consumption**
Odds Ratio(95% CI)		3.6 (1.5, 8.8)	0.3 (0.1, 0.8)	3.6 (1.3, 10)	0.3 (0.1, 0.8)
Significance		0.005	0.019	0.012	0.018
Multivariable Predictor 3	**None**	**Female**	**Female**	**None**	**None**
Odds ratio (95% CI)		2.1 (1.1, 4.1)	2.8 (1.4, 5.8)		
Significance		0.03	0.004		

POD: postoperative day; DOS: day of surgery; CI: confidence interval

NVR: patient who reported any nausea, vomiting, and/or retching on the Quality of Recovery 40-item scale during the listed assessment preoperatively (“baseline”) or on POD 1-4