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Chronic pain following breast surgery

Chad M. Brummett, MD

From the Department of Anesthesiology, Division of Pain Medicine, University of Michigan Health System, Ann Arbor, Michigan.

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Chronic pain after breast surgery has been known to be a problem for many years. Recent large studies of noncosmetic breast surgery cohorts have found the prevalence to be between 29% and 47%, with up to 13% of those patients reporting their pain as severe. The pain is frequently neuropathic in nature and generally affects the ipsilateral breast, axilla, and arm. A number of risk factors have been found to be associated with the development of pain, including younger age, demographic variables, preoperative pain in the chest/breast, pain in other locations, psychological variables, the surgery performed, acute pain severity, radiation, chemotherapy, hormonal therapy, fear of recurrence, and genetic polymorphisms. Few studies include an adequate preoperative assessment along with the appropriate longitudinal assessment, and many studies are underpowered to account for the many variables involved. As such, a clear understanding of high-risk patients is still lacking. Alterations in central pain processing, as seen in fibromyalgia, might explain some of the variation between patients despite similar surgeries, anesthesia, and perioperative pain care. Prospective studies of cohorts of patients having noncosmetic breast surgery are needed to better identify the key risk factors for the development of pain. Such studies should include preoperative and longitudinal assessments of pain, pain descriptors, and other key variables. The present review will discuss the epidemiology and descriptions of chronic pain after breast surgery and the risk factors described. In addition, potential means for prediction and acute pain interventions will be discussed.

The issue of chronic pain following breast surgery has been more widely recognized in recent years. Whereas physicians have long been concerned about pain during cancer treatment, much of the focus has revolved around curing the cancer. As breast cancer therapies have improved, survival and life expectancy have increased. Clinicians and researchers are now more focused on the long-term sequelae of cancer and its treatment, including chronic pain. Chronic pain after breast surgery was once thought to be quite rare, but it is now appreciated as a common occurrence.[1] Unlike some of the other commonly described surgical conditions associated with a higher incidence of chronic postsurgical pain, the breast surgery population is more difficult to study because of other factors possibly affecting their potential for pain, including chemotherapy, radiation, and concern for recurrence. As with all forms of chronic pain, the impact can be significant with physical and emotional effects, as well as potential loss of ability to work and costs associated with treatment. The present review will discuss the epidemiology and descriptions of chronic pain after breast surgery, in addition to the risk factors that have been studied to date. In addition, potential means for prediction and acute pain interventions will be discussed. Although pain following cosmetic breast surgery is well reported, the present review will focus on surgeries for breast masses and cancer.

Address reprint requests and correspondence: Chad M. Brummett, MD, University of Michigan Health System, Department of Anesthesiology, Division of Pain Medicine, 1500 East Medical Center Drive, 1H247 UH, Box 5048, Ann Arbor, MI 48109.
E-mail address: cbrummet@umich.edu.

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Chronic postsurgical pain

Although chronic pain after surgery has certainly been a problem since the first incisions were made, it has only been the subject of open discussion and intensive research in recent years. Groups have begun to elucidate the scope of the problem in surgical conditions commonly associated with high rates of chronic pain, including thoracotomy, breast surgery, hernia repair, amputation, coronary artery bypass surgery, and Cesarean section.[1] The prevalence of pain following these surgeries ranges from 10% to 50%. Although these surgeries are the most widely described conditions associated with high rates of chronic postsurgical pain, there appears to be a subset of patients with chronic pain following almost all surgeries. The invasiveness of the surgical insult likely plays a role, but the individual factor of the patient is probably more important. Some risk factors have been proposed, including age, sex, type of surgery, preexisting pain, pain in other locations, psychological factors (anxiety, depression, catastrophizing), and severity of acute pain. These factors, along with genetic predictors, are the source of a great deal of ongoing research.

Prevalence of chronic pain after breast surgery

The prevalence of pain after breast surgery is somewhat difficult to estimate because of methodological limitations in the work performed to date and the many other treatments patients with breast cancer often receive. Few prospective studies include a preoperative assessment of pain, and the definitions of chronic pain after surgery vary. Estimates range between 10% and 60% for patients reporting some level of chronic pain, with about 5% to 10% reporting severe or disabling pain.[1,2] When compared with age-adjusted samples from the general population in Denmark, Peuckmann et al[3] found higher levels of chronic pain in women who had breast surgery, with the largest discrepancies seen in the younger population. This study found the prevalence of pain related to breast cancer to be 29% for the more than 1300 breast cancer survivors more than 5 years after surgery. For some women, the symptoms were rated as slight and infrequent, but many women complained of daily pains that were more severe in nature. In one of the largest and most granular studies performed to date, Gärtner et al[4] surveyed more than 3000 women 2 to 3 years after breast surgery and found a 47% self-report rate of pain, with 13% reporting severe pain. Although there are certainly conflicting data regarding prevalence, severity, and impact,[5] the data presented by Gärtner et al[4] are probably the best estimates available until future prospectively collected, granular data are presented.

Excluding cosmetic surgeries, breast surgery is most commonly conducted for the treatment of cancer or because of concern regarding a potentially cancerous mass. Genetic associations for breast cancer have led to prophylactic mastectomy in some high-risk populations, however. Despite not having chemotherapy and radiation, the incidence of chronic pain in some studies with small sample sizes still appears high. One study of 55 patients found that 69% reported some level of chronic pain, mainly in the lateral and anterior breast area following prophylactic mastectomy.[6] Much of the pain described was evoked by touch, pressure, and physical activity.

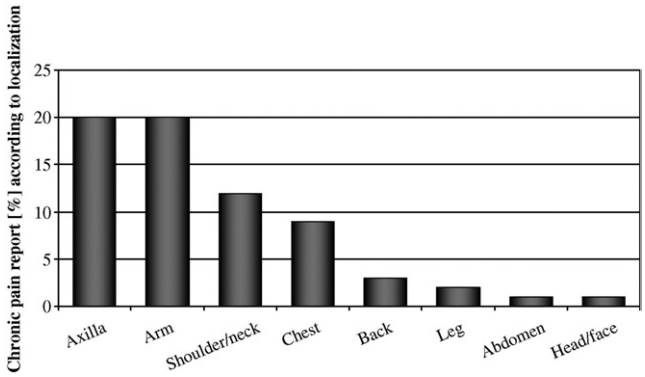

Figure 1 Locations outside of the chest/breast area in which patients complained of pain. Reprinted from Peuckmann et al.[3]

Location and description of pain

Surgical trauma is often thought to be the cause of chronic postsurgical pain, but as previously noted, there are multiple reasons for which breast surgery patients can report pain. Complaints are generally limited to the ipsilateral chest/breast, although other areas such as the axilla, arm, and side of the body are also common (Figure 1).[3,4] Pain in the arm and axilla was significantly more common in women having axillary node dissection. Patients who were younger (age 18-39 years, adjusted odds ration 3.62), had axillary lymph node dissections (adjusted odds ratio 1.77), and reported pain in other locations were more likely to report pain.[3,4] Some experts have advocated for a more granular description of the location of pain to differentiate neuropathic pain and as a means to better understand the associated pathophysiology and potential underlying surgical factors.[5]

Common descriptions of pain include allodynia, pressure, and paresthesias.[3,5] Swelling and lymphedema are also common complaints and are associated with younger age and radiation therapy (Figure 2).[3] A subset of women complain of phantom breast sensations and/or pain following mastectomy.[3,5] These sensations are described in about 6% to 19% of women after mastectomy.[3] Jung et al[2] created a classification system for the different types of neuropathic pain following breast surgery with the goal of better studying the epidemiology, mechanisms, and treatment for the varied types of pain seen after breast surgery (Table 1).

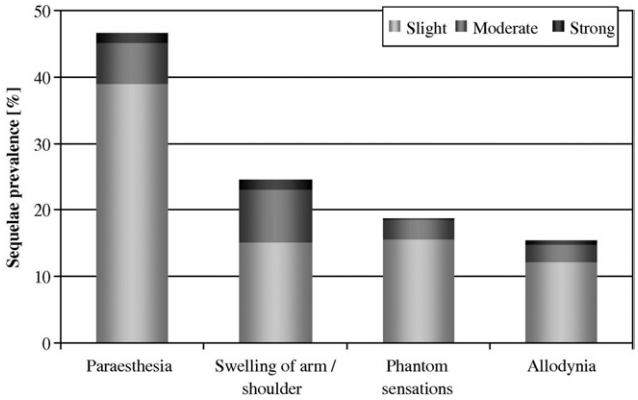

Figure 2 Prevalence of patients reporting pain who described concomitant paresthesia, swelling, allodynia, and phantom sensations and the intensity of the symptoms. Of the sequelae other than pain related to breast surgery, 47% of women reported paresthesia in the surgery and radiation treatment areas, 25% reported swelling of the arm/shoulder, 19% reported phantom sensations, and 15% reported allodynia. Most patients described their pain as "slight". Reprinted from Peuckmann et al.[3]

Risk factors for the development of chronic pain

Pain researchers are beginning to appreciate that there are likely phenotypic and genotypic associations with most forms of chronic pain, including pain after surgery. Despite the fact that most patients have similar anesthesia, surgical trauma, and perioperative analgesic regimens within institutions, only some manifest chronic pain. There have been multiple risk factors proposed, but large prospective studies including a granular preoperative assessment are still lacking.

Phenotypic characteristics

Multiple patient characteristics have been associated with higher potential for chronic postsurgical pain, including pain after breast surgery. Younger age has been associated with increased risk of pain in multiple studies.[3,7] Some researchers have speculated that the age-related factors are the result of older patients misattributing their pain to normal aging. Less education and being single but previously married (divorced, separated, or widowed) have also been described as risk factors.[3] Associations between race and pain in cancer survivors have previously been described.[8] A few studies have demonstrated that Caucasians are at a lower risk for chronic pain when compared with all other races.[9] The importance of race (which is likely associated with genetic risk) on the development of pain is still poorly understood, however. Some researchers have demonstrated racial disparities in acute, chronic, and palliative pain care in both cancer and noncancer patients.[10] Whether disparities in care are causal in the association between race and pain in chronic pain after breast surgery is unclear.

Preoperative pain either in other locations or at the site of surgery may predict the potential for new or worsened breast/chest wall/arm pain.[5] Chest/breast pain without surgery or trauma is not a common complaint, but the masses identified can be described as painful preoperatively. It is, therefore, important to ensure understanding of the preoperative intensity and descriptors because worsened and/or changed pain (eg, more neuropathic pain complaints) can be observed. Patients with pain in other locations may also be at higher risk for chronic pain after breast surgery, as reported by Gärtner et al.[4] Pain in other locations could be part of a phenotype of pain-prone patients, as described in the "Pain-Prone Patient" section below.

Some studies have implicated obesity as a potential risk factor;[9,11] however, data are conflicting.[12] Although it may be that obesity leads to worsening lymphedema, the data regarding its effects in pain are less clear. Experts believe that obesity may play a factor in the way in which the intercostobrachial nerve is handled, thereby increasing the potential for neuropathic pain.

Psychological variables, such as depression, anxiety, and catastrophizing, have been reported as poor predictors.[13] The importance of accounting for and assessing psychological measures has been described in a number of pain conditions,[14] and studies show the importance of these psychological factors in acute pain, analgesic consumption, and chronic postsurgical pain.[15,16] Given the commonalities be-

Table 1 Classification of Chronic Neuropathic Pain Syndromes following Breast Cancer Surgery

Syndrome	Description
Phantom breast pain[a]	Sensory experience of a removed breast that is still present and is painful
Intercostobrachial neuralgia (includes postmastectomy pain syndrome)	Pain, typically accompanied by sensory changes, in the distribution of the intercostobrachial nerve following breast cancer surgery with or without axillary dissection
Neuroma pain (includes scar pain)	Pain in the region of a scar on the breast, chest, or arm that is provoked or exacerbated by percussion
Other nerve injury pain	Pain outside the distribution of the intercostobrachial nerve consistent with damage to other nerves during breast cancer surgery (e.g. medial and lateral pectoral, long thoracic, thoracodorsal, and other intercostal nerve

[a]To be distinguished from non-painful phantom breast sensations.

tween neurotransmitters affecting pain and those regulating mood and anxiety, it is not known whether psychopathology has an association with the report of postsurgical pain or if it is simply part of the phenotypic expression of a subset of pain-prone patients. Much of the focus to date has been on negative affect in chronic postsurgical pain, whereas positive affect and resiliency have not been studied in this arena.[17]

Surgery

Radical mastectomy was once a common treatment for breast cancer. Large studies of women undergoing modified radical mastectomy with lymph node dissection described rates of chronic pain of approximately 50%.[7] Surgeries today are usually less invasive and aim to be more individualized to the patient and their cancer, but overall rates of chronic pain remain high. Breast-conserving surgeries with and without sentinel lymph node biopsy or axillary lymph node dissection are now much more common than mastectomies. To the author's knowledge, there have not been randomized, controlled trials comparing rates of postsurgical pain following mastectomy versus lumpectomy with or without node dissection. Although there are certainly other benefits to lumpectomies over mastectomies, it is not clear whether these less invasive approaches affect the potential for pain.[18] One study showed that the prevalence of pain complaints was not significantly different between patients who had mastectomies when compared with those who had breast-conserving surgery; however, the pain reported in the mastectomy population was significantly more intense.[4] Differentiating among the patients receiving only a sentinel node biopsy from those who have a full node dissection is important in determining the potential for chronic pain.[19] The proximity to the brachial plexus, as well as damage to the intercostobrachial nerve from transection and traction, is thought to be the reason for increased pain in axillary node dissections.[2] Rarely, more serious nerve damage can occur, leading to pectoral weakness or "winging" of the scapula. Women who have immediate reconstruction after a mastectomy may be at higher risk for chronic pain.[20]

Surgical experience may play also be a factor in the development of pain, with some studies showing that high-volume hospitals had lower rates of pain.[13] Other studies have failed to detect a difference, however.[3] Improved outcomes with greater surgical experience have also been described under other conditions, including knee replacement.[21] Although surgical experience may be important in pain outcomes, it has not been included as a variable in many of the larger studies done to date.

Acute pain intensity

A well-described association exists between the intensity of acute postsurgical pain and the development of chronic pain after surgery.[1] The concept of central sensitization was described by Clifford Woolf more than 25 years ago and is the source of ongoing research.[22-24] This finding has been demonstrated in the breast surgery population.[13,19,25] There are limited prospective data accounting for the severity of acute pain, with many studies relying on recall. Most of the work linking preoperative pain sensitivity (experimental pain testing) and the severity of acute pain with the development of chronic postsurgical pain has been performed in the hernia population.[26,27] Many phenotypic factors associated with the risk of acute postoperative pain are the same as those associated with chronic pain.[16] It is possible that the associations between acute and chronic postsurgical pain are the result of a patient population that is predisposed to both. That said, it may be that these are the patients in whom aggressive management of acute pain may prevent the development of chronic pain.[23,28] As is noted in the "Future Directions" section below, researchers must focus on a prospective measurement of pain that accounts for preoperative, acute postoperative, and chronic pain assessments.

Radiation therapy

Radiation is a common portion of the multimodal treatment for breast cancer. Studies of older algorithms of high-dose radiotherapy in the 1960s clearly demonstrate the ill effects that radiation can have on the nerves of the chest, breast, and arms, leading to neuropathies.[29] Despite changes in the ways in which radiation is conducted, including more targeted treatment and lower dosing, radiotherapy remains a relevant risk factor in the development of chronic pain.[3,13] Radiotherapy appears to have a significant effect on the likelihood of neuropathic complaints (eg, allodynia) and swelling/edema.[3,4,7,11] In addition, it is associated with higher rates of paresthesias, swelling, and phantom sensations.[3] Given the survival benefit from patients receiving radiation, it will likely remain a portion of standard breast cancer treatment and a cause of pain.

Chemotherapy

Chemotherapy-induced neuropathy and pain is a well-established problem, but the impact of chemotherapy on chronic pain after breast surgery is less clear. Most studies do not define the chemotherapeutic regimens despite the fact that there are known differences in toxicity between the different agents. Gärtner et al[4] included a defined chemotherapy regimen (cyclophosphamide, epirubicin, and fluorouracil) in their multivariate analysis and did not find this regimen to be an independent risk factor. Chemotherapy alone may not lead to increased rates of chronic pain; however, combinations of chemotherapy and radiation may lead to pain.[7]

Hormonal therapy

Aromatase is an enzyme that acts to create estrogen, and it is therefore a treatment target in estrogen-responsive breast cancers. Aromatase inhibitors are superior to tamoxifen alone in terms of cancer recurrence and survival.[30] Although there is a survival benefit from the addition of hormonal therapy, many patients who take these medications will describe diffuse arthralgias. Patients generally complain of symptoms just more than 1 year after treatment; however, some describe severe symptoms within 2 months.[31] Arthralgias are more common in patients taking aromatase inhibitors when compared with tamoxifen. History of chemotherapy prior to hormonal therapy does increase the incidence of complaints of arthralgias. Although the mechanism by which these drugs cause pain is not completely clear, it is thought that estrogen has antinociceptive effects and can act to decrease central sensitization. The decreased estrogen production caused by aromatase inhibitors is therefore thought to allow for central augmentation of nociceptive processing rather than true joint pathology. Less is known as to whether the same pronociceptive effects of low estrogen levels adversely affect pain complaints in areas of surgical pain. Regardless, it is important to differentiate the pain associated with the surgical incision and dissection from the widespread arthralgia-type pain from aromatase inhibitors. In addition, a preoperative assessment of pain in the surgical area and elsewhere is essential to distinguish that which is new from a preexisting rheumatologic condition. It has been estimated that about half of the women who complain of arthralgias associated with aromatase inhibitors described their symptoms as a worsening of preexisting symptoms.[30] Studies that simply assess the patient's overall pain score without differentiating the location and/or descriptors may misinterpret arthralgia pain as chronic postsurgical pain.

Fear of recurrence

Improvements in the treatment of breast cancer have increased survivorship. Understandably, women are frequently concerned about the potential for recurrence, and pain was found to be a strong predictor of this fear.[32] Some clinicians believe that the fear of recurrence is a portion of what drives the high rate of self-report of chronic pain after breast cancer surgery. It is not known whether this is true, but it seems unlikely that the fear of recurrence would lead to pain in a large subset of women. It is possible, however, that the self-reported intensity and impact could be affected. Future research is needed to better understand the impact of fear of recurrence on the self-report and impact of pain.

Genetics

There has been a large increase in clinical and preclinical genetics research in virtually all fields of medicine. There have been many genetic alterations implicated in the development of pain, but the true genetic underpinnings of pain are still poorly understood.[33-37] In a recent study, Nissenbaum et al[38] used a mouse model to determine that CACNG2 had a role in neuropathic pain processing, likely through alterations in glutamatergic transmission. This polymorphism was associated with neuropathic pain complaints in a cohort of more than 500 women describing neuropathic pain after breast surgery.

Although much of the work to date in pain medicine has been performed using a candidate gene approach, there are large, ongoing studies that will hopefully begin to use a whole-genome approach. An enhanced understanding of the genetic factors influencing the development of pain will certainly help to move the field forward both in the prevention and in the treatment of pain. Once genetic polymorphisms associated with pain are determined, researchers can begin to understand the physiological effects of these alterations and potentially create more targeted therapies. Point-of-care genetic testing could also be used to detect high-risk populations and create personalized analgesic regimens.

Pain-prone patient

The risk factors for chronic pain following different surgeries, including breast surgery, continue to be the subject of research. Although there are likely factors unique to surgery, there may be common characteristics among all patient patients regardless of etiology. The factors distinguishing these patients are the insult (eg, surgery, diabetes, herpes zoster, etc.) or lack thereof (eg, fibromyalgia, temporomandibular joint pain, etc.). Although the diagnosis of fibromyalgia has been a source of controversy and skepticism, years of quality research have validated its existence.[39,40] Whereas patients with fibromyalgia manifest different comorbid symptomatology (eg, fatigue, trouble thinking, depression, anxiety) and disorders (eg, temporomandibular joint disorder, migraine, irritable bowel), the common central theme is widespread body pain. In fact, regardless of the sensory stimulus, fibromyalgia patients are more sensitive to virtually all forms of sensory testing, including proprioceptive and auditory stimuli.[41,42] Research has demonstrated that patients with fibromyalgia have lower central levels of neurotransmitters associated with the inhibition of pain, including low norepinephrine, serotonin ($5HT_{1a,b}$), and GABA, as well as higher central levels of those that enhance pain, including glutamate.[40,43,44] Fibromyalgia patients also have less free opioid receptor availability when compared with healthy controls.[43]

Whereas fibromyalgia is accepted as an independent diagnosis, research has demonstrated that fibromyalgia patients display differences in terms of comorbid symptomatology with varied levels of intensity. The American

College of Rheumatology has adopted a new self-report questionnaire in lieu of the tender point examination.[45,46] As such, the combined score for the assessment of Widespread Pain Index (19 selected areas associated with rheumatologic complaints) and the comorbid Symptom Severity Scale (eg, fatigue, trouble thinking, etc.) is used to create a "fibromyalgia-ness" score of 0 to 31. A score of ≥13 along with the exclusion of other diagnoses that could otherwise explain the pain and symptoms meets the American College of Rheumatology cutoff for the diagnosis of fibromyalgia. More importantly, the fibromyalgia-ness score can be used to view the patient's sensitivity as a continuum rather than a binary categorization. As such, this scale may allow for prediction of patients who may respond poorly to surgical pain and potentially go on to develop chronic pain. Most research in fibromyalgia has been focused on the chronic condition and outpatient management. Whether the concepts and management of fibromyalgia are applicable to the perioperative setting is not known but remains the subject of ongoing research.

A number of predictors for chronic postsurgical pain have been proposed, as previously discussed. Although these factors explain some of the risk, the reasons for which patients respond so differently to similar surgical stimuli with similar perioperative analgesic regimens are still unclear. It is possible that the same patients predisposed to other types of chronic pain (low back pain, painful osteoarthritis, etc.) are more likely to develop chronic pain after surgery. As noted previously, patients with preexisting pain in other locations are at higher risk for chronic postsurgical pain. Fibromyalgia is associated with known pathophysiologic changes in central pain processing and may explain some of the differences noted. Although patients may not carry a formal diagnosis of fibromyalgia, a phenotype of central pain as measured by high fibromyalgia-ness could describe a pain-prone patient.

Can we prevent chronic pain after breast surgery?

Multiple studies of chronic postsurgical pain describe an association with the duration and severity of acute pain after surgery. Some experts believe that the association is caused by a pain-prone phenotype in which the same person at risk for severe acute pain is also prone to develop chronic pain. Some believe, however, that aggressive treatment of acute pain will decrease the potential for the development of chronic pain. Some studies have addressed this question, although clear guidance is difficult based on the limited data. Most studies conducted on interventions or analgesic regimens are small and too heterogeneous in nature to allow for conclusions.[5] Many of the risk factors noted previously should be included to create appropriate randomization of high- and low-risk groups. Recommendations for perioperative care along with supporting evidence for selected surgical procedures, including noncosmetic breast surgery, have been proposed by the Procedure-Specific Postoperative Pain Management group (PROSPECT).[a]

Pharmacologic therapies

The most common analgesics in acute pain are in the opioid class. Although these will almost certainly remain a key portion of the overall management of acute pain, there has been a strong push toward multimodal analgesia to improve pain relief while minimizing side effects.[47] The most commonly used adjunctive treatments are the gabapentinoids. In a small prospective, randomized, controlled trial, gabapentin reduced acute analgesic requirements in breast surgery patients but did not impact pain reporting at 3 or 6 months after surgery.[48] Patients in the gabapentin group did, however, report significantly less burning pain, potentially showing a neuropathic pain benefit.[48] When combined with a ropivacaine axillary brachial plexus block and topical anesthetic cream, gabapentin reduced the pain complaints at 3 months, but the effect was no longer significant at 6 months. In a randomized, placebo-controlled, double-blind trial, Buvanendran et al[49] showed that a single preoperative dose of 300 mg followed by 14 days of twice-daily dosing of pregabalin significantly decreased neuropathic pain complaints following total knee arthroplasty. Given the high reported rate of neuropathic complaints after breast surgery, it is reasonable that gabapentinoids may be beneficial, but future research is needed.

A number of other adjunctive medications have been described in multimodal analgesia.[47] Antidepressants that block reuptake of norepinephrine in addition to serotonin are widely used in the treatment of pain, especially neuropathic peripheral and central pain states. A study of 150 women randomized to 1 of 3 treatment groups (venlafaxine, gabapentin, or placebo) found that venlafaxine was effective in reducing the rates of chronic pain at a 6-month follow-up when compared with gabapentin or placebo.[50] Duloxetine has been shown to decrease acute morphine consumption following total knee replacement, but its effects on the development of chronic pain in breast surgery are not known.[51] Ketamine is widely described as a pharmacologic tool to prevent chronic pain. Although the acute opioid-sparing effects are clear, limited data exist regarding the prevention of chronic pain. A study of total hip arthroplasties found that a preincisional bolus of ketamine (0.5 μg/kg) followed by a 24-hour infusion (2 μg/kg/min) significantly decreased the report of pain at rest.[52] Nonsteroidals may also be of benefit in reducing the acute peripheral inflammatory response associated with incision and dissection, but the risk of bleeding and axillary hematoma generally limits their use.

Although data certainly exist to support the reduction in acute pain and opioid consumption using multimodal analgesia, data to guide dosing and recommended duration of use after surgery are limited. Many studies include multiple

[a] http://www.postoppain.org. Accessed 4 July 2011.

Table 2 Checklist for Future Studies on PPBCT; Checklist over Potential Risk Factors to Be Accounted for in Future PPBCT Studies

	Item	Description
Design	Method	Prospective/retrospective/RCT
	Questionnaire	Procedure-specific questionnaire
	Clinical examination	
	Follow-up	Protocol for questions and examinations
	Pain evaluation:	>3 months, details on time
		NRS/VRS
		Pain characteristics
		Anatomical localization
		Pain in rest
		Pain in movement
		Pain-related functional impairment
Exclusion criteria	Recurrent cancer	Systematic examination
	Metastasis	Systematic examination
	Previous surgery in area	Medical records, clinical examination
	Breast reconstruction	
Preoperative	Demographics:	Included in analysis
	Age	TNM, receptor status
	BMI	Analgesics, psychotherapeutic agents
	Socioeconomic	
	Ethnicity	Neuropathy, cardiac disease
	Disease status	NRS
	Preoperative medication	Muscle and joint pain, location and intensity
	Comorbidity	
	Nociceptive function	Validated instrument (eg. HADS)
	Pain in breast area	
	Pain other locations	
	Psychological assessment	
	Blood sample for genetic analysis	
Intraoperative	Surgical procedure on breast	Description of procedure
	Surgical procedure on axilla	Description of procedure, concomitant with or separate from breast procedure
	Handling of nerves	Preservation of ICBN
	Analgesics	Preemptive analgesia
Postoperative	Early postoperative pain	NRS
	Analgesics	Postsurgical pain regimen
	Adjuvant therapy:	Radiotherapy
		Radiation field
		Radiation dose
		Timing
		Chemotherapy
		Regime
		Cumulative dose
		Timing
		Endocrine therapy
		Regime
		Dose
		Timing
	Lymphedema	Subjective/clinical examination
	Complications	Seroma, hematoma, infection
	Sensory disturbances	Subjective/clinical examination/QST
	Social/physical consequences	Validated instrument

adjunctive medications making analysis of the analgesic and side effects of the individual medications nearly impossible. Many experts feel that the lack of effect seen in some trials is the result of failure to maintain therapy throughout the acute pain course. The side effects associated with these medications, including sedation, dizziness, and confusion, are dose dependent and can be a source of concern. Multimodal analgesia is certainly an area of active research, which will hopefully provide additional clarity and management recommendations.

Interventional modalities

Given that many of the surgeries performed for breast cancer today are less invasive than in the past, most surger-

ies in the United States are performed in an outpatient setting. As such, interventional techniques are limited to single-shot blocks rather than indwelling catheters. Intercostal nerve blocks in the T3–T6 region can be used to anesthetize the breast and attenuate acute postoperative pain, but the use of a paravertebral block may be preferable.[53] Using the same concept of intercostal nerve blocks for anesthesia of the dermatomes of the breast, researchers have demonstrated that the use of paravertebral blocks can lessen acute pain, decrease opioid consumption, decrease sedation, decrease acute perioperative nausea and vomiting, and improve acute postoperative coordination.[54] A follow-up study by the same group indicated that preincisional paravertebral blockade may decrease the incidence of chronic postsurgical breast pain.[55] The increase in experience and comfort with ultrasound seems likely to improve the success of these blocks while potentially minimizing serious side effects, such as pneumothorax.[56]

Future directions

Although chronic pain after breast surgery is clearly a common problem, the true incidence and impact are still issues of controversy. Many of the studies performed to date have methodological limitations that impact the utility of the findings. Large, prospective studies of all types of chronic postsurgical pain are needed. These studies must incorporate the many factors thought to affect the likelihood of developing pain such that high-risk populations can be identified and potentially modifiable factors can be addressed. Guidelines for future studies of postsurgical pain have been published, and a specific set of guidelines was recently described by Andersen and Kehlet (Table 2).[5] Once we have models in place to assess risk for postsurgical pain, we can begin to conduct efficient and targeted prospective trials of acute pain interventions and perioperative analgesics to determine whether we can actually prevent the development of chronic pain. Prevention of the development of chronic pain must be the goal, because although it is often possible to improve pain and function in a patient with chronic pain after surgery, a true cure is elusive.

Conclusions

Chronic pain after breast surgery is a common complaint, and multiple risk factors have been proposed. Prediction and prevention of pain are essential because many chronic postsurgical pain patients fail to improve despite treatment. Hopefully through continued research, high-risk populations can be identified preoperatively as a means to create personalized perioperative treatment plans to prevent chronic pain.

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