Chronic pain management after surgery

Kiran K Koneti
Joel S Perfitt

Abstract

Chronic post-surgical pain is a common problem affecting between 2% and 10% of adults after surgery and a significant health burden. The development of chronic post-surgical pain involves multiple mechanisms including peripheral and central sensitization and nerve injury, thought to be the most significant factor. There are many risk factors including preoperative pain, chemo/radiotherapy, surgical, psychological and genetic factors. The prevention of chronic post-surgical pain is challenging but progress is being made in identifying at-risk groups, improved surgical technique and preventative analgesia including regional analgesia. Accurate diagnosis is essential for proper management, including identification of neuropathic pain. Management involves identifying any surgically or medically treatable cause, followed by pharmacological, psychological, physical and interventional management. It is essential for all clinicians involved in the care of surgical patients to have an awareness of chronic post-surgical pain, its prevention, diagnosis and treatment.

Keywords Acute on chronic pain; acute pain; chronic pain; CPSP; pain management; persistent pain; post surgical pain; PPSP

Background

Chronic post-surgical pain (CPSP) is a significant problem and represents a major health burden. Between 2% and 10% of adults undergoing surgery experience chronic post-surgical pain,[1] and with over 4 million operations performed in the UK every year the incidence of CPSP may be over 100,000 patients per year. Chronic pain is often the most common surgical complication and yet it is only within the last 10–15 years that the magnitude of the problem has been recognized.[2]

The reported incidence and severity of CPSP varies greatly due to methodology. Despite methodological differences it is clear that the likelihood of developing CPSP varies with type of surgery[3] (Table 1).

A definition of CPSP was proposed in 1999 and recently revised in 2014.[4] The current definition recognized by the International Association for the Study of Pain (IASP) broadly follows the one Werner proposed in 2014. CPSP is due to be included in the next edition of the International Classification of Diseases – ICD11. The IASP definition[5] is shown in Box 1.

Effects of different surgeries on incidence of postoperative chronic pain

Type of surgery	Incidence of chronic pain (%)
Amputation	30–85
Thoracotomy	5–67
Mastectomy	11–57
Inguinal hernia repair	0–63
Sternotomy	28–56
Cholecystectomy	3–56
Knee arthroplasty	19–43
Breast augmentation	13–38
Vasectomy	0–37
Radical prostatectomy	35
Gynaecological laparotomy	32
Iliac crest bone harvest site	30
Hip arthroplasty	28
Saphenectomy	27
Hysterectomy	25
Craniotomy	6–23
Rectal amputation	12–18
Caesarean section	12
Dental surgery	5–13

Table 1

Pathophysiology

Transition from acute to chronic pain

Almost all surgery has the potential to cause acute pain due to activation of peripheral nociceptors, and sensitization of these nociceptors by inflammatory processes at the site of injury. Central sensitization occurs due to prolonged noxious stimuli, lowering of the threshold for nociceptive transmission in the brain and spinal cord. This involves mechanisms such as reduced descending inhibitory control, microglial activation and activation of wide dynamic range interneurons. In some cases these changes persist after tissue healing and pain becomes chronic.[6]

Nerve injury

Neuropathic pain is 'pain which arises from a direct consequence of a lesion or diseases affecting the somatosensory system'

IASP definition of CPSP

- Pain persisting at least 3 months after surgery
- Pain not present before surgery or that has different characteristics or increased intensity from preoperative pain
- Pain is localized to the surgical site or referred area
- Other possible causes of the pain are excluded (e.g. cancer recurrence, infection)

Box 1

Kiran K Koneti *FRCA is a Consultant in Anaesthesia and Pain Management at City Hospitals Sunderland NHS Trust, Sunderland, UK. Conflicts of interest: none declared.*

Joel S Perfitt *MbChB FRCA FFPMRCA is an ST7 in Anaesthesia and Pain Medicine at Sheffield Teaching Hospitals NHS Foundation Trust, Northern General Hospital, Sheffield, UK. Conflicts of interest: none declared.*

(IASP). It deserves special consideration because it is often under-diagnosed, unrecognized and undertreated. Neuropathic features appear in approximately 30% of patients with CPSP and the incidence of neuropathic pain is higher in operations likely to be associated with nerve injury (e.g. thoracotomy, axillary dissection). Iatrogenic nerve injury is likely the biggest single causative factor in the development of CPSP.[1]

Nerve injury causes a cascade of inflammatory processes within the axon to release neurotransmitters and growth factors acting locally and spinally. Damaged nerves may discharge spontaneously leading to pain. Neuroplastic change within the peripheral and central nervous system after nerve injury results in evoked and spontaneous neuropathic pain symptoms.

Severity of symptoms correlates poorly with the magnitude of nerve trauma. Not all patients with symptoms and signs of nerve damage after surgery have pain, and not all patients who undergo operations involving nerve transection, such as rib resection, develop pain.

Risk factors

Many risk factors for the development of CPSP have been identified and are summarized below [7] (Box 2).

Perioperative

Preoperative pain is a risk factor for CPSP, both when the pre-existing pain is in the area of surgery and when the pain is in a distant site. This implies that central mechanisms are involved; pre-existing pain may cause central sensitization, increasing post surgical pain.

Female gender and younger age have identified as risk factors for the development of CPSP.

Risk factors for developing chronic post surgical pain

Preoperative
- Anxiety, catastrophizing, depression
- Chronic pain or pain at site of surgery
- Radiotherapy/chemotherapy

Intraoperative
- Site of surgery (thoracotomy, sternotomy, mastectomy, amputation)
- Extent of surgery
- Duration of surgery
- Incision type
- Low volume surgical unit
- Intraoperative nerve damage

Postoperative
- Unrelieved pain
- High use of analgesics
- Re-operation

Social
- Low income
- Low self-rated heath
- Low educational status
- Lack of social support
- Solicitous responding from significant others

Box 2

Patients receiving chemotherapy or radiotherapy, such as in breast cancer surgery are at higher risk of developing CPSP likely due to the neurotoxic effects of these treatments.

Poorly controlled postoperative pain and longer duration of pain, as well as greater use of analgesics postoperatively is a risk factor for CPSP.

Surgical

Surgical risk factors include; procedures with high risk of nerve damage, extent and duration of surgery and units performing low volumes of surgery. Surgical nerve damage may be due to surgical section of nerves (deliberate or otherwise), compression, ischemia or stretching. Surgical procedures associated with a high risk of neuropathic pain include; axillary dissection, thoracotomy, inguinal herniorrhaphy, limb amputation and mastectomy.

Reoperation at the site of previous surgery is also a risk factor for CPSP.

Psychological

Psychological factors such as preoperative anxiety, catastrophizing, fear of surgery and major depression are associated with a greater risk of CPSP across many different surgical procedures. In the postoperative period, pain catastrophizing and anxiety increase risk of CPSP.

Genetic

Variability in response to experimental pain has been demonstrated in a number of genotypes. COMT polymorphisms are associated with increased pain sensitivity and the development of CPSP.

Variability in drug metabolism due to genetic difference is known to affect response to commonly used analgesics.

Perioperative risk assessment

Identification of perioperative risk factors early in the patients' surgical journey is important. Attempts to address these risk factors may be made along with discussion with the patient regarding the risks and benefits of surgery. Collaboration between the surgeon, anaesthetist and patient, along with pain specialists is important for patients at high risk of CPSP. Preventative strategies may be employed when high risk patients are identified.

Prevention

Given that the two proposed mechanisms for the development of CPSP are sensitization (peripheral and central) and nerve injury, it follows that these are the targets for prevention.

Processes of sensitization at the spinal cord level are driven in part by ongoing nociceptive stimuli from the periphery. Effective multimodal analgesia aims to limit this nociceptive barrage and reduce sensitization. Modification of surgical technique aims to limit tissue trauma and nerve injury.

Surgical

The surgical insult is a major determinant of both acute post-surgical pain and CPSP. Reducing tissue damage is expected to reduce pain. Techniques aimed at reducing nerve injury include nerve-sparing techniques, avoiding excessive traction on nerves, and careful placement of surgical clips. These may reduce the incidence of iatrogenic nerve damage.

Avoidance of unnecessary surgery is an important strategy in the prevention of CPSP. Non-operative management may be preferable in some cases if the risk of CPSP is high. Of course the essential role of surgery in the management of a wide range of often serious and sometimes life threatening diseases is not questioned. Patients often believe that surgery may improve existing chronic pain, such as in cases of lower back, abdominal and pelvic pain. This is however not often the case and repeated surgery is likely to worsen an existing chronic pain problem.

Pharmacological

Multimodal perioperative analgesia is recommended to provide effective analgesia for acute pain while limiting side effects from these drugs, particularly opioids. Drugs used for current multimodal analgesia includes paracetamol, NSAIDS, gabapentinoids, local anaesthetics, α-2 agonists (clonidine) and opioids.

Preventative analgesia reduces acute and chronic pain by inhibiting nociceptive input during the perioperative period, with an effect that extends beyond the pharmacological effect of the drug. Severity of acute post surgical pain correlates with CPSP, and optimization of postoperative analgesia has shown benefits in reducing CPSP.

The use of perioperative gabapentinoids (gabapentin and pregabalin) has received considerable interest as a method of improving postoperative analgesia and reducing the incidence of CPSP. There is some evidence for their efficacy in preventing CPSP after knee arthroplasty and lumbar discectomy. Overall there is insufficient to recommend their use routinely but there may be a role in some patients.

The NMDA receptor antagonist ketamine has shown some beneficial effects and may have a role in preventing CPSP. It was the only pharmacological method found to have a preventative effect in the 2013 Cochrane review.[7] It decreases nociceptive amplification at spinal cord level and reduces opioid induced hyperalgesia.

Regional anaesthesia

Regional anaesthesia is the most effective method of preventing moderate to severe acute post operative pain. Complete blockade of nociceptive transmission is possible for the duration of the anaesthetic block. This reduces perioperative pain and may reduce sensitization. A 2018 Cochrane review of the effect of regional anaesthesia on CPSP reported that for thoracic surgery, caesarian section and breast surgery, regional anaesthesia reduced the risk of CPSP when compared to standard non-regional anaesthesia.[8]

Psychological/other

Psychological risk factors are well recognized in the development of many chronic pain states including CPSP. Specific perioperative psychological management is not well established; however, such programmes do exist for established chronic pain.

Unhelpful pain beliefs should be challenged by healthcare staff to reassure patients some post surgical pain is expected and does not equal further harm. Patients should be educated on appropriate use of analgesics regarding dosing, timing and expectation.

Management

General chronic pain management

The modern approach to chronic pain management is based on the biopsychosocial model. Biologically modifiable factors should be identified and where possible treated. Psychosocial elements are equally, if not more important in many cases and these should be identified and addressed. Without assessment of the complex elements contributing to the patient's pain experience, a favorable outcome is unlikely.

Very often in the management of CPSP, absolute pain reduction is often not an achievable aim. Improvements in function and quality of life are aims more likely to be achievable and should be pursued.

The biological component of pain includes any biological pain generators. This includes the amount of tissue disruption at the time of surgery, potential nerve injury and scarring or adhesions, which may contribute to pain. Potentially reversible causes of pain should be considered such as infection, recurrence of previous pathology and specific complications from surgery such as damaged prosthesis. The patient should be reviewed by an experienced surgeon to rule out these causes. In many cases a clear cause cannot be identified.

Pharmacological

Opiates are the mainstay of a multimodal strategy for acute post surgical pain management for moderate to severe pain. In contrast to their well-accepted role in the management of acute pain, opiates have poor efficacy in the management of CPSP. The long-term side effects of opiates include tolerance, addiction, hyperalgesia, endocrine dysfunction and death. There is little evidence that they are effective in improving pain, function and quality of life in the long term. The recent 'opioid crisis' in the US has shown the disastrous effect of uncontrolled prescribing of strong opiates for chronic pain.

Recent guidance from the 'opioids aware' publication by the Faculty of Pain Medicine[9] is summarized below (Box 3).

Weak opiates carry lower side effects and risk than strong opiates and uncontrolled dose escalation is less likely. They therefore are preferred as long as they are effective, used when needed and side effects are tolerable and managed.

Opioids: benefits and cautions

- Opioids ire very good analgesics for acute pain and for pain at the end of life but there is little evidence that they are helpful for long term pain
- A small proportion of people may obtain good pain relief with opioids in the long-term if the dose can be kept low and especially if their use is intermittent (however it is difficult to identify these people at the point of opioid initiation)
- The risk of harm increases substantially at doses above an oral morphine equivalent of 120 mg/day, but there is no increased benefit tapering or stopping high dose opioid needs careful planning and collaboration
- If a patient has pain that remains severe despite opioid treatment it means they are not working and should be stopped, even if no other treatment is available
- Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they arc on high opioid doses, a very detailed assessment of the many emotional influences on their pain experience is essential

Box 3

Pharmacological management of neuropathic pain

All treatment (except trigeminal neuralgia)

- Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment tor neuropathic pain (except trigeminal neuralgia)
- If the initial treatment it not effective or it not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated
- Consider tramadol only if acute rescue therapy is needed
- Consider capsaicin cream for people with localized neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments

Box 4

Treatment of neuropathic pain

The management of neuropathic pain is distinct from somatic pain and therefore accurate diagnosis is required for the most effective treatment.

Several questionnaire-based diagnostic tools exist for the diagnosis of neuropathic pain. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) offers sensitivity and specificity of over 80% and is easy to administer consisting of 5 symptoms and two clinical signs.

Nerve conduction studies can be used in selected cases to demonstrate a nerve lesion, however neuropathic pain can be present even with normal nerve conduction studies. The majority of cases of neuropathic pain are diagnosed clinically.

NICE clinical guideline 173 published in 2013[10] recommends the pharmacological management of neuropathic pain in non-specialist settings. The recommendations are summarized in Box 4.

Interventional management

Intervention management of CPSP largely involves targeted needle based therapies either using radiofrequency or drugs as well as spinal cord stimulation.

Pulsed radiofrequency (PRF) is an emerging treatment for neuropathic pain including CPSP. It involves application of short bursts of high frequency alternating current to nerves to modulate pain transmission and reduce pain. There is minimal heating effect and no histological damage to the nerve, in contrast to conventional (thermal) radiofrequency. The underlying mechanism is poorly understood but alteration in gene expression has been detected in targeted nerves.

Interventional therapies involving the targeted application of local anaesthetics and steroids are employed for diagnostic and therapeutic purposes.

Spinal cord stimulation therapy is a recognized treatment for neuropathic pain syndromes including CPSP. Its evidence is best for the treatment for neuropathic leg pain following spinal surgery. Prolonged reduction in pain can be achieved in patients who respond. This treatment is clearly invasive and not without risk of complications.

Surgical

Patients should be reviewed by an experienced surgeon to establish if there is ongoing treatable surgical pathology. If the surgery has failed to achieve it's desired aim, was performed incorrectly or if there has been a treatable surgical complication then re-operation may be appropriate. If, however, there is nothing identified likely to be causing the pain that can be treated surgically, then surgery is not indicated. Surgical re-exploration due to pain is highly likely to contribute to ongoing pain rather than resolve it given the already sensitized state of the somatosensory system.

Psychological

Psychological therapies are well recognized in the management of chronic pain. It is important to note that the use of psychologically based therapies in the management of pain does not imply that the pain is 'psychological', or 'made up' by the patient. Instead, the use of psychological therapies is an acknowledgement of the complexity of pain and its impact on the psychological functioning of a person.

Therapies such as cognitive behavioral therapy (CBT) and more recently acceptance and commitment therapy (ACT) are well evidenced for the treatment of a wide range of chronic pain conditions.

Pain management programmes are group based, psychologically informed programmes which aim to improve function and quality of life for patients living with persistent pain. These programmes usually incorporate elements of movement based therapy, relaxation and meditation as well as pain education.

Conclusion

Much progress has been made in the last 13 years since the publication by Kehlet drawing attention to the burden of chronic post surgical pain.[1] Much needs to be done however to raise awareness and improve outcomes for patients who are left with the long term impact of pain after surgical procedures. Recognition by the medical community of this important cause of long term pain and disability should lead to better prevention and treatment. ◆

REFERENCES

1 Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006 May 13; **367:** 1618–25.

2 Macrae WA. Chronic post-surgical pain: 10 years on. *Br J Anaesth* 2008 Jul; **101:** 77–86.

3 Visser EJ. Chronic post-surgical pain: epidemiology and clinical implications for acute pain management. *Acute Pain* 2006; **8:** 73–81.

4 Werner MU, Kongsgaard UEI. Defining persistent post-surgical pain: is an update required? *Br J Anaesth* 2014 Jul; **113:** 1–4.

5 International Association for the Study of Pain. Global year against pain after surgery. Fact sheet No. 4. 2017. accessed 22nd January 2019, https://s3.amazonaws.com/rdcms-iasp/files/production/public/2017GlobalYear/FactSheets/4.%20Chronic%20Postsurgical%20Pain.LavandHomme-Zahn-EE_1485789834697_3.pdf.

6 Shipton EA. The transition from acute to chronic post surgical pain. *Anaesth Intensive Care* 2011 Sep; **39:** 824–36.

7 Chaparro LE1, Smith SA, Moore RA, Wiffen PJ, Gilron I. Pharmacotherapy for the prevention of chronic pain after surgery in adults. *Cochrane Database Syst Rev* 2013 Jul 24;(7): CD008307.

8 Weinstein EJ, Levene JL, Cohen MS, et al. Local anaesthetics and regional anaesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children. *Cochrane Database Syst Rev* 2018 Apr 25; **4**: CD007105.

9 Faculty of Pain Medicine. Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. 2019. accessed 22nd January 2019, https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware.

10 NICE clinical guideline (CG173) published November 2013 updated April 2018. Neuropathic pain in adults: pharmacological management in non-specialist settings. 2013. accessed 22nd January 2019, https://www.nice.org.uk/guidance/cg173.

