Transition from acute to chronic pain after surgery

Patricia Lavand'homme*

1. Introduction

Any tissue trauma can lead to “chronic pain,” which by definition is pain that persists past the normal healing time. This type of pain is frequent after surgery. In 1998, Crombie et al. noted that 22.5% of patients attending pain clinics attributed their pain to a previous surgery, and since then, numerous original research articles, review articles, and editorials have addressed chronic pain after surgery. Long-term pain after surgery causes disability and suffering associated with reduced quality of life and increased use of health care resources. For that reason, chronic postsurgical pain (CPSP) has become a health priority and will be included in the new version of the International Classification of Diseases (ICD-11), as a result of the combined efforts of the World Health Organization (WHO) and the IASP. Adequate pain treatment is a human right, and the inclusion of CPSP in the ICD-11 is expected to increase recognition of the problem and promote interdisciplinary research in the field. Indeed, CPSP is now accepted as an important outcome of surgery. Researchers have determined its prevalence in the adult population and examined its incidence after various procedures. However, while the global volume of surgeries is increasing worldwide, the occurrence of CPSP has not really decreased over the years because preventive strategies are not clearly defined and thereby not applied in clinical practice, in contrast to the progress made in basic research in the understanding of incisional pain physiology.

In daily clinical practice, the transition from acute postoperative pain to CPSP is often subtle and unpredictable. Rather than focusing on pathophysiological mechanisms, the following discussion will address clinical aspects, ongoing improvements in management, and future challenges.

2. The “problem” of chronic postsurgical pain: evolution and new approaches

Chronic postsurgical pain may occur irrespective of the type of procedure, although some surgeries carry a higher risk in relation to the degree of tissue damage and the potential for a major inflammatory reaction or nerve injury. An editorial dedicated to acute postoperative pain summarized the situation as follows: “CPSP develops in 1 of 10 surgical patients and becomes an intolerable pain condition after 1 of every 100 operations.” In 2016, studies from large cohorts of patients and prospective studies still showed the same prevalence (Table 1), despite a significant evolution in surgical techniques. Laparoscopic procedures and minimally invasive approaches have only slightly modified the incidence of CPSP, but their impact on the intensity and duration of CPSP deserves further assessment. A recent multicenter observational study on CPSP in Europe reports a 12-month incidence of 11.8% for moderate CPSP and 2.2% for severe CPSP (defined by a score >6 on a numeric rating scale ranging from 0-10).

The nature of CPSP is often poorly characterized in clinical studies. However, a neuropathic component may exist in around 35% of cases. The reported prevalence of a neuropathic component differs among surgical procedures, depending on the likelihood of surgical iatrogenic nerve injury and the method or tool used to assess its presence. Signs of neuropathic pain are important to detect because they are always associated with higher pain intensity and a poorer quality of life. Furthermore, neuropathic pain requires a specific therapeutic approach.

For several years, CPSP has been assessed in adult hospitalized patients undergoing major surgical procedures such as thoracic surgery or limb amputation. Recently, orthopedic procedures and specifically joint replacements have been considered as a major risk for development of CPSP. The volume of knee and hip arthroplasties is growing because the population is growing older and inflammatory diseases as well as obesity are becoming more frequent. Although outcomes in terms of pain relief and mobility are highly successful for most patients undergoing joint arthroplasty, 20% of them will develop CPSP after knee arthroplasty and 10% after hip arthroplasty.

The intensity of CPSP is greater after joint arthroplasty than after visceral or gynecological surgery.

It is unfortunate that CPSP data are still missing for specific populations and subgroups of patients because they might yield important findings for a better understanding of the chronification of acute postoperative pain. Only recently, CPSP was found to be an important problem in children. The prevalence of CPSP is lower when surgery is performed at a younger age, perhaps because surgical procedures are simpler and recovery is faster during childhood. Nevertheless, CPSP has a significant impact on any child’s quality of life and is associated with poor long-term outcomes. Therefore, better understanding of the context of CPSP development in children is mandatory to prevent pain persistence into adulthood. Furthermore, studying CPSP in children is a unique opportunity to assess the role of pain at a critical period of development and to determine the impact of protective factors vs risk factors, including hormonal factors and social variables such as parental influence.

