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# Regional Anesthesia in the Prevention of Chronic Postoperative Pain

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## Abstract

Chronic postsurgical pain (CPSP) develops after a surgical procedure but increases its intensity and persists beyond the healing process without another cause to explain it. The incidence ranges from 5–85%, according to the type of surgery. Patients who develop CPSP may have a protracted ambulation, cardiac and pulmonary complications and increased morbidity and mortality. Several risk factors have been found related to the development of CPSP: female gender, young age, genetic predisposition, and psychosocial problems, hence prevention, early identification and treatment of these factors is essential. Several guidelines recommend the use of multimodal analgesia to treat postoperative pain, and the perioperative management seems to have a preventive role in the development of CPSP. Regional anesthesia (RA) either neuraxial or peripheral nerve blocks, by modulating signaling created by a surgical incision, play a key role in the prevention of CPSP. Local anesthetics have anti-inflammatory properties which decrease sensitization, reduce ectopic firing of neurons, cytokines expression and decrease neutrophil priming. RA reduces pain signals to the spinal cord and supraspinal and cortical nociceptive centers. RA along with other pharmacologic interventions can improve the CPSP as well as the physical and social functionality.

**Keywords:** acute pain, chronic pain, multimodal, regional analgesia, ultrasound

## 1. Introduction

Pain is a universal experience but unique for every individual. Any surgical intervention is a common pain source, that results from a planned incision at a specified point in time, often approached and managed sub optimally or without proper prevention, for this reason it should be prevented or controlled. However, there are many factors that contribute to the development and persistence of Chronic Postsurgical pain [CPSP], and only some of these are related to the surgery. As with nonsurgical chronic pain, psychological and social factors have an important influence [1].

Poor pain management will contribute to a worse experience of the disease for the patient, lower satisfaction, delayed ambulation, increased incidence of cardiac and pulmonary complications, and increased morbidity and mortality. It also has

a negative impact on the health system by having short-term and long-term consequences such as late discharge and slow recovery and late rehabilitation [2].

All clinicians should have some knowledge on CPSP and how to manage established cases, which can persist for months or years after the procedure. As with many other chronic conditions, early intervention is likely to improve outcomes, so identifying patients at risk is crucial. The incidence of chronic postoperative pain varies according to the type of surgery and may be severe and disabling. Chronic pain is difficult to treat and is often permanent. For this reason, efforts to prevent its development after surgery are especially important [3].

An accurate clinical history and physical examination are essential to identify known risk factors leading to postoperative acute and chronic pain. The outcome improves with pharmacological and non-pharmacological multimodal analgesia, peripheral regional anesthesia or neuraxial techniques are some current tools that may reduce the incidence and severity of CPSP.

## 2. Postoperative pain

The International Association for the Study of Pain (IASP) describes pain as an unpleasant sensory and emotional experience associated with an actual or potential injury or described in terms of such injury [4].

Acute postoperative pain is a result of noxious stimulation of skin, subcutaneous tissues, viscera and neural structures. The 11th revision of the International Classification of Diseases defines CPSP as pain developing or increasing in intensity after a surgical procedure, in the area of the surgery, persisting beyond the healing process (at least 3 months) and not better explained by another cause such as infection, malignancy, or a pre-existing pain condition [5].

The prevention of CPSP is an important goal, for this reason the IASP named 2017 as the Global Year Against Pain After Surgery [6, 7]. Substantial rates of chronic postoperative pain after a variety of surgical procedures, have revealed important demographic, genetic and psychosocial risk factors, which allow us in cases of elective surgery, to investigate or and prevent some of them that may influence pain chronicity. While traumatic injury is clearly not predictable [8].

### 2.1 Incidence

CPSP has been reported after almost all types of surgery with a high prevalence >20%, the incidence of CPSP varies depending on the surgical procedure ranging from a low of 5% to a high of 85% [9]. Some studies following limb amputation have reported incidences ranging from 50–85%, following mastectomy 11–57%, after thoracotomy 5–65%, and 5–63% following hernia repair [10, 11].

The high prevalence after these procedures may be attributed to the increased risk of nerve injury and central sensitization on this type of surgeries; but also, there could be other explanations, including persistence of a pre-existing pain in the operated area [12].

### 2.2 Risk factors for chronic postsurgical pain

Several studies have attempted to identify specific surgical factors that increase the risk of developing chronic postoperative pain. The surgical location, duration, and extent, as well as the experience of the surgical team, have been implicated [13, 14]. There are predictors for developing persistent pain, which are divided into preoperative, perioperative, or immediate postoperative and late postoperative.

Among the predictors in the preoperative period are patient factors including female gender, being a young adult, genetic predisposition, and psychosocial factors like depression tendency to catastrophize, preexisting patient conditions, for example, pain present preoperatively, and any preexisting painful conditions [15, 16].

Perioperative factors include duration and type of surgery, extent of nerve damage intraoperatively, longer duration and an open vs. laparoscopic approach [15, 16]. Modifying surgical technique to minimize nerve damage and using minimally invasive approaches may decrease chronic postoperative pain risk [13].

In the postoperative period, the predictors will be related to the analgesic treatment, psycho-social factors, or patient factors such as chemotherapy or radiotherapy treatments, because they could be related to other states of hyperalgesia [17].

The time-point of chronic postoperative pain assessment, ranging from months to several years after surgery, may impact incidence estimates, with longer follow-up times corresponding to lower incidence rates [18].

### **2.3 Transition from acute to chronic pain**

The intensity of acute pain is one of the strongest predictors of chronic postoperative pain, likely because acute pain itself is a product of biopsychosocial variables [19]. Pain is not only a sensation to protect the body from harm, but also a process where nociceptive information is transformed into a complex, subjective, unpleasant, sensory, and emotional experience with different factors that define it [20]. Acute pain responds to tissue damage, a certain pathology or abnormal function of a muscle or viscera. It is protective, adaptive and self-limited, its evolutionary function is to restrict behaviors that increase the risk of inadequate tissue recovery [21]. Nociception is a protective process that helps prevent further tissue damage by triggering reflex withdrawal responses and modification of behavior to avoid injury [22].

Tissue damage triggers profound changes in peripheral and predominantly central somatosensory circuits. Chronic pain does not have a specific function, it is related to inadequate and aberrant adaptation that can include some states of neuroplasticity [23].

Neuropathic pain is defined by the IASP as pain caused directly by an injury or disease that affects the somatosensory nervous system, it is characterized by spontaneous pain with abnormal sensory symptoms [24].

Persistent pain following surgery can have neuropathic characteristics, and many of the surgeries associated with persistent pain, such as thoracotomy, breast surgery and amputation, involve major nerves in the surgical field [13]. Following nerve injury, nociceptive neurons fire rapidly leading to changes in N-methyl-D-aspartate receptors NMDAR composition and activation. NMDARs are highly permeable to calcium, whose influx triggers neuron-specific cascades that underlie synaptic plasticity and, in extreme cases, cause excitotoxicity and neuronal death. In a neuropathic pain model, the conditional deletion of spinal NMDARs prevents calcium-dependent neuronal death and the transition from acute to persistent pain-like behaviors. This shows that glutamate, NMDARs, and calcium influx play an essential role in the development of chronic pain [25].

However, intra-operative nerve transection does not inevitably result in neuropathic pain and avoiding nerve transection does not necessarily prevent chronic pain [26]. Risk factors for persistent postoperative pain, other than nerve injury and ongoing inflammation, include pre-operative pain, younger age, female sex, genetic factors, and psychological vulnerability [13].

The pathophysiological mechanism is considered mostly neuropathic when finding an important association between persistent postoperative pain and sensory

abnormalities, the evidence indicates that there are other components involved such as inflammatory processes, central sensitization, damage to nerves or somatic/visceral structures, or a combination of the above [27].

### **3. Multimodal analgesia**

Some risk factors for postoperative chronic pain can be modifiable especially if surgery is elective, like body-mass index, preoperative pain, and some comorbidities, whereas others like demographics, genetics, and pain sensitivity are not. The site, timing and intensity of surgical damage are predictable. An analgesic regimen can be designed to anticipate, prevent, or modify the nociceptive barrage, thereby preventing central sensitization [28].

Multimodal analgesia has become an important concept in the field of modern pain management. The use of multimodal analgesia is highly recommended for postoperative pain management. It is defined as the use of a variety of drugs and combined techniques, with different mechanisms of action at the central and/or peripheral nervous system level and may have an additive effect or synergism. Some of these agents include  $\alpha_2$  agonists, NMDA receptor antagonists, gabapentinoids, dexamethasone, NSAIDs, acetaminophen, and duloxetine [29].

Advantages include superior analgesia secondary to the synergistic effects of multiple agents acting via different pain pathways, the ability to limit parenteral opioid administration, and minimizing opioid-related side effects [28].

The site, timing and intensity of surgical damage are predictable. An analgesic regimen can be designed to anticipate, prevent, or modify the nociceptive barrage, thereby preventing central sensitization. Pain management plays a fundamental role in enhanced recovery after surgery (ERAS) pathways. The concept of multimodal analgesia in providing a balanced and effective approach to perioperative pain management is widely accepted and practiced, with regional anesthesia playing a main role [30].

There are evidence-based guidelines for the management of postoperative pain, like the American Society for pain management, the European guidelines PROSPECT (Procedure Specific Postoperative Management) and ERAS guidelines (Enhanced Recovery After Surgery), all of them have similar objectives; an early mobilization, a reduction in hospital stay times, a decrease in morbidity and mortality, an increase in patient satisfaction and the use of multimodal analgesia, specially regional anesthesia [30–32]. A multidisciplinary team-based approach for defining the goals is essential, based on each patient's needs, and incorporating patient, surgical, and social factors.

### **4. Regional anesthesia**

The guidelines on postoperative pain management created by multiple societies advocate for the use of site-specific regional anesthetic techniques as part of a multimodal analgesic regimen, which is effective in several surgical procedures including thoracotomy, joint replacement surgery, and cesarean sections. Central neuraxial blocks alone or in combination with catheter techniques are performed in order to decrease stress surgically induced and inflammation, and they could improve pulmonary functions, and reduce the period of hospitalization with better pain control [30].

Effective regional anesthesia may prevent central sensitization by blocking nociceptive input into the spinal cord. Epidural anesthesia and paravertebral blocks

reduce the risk of persistent pain after open thoracotomy and breast cancer surgery, respectively [33]. These findings are interesting also in view of the apparent beneficial effect of regional anesthesia in reducing tumor recurrence [34]. Regional anesthesia has been advocated in oncological surgery to reduce the risk of cancer recurrence, based on some evidence by the inhibition of tumor cell seeding and growth by various pathways. These include effective suppression of the adrenergic and inflammatory response to surgery, preservation of immune function and direct action of systemic local anesthetics on tumor cell apoptosis, and indirectly through reduction in the use of opioids which may have their own pro-metastatic effects [35].

Improvement in ultrasound technology may increase clinical applications not only for epidural and paravertebral blocks but also for peripheral nerve and truncal blocks. The use of real time of ultrasound while performing the block may reduce the complications, performance time, and local anesthetic requirements. The rate of success may increase with clinical experience. Peripheral nerve blocks seem to lack systemic side effect related to sympathetic blockade and lesser incidence of minor complications including urinary retention when compared with central neuraxial blocks or catheter applications. For what they seem to be safer than either central neuraxial blocks or general anesthesia, especially in patients with severe coexisting disease [36].

The potential beneficial effect of local anesthesia on inflammation and immune function has long been suggested [37]. Local anesthetics have anti-inflammatory properties which may also decrease sensitization. The clinical anti-inflammatory effect of intravenous lidocaine is today reasonably well documented. The exact mechanisms of action are not clear but seem to involve a reversible interaction with membrane proteins and lipids, thus regulating cell metabolic activity, migration, exocytosis, and phagocytosis [38].

The shift toward peripheral and regional anesthetic techniques has largely been driven by the advent of ultrasound-guided regional anesthesia, it provides real-time visualization and targeting of major nerves that were previously located with landmark-based “blind” techniques, therefore, it has made regional anesthesia safer, more efficient, and more accessible to general anesthesiologists [39]. There is a growing interest in the potential preventative impact of regional anesthesia on chronic postoperative pain, especially with ongoing development of new techniques.

## **5. Conclusions**

The role of regional anesthesia in peri-operative care and acute pain management is more important now than it has ever been. Postoperative pain management continues to be a challenge for the health professional, due to the combination of factors that produce it. If not treated correctly, postoperative pain may become chronic which can cause functional limitation and psychological distress to patients. We should identify the risk factors in a patient undergoing surgery and institute appropriate preventive measures.

When seeking satisfaction in the patient, it must be understood that suboptimal pain management may be due to the lack of an updated and multidisciplinary approach. The use of regional techniques in the pre, intra and postoperative period, based on the recommendations of the multimodal therapy guidelines, implemented according to the setting and the availability of the health center, hence it can make a difference in terms of acute postoperative pain and long-term preventable consequences.

The ability of regional anesthesia to target many areas of the surgically induced pain pathways makes it a powerful tool in reducing neural activation from surgical injury, making it the centerpiece of a well-rounded multimodal approach. Several ongoing studies addressing innovative blocks will likely continue to inform preventative treatment options. Successful approaches to decrease chronic postoperative pain incidence should start at the time of pre-operative planning and extend into the recovery period.

Adoption of ultrasound guidance as the gold standard has been key to this; recently new techniques have been developed. Fascial plane blocks have been an important step in increasing the reach of regional anesthesia, although more research is needed to clarify their role in peri-operative pain management, reason why is particularly important to continue investing into regional anesthesia education. Advances in technology, technique development and pharmacology over the last decade have significantly improved efficacy and safety of regional anesthesia.

### Conflict of interest

The authors do not have any potential conflict of interest related to this chapter.

### Abbreviations

CPSP	Chronic Postsurgical pain
RA	Regional anesthesia
IASP	International Association for the Study of Pain
NMDARs	N-methyl-D- aspartate receptors
PROSPECT	Procedure Specific Postoperative Management
ERAS	Enhanced Recovery After Surgery

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