Original Article

Reduction in opioid consumption, pain, and antiemetic use following use of an enhanced recovery after surgery protocol for breast cancer patients undergoing mastectomy

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Background: Patients undergoing mastectomy, both with and without immediate reconstruction, frequently experience postoperative pain, nausea and vomiting. Enhanced recovery after surgery protocols have been designed in part to minimize these postoperative complications. The aim of this study was to test an enhanced recovery after surgery protocol specifically designed to effectively manage postoperative pain, nausea and vomiting among women undergoing mastectomy.

Methods: A retrospective cohort analysis was designed to examine the difference between patients who experienced traditional recovery after surgery (TRAS) and patients who experienced enhanced recovery after surgery regarding pain, opioid consumption, and antiemetic administration. The sample (N=204) included women undergoing mastectomy both with (n=102) and without (n=102) immediate reconstruction. No significant differences were found between these groups. Similarly, no significant differences were found related to the following sample characteristics; age, body mass index (BMI), opioid use, and pain scores on admission.

Results: Significant differences were found between groups related to pain on day of surgery (P<0.001), and postoperative day one (P<0.001). In addition, significant differences were found on both days (day of surgery P<0.001 and postoperative day one P<0.001) for opioid consumption and antiemetic administration (day of surgery P<0.009 and postoperative day one P<0.005). Mean, standard deviation, and frequency differences in the variables range from moderate to strong.

Conclusions: Results of this study among women with breast cancer undergoing mastectomy with and without reconstruction suggest that this enhanced recovery after surgery protocol can improve pain management, reduce opioid consumption, and diminish anti-emetic intake.

Keywords: Enhanced recovery after surgery; mastectomy; breast cancer; PECS blocks; acute pain management

Received: 30 September 2020; Accepted: 21 February 2021; Published: 30 June 2021.

doi: 10.21037/abs-20-118

View this article at: http://dx.doi.org/10.21037/abs-20-118

Introduction

Acute surgical pain and postoperative nausea and vomiting (PONV) are frequently reported in patients undergoing breast cancer surgery. Management of these symptoms continues to improve as health care providers initiate new approaches. In the 1990s, Professor Henrik Kehlet introduced the concept of Enhanced Recovery After Surgery (ERAS) protocol to alter the physiological and psychological responses to surgery (1). ERAS protocols have been shown to cause a reduction in complications and shorten hospital stay while improving cardiopulmonary function, enhancing the return of bowel function, and allowing for earlier return to normal activities (2,3). An evidence-based ERAS protocol designed to minimize postoperative pain and PONV among patients undergoing mastectomy with or without immediate reconstruction was tested in a 393-bed Magnet re-designated community hospital. This protocol was developed by a multidisciplinary team that included surgeons, certified registered nurse anesthetists, anesthesiologists, pharmacists, and nursing staff. It included the key principles of ERAS protocols: preoperative patient education, the use of a non-opioid multimodal approach for pain, a multimodal prophylactic approach to PONV management, intraoperative ultrasound-guided pectoral nerve blocks (PECs), and an opioid-sparing anesthetic. Traditional recovery after surgery (TRAS) differs in that it utilizes a conventional approach to anesthetic management, pain, and nausea reduction that relies heavily on opioids while often limiting antiemetic agents to a single modality.

Inadequate pain management following surgery is associated with reduced quality of life, impaired physical function, and extended recovery time (4). A multimodal approach to pain and antiemetic management has been shown to reduce the length of hospital stay and postoperative opioid consumption in patients undergoing mastectomy with immediate reconstruction (5). Multimodal analgesia offers many benefits such as reduced intensity of pain, utilization of postoperative opioids, and adverse events related to opioid use (4). Members of the American Society of Breast Surgeons agree that an ERAS protocol that includes multimodal analgesia and regional anesthesia should be considered a positive approach to surgical care (6). In addition to the management of pain, this ERAS protocol includes a multimodal prophylactic approach to PONV. Evidence suggests that patients included in an ERAS protocol following mastectomy demonstrate a lower incidence of PONV, as measured by antiemetic medication utilization (7). The aim of this study was to compare postoperative pain scores, opioid consumption, and antiemetic administration among women undergoing mastectomy with and without reconstruction who received either TRAS or ERAS. This study differs from prior research in that PECS blocks were utilized for all ERAS participants. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/abs-20-118).

Methods

Study design

A retrospective cohort analysis was used to compare variables of interest between a group of patients undergoing mastectomy who experienced TRAS and a group that experienced ERAS both with and without reconstruction. A sequential chart review was conducted over two years. Group assignment (TRAS and ERAS) was determined by date of surgery. To ensure consistency of care for participants in each group, only patients of one surgeon, who prescribed the ERAS protocol to all of his patients after the protocol was adopted by the multidisciplinary team, were included. All patients undergoing mastectomy surgery were included in this study. All of the patients in this study were female. Data were collected to examine differences in three variables: pain, opioid consumption, and antiemetic use. An a priori power analysis was performed for sample size estimation. With an effect size of 0.5, an alpha level of 0.05, and a power of 0.8, the projected sample size needed was an N of 204 (TRAS 51 with reconstruction, 51 without and ERAS 51 with reconstruction, 51 without). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board at Baptist Health Lexington, Lexington, Kentucky (No.: BHL-16-1375) and individual consent for this retrospective analysis was waived.

Sample

Clinical and demographic information collected were: age, body mass index (BMI), opioid use upon admission (yes/no), pain score on admission (visual analog scale), and type of surgery (unilateral or bilateral mastectomy, with/without immediate reconstruction). Data analysis revealed no significant differences related to these sample characteristics between groups (*Table 1*).

Table 1 Participant characteristics

Characteristics	Traditional recovery	Enhanced recovery	P value
Total patients	102	102	–
Age (years)	58.2±13.4	55.3±14	0.13
BMI	29.7±6.4	28.9±5.9	0.34
Opioid use upon admission			0.31
No	96 (94%)	99 (97%)	
Yes	6 (6%)	3 (3%)	
Mastectomy			0.62
Unilateral	26 (25%)	23 (22%)	
Bilateral	76 (75%)	79 (78%)	
Pain score on admission	0.38±1.2	0.39±1.6	0.94

The data are reported as mean ± standard deviation or n (%).

ERAS protocol

The protocol developed for this population consists of three phases: preoperative, intraoperative, and postoperative. The preoperative phase addresses patient and family education, and non-opioid medications to be given on the day of surgery. During the intraoperative phase, an opioid-sparing anesthetic that includes regional anesthesia (PECS Blocks), and a multimodal prophylactic antiemetic regimen were administered to patients. Notable characteristics of the postoperative phase include scheduled non-opioid medications for pain management, early mobilization, early nutrition and discharge planning related to pain management. *Table 2* provides a detailed description of the protocol.

Ultrasound-guided pectoral nerve blocks (PECs)

The utilization of regional anesthesia in ERAS protocols allows for immediate postoperative pain control and reduces the amount of general anesthetic agents and opioids required in the intraoperative phase of care. The ability to minimize these pharmacologic agents intraoperatively plays a role in the reduction of PONV. Although several regional anesthetic techniques have been described in the anesthesia literature for breast surgery, this ERAS protocol utilized PECS blocks (8). PECS blocks are a novel fascial plane block first introduced by Blanco in 2011 (9). For this study, the block was performed with ultrasound-guidance immediately after the induction of general anesthesia. The PECS block features two separate injections, PECS I and PECS II. PECS I targets the interfacial planes between the pectoralis major and the pectoralis minor muscles at the fourth rib level. The PECS II injection occurs between the serratus anterior muscle and pectoralis minor muscle at the same rib level. Anatomically, the block provides analgesia of the pectoral muscles and the sensory dermatomes T2-T6, thus targeting the whole breast and axilla. This study utilized 0.25% bupivacaine, preservative-free dexamethasone 2 mg, and buprenorphine 300 mcg for all PECS block injections. The PECS I injection received 10 mL, while the PECS II injection received 20 mL. In bilateral mastectomy patients, the injections were repeated on both sides unless the patient was less than 65 kg, which required the dilution of the bupivacaine to avoid exceeding the maximum allowable dose.

Statistical analysis

Statistical analyses were performed using SPSS version 26. Differences in demographic and clinical variables were analyzed using independent sample *t*-tests for age and BMI. Chi-square analysis was used for chronic opioid use in order to detect differences between the two groups. *T*-test and chi square (χ^2) analyses were used on the three variables of interest: pain, opioid consumption, and additional antiemetic use.