Studies addressing recovery from CPSP in the context of outpatient surgery are scarce. Although outpatient surgery might be different in terms of tissue damage and anesthetic

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Chronic postsurgical pain is either a continuum of acute postsurgical pain; new studies should assess all patients at several time points. Not only the incidence but also the intensity of CPSP decreases with time. Furthermore, studies focusing on neuropathic pain reach their lowest level by 3 months after surgery. The cutoff for CPSP has now been fixed at 3 months after surgery. Chronic postsurgical pain shows greater intensity or different components of CPSP have highlighted the variability of these aspects over time. Several problems arise when investigating CPSP, and the first involves its definition. Werner and Kongsgaard proposed an updated definition based on observations and the most important concerns raised during the last few years (Table 1). These criteria will factor into the definition of CPSP that will be included in the ICD-11. The major points are as follows:

1. Chronic postsurgical pain is either a continuum of acute postsurgical pain or develops after an asymptomatic period.
2. Chronic postsurgical pain shows greater intensity or different pain characteristics than preoperative pain (an important point regarding CPSP after orthopedic procedures, where preoperative pain may affect up to 80% of patients undergoing surgery).
3. The cutoff for CPSP has now been fixed at 3 months after surgery because healing times differ among different procedures; for major orthopedic surgeries such as hip and knee arthroplasties, pain reaches its lowest level by 3 months after surgery.

### 3. The resolution of pain after surgery: pointing to a novel definition of chronic postsurgical pain

Fortunately, CPSP resolves over time. Of all patients with CPSP 6 months after surgery, 55.8% will be pain free at 12 months, whereas 2.9% of patients without pain at 6 months will report some pain at 12 months. Such findings reinforce the fact that CPSP does not always develop on a continuum from acute postsurgical pain; new studies should assess all patients at several time points. Not only the incidence but also the intensity of CPSP decreases with time. Furthermore, studies focusing on neuropathic components of CPSP have highlighted the variability of these aspects over time. Several problems arise when investigating CPSP, and the first involves its definition. Werner and Kongsgaard proposed an updated definition based on observations and the most important concerns raised during the last few years (Table 1). These criteria will factor into the definition of CPSP that will be included in the ICD-11. The major points are as follows:

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### 4. Predictive tools: strengths and weaknesses

Chronic postsurgical pain may develop after any surgical procedure, and the fact that the pain is sometimes disproportionate to the degree of tissue trauma underlines the major role of individual factors. In pain clinics, the suffering expressed by patients results from both pain amplification and psychological distress. As prevention is always better than a cure, the development of reliable predictive tools to detect the high-risk patients for CPSP is mandatory. Studies investigating the association of CPSP with 90 genetic markers found no evidence for genetic predisposition in a subset of 1000 patients, whereas 6 clinical factors predicted 73% of the chronic postsurgical pain that developed. Today, despite the hopes and promises of genetic research, which has revealed several links between gene polymorphisms and sensitivity to pain, clinical risk factors remain the best available predictors of CPSP. However, in daily practice, even if the risk factors are well known, the proposed risk index is still not sensitive and specific enough to determine which patients are at most risk.

The chronicization of postoperative pain often remains subtle, and the risk factors involved in the transition from acute to chronic postsurgical pain probably differ from those involved in maintaining chronic pain once it has developed. The most important risk factors involved in the development of CPSP are as follows:

1. The intensity of acute postoperative pain;
2. The presence of preoperative pain in the body part to be operated on or elsewhere (including coexisting chronic painful conditions such as fibromyalgia, headache, low back pain, or restless leg syndrome);
3. Symptoms of psychological distress and major stress such as depression, extreme anxiety, or catastrophizing.

Acute postoperative pain intensity, “recalled pain” in retrospective studies, is a highly prominent risk factor although the association between acute postoperative pain and CPSP is not

### Table 1

<table>
<thead>
<tr>
<th>Population</th>
<th>Preoperative pain</th>
<th>Severe acute postoperative pain</th>
<th>CPSP moderate/severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crombie et al,8</td>
<td>Adult patients in pain clinics</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Macrae,25</td>
<td>Adult population</td>
<td>10%-50%/4%-10%</td>
<td></td>
</tr>
<tr>
<td>Johansen et al, 2012</td>
<td>General adult population</td>
<td>18.3% (6.2% without preoperative pain)</td>
<td></td>
</tr>
<tr>
<td>Fletcher et al,13</td>
<td>Adult inpatients</td>
<td>35%-60%</td>
<td>30%</td>
</tr>
<tr>
<td>Hooftwijk et al,18</td>
<td>Adult outpatients</td>
<td>37.7%</td>
<td>26.7%</td>
</tr>
<tr>
<td>Nikolajsen and Brøx29</td>
<td>Pediatric population</td>
<td>13% (with NRS &gt; 3)*</td>
<td></td>
</tr>
</tbody>
</table>

*NRS: Numeric rating score on a scale from 0 (no pain) to 10 (worst possible pain).

CPSP, chronic postsurgical pain.

