Hite *et al. J Unexplored Med Data* 2019;4:9
DOI: 10.20517/2572-8180.2018.003

Journal of Unexplored Medical Data

Review

Open Access

Narcotics and breast surgery: a review of current literature

Melissa Hite, Nancy Klauber-DeMore, Andrea M. Abbott

Division of Surgical Oncology, Medical University of South Carolina, Charleston, SC 29425, USA.

Correspondence to: Dr. Andrea M. Abbott, Division of Surgical Oncology, Medical University of South Carolina, 114 Doughty Street Room 237, MSC 295, Charleston, SC 29425, USA. E-mail: abbottan@musc.edu

How to cite this article: Hite M, Klauber-DeMore N, Abbott AM. Narcotics and breast surgery: a review of current literature. *J Unexplored Med Data* 2019;4:9. http://dx.doi.org/10.20517/2572-8180.2018.003

Received: 31 Dec 2018 **First Decision**: 18 Jul 2019 **Revised**: 24 Sep 2019 **Accepted**: 7 Nov 2019 **Published**: 18 Nov 2019

Science Editor: Kandace McGuire **Copy Editor**: Cai-Hong Wang **Production Editor**: Jing Yu

Abstract

Opioid consumption in the United States is the highest of all nations, with 42,000 people dying from opioid overdose in 2016. Patients with breast cancer undergoing curative-intent surgery are particularly vulnerable to developing persistent opioid use. It is anticipated that postoperatively nearly all of these women will receive prescription pain medication and that 20%-50% of patients will go on to develop acute and chronic pain after breast cancer surgery. In this review, we aim to better understand opioid use and ongoing efforts to reduce opioid abuse in breast cancer surgery patients.

Keywords: Breast cancer, opioids, narcotic addiction, enhanced recovery after surgery protocol

INTRODUCTION

The United States population consumes the highest total number of opioids in the world[1]. Abuse of opioid pain medications is estimated to affect over 12 million Americans, and prescription opioids contribute to more overdose deaths than cocaine and heroin combined[1,2]. In 2016, 42,000 people died from opioid overdose in the United States with nearly 530 deaths reported every week[3,4]. Opioids are linked with many adverse health effects including increased risk of falls, fractures, respiratory distress, and bowel obstruction. Opioid abuse, especially as a result of prescription narcotics, is becoming one of the most widely researched and published health issues in the United States. As of 2014, drug overdose has become the leading cause of accidental death in the United States, with 40% of those deaths being attributed to physician prescribed pain reliever overdose[5].

As a result of the increasing incidence of prescription related opioid overdoses, new studies are investigating the role of physicians in resolving this epidemic[6]. Patients with cancer undergoing curative-intent surgery are particularly vulnerable to developing persistent opioid use[7]. Studies suggest that physicians underestimate the susceptibility of cancer patients to opioid dependence[1]. Breast cancer affects 12% of women born in North America. It is currently the most commonly diagnosed cancer among women with an estimated 266,000 cases being diagnosed in 2018[8]. Surgical resection remains part of the treatment regimen and standard of care for women with stage 0-III disease. It is anticipated that postoperatively nearly all of these women will receive prescription pain medication and that 20%-50% of patients will go on to develop acute and chronic pain after breast cancer surgery[9]. In this review, we aim to better understand opioid use and ongoing efforts to reduce opioid abuse in breast cancer surgery patients.

A literature review was performed using PubMed and the search terms: opioids and breast surgery, breast cancer surgery and opioids, breast surgery and opioid crisis, breast surgery and narcotics, breast cancer surgery and narcotics, and breast cancer and opioids. Twelve articles and three websites are included in the review. Studies that evaluated current prescribing practices and evaluated strategies to reduce perioperative narcotic use are included in this review. Alternative medicine strategies such as acupuncture, aromatherapy, meditation, *etc*., as methods of reducing postoperative pain, are not included.

OPIOID USE

Persistent opioid use and overprescribing of opioids is well studied within the surgical oncology patient population[10]. In a study by Lee *et al.*[11], the authors aimed to understand the risk of developing new persistent opioid use after curative-intent cancer surgery. By reviewing insurance claims from multiple databases, they were able to identify 68,463 cancer patients undergoing curative-intent surgery who filled postoperative opioid prescriptions. Of those patients, 10.4% of the opioid naïve patients developed persistent opioid use, defined as continued filling of high dose daily prescriptions one year out from surgery. They were also able to identify adjuvant chemotherapy as an associated risk factor for persistent opioid use[11]. In a separate study by Marcusa *et al.*[1], characteristics and long-term opioid use in initially opioid-naïve patients undergoing mastectomy followed by immediate reconstruction were evaluated. They found that 90% of the patients filled their opioid prescriptions and 10% were filling opioid prescriptions three months following surgery[1]. In this study, they were able to identify patient and surgical factors associated with increased filling of opioid prescriptions including depression, anxiety and those undergoing bilateral reconstruction and repair by prosthesis compared to those undergoing autologous pedicle reconstruction or free tissue transfer. They found, consistent with prior studies, that 80% of patients filled opioid prescriptions after low risk surgical procedures and, regardless of major *vs*. minor procedure, 5%-15% of the opioid-naïve patients continued to fill opioid prescriptions and 10% of these patients filled them for over four months after surgery[1]. Studies have shown that patients using opioids for longer than 90 days are likely to still be using opioids five years later[1].

PERI OPERATIVE PAIN MANAGEMENT

Several efforts have been made to optimize pain control in the perioperative period while decreasing the number of opioids prescribed. Hart *et al.*[10] performed a unique analysis of opioids, pain control, and patient satisfaction following ambulatory breast surgery, including breast reduction and secondary breast reconstruction (implant exchange, capsulectomy/capsulotomy, fat grafting, scar revision, nipple reconstruction and/or combination of procedures). They found clear evidence of opioid over-prescribing for this patient population[10]. To evaluate opioid prescribing habits, patients were surveyed on pre- and postoperative narcotic use, pain level and satisfaction with pain control. The authors reported that there were over 1500 unused tablets for the entire cohort by postoperative Day 30. Interestingly, there was no significant difference in average pain scores or interference with enjoyment of activity reported between

those patients who did or did not take pain medication. They did find a difference between breast reduction and breast reconstruction and narcotic use. Patients undergoing breast reduction stopped all narcotics by postoperative Day 30, whereas 7.1% of patients undergoing secondary breast reconstruction continued to use narcotics beyond postoperative Day 30. This supports the data that suggest breast cancer patients are at increased risk of chronic opioid use, perhaps due to patient risk factors such as confounding anxiety and/or depression often associated with the diagnosis of breast cancer[1,10]. The authors warned physicians to be cognizant of patient factors, such as a new cancer diagnosis, that put patients at higher risk of opioid dependence[10].

In a Canadian prospective, randomized controlled study by Mitchell *et al.*[6], the researchers aimed to compare Tylenol 3 (T3: acetaminophen, codeine, caffeine) to acetaminophen and ibuprofen combination (AcIBU) for pain management after outpatient general surgery procedures. In this study, they found that AcIBU for postoperative pain control after outpatient breast surgery was at least as effective as T3. Study outcomes included pain intensity, recorded four times a day, pain relief with analgesic, days until freedom from pain, adverse effects, discontinuation of a drug as a result of adverse effects, and patient satisfaction. Importantly, 92% of AcIBU patients were satisfied with pain control compared to 89% of T3 patients, and there was no significant difference in average pain intensity over seven days postoperatively. They found that the AcIBU combination did not worsen any secondary outcomes and was associated with fewer adverse side effects, such as nausea, vomiting, decreased GI motility, urinary retention, pruritus, bradycardia, and altered consciousness[6].

Chronic neuropathic pain can be a common problem after surgery, especially in the breast cancer surgery population and those undergoing axillary lymph node dissections. A meta-analysis by Jiang *et al.*[12] aimed to determine the effect of gabapentin on pain control after breast surgery. This review included nine randomized controlled trials that studied women undergoing breast cancer surgery who were randomized to placebo *vs.* gabapentin. Outcomes included postoperative pain control, total morphine consumption, incidence of nausea and chronic pain. Gabapentin was shown to positively impact all outcomes studied. They also found high dose gabapentin (> 900 mg/day) to be more effective than low dose gabapentin (< 900 mg/day), although they did not conclude an optimal dose for breast cancer surgery. There was significant heterogeneity in pain score outcomes, which they partly contributed to patients undergoing axillary lymph node dissection and the likelihood of more chronic pain development after surgery, which gabapentin is thought to have less of an effect on treatment. They concluded that preoperative use of gabapentin was successful in reducing acute postoperative pain and chronic pain incidence, but encouraged future studies to understand its effect when used postoperatively[12].

THE ROLE OF REGIONAL ANESTHESIA IN BREAST SURGERY CASES

In addition to non-narcotic multi-modals, the use of regional anesthesia to control pain in the perioperative period is also being explored. It is known that injuries to muscle and nerves during breast surgery in the acute postoperative period and more severe acute postoperative pain are risk factors for chronic pain[13,14]. A randomized study by Karmakar *et al.*[15] assessed the development of chronic pain after modified radical mastectomy in patients who received thoracic paravertebral block (TPVB) *vs.* placebo and found that patients who received the TPVB exhibited fewer symptoms and signs of chronic pain[15]. FitzGerald *et al.*[16] noted the significance of regional anesthesia as an important adjunct to perioperative care of breast surgery patients. They stated that the complex innervation of the breast provides multiple neural target and interfacial planes through which the delivery of regional anesthesia can benefit the patient in the postoperative setting. Regional blocks for breast surgery can include thoracic paravertebral, fascial plane, retrolaminar and mid-point transverse process to pleura blocks[16] and there are several studies which suggest that paravertebral blocks provide adequate anesthesia while decreasing the use of intraoperative and postoperative opiate

use[17]. New techniques, such as fascial plane blocks and paravertebral nerve blocks, offer comparable analgesia with lower risk of complications, thereby superseding the traditional thoracic epidurals, while the use of ultrasound guidance has improved efficacy and safety of these blocks[16]. The use of regional blocks as an adjunct to general anesthesia, the type of medication used in the block, and even the use of blocks as an alternative to general anesthesia are all topics of ongoing research. Several studies have found that the addition of regional anesthesia can provide a decrease in the use of postoperative narcotics, may decrease postoperative nausea and vomiting, is associated with fewer postoperative pulmonary complications and is associated with faster recovery times[17,18].

Thoracic paravertebral anesthesia (TPVA) is one of the most well-studied methods of regional anesthesia for patients undergoing cancer surgery. Studies have found that the use of TPVA in addition to general anesthesia for breast surgery provides superior pain relief when compared to general anesthesia alone[15,19,20]. There are further studies looking at the composition of regional anesthesia for achieving optimal pain control. In a randomized study of 72 breast cancer patients undergoing surgery with general anesthesia by Jin *et al.*[21], 36 patients received TPVA using the combination of bupivacaine and dexmedetomidine compared to TPVA with bupivacaine alone. They found that patients receiving combination therapy had a longer time to initial postoperative administration of analgesia ($P = 0.04$) and less tramadol consumption ($P = 0.04$) compared to bupivacaine alone. This suggests that the addition of dexmedetomidine to the TPVA with bupivicaine had a positive effect on anesthesia as well as a similar safety profile in breast cancer patients[21]. While TPVB is the gold standard for regional anesthesia technique for breast surgery, several studies investigated the use of the pectoral nerve block as less invasive with less complications compared to other procedures. In a randomized controlled trial by Wahba and Kamal, they compared traditional paravertebral block to pectoral nerve block and found that, among patients undergoing modified radical mastectomy, those who received pectoral block had less morphine consumption and lower intensity of pain in the first 12 h compared to patients who received paravertebral block[22]. Moon *et al.*[13] presented a case in which a pectoral nerve block was used in a patient who underwent monitored anesthesia care, thereby avoiding complications related to general anesthesia. The advantages of the pectoral block include no risk of sympathectomy and less restrictions on use of anticoagulants with studies showing a reduced postoperative morphine consumption in the first 24 h and lower pain scores in the first 12 h in the pectoral block group compared to TPVB in modified radical mastectomy. They found the pectoral block to be a safe and useful alternative for outpatient surgery as well as for shortening hospital stay and improving bed rotation rate[13]. Bashandy and Abbas similarly found that the combination of a pectoral nerve block and general anesthesia was superior to general anesthesia alone while FitzGerald *et al.*[16] agreed with the use of pectoral block as suitable for day-case procedures for appropriate anesthetic[16,20]. In analyzing the literature, it is obvious that, with appropriate patient selection, the use of regional anesthesia should be considered as an important adjunct for perioperative pain control while decreasing the number of opioids taken in the postoperative period.

ENHANCED RECOVERY AFTER SURGERY

Enhanced recovery after surgery (ERAS) protocols have been established to help patients recover from surgery and return to ambulation, normal bowel function, and regular diet in an expedited fashion. One aspect of these protocols includes specific perioperative pain management. These protocols have been effective in several surgical subspecialties, most notably colorectal surgery[23]. Recently, the ERAS Society performed a systematic review of perioperative care around breast reconstruction. In this review, pre- and postoperative analgesia regimens were analyzed, including the use of multi-modal and opioid sparing therapies. They found that regional anesthesia was associated with decreased postoperative narcotic use. They were also able to link opioid reduction to reduction in postoperative nausea, vomiting, and constipation, as well as facilitating early mobilization[23].

Rojas *et al*.[3] further implemented and reported outcomes on an ERAS protocol focused on breast surgery procedures with a goal of eliminating narcotic prescriptions after discharge. Their ERAS protocol used opioid-sparing techniques to eliminate narcotic prescriptions at discharge without sacrificing perioperative pain control. The protocol included preoperative counseling, preoperative oral pain medication (acetaminophen and gabapentin), long-acting local analgesia (a 1:1 mixture of 1.3% liposomal bupivacaine and 0.5% bupivacaine hydrochloride) prior to incision along with liposomal bupivacaine infiltration (20 cm^3) prior to closure, toradol during closure, and alternating ibuprofen with Tylenol every 8 h for 4-5 days postoperatively. It also included standard ERAS protocol strategies such as intra-operative maintenance of euvolemia, normothermia, anti-emetics, early cessation of intravenous fluids, early ambulation and unrestricted diet. The control group, defined as "Usual Care" (UC) patients, did not receive preoperative Tylenol, gabapentin, or intraoperative ketorolac. They were discharged with a median 54.5 morphine milligram equivalents (MMEs) (range 0-120 MMEs). In the results of their study, under the ERAS protocol, patients undergoing lumpectomy were discharged with no narcotics. Pain scores were evaluated at one day and one week postoperatively, and scores were reported on a 1-10 scale. They found no significant difference in pain scores for the ERAS *vs*. control group patients in surgeries including lumpectomy, sentinel lymph node biopsy, and axillary lymph node dissection at both postoperative Day 2 and Week 1[3].

PATIENT EDUCATION

Physicians must also understand their role in education and managing expectations for patients undergoing surgery. Lee *et al*.[7] designed and implemented an intervention focused on education and prescribing guidelines with the goal of reducing opioid prescribing after breast and melanoma procedures[7]. The intervention included mandatory education for prescribers, evidence based prescribing guidelines and standardized patient instructions. Prescriber education included a written protocol as well as mandatory educational conferences three times a year. The prescribing guidelines were distributed within the written protocol along with required online modules for surgical residents prior to their surgical oncology rotation. Patient hand-outs were developed that provided education on when to use opioids *vs*. non-opioid therapy as well as instructions on safe storage and disposal[7]. The authors then used an interrupted time series analysis to compare mean quantity of opioids prescribed before and after the intervention and evaluated the frequency of opioid prescription refills. They were able to decrease mean quantity of opioids prescribed immediately after the intervention by 37% after mastectomy and 42% after lumpectomy or breast biopsy. Opioid prescription refills did not significantly change for either group[7]. Yorkgitis and Brat[2] developed a comprehensive algorithm to assist surgeons with opioid prescribing. Their algorithm, "Getting it RIGHTT", encourages surgeons to understand six key parts to a patient's care: Risk for adverse event, Insight into pain, Going over pain plan, Halting opioids, Tossing unused opioids, and Trouble identification. These concepts were designed to help surgeons better prepare themselves for the complex treatment of surgical patients[2]. The University of Michigan published recommended prescribing guidelines for basic general surgery procedures, including lumpectomy, mastectomy, sentinel lymph node biopsy and axillary lymph node dissection[24]. These guidelines and additional resources are available to both physicians and patients on the open prescribing engagement network website (https://michigan-open.org/prescribing-recommendations/)[25].

CONCLUSION

Narcotic addiction after breast surgery is a growing problem in the United States. Studies show that cancer patients are at an increased risk of developing narcotic addiction and physicians must be cognizant of these risks. Development of multi-modal pain regimens and ERAS protocols incorporating multimodal agents and regional anesthesia may improve patient satisfaction. Physician engagement is essential in stemming the rising number of patients who develop opioid abuse after breast surgery. Patient education

through hand-outs and discussion with health care providers regarding pain control expectations may also help to curb the risk of addiction. Physicians have a responsibility to identify patient factors and surgical procedures that put patients at higher risk of developing narcotic dependence after surgery, provide education preoperatively, utilize opioid-minimizing strategies (use of multimodal pain regimens and regional anesthesia), and support and monitor patients postoperatively to provide adequate pain relief for a successful recovery while preventing chronic opioid use.

DECLARATIONS

Authors' contributions

Contributed literature review, writing, and review: Hite M
Contributed to editing and review: Klauber-DeMore N
Contributed framework, writing, editing, review: Abbott AM

Availability of data and materials

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Marcusa DP, Mann RA, Cron DC, Fillinger BR, Rzepecki AK, et al. Prescription opioid use among opioid-naïve women undergoing immediate breast reconstruction. Plast Reconstr Surg 2017;140:1081-90.
2. Yorkgitis BK, Brat GA. Postoperative opioid prescribing: getting it RIGHTT. Am J Surg 2018;215:707-11.
3. Rojas KE, Manasseh DM, Flom PL, Agbroko S, Bilbro N, et al. A pilot study of a breast surgery enhanced recovery after surgery (ERAS) protocol to eliminate narcotic prescription at discharge. Breast Cancer Res Treat 2018;171:621-6.
4. Brummett CM, Waljee JF, Goesling J, Moser S, Lin P, et al. New persistent opioid use after minor and major surgical procedures in US adults. JAMA Surg 2017;152:e170504.
5. Hoback J. Overdosed on opioids: a deadly epidemic sweeping the country has lawmakers working hard to find solutions. State Legis 2016;42:9-13.
6. Mitchell A, McCrea P, Inglis K, Porter G. A randomized, controlled trial comparing acetaminophen plus ibuprofen versus acetaminophen plus codeine plus caffeine (Tylenol 3) after outpatient breast surgery. Ann Surg Oncol 2012;19:3792-800.
7. Lee JS, Howard RA, Klueh MP, Englesbe MJ, Waljee JF, et al. The impact of education and prescribing guidelines on opioid prescribing for breast and melanoma procedures. Ann Surg Oncol 2019;26:17-24.
8. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts - Female Breast Cancer. Available from: https://seer.cancer.gov/statfacts/html/breast.html. [Last accessed on 11 Nov 2019]
9. Fecho K, Miller NR, Merritt SA, Klauber-Demore N, Hultman CS, et al. Acute and persistent postoperative pain after breast surgery. Pain Med 2009;10:708-15.
10. Hart AM, Broecker JS, Kao L, Losken A. Opioid use following outpatient breast surgery: are physicians part of the problem? Plast Reconstr Surg 2018;142:611-20.

11. Lee JS, Hu HM, Edelman AL, Brummett CM, Englesbe MJ, et al. New persistent opioid use among patients with cancer after curative-intent surgery. J Clin Oncol 2017;35:4042-9.
12. Jiang Y, Li J, Lin H, Huang Q, Wang T, Zhang S, et al. The efficacy of gabapentin in reducing pain intensity and morphine consumption after breast cancer surgery. Medicine (Baltimore) 2018;97:e11581.
13. Moon EJ, Kim SB, Chung JY, Song JY, Yi JW. Pectoral nerve block (Pecs block) with sedation for breast conserving surgery without general anesthesia. Ann Surg Treat Res 2017;93:166-9.
14. Poleshuck EL, Katz J, Andrus CH, Hogan LA, Jung BF, et al. Risk factors for chronic pain following breast cancer surgery: a prospective study. J Pain 2006;7:626-34.
15. Karmakar MK, Samy W, Li JW, Lee A, Chan WC, et al. Thoracic paravertebral block and its effects on chronic pain and health-related quality of life after modified radical mastectomy. Reg Anesth Pain Med 2014;39:289-98.
16. FitzGerald S, Odor P, Barron A, Pawa A. Breast surgery and regional anaesthesia. Best Pract Res Clin Anaesthesiol 2019;33:95-110.
17. Eden C, Esses G, Katz D, DeMaria S Jr. Effects of anesthetic interventions on breast cancer behavior, cancer-related patient outcomes, and postoperative record. Surg Oncol 2018;27:266-74.
18. Garg R. Regional anaesthesia in breast cancer: benefits beyond pain. Indian J Anaesth 2017;61:369-72.
19. Klein SM, Bergh A, Steele SM, Georgiade GS, Greengrass RA. Thoracic paravertebral block for breast surgery. Anesth Analg 2000;90:1402-5.
20. Bashandy GM, Abbas DN. Pectoral nerves I and II blocks in multimodal analgesia for breast cancer surgery. Reg Anesth Pain Med 2015;40:68-74.
21. Jin LJ, Wen LY, Zhang YL, Li G, Sun P, et al. Thoracic paravertebral regional anesthesia for pain relief in patients with breast cancer surgery. Medicine (Baltimore) 2017;96:e810.
22. Wabha SS, Kamal SM. Thoracic paravertebral block versus pectoral nerve block for analgesia after breast surgery. Br J Anaesth 2016;117:382-6.
23. Temple-Oberle C, Shea-Budgell MA, Tan M, Semple JL, Schrag C, et al. Consensus review of optimal perioperative care in breast reconstruction: enhanced recovery after surgery (ERAS) society recommendations. Plast Reconstr Surg 2017;139:1056e-71.
24. Michigan OPEN Website. Opioid Prescribing Recommendations for Surgery. Available from: https://opioidprescribing.info/. [Last accessed on 11 Nov 2019]
25. Michigan OPEN Website. Surgical prescribing recommendations. Available from: http://michigan-open.org/surgical-prescribing-recommendations/. [Last accessed on 11 Nov 2019]