Table 2 Current enhanced recovery after surgery protocol at Baptist for breast cancer

Phases	Protocol	Details
Phase 1: preoperative	Patient and family education during pre-admission testing	
	Preoperative medication	
		Acetaminophen 1,000 mg, oral
		Celecoxib 200 mg, oral
		Pregabalin 75 mg, oral
		Scopolamine patch 1.5 mg transdermal
Phase 2: intraoperative	Multimodal analgesia	General anesthesia
		Pectoral nerve blocks after induction of anesthesia
		Pectoral nerve block I: 10 mL
		Pectoral nerve block II: 20 mL
		Avoid/minimize opioids
	Nausea/vomiting prophylaxis	Dexamethasone
		Propofol infusion
		Ondansetron
	Minimize excess fluid administration	
	Normothermia	
	Normoglycemia	
Phase 3: postoperative	Early nutrition—advance diet as tolerated day of surgery	
	Early mobilization	Walking 3 times per day
		Up in chair for all meals
	Multimodal analgesia	Acetaminophen 1,000 mg oral, every 6 hours
		Celecoxib 200 mg oral, twice per day
		Carisoprodol or cyclobenzaprine oral, every 8 hours, as needed for muscle spasm
		Tramadol 50 mg every 6 hours as needed for pain ≤4
		Oxycodone 5–10 mg oral, every 4 hours as needed for pain >5
		Hydromorphone intravenous 0.3–0.5 mg every two hours as needed for pain >7
	Nausea/vomiting treatment	Ondansetron 4 mg IV every 6 hours as needed
	Minimize excess fluid administration	
	Defined discharge criteria and patient education	Acetaminophen 1,000 mg every 8 hours for 96 hours
		Physician choice over the counter non-steroidal anti-inflammatory drug for 96 hours
		Oxycodone 5 mg every 6 hours as needed
		Opioid prescribing reduced to 12 pills

Table 3 Mean pain scores

Day	Traditional recovery		Enhanced recovery		P value
	Mean	SD	Mean	SD	
Day of surgery	3.45	1.28	2.07	1.28	<0.001
Post-operative day 1	2.8	1.76	1.6	1.7	<0.001

Table 4 Total morphine equivalents administered

Day	Traditional recovery		Enhanced recovery		
	Mean	SD	Mean	SD	P value
Day of surgery	53.9	30.3	24.2	23.7	<0.001
Post-operative day 1	28	23.5	8.1	11.5	<0.001

Table 5 Additional anti-emetic administered

Day	Recovery group				χ^2 value	P value
	Traditional recovery		Enhanced recovery			
	Yes	No	Yes	No		
Day of surgery	46 (45%)	56 (55%)	28 (27%)	74 (73%)	6.8	0.009
Post-operative day 1	16 (16%)	86 (84%)	4 (4%)	98 (96%)	7.98	0.005

Results

Four groups of participants (N=204) were identified from the charts TRAS (51 with reconstruction, 51 without reconstruction) and ERAS (51 with reconstruction, 51 without reconstruction). There were no significant differences between the TRAS and ERAS groups in relation to age, BMI, chronic opioid use, pain score on admission, and type of mastectomy performed (unilateral or bilateral) (*Table 1*).

In this study, mean pain scores were recorded for the day of surgery and postoperative day one. Statistically significant differences in mean pain scores were noted between the TRAS and ERAS groups on both the day of surgery (P<0.001) and postoperative day one (P≤0.001) (*Table 3*). Opioids administered throughout the day of surgery and postoperative day one were recorded. Data using morphine equivalents were analyzed and were significantly different (P<0.001) (*Table 4*). Postoperative nausea was measured as the need for additional antiemetic medication on both the day of surgery and postoperative day one. Similarly, significant findings in additional antiemetic use were shown for both days (day of surgery P=0.009, postoperative day 1, P=0.005) (*Table 5*).

Analyses of data on the three variables of interest between TRAS and ERAS groups with and without reconstruction were also conducted. Findings were similar to analyses conducted on the total group (*Tables 6*,*7*).