### Table 2

**Updated definition of chronic postsurgical pain.**

- Pain developed after a surgical procedure or increased in intensity after the surgical procedure.
- Pain should be of at least 3 mo duration with a significant negative effect on the quality of life.
- Pain is a continuation of acute postsurgical pain or may develop after an asymptomatic period.
- Pain is localized to the surgical field or to a referred area (eg, innervation territory, referred dermatoma for visceral surgery).
- Other possible causes for the pain have been excluded (eg, infection, cancer recurrence).

Italic characters concern the modifications proposed and added to the initial definition (from Macrae WA, 2008; and Werner MU and Kongsgaard UE, 2014). The current definition of chronic postsurgical pain has been accepted by the IASP Task Force on Chronic Pain and will be included in ICD-11.
necessarily a causal one. An estimated 30% of patients endure severe pain (numeric rating scale > 6) during the first 24 hours after surgery, even after minor procedures. Fortunately for the patients, not all of those who experience severe acute postoperative pain will develop CPSP. Conversely, and unfortunately for the patients’ caregivers, optimal control of acute postoperative pain is not a guarantee that CPSP will not develop, as highlighted by the failure of current perioperative treatments such as multimodal analgesia and local and regional techniques to significantly reduce the incidence of CPSP. Indeed, epidural analgesia may prevent CPSP after thoracotomy in 1 of 4 patients, and paravertebral block may prevent CPSP after breast cancer surgery in 1 of 5 women, which supports the mandate to target high-risk patients and to individualize perioperative management. Postoperative pain and the development of CPSP not only vary among individuals but are dynamic processes. The fact that a 10% increase in the percentage of time in severe pain is associated with a 30% increase in the incidence of CPSP at 12 months certainly demonstrates that acute postoperative pain intensity is a risk factor for some patients. However, it does not allow us to determine which patients are at high risk.

The resolution of postoperative pain matters more than the initial pain intensity. The development of “pain trajectories” should allow us to characterize an individual’s postoperative pain and thereby identify abnormal resolution of acute pain. In a study that mapped pain trajectory patterns, and specifically the slope of the trajectory (ie, pain resolution), during the first week after surgery, 25% of patients showed no pain resolution (a flat slope), whereas 12% of patients had a greater postoperative pain (a rising slope). In a study on pain after total knee replacement, patients whose pain was increasing a week after surgery were still in severe pain 3 months after surgery, and their CPSP had a neuropathic component.

There are 2 lessons to be learned from these observations. First, the control of acute postoperative pain should include correct assessment of pain and early intervention with accurate treatment. The diagnosis of a neuropathic component in the early postoperative period is feasible with the use of adequate tools. Back in 2002, Hayes et al. pointed out that acute pain services often neglected to assess neuropathic pain. They reported that among the 3% of patients diagnosed with neuropathic pain by their acute pain service, 78% had ongoing pain at 6 months and 56% at 12 months.

Second, the characteristics of pain are important in identifying patients at high risk for CPSP. Unfortunately, most clinical trials do not provide many details regarding the type of pain, either postoperative or chronic; for example, only 40% of trials assess pain related to mobilization (ie, evoked pain), which plays a major role in rehabilitation after surgery. After laparoscopic cholecystectomy, 3 components contribute to the overall burden of pain: incisional pain (somatic pain), deep abdominal pain (visceral pain), and shoulder pain (referred pain). The 3 components show distinct pain trajectories, with incisional pain having the highest pain scores. Surprisingly, the risk of chronic pain after laparoscopic cholecystectomy is significantly related to the visceral pain response during the first week after surgery. In patients with osteoarthritis with joint pain, there is a growing recognition of the importance of distinguishing between pain at rest and pain on movement, owing to different underlying pain mechanisms and a different response to analgesic treatments. A recent study intended to explore the relationship between acute postsurgical pain and preoperative pain on one hand and CPSP on the other hand after knee and hip replacement secondary to osteoarthritis, considering both pain at rest and movement-evoked pain. The main findings of the study are the preponderant influence of preoperative pain either at rest (for hip arthroplasty) or on movement (for knee arthroplasty) in predicting the intensity of postoperative pain at rest or on movement.

Preoperative pain at the surgical site or elsewhere also stands as a major risk factor for persistent pain after surgery. Two explanations underlie the phenomenon: the link between pain and sensitization to further pain and the impact of taking preoperative analgesics. Patients taking opioid analgesics before surgery report higher acute postoperative pain and are at a greater risk for painful prolonged recovery, particularly after orthopedic procedures. Is sensitization caused by opioid intake the explanation? The answer is not so simple. Opioid analgesics are not very effective against evoked pain (ie, pain associated with movement). A prospective study on CPSP in outpatients scheduled for orthopedic surgery found that in patients achieving effective pain relief with preoperative analgesics, only 8% developed CPSP. By contrast, 32% of patients taking preoperative analgesics without achieving effective pain relief developed CPSP. These data underline the complexity of the relationship between preoperative pain, its control, and CPSP. Further studies should focus on preoperative pain control as a preventive measure to reduce both the incidence of severe acute pain and the development of persistent pain after surgery. The experience of pain results from both pain amplification and psychological distress, and some patients are more prone to develop severe pain both immediately after tissue lesion and subsequently. Thereby, progress in preventive strategies is strongly linked to individualization of treatments based on the knowledge of the patient’s pain phenotype. The use of quantitative sensory testing allows clinicians to determine a patient’s endogenous pain modulation profile and thereby might allow mechanism-based pain management as more appropriate pain therapy. Around 68% to 82% of patients scheduled for joint replacement present with preoperative pain caused by osteoarthritis. In those patients, nociceptive peripheral pain is associated with a central sensitization process in 30% of cases, particularly when a neuropathic component is present. However, individualized perioperative treatments are rarely provided because the patient’s pain phenotype is not taken into account.

Mental health has an important impact on the patient’s ability to recover after surgery. There is a vulnerable population of individuals with a reduced ability to cope with pain, to anticipate pain, and to control pain when confronted with it. A tendency toward anxiety, psychological distress such as depression, hypervigilance, and catastrophizing are all risk factors for both severe acute postoperative pain and CPSP. However, the importance of these psychological factors varies from one surgical population to another. Catastrophizing has only a minor impact on pain after cesarean section in comparison with its role in pain after breast cancer surgery. Models of postoperative pain in children display 2 distinct trajectories: early recovery (49.8%) and late recovery (11.2%). While child catastrophizing has no impact, parental pain catastrophizing before surgery significantly predicts late recovery. Furthermore, as time from surgery increases, parents exert more and more influence over the pain response of their children.

Chronic postsurgical pain should be considered a “mixed pain syndrome” in which neuropathic pain represents one of the components that, when present, contributes to pain severity and chronification. As a neuropathic component is present in at least one-third of CPSP cases, determining the factors that contribute to whether or not a nerve lesion will become painful is...
highly relevant. Indeed, not all lesions in the somatosensory system lead to neuropathic pain.36 In the first 48 hours after surgery, higher pain intensity, a positive neuropathic pain score, and evidence of secondary hyperalgesia (a clinical correlate of central nervous system sensitization) are all predictive of CPSP involving a major neuropathic component.25 A history of previous neuropathy is also a risk factor,11 which highlights the role of genetic predisposition to less-successful nerve regeneration after injury in the development of CPSP.38

5. The subacute pain period: the role of transitional pain services

After hospital discharge, postoperative pain can last for several weeks. This “subacute pain” period remains a rather neglected area, a “gray zone” of clinical investigations, despite its crucial role in rehabilitation and the patient’s return to his or her preoperative status.22 A few prospective studies have underlined the predictive value of 30-day or 6-week postoperative pain intensity as a risk factor for the development of CPSP, for example, after inguinal hernia repair and cosmetic breast surgery.22 In clinical studies using long-term pain trajectories after surgery, analysis conducted between 6 weeks and 3 months shows subgroups of patients who will or will not resolve their pain after knee arthroplasty.30 The intensity of subacute pain 30 days after knee replacement is a risk factor for severe CPSP at 3 and 6 months.15 Pain intensity may even increase during the subacute period, revealing the presence of a neuro- pathic pain process, as observed after hernia repair or orthopedic surgery in rehabilitation units.30 It is worth noting that not only pain intensity but also pain unpleasantness (the emotional aspect of pain) might be an important predictor of subsequent CPSP development, as highlighted in a pediatric population during the subacute period (eg, at 6 weeks).31 In pain clinics, patients who attribute their chronic pain to a specific cause often report a higher level of emotional distress and pain intensity.8 For a large majority of patients, the worst pain period occurs at home (eg, outpatients) and during rehabilitation efforts (eg, orthopedic patients), which supports the implementation of transitional pain units as an integral part of “perioperative medicine” to provide the most effective pain treatment and to attract the attention of caregivers, patients, and their relatives. As stated above, chronic postsurgical pain results from pain amplification and emotional distress. Although the risk factors are well known, they do not allow clinicians to identify patients at very high risk or to provide effective preventive treatments. Future challenges include the optimization of predictive tools. Screening of new populations including pediatric patients, the use of pain trajectories including observation of patients during the subacute pain period, and the implementation of transitional pain units as part of perioperative medicine are exciting projects that should help caregivers to find a better approach to the transition from acute to chronic postoperative pain.

Conflict of interest statement

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