

# Chronic pain after surgery and trauma: current situation and future directions

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## Abstract

Chronic post-surgical pain (CPSP) stands as a major health issue. The unchanged incidence over the last two decades underlines both the failure of predictive models developed until now and the lack of efficacy of common “preventive” strategies (pharmacotherapy and regional analgesic techniques) applied in current clinical practice. The recognition of CPSP as a disease and the release of a common definition of the condition is an important progress in the field. CPSP predictive scores exist but none has presently demonstrated an impact on patient care. New clinical directions based on the resolution of postoperative pain, a complex and highly dynamic process supported by individual pain trajectories, argue for predictive models and preventive strategies extended to the subacute pain period i.e. after hospital discharge.

**Keywords:** Chronic PostSurgical Pain, postoperative pain, risk factors, predictive risk models, preventive strategies, sub-acute postoperative pain.

## Introduction

Although pain itself is not immediately life threatening, chronic pain is the leading cause of years lived with disability<sup>1</sup>. Persistent pain after surgery is common and may even progress to a chronic pain condition i.e. chronic post-surgical pain, CPSP. Any chronic pain condition decreases the quality of life because pain impairs functional status and causes psychologic distress. Furthermore, psycho-social problems and sleep disturbances often are associated to pain and to chronic drugs intake like pain killers and psychotropic medicines which are wellknown sources of drug addiction. For the aforementioned reasons, the World Health Organization (WHO) has sought to include chronic pain in the new international classification of diseases i.e. ICD-11. Among the common chronic pain conditions, chronic post-surgical pain (CPSP) and chronic post-traumatic pain have deserved their own classification as a formal recognition of an existing problem and major health issue<sup>2</sup>. The inclusion of CPSP in ICD-11 will increase the

visibility of the problem and hopefully will promote collaborative efforts to better control the situation.

## Chronic Post-Surgical Pain: little progress made over two decades

CPSP prevalence has not changed over the last two decades, since its first description by Crombie in 1998 who stated that surgery contributed to pain in 22.5% of patients attending the Pain Clinics (trauma also was a cause of pain in 18.7% of patients)<sup>3</sup>. Since then, numerous retrospective and prospective studies have assessed the prevalence of chronic pain after various surgical procedures. According to the study design and the definition used for chronic pain (i.e. cut off used for pain intensity and duration), CPSP incidence may widely differ (range from 5% to 85%)<sup>2</sup>. The prospective and retrospective observational cohort studies published in the last decade, including common procedures, both in- and out-patients surgeries<sup>4</sup>, report similar incidences (see Table I)<sup>5-15</sup>. It is worth noting that the presence of a neuropathic component is often mentioned in

**Table I.** — Incidence of Chronic Post-Surgical Pain (CPSP) in different populations.

Study Prospective [P], retrospective [R]	N	Type of surgery	CPSP Incidence (severe to moderate pain)	Neuropathic pain component
<u>Adult population</u> Johansen et al. 2012 (TROMSO population study) [R] <sup>12</sup>	2043	All types	At 3 months and later : 6.2% (6.6-11.7%)	24.5%
Fletcher et al. 2015 [P] <sup>11</sup> Hoofwijk et al. 2015 [P] <sup>4</sup> Khan et al. 2021 [P, secondary analysis of VISION study] <sup>13</sup>	1044 908 14831	All types Out-patients – all types All types, non cardiac surgery	At 12 months: 2.2% - 11.8% At 12 months: 2.3% - 15.3% At 12 months: 3.1% - 3.6%	35.4% - 57.1% --- 81%
<u>Adult population post-trauma</u> Edgley et al. 2019 [P] <sup>10</sup>	303	Orthopedic (trauma fixation)	At 3 months: 59% - 71%	---
Aulenkamp et al. 2022 [P] <sup>5</sup>	127	Orthopedic (trauma fixation)	At 12 months: 42.7%	17.1%
<u>Elderly population (over 65 years old)</u> Goto et al. 2020 [P] <sup>7</sup> Diakomi et al. 2020 [P] <sup>6</sup>	72 182	Hip fracture open repair Hip fracture open repair	At 2 months and later: 30.6% At 3 – 6 months: 60% - 45%	--- ---
<u>Pediatric population (less than 17 years old)</u> Fortier et al. 2011 [P] <sup>9</sup>	113	All types (mostly orthopedic)	At 4 months: 13%	---
Batoz et al. 2016 [P] <sup>8</sup>	291	All types (major procedures)	At 3 months: 3.9% - 10.9%	64.3%
Rosenbloom et al. 2019 [P] <sup>15</sup>	265	All types (major procedures)	At 6 months: 35% - 38%	---
Narayanasami et al. 2022 [P] <sup>14</sup>	109	Scoliosis and pectus surgery	At 6 - 12 months: 25.7% - 28.2%	---

CPSP and always associated to higher pain severity, more disability and poorer quality of life<sup>16</sup>.