Discussion

There has been a radical shift in the surgical care of patients following the implementation of ERAS protocols. Multiple protocols have been developed and used by healthcare providers in the care of colorectal, vascular, thoracic, gynecologic, urologic, orthopedic, and breast cancer patients. In relation to mastectomies associated with breast cancer, findings to date suggest that protocols that include comprehensive preoperative counseling of patients and multimodal pain management can lead to decreased opioid analgesia and an improvement in the treatment of pain (10). Findings related to the three variables examined in this study, pain scores, opioid consumption and use of additional antiemetic medication to reduce nausea, support prior

Table 6 Mean pain scores and opioid consumption by group

Day	Surgery type and recovery group					
	With reconstruction			Without reconstruction		
	Traditional recovery	Enhanced recovery	P value	Traditional recovery	Enhanced recovery	P value
Mean pain Score						
Day of surgery						
Mean	3.75	2.25		3.15	1.9	
SD	1.25	1.7	<0.001	1.25	1.8	<0.001
Post-operative day 1						
Mean	3.45	1.6		2.1	1.21	
SD	1.6	1.8	<0.001	1.67	1.6	0.008
Total morphine equivalent mg						
Day of surgery						
Mean	49.4	21.8		58.3	26.7	
SD	25.9	23.3	<0.001	34	24	<0.001
Post-operative day 1						
Mean	35.1	11.5		20.8	4.7	
SD	25	13.6	<0.001	19.8	7.7	<0.001

Table 7 Additional anti-emetic administered by group

Anti-emetic administered	With reconstruction				Without reconstruction			
	Traditional recovery	Enhanced recovery	χ^2 value	P value	Traditional recovery	Enhanced recovery	χ^2 value	P value
Day of surgery								
Yes	25 (49%)	18 (35%)			21 (41%)	10 (20%)		
No	26 (51%)	33 (65%)	1.97	0.16	30 (59%)	41 (80%)	5.6	0.018
Post-operative day 1								
Yes	9 (18%)	3 (6%)			7 (14%)	1 (2%)		
No	42 (82%)	48 (94%)	3.4	‡	44 (86%)	50 (98%)	4.9	‡

‡, expected cell count too small for chi-square analysis.

research.

Results of this study showed a decrease in both pain scores and opioid consumption among patients undergoing mastectomy with and without reconstruction who experienced ERAS. Separate analyses of both reconstruction and no reconstruction groups showed little difference from the total sample. While the difference in mean pain scores for both day of surgery and post-operative day one was moderate (<2) a definite trend is apparent regarding a decrease in pain scores for the ERAS group. A strong clinically meaningful difference was found regarding opioid consumption. Given that patients with cancer undergoing curative-intent therapies are at increased risk of developing opioid misuse and dependency effective pain management minimizing the use of opioids is essential (11).

In relation to antiemetic use to treat PONV, differences

were also found between groups with participants in the ERAS group taking fewer doses of antiemetics on the day of surgery and postoperative day one. Studies have shown that the incidence of PONV can be as high as 80% following mastectomy (4). Additionally, PONV is associated with longer stays in the post-anesthesia care unit, longer hospital stays, and an increase in health care costs (12). The inclusion of multimodal prophylactic antiemetics in this ERAS protocol produced a significant difference in our patient population.

In addition to approaches to care included in ERAS, a consistent approach to patient care is also a strength of these protocols. For example, a cancer diagnosis carries inherent psychosocial distress and involves multiple invasive and surgical procedures as well as ongoing adjuvant treatment under the care of a multidisciplinary team. Based on the findings of this study it appears that consistent use of a protocol can provide care that limits the use of opioids for pain while care that is not carefully directed may lead to an increased number of opioid prescriptions per patient.

In summary, results of this study provide evidence that use of this ERAS protocol can improve the management of pain, reduce opioid use, and diminish antiemetic intake in patients with breast cancer undergoing mastectomy with and without reconstruction. Recommendations include use of the ERAS protocol for both patients who undergo mastectomy with reconstruction and without reconstruction. In addition, the value of a consistent approach to care outlined by ERAS is strongly supported. Limitations of the study include: (I) data reflect participants given care at one community hospital and (II) patients at this hospital are, in general middle class and insured. Future research using multiple sites is suggested.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/abs-20-118

Data Sharing Statement: Available at http://dx.doi.org/10.21037/abs-20-118

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/abs-20-118). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional review board at Baptist Health Lexington, Lexington, Kentucky (No.: BHL-16-1375) and individual consent for this retrospective analysis was waived.

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doi: 10.21037/abs-20-118
Cite this article as: Abou-Jaoude W, Edwards JM 3rd, Yackzan SG, Stanifer S, Monroe M, Dollar SD, Self B, Shearin H, Young TJ. Reduction in opioid consumption, pain, and antiemetic use following use of an enhanced recovery after surgery protocol for breast cancer patients undergoing mastectomy. Ann Breast Surg 2021;5:15.

