Journal of Pain & Relief
ISSN: 2167-0846

Research Article Open Access

A Proposed Multimodal Pain Control Regimen for Patients Undergoing Post Mastectomy with Reconstruction and Its Effect on Minimizing Narcotic Use and Hospital Length of Stay

Grace Lepis, Ashley Toussaint, Vincent Almagno, Adam Shalek, Alexis Coleman, Ethan Paulin, Manpreet Kohli and Gregory Greco*

Robert Wood Johnson Barnabas Health Monmouth Medical Center, New Jersey, USA

Abstract

Background: There are few studies outlining an adoptable enhanced recovery pathway after mastectomy and reconstruction. This study analyzed a constructed and employed multimodal pain control regimen and the data extrapolated demonstrates how it may influence narcotic use and length of stay in the hospital.

Methods: A retrospective electronic medical record review from 2016 to 2016 under the care of two surgeons from a community hospital included 47 patients.

Results: After implementation of the regimen, average length of stay in the hospital decreased by nearly 10 hours with about 1/3 of the patients having a completely narcotic free hospitalization.

Conclusion: By employing these techniques, adequate pain control is possible, patient satisfaction would increase and length of hospital stay would decrease. Encouraging results of this study propose a regimen that could easily and affordably be adopted amongst other hospitals and surgeons across multiple specialties.

Keywords: Multimodal analgesia, Mastectomy with reconstruction, Postoperative pain control

Introduction

Adequate pain management is an obligation in healthcare, but despite considerable advancements in the regimens designed, the adverse implications of unmanaged pain remain substantially unresolved. Inadequate pain control for patients can decrease the likelihood of desirable outcomes both clinically and psychologically, as well as negatively impact the patients' overall quality of life. As clinicians, it is essential to recognize the deleterious effects that come with inadequate pain control for patients, making the need for improvements in this particular area of patient care imperative. Surgeons have historically prescribed narcotics to their patients with an aim to tackle postoperative pain. Narcotics, although used for many years for analgesia after surgery, unfortunately have the potential to carry very unpleasant side effects for patients. Given the recent opioid epidemic in the United States, there has been a nationwide emphasis on decreasing the amount of narcotic usage across all medical specialties. Although research and advancements in improved practice protocols have documented progressive improvements in the management of acute and postoperative pain, there is very little awareness of the effectiveness of best practices in current literature.

Among women that are diagnosed with breast cancer, approximately 30-40% undergo mastectomy for treatment [1]. Inadequate pain control postoperatively has been shown to be associated with decreased quality of life through impaired sleep and physical function. It has also become one of the most common reasons for post-surgical hospital readmission [2].

Enhanced recovery after surgery (ERAS) pathways for various surgical subspecialties have been successfully implemented through evidence-based practices, with goals to reduce opioid consumption, decrease post-operative nausea and vomiting, as well as decrease the length of hospital stays. There are few studies outlining an adoptable enhanced recovery pathway after mastectomy with immediate reconstruction.

Offodile et al performed a meta-analysis appraisal for the evidence for ERAS pathways in breast reconstruction. A systematic search of Medline, EMBASE, and Cochrane databases was performed to identify reports of ERAS protocols in post-mastectomy breast reconstruction 260 articles were identified and a total of 1191 patients were reviewed. Researchers looked at length of stay (LOS), opioid use, or major complications. ERAS pathways significantly reduce opioid use [Mean difference (MD) = − 183.96, 95% CI −340.27 to 27.64, p = 0.02) and length of stay (MD) = − 1.58, 95% CI − 1.99 to 1.18, p < 0.00001] versus traditional care[3].

One study performed by Kennedy et al had a small patient population undergoing mastectomy with implant-based reconstruction who were treated with perioperative gabapentin, acetaminophen, and NSAIDs; data regarding clinical course and medication requirement was compared to a historical control cohort receiving usual care after mastectomy. The study suggested that patients treated with the proposed ERAS protocol required significantly reduced doses of pain medication over postoperative days 0-2 as well as a significantly shorter mean length of hospital stay (1.3 vs. 2.5 days, p = 0.037)[4].

Chiu et al performed a retrospective study after implementing an evidence-based, multimodal ERAS pathway for all patients undergoing total skin-sparing mastectomy surgery with immediate reconstruction at a single 23-hour stay surgery center. Highlights of the ERAS pathway in this study included: preoperative acetaminophen, gabapentin, and scopolamine; regional anesthesia for the breast (pectoral blocks type 1

***Corresponding author:** Gregory Greco, Robert Wood Johnson Barnabas Health Monmouth Medical Center 300 Second Avenue Long Branch, New Jersey, USA 07740 , Phone : (732) 923-6769, E-mail: plasdoc39@msn.com

Received May 13, 2020; **Accepted** June 24, 2020; **Published** July 01, 2020

Citation: Lepis G, Toussaint A, Almagno V, Shalek A, Coleman A, et al. (2020) A Proposed Multimodal Pain Control Regimen for Patients Undergoing Post Mastectomy with Reconstruction and Its Effect on Minimizing Narcotic Use and Hospital Length of Stay. J Pain Relief 9: 350.

and type 2 or paravertebral block); and intraoperative dexamethasone and ondansetron. This study compared 96 patients who were in the ERAS pathway to a retrospective cohort of 276 patients treated traditionally. Patients in the ERAS group had significantly lower total perioperative opioid consumption compared to the traditional group (mean (SD): 111.4 mg (46.0) vs. 163.8 mg (73.2) oral morphine equivalents, $p < 0.001$). In addition, patients in the ERAS group had a lower incidence of postoperative nausea and vomiting (PONV) (28% vs. 50%, $p < 0.001$), less pain in the recovery room (median [interquartile range (IQR)]: 4 (2,6) in ERAS group vs. 6 (4,7) in traditional group, $p < 0.001$). The difference in the length of stay was not clinically significant between the two groups (median [IQR]: 1144 min (992, 1259) in ERAS group vs. 1188 (1058, 1344) in traditional group, $p = 0.006$) [5].

Due to the recent opioid-abuse epidemic, it has never been more important for clinicians to recognize prescribing patterns and assess where improvements can be afforded. Therefore, it is vital for surgeons to recognize that effective management of acute pain can result in improved patient outcomes and increased patient satisfaction, inspiring them to habitually explore and stay current with evidence-based practices.

As with all surgical subspecialties, there is a desire to standardize and accelerate the postoperative period while maintaining safe outcomes. This study aims to provide valuable insight into alternatives of post-mastectomy pain control and should prompt physicians to recognize the need for multimodal regimens in order to adequately care for patients. Using the data from a singlebreast surgeon and a single plastic surgeon at a community hospital in New Jersey, we take an in-depth look at a particular multimodal pain regimen that they have employed to control pain for their patients over several years. The data extrapolated demonstrates how our experiences using a multimodal pain control regimen may decrease narcotic use amongst patients over time and how adequate pain control can influence a patient's length of stay. The study will provide readers with an adoptable example of a multimodal pain control regimen that a variety of medical specialties could effortlessly adopt into their everyday practice to aid in adequate pain control for their patients while tackling the opioid epidemic head on opioid epidemic head on (Figure 1).

Methods

The study consisted of a retrospective electronic medical record review from 2016 to 2019 of patients 18 years or older at a community hospital in New Jersey who underwent a mastectomy with immediate reconstruction, managed independently by a single breast surgeon (M.K.) and a single plastic surgeon (G.G.).

A total of 47 patients were included in this study. The mastectomies performed on these patients significantly varied from unilateral, bilateral, prophylactic, nipple sparing and skin sparing with or without sentinel lymph node biopsy and/or axillary lymph node dissections. Of these patients included in this study, 34 (72.3%) of these patients underwent mastectomy with direct-to-implant reconstruction, while the other 13 (27.6%) patients underwent mastectomy with multiple stage reconstruction, with the majority using tissue expanders and acellular dermal matrix (Alloderm LifeCell Corporation® or DermaCell Stryker Corporation®).

Patients excluded from the study were those who underwent a same day breast surgery (i.e. excisional biopsy) or mastectomies performed alone without reconstruction. Any patients that underwent an autologous reconstruction were not included in the study.

Once the regimen was initially incorporated into practice, patients were offered similar medications preoperatively, intraoperatively and postoperatively. In the preoperative period, patients were educated and provided with materials about what to expect with their care as well as reviewing expectations regarding postoperative analgesia.

The design and implementation of the regimen utilized in this study has undergone adjustments (i.e. addition of medications, dose changes) throughout the course of this study. Patients were instructed to take gabapentin, 600 mg 2 hours prior to incision time and were ordered to receive it every 12 hours postoperatively, for a total of 3 doses. All patients received SCIP (Surgical Care Improvement Project) preoperative antibiotics.

Intraoperatively, patients received 50 mg of intravenous ketamine (regardless of weight) administered prior to initial incision and 1000 mg of IV acetaminophen was administered 1 hour prior to incision closure. Intercostal nerve blocks using Exparel® liposomal Marcaine were performed by the plastic surgeon. The mixture consisted of 20 cc (266mg) of Exparel®, 30 cc of 0.5% Marcaine and 10 cc of normal saline totaling 60 cc to be dispersed bilaterally. Approximately 2.5 cc was injected in each intercostal space from T2 to T8 and about 8 cc was injected to perform a field block.

Postoperatively, 400mg celecoxib was administered in a post-anesthesia care unit and every 12 hours as needed for pain control. The addition of celecoxib was appended to the regimen later in the study. IV acetaminophen was prescribed every 6 hours as needed for pain control and Valium, 5 mg, prescribed as needed for pain control/muscle spasms every 6 hours. Oxycodone 5mg and 10 mg were prescribed and only administered on an as-needed basis based on the patient's pain score to provide additional pain control. No standing narcotic orders were provided. Patients were discharged home with a prescription for Valium 5mg (10 tablets, to be taken as needed for pain) and Percocet 5-325mg (10 tablets, to be taken as needed for pain). Refills were rare and were considered based on patient need and clinical assessment on outpatient follow-up visits. Over-the-counter pain medications (*i.e.*, acetaminophen, ibuprofen, or other nonsteroidal anti-inflammatory drugs) were allowed at the patient's discretion. Patients were examined postoperatively for complications such as seroma or hematoma formation, erythema, red breast syndrome, and mastectomy flap necrosis and data was collected.

Multiple factors were collected from electronic health records which included the patient's age, race, comorbid conditions, body mass index (BMI), patient's pre-operative breast size, the initial diagnosis and procedure, the breast tissue pathology, the gram weight of the specimens and the pathologic stage. In addition, data was collected regarding the various incisions, location of implant (sub muscular vs. prepectoral), the type of implant, and both the type and size of ADM used.

Information was collected from the electronic health records on narcotic use, hospital length of stay and complications. The records were retrospectively reviewed to study in-hospital narcotic and other non-narcotic medication usage in both the post-anesthesia care unit and postoperatively up until the patient's discharge. The study focused on the initial hospital stay when the index operation was performed, therefore any additional hospitalizations and revisional procedures were not analyzed. The primary outcome studied was narcotic administration during hospitalization analyzed by evaluating narcotic consumption from the patient's arrival in preoperative holding, to the operating room, to the post-anesthesia care unit and on the hospital floor prior to discharge from the hospital. Secondary outcomes included hospital length of stay.

Statistics

Data were reported as mean (standard deviation) for normally distributed continuous variables and as count (percentage) for binary variables as show in (Tables 1 and 2). The Cochrane Armitage trend test was used to assess the changes in post-operative length of stay and proportion of patients who had narcotic free hospital stays. A stepwise logistic regression model with backward selection using the Akaike information criterion was used to identify independent predictors of narcotic free hospital stays amongst patients as shown in Table 3. Associations between variables and narcotic free hospital stays were reported using the beta estimate and standard error. Statistical significance was defined as $p < 0.05$ and all analyses were performed using the Statistical Analysis System (SAS) statistical software package, version 11.1.3 (SAS Institute Inc; Cary NC, USA).

Results

A total of 47 patients were included in the study. All 47 patients underwent surgery during the implementation of the pain control protocol that was adopted. The demographic information of the patients included age, BMI, race and comorbid conditions were included in the model as shown in (Table 1) and there were no statistically significant differences amongst patients in the group. From the population in question, the surgeon performed 87 mastectomies (7 unilateral, 40 bilateral); 34 mastectomy cases underwent immediate single-stage reconstruction with permanent silicone implant and placement of ADM, and 13 cases underwent multi-stage reconstruction with tissue expanders and later placement of permanent implants with or without nipple reconstruction as depicted in (Table 1).

(Table 2) shows postoperative outcomes, including overall complications, length of stay, in-hospital mortality, readmission after 30 days, percent of patients discharged home, and narcotic-free hospital stays. The complications were evaluated between patients, totaling 12 incidences reported respectively. Complications included seroma (with and without intervention), skin-flap necrosis requiring revision, implant exchanges, and one episode of red breast syndrome requiring inpatient care after 30 days of initial hospital admission.

The average length of stay in the hospital amongst all the patients included in the study was 31 hours. As (Figure 2) depicts, there was a dramatic change noted in average length of stay in patients who underwent mastectomy with reconstruction between 2016 and 2019. In 2016, the average length of stay was 38.4 hours, which significantly decreased to an average length of stay of approximately 28.8 hours by 2019.

The possibility of a narcotic-free hospital stay was evaluated. In total, 31.75% of patients in the study had a completely narcotic-free hospital stay. According to their electronic medical record, no narcotics were administered during their stay in the post anesthesia care unit or on the floors up until the time of discharge. (Figure 2) shows the progression of narcotic-free hospital stay from 2016 to 2019. Between the two surgeons, narcotic-free hospital stays in post-mastectomy patients undergoing immediate reconstruction steadily increased from 0% in 2016 to greater than 40% in 2018 and 2019. Factors that were significantly associated with a narcotic-free hospital stay were placement of implants in the prepectoral space (p-value 0.002) and increasing age (p-value 0.026).

There were no patients readmitted to the hospital within 30 days of their initial hospital stay; there were no incidences of in-hospital mortality, and all of the patients included in this study were discharged home on postoperative day 1 or 2.

Between 2017 and 2018 there was a dramatic decrease in hospital length of stay and associated increase in the probability of a patient having a narcotic-free hospitalization. The exact reason remains unclear. Considering only two surgeons were involved with the patient population, it is unlikely there were any deviations from the protocol outside of adjusting preoperative and postoperative medications and dosages. There were no changes noted upon review of electronic medical records that could have made a dramatic difference and all minor adjustments to the regimen were made on a case-to-case basis. It is possible that surgical technique and experience improved over this time period. It is also possible that the patient population examined during this time consisted mostly of opioid-naïve patients which, in a small sample size, could have such dramatic effects. Improved communication with anesthesia or better patient education could also have had these effects on our results.

Variable	Distribution
Age (years)	50 ± 10
BMI (kg/m^2)	25.8 ± 6
Race (n) (%) Caucasian Other	 40 (85) 7 (15)
History of Diabetes Hypertension Hyperlipidemia	 0 (0) 4 (9) 3 (6.3)
Procedure Characteristics	
Single Staged Multi Staged	34 (72) 13 (28)
Laterality Unilateral Bilateral	 7 (15) 40 (85)
Placement of prosthetic Pre-pectoral Sub-muscular	 14 (30) 33 (70)
Prosthetic Tissue expander Permanent implant	 14 (30) 33 (70)
Breast Size (grams) Right Left	 736 ± 599 725 ± 586

Table1: Baseline demographic and clinical characteristics.

Variable	Distribution
Complications (n) (%) Seroma	
Post-op LOS (hours)	31 ± 7
In-hospital mortality (n) (%)	0 (0)
Re-admission (30-days)	
Discharge (n) (%) Home	 47 (100)
Narcotic free hospitalizations (n) (%)	15 (32)

Table 2: Post-operative outcomes.

Variable	beta estimate (S.E)	p value
Age (per 1-yr increase)	0.1 (0.05)	0.026
Weight of L breast (g)	-0.004(0.002)	0.072
Placement of bioprosthetic Pre-pectoral vs. Others	 1.56 (0.51)	 0.002
S.E: Standard Error		

Table 3: Results of a stepwise logistic regression model showing independent predictors of narcotic free hospital stay.

Figure 1: Schematic representation of pain regimen/protocol.

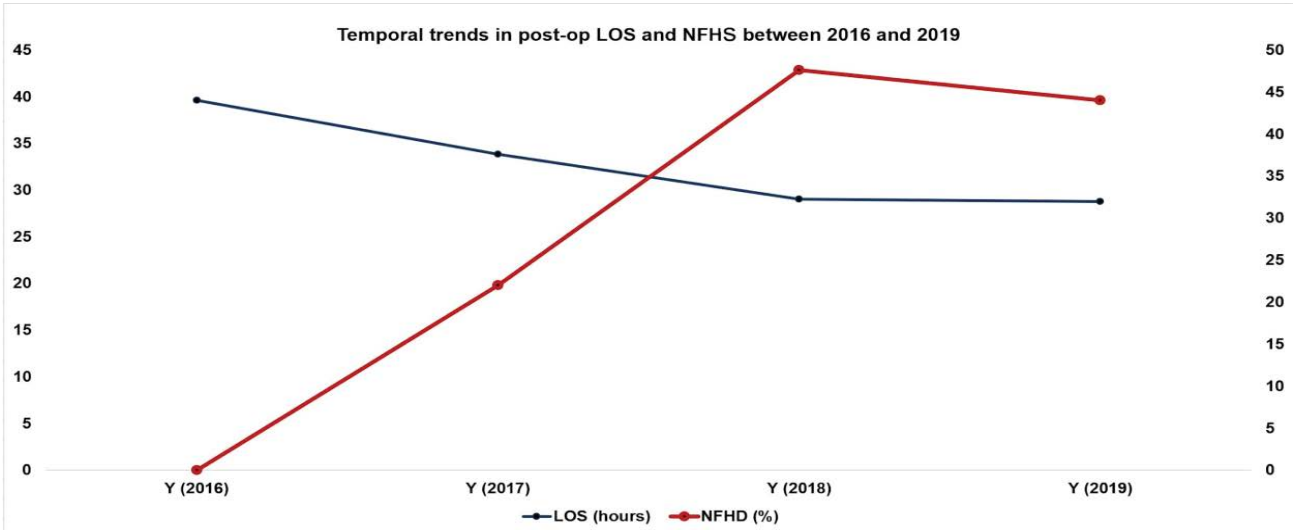

Figure 2: Temporal trends in length of stay and narcotic free hospitalizations.

Discussion

A multimodal pain control regimen for patients undergoing mastectomy with immediate reconstruction was designed and implemented in a community hospital in New Jersey with only two surgeons, and the results across the years were astonishing. From 2016 to 2019, there were dramatic improvements in postoperative analgesia, the possibility of a narcotic-free hospital stays, and shorter length of stay in the hospital. Having reviewed the literature, this particular regimen is similar to other protocols developed for postoperative analgesia after breast or plastic surgery, but what makes this particular ERAS regimen unique is the incorporation of local anesthetic blocks as part of the regimen. Once adopted, this approach could be easily replicated in practice. The authors of this study recognize that it is not scientifically sound to say that the implemented protocol is what led to decreased length of stays in the hospital as well as the possibility of narcotic free stays, but the experience is certainly worth sharing.

Systemic medication administered preoperatively included gabapentin. Gabapentin has specifically been shown to provide effective postoperative analgesia and decrease narcotic consumption post-operatively by binding to the voltage dependent calcium channels. Such interaction blocks the neuronal calcium influx, which decreases excitatory amino acid (glutamate) release [6]. This allows the anti-hyperalgesic actions pre-operatively and decreases postoperative opioid use [7]. Rai et al performed a systematic revision and meta-analysis of randomized controlled trials to evaluate the effects of gabapentin and pregabalin on postoperative pain among patients undergoing breast cancer surgery. They reviewed twelve studies enrolling adult patients undergoing breast cancer surgery who were randomly assigned to preoperative gabapentin or pregabalin versus placebo or active control and assessed acute (≤24 hours) or chronic (≥2 months) pain. They found that gabapentin (mean difference [MD] -1.68 on a 0-10 Numeric Rating Scale (NRS), 95% CI -2.59 to -0.77; minimally important difference is 1 point; relative risk [RR] for mild pain (<4/10) 1.71, 95% CI 1.33-2.02; moderate QoE) and pregabalin (MD -6.71 mg, 95% CI -10.73 to -2.70; low QoE) seemed to reduce opioid consumption in the recovery room and gabapentin (MD -0.52, 95% CI -1.02 to -0.01; RR for mild pain 1.07, 95% CI 1.00-1.13; very low QoE), but not pregabalin (MD -0.38, 95%, CI -0.96 to 0.21; moderate QoE), reduced pain at 24 hours after breast cancer surgery [8].

Ofirmev is used for its analgesic and antipyretic properties and has been proven effective to control post-operative pain and reduce opioid consumption. Celecoxib is a highly selective reversible inhibitor of COX-2 and inhibits the transformation of arachidonic acid to prostaglandin precursors. This creates an analgesic and anti-inflammatory effect.

Ketamine has become part of multimodal postoperative analgesia regimens because of its potential to reduce opioid consumption in postoperative patients. Administration of 50 mg Ketamine, informally termed the "nifty fifty," before surgical incision blocks the NMDA receptors in the midbrain and prevents transmission of impulses to the cortex for interpretation, thus avoiding the "wind- up" phenomenon associated with the pain response cascade [9]. This plays an important role in the development of chronic pain. It also interacts as an agonist at opioid receptors. This allows the medication to be used to control pain, reduce opioid use, nausea, and vomiting after surgery. In 2018, consensus guidelines on the use of intravenous ketamine for acute pain were published from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. These guidelines are based on consensus of experts and offer reasonable guidance, with the proviso that this is an area of great interest and emerging experience [10]. A systematic review and meta-analysis of trials of perioperative IV ketamine in 2011 showed a reduction in total opioid consumption and an increase in the time to first analgesic. Patients having the most painful surgical procedures, including thoracic, upper abdominal, and major orthopedic operations, had improvement in pain scores despite a decrease in opioid consumption [11].

There exists a multitude of non narcotic pain medications and various nerve blocks that can help reduce narcotic use in postsurgical patients. They include local anesthetic infiltration, regional nerve blocks and systemic medications. Local anesthetics can provide immediate postoperative pain control that lasts several hours and-if appropriately administered-can provide excellent pain control to patients. Regional nerve blocks can include the paravertebral nerve block and the pectoral nerve block. The pectoral nerve block aims to block the pectoral

nerves; the intercostobrachial nerve, intercostal nerves III, IV, V and VI as well as the long thoracic nerves [12]. The pectoral nerve block and intercostal nerve blocks have shown to result in decreased pain scores within the perioperative period when compared directly to paravertebral blocs [13]. Our study is unique in that intercostal as well as pectoral blocks were performed. Dissection of the pectoralis muscle and the subsequent stretch placed upon the muscle by implant placement often results in muscle spasm with associated post-reconstruction discomfort. These blocks prove to be imperative as part of a multimodal pain control regimen. Hospital length of stay was noted to decrease dramatically after incorporating the multimodal pain regimen into practice. Although most research evaluates ERAS protocols typically after procedures with longer hospitalizations, the value of implementing our protocol in the limited stay setting lies in improved quality of care and patient experience by reducing narcotic use and maximizing the patient's chance of successful discharge home. In light of the current opioid epidemic, it is imperative that we continue to embrace narcotic-sparing practices, particularly if patient outcomes are similar or improved in the acute postoperative setting.

Limitations

Various limitations were noted while conducting this study, including a limited sample size, the potential for unknown, confounding individual patient variables, variations in intraoperative anesthesia techniques, uniform administration of intercostal nerve blocks, and varying approaches to postoperative care from ancillary staff uneducated about alternative modes of pain management.

The purpose of the study was to focus on how patient outcomes in a specific patient population operated upon by a specific breast surgeon and a specific plastic surgeon have changed over several years. The breast surgeon involved in the study initiated practice in 2015, therefore there were no patients to consider for a traditional pregroup or comparison group, unless other breast surgeons were incorporated into the study.

This study included a small sample size of 47 patients, at a single institution, under the exclusive care of the aforementioned two surgeons. To alleviate this, a retrospective study of patient outcomes, involving several institutions whom also utilize multimodal pain regimens could be performed.

In order to optimize the study, patients with a known history of substance abuse, a diagnosis of chronic pain, or patients actively taking prescription opioids were excluded. Unless identified pre-operatively during routine history-taking, the physicians involved made no specific attempts to obtain information about all patients' previous opioid history, particularly regarding naive status versus chronic usage. Knowing this information may have added power to the study. Although the risk of reporting bias and recall bias exists with patient reported information, perhaps a screening questionnaire or greater detailed patient history could have been obtained to add power to this portion of the study.

Intraoperative medications via direct administration from the anesthesia care provider was not studied. It is understood that anesthesia technique can be variable and in turn influence postoperative pain experience. Intercostal nerve blocks were performed in the same fashion on all patients in the study. A comparison between patients who received the block and who did not would aid in the validity of the study, however this did not occur within our patient population. A prospective trial focusing on intercostal nerve blocks alone as a factor in postoperative pain control, may provide insight to the benefits of nerve blocks in mastectomy patients undergoing reconstruction.

As surgeons, changes to improve patient care should always be on the forefront of our minds and the driving force behind the care we render. Since the implementation of the protocol, there were additions to the postoperative medications prescribed and changes to the medications utilized. The authors and clinicians involved with this paper recognize that effective management of acute pain requires habitual exploration, education and safe utilization of current evidence-based practices. Research is currently underway determining the effects of the individual medications on the patient's postoperative analgesia within our practice. Information on postoperative nausea and vomiting will be collected and studied, as this is an element of the postoperative patient experience that has historically been impacted by opioid use. Additionally, we plan to shift focus onto quality of care metrics, such as patient satisfaction, quality of life measures, post-discharge opioid consumption and instance of development of chronic post-surgical pain.

As we transition to focus on quality care metrics, it is vital that postoperative nursing care is involved in executing techniques to minimize the use of narcotics. With strong reliance on the patient pain scale, it is imperative to provide appropriate education on the multimodal approach to pain management to those rendering postoperative care to this patient population. Alternative pain management options must be openly discussed with the patient, anesthesia providers, surgical team members and nursing staff as means of health promotion and optimal care for patients.

Conclusion

This study highlights the findings of a novel multimodal ERAS protocol employed by two surgeons at a single institution performing mastectomy with immediate implant-based reconstruction. The emphasis on multimodal analgesia with intercostal nerve blocks potentially influenced a reduction in narcotic consumption and in-hospital length of stay, suggesting adoption of this regimen or similar multimodal-based analgesics could result in overall higher patient satisfaction. The encouraging results of this study propose a regimen that could easily and affordably be adopted by other hospitals and surgeons across multiple subspecialties. Further studies are needed to determine which interventions contribute most to the quality of analgesia in the perioperative period. This can be achieved by assessing patient satisfaction, quality of life measures, post-discharge opioid consumption, or the development of chronic post-surgical pain.

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