The reality of CPSP is also highlighted in reports from the recently developed “Transitional Pain Services, TPS”. These services have been developed as humanistic projects to fill the gap between the acute pain services developed in the 1990’s and the traditional Pain Clinics. The majority of the patients referred to the TPS have undergone either thoracic or orthopedic (limbs and spine) procedures and around 70% of them present with allodynia and hyperalgesia i.e. a neuropathic component in their pain<sup>17,18</sup>. Unchanged incidence of CPSP over the last decades underlines the failure of existing predictive models and preventive strategies.

However, knowledge about CPSP are still progressing as CPSP is now assessed in various patient populations like pediatric patients (from 6 to 17 years old), elderly (older than 65 years old) including frail patients and recently after trauma surgery (Table I). Emerging research suggests that pain may persist for several months after surgery in children and adolescents<sup>19</sup>. In this meta-analysis and systematic review including 12 studies, Rabbitts et al report a CPSP incidence of 20% (IQR 14.5 – 38%) at 12 months after major surgical procedures, mainly orthopedic surgery. Pain in children of

school bearing age has major consequences on health, social functioning and education. To date CPSP management in children has received little attention. While the French study from Batoz et al found 64% of children presenting with a neuropathic pain component at 3 months after surgery, no patient received adequate treatment with antiepileptic or antidepressant drug<sup>8</sup>. Also interesting to note, in the Canadian study from Rosenbloom et al, among children reporting CPSP at 12 months, around 6.75% received chronic opioid treatment<sup>15</sup>. Such observations point out the extremes of chronic pain management in a population of children and emphasize the need for more consensus. The presence of CPSP in elderly patients (older than 65 years) also has received little attention until now despite that population aging should suggest the occurrence of a major health issue. Chronic pain conditions are common in older adults and may be associated to the presence of frailty<sup>20</sup>. Frailty syndrome which is characterized by limited physiologic reserve and reduced ability to withstand stressors, is predictive of poor surgical outcomes. In a prospective study, preoperative frailty was found to be associated with an almost five times increased risk of CPSP in adults over 65-years old undergoing non cardiac surgery<sup>21,22</sup>. The problem of chronic pain

after hip fracture repair remains poorly explored, large trials usually having focused on survival and functioning. Recent studies however have pointed out a non negligible incidence of CPSP associated to poor recovery and disability in patients over 75 years old after hip fracture repair: 30.6% CPSP incidence during mobilization at 8 weeks (N=72; age 83 + 7 years) 7 and 45% CPSP at 12 months (N=182; age 78+10 years)<sup>6</sup>. It is worth noting here that the presence of preoperative frailty was not assessed in those studies. Finally, in the adult population, orthopedic surgery carries a 3-fold higher risk of CPSP in comparison with other surgeries<sup>11</sup>. Despite this observation, CPSP incidence and risk factors after trauma surgery i.e. fracture fixation remain understudied<sup>5</sup>. A prospective observational study (N=127) reported a 57% CPSP incidence at 3 months and 43% (with 17% neuropathic pain) at 12 months, that is higher than CPSP incidence observed after elective limb orthopedic surgery<sup>5</sup>. Importantly, the study results suggested that chronic pain was more related to the initial fracture-related trauma than to the surgical trauma.

### First progress about CPSP: a common definition and its recognition as a disease

More than 300 millions surgical procedures are performed globally each year and when the total volume of surgical procedures performed on an annual basis is taken into consideration, the global burden of CPSP are likely to be high. These facts have prompted the recognition of CPSP as a disease and the necessity to have a common definition of the condition<sup>2</sup>. Persistent postoperative pain is common after surgery, particularly after major procedures. Persistent postoperative pain is a term for pain that continues to be present beyond normal healing while CPSP implies chronicity (cut off has been fixed at 3 months after surge, impact on the quality of life (what may differ from pain intensity alone which

**Table II.** — Definition of Chronic Post-Surgical Pain (Schug et al, Pain 2019)<sup>2</sup>

<ul style="list-style-type: none"> <li>• The pain developed after a surgical procedure or increased in intensity or presented novel characteristics (e.g. neuropathic component) after the surgical procedure</li> <li>• Duration at least 3 months with a significant negative effect on the Quality of Life</li> <li>• Pain is a continuation of acute postoperative pain or develops after an asymptomatic period</li> <li>• Pain is localized in the surgical field or in referred area</li> <li>• Exclusion of other possible causes for the pain (infection, cancer recurrence...)</li> </ul>
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is highly subjective), different characteristics from preoperative pain in terms of features and intensity and exclusion of common causes for chronic postsurgical pain such as diagnosed infection or cancer recurrence (see Table II).

### From perioperative risk factors to predictive models of CPSP: where is the failure?

CPSP may develop after any surgical procedure and, as a correlate, individual factors play a major role in the process of pain chronification. Over the last decades, numerous studies have assessed the risk factors associated with CPSP development (see Table III). By contrast to genetic factors, clinical risk factors have always shown a better predictive value as they could predict 70 percent of CPSP risk<sup>23</sup>, specifically the surgical procedure itself, physical health, mental health and the presence of preoperative pain in the surgical field or elsewhere (e.g. chronic pain condition like low back pain, headaches, fibromyalgia...). Besides, numerous studies have also highlighted the presence of severe acute postoperative pain as an important risk factor of future CPSP<sup>24</sup>. What does it mean? On one hand, some peoples are clearly predisposed to develop severe pain after surgery or trauma (“pain begs pain”)<sup>24</sup>. On the other hand, postoperative pain stands as an important factor on which some preventive actions might be directed. By consequence, the relationship between severe acute postoperative pain and CPSP development deserves attention. A recent review assessing the relationship between acute postoperative pain and CPSP found the relation to be moderate at best<sup>24</sup>. Although the lack of association probably was in relation with the measurement methods used, when pain intensity was reported, the severity of acute pain during mobilization predicted the severity of CPSP.

Several predictive models of CPSP have been developed on the basis of predictive factors. In a recent systematic review<sup>26</sup>, 19 prediction models have been identified. Predictors most frequently presented in final development models included preoperative pain in the surgical area (85% of the models), preoperative pain in other areas (43%), sex or gender (31%), and acute postoperative pain severity (31%). Intraoperative factors like surgical procedure and technique and postoperative pain intensity are only included in a few current models. Nevertheless, the unchanged incidence of CPSP questions the clinical utility of these existing predictive models.

The resolution of postoperative pain is a complex and dynamic process as highlighted by the concept

**Table III.** — Perioperative risk factors associated with CPSP development.

Domain of risk factor	Preoperative period	Intraoperative period	Postoperative period
Demographic	Age (younger) Sex (female)		
Genetic	Several mutations		
<b>Pain</b>	<b>Preoperative chronic pain</b> -At surgery site -Elsewhere		<b>-Severe acute and subacute pain</b> (at mobilization) -Presence of secondary hyperalgesia <b>-Presence of neuropathic features in the pain</b>
<b>Psychological / mental health</b>	<b>Psychological vulnerability</b> (depression, stress, catastrophizing, anxiety)		<b>Psychological vulnerability</b> (depression, stress, catastrophizing, anxiety)
<b>Surgical</b>		<b>-Type of surgery</b> (bone surgery) <b>-Nerve injury</b> <b>-Traumatic approach</b>	
<b>Clinical / physical health</b>	<b>-Preoperative opioid use</b> -Sleep disturbances -Severity of comorbidities and disability		-Longlasting opioid use and dependance -Radiotherapy -Chemotherapy -Kinesiophobia
Perioperative risk factors involved in the development of CPSP according to published narrative reviews (Schug & Bruce) <sup>24</sup> , systematic reviews (Papadomanolakis-Pakis et al, Giusti et al) <sup>26,39</sup> and prospective studies (Montes et al, van Driel et al) <sup>23,36</sup> . <b>In bold</b> : major risk factors currently known (all being clinical risk factors).			

of “pain trajectories” developed by Chapman a few years ago<sup>27</sup>. Since then, the concept of pain trajectories has gained in interest and has now evolved to the concept of “trajectories of recovery”. Further, optimal versus non-optimal pain trajectories are now dichotomized, non-optimal trajectories being associated with pain persistence and CPSP<sup>28</sup>. This concept fits with earlier observations which reported that the time spent in severe pain after surgery<sup>11</sup>, and particularly within the first 5 days<sup>29</sup> was associated with an increased risk of CPSP. Recently, the role of sub-acute pain, a “gray zone” extending between hospital discharge and the CPSP suggested cutoff time (usually a time period between 10-days and 3 months after the procedure) has emerged as an very important factor<sup>30</sup>. The sub-acute pain period deserves all our attention as an important time for the transition from acute to chronic pain. Therapeutic actions during that period might work as preventive strategies of CPSP<sup>31</sup>. Despite the value of subacute pain as a risk factor for the development of CPSP (demonstrated in various surgical procedures like inguinal hernia repair<sup>32,33</sup>, orthopedic surgery<sup>34</sup>...), pain after hospital discharge is rarely included in the predictive models of CPSP 26 35. A very recent publication by Van Driel et al reports the development and validation of a new prediction model for the early prediction of CPSP after major surgical procedures<sup>36</sup>. The model (N=344 for its development; N=150 for its validation) is based on four easily obtainable predictors in clinical practice and thereby could alert health care providers to further assess and treat the

individual patients at risk. The four predictors are preoperative treatment with opioids (odds ratio (OR): 4.04, 95% CI: 2.13-7.70), bone surgery (OR: 2.01, 95% CI: 1.10-3.67), pain score on postoperative day 14 (OR: 1.57, 95% CI: 1.34-1.83) and the presence of painful cold within the painful area two weeks after surgery (OR: 4.85, 95% CI: 1.85-12.68). This new model certainly questions the best timing of prediction i.e. preoperative versus pre- and post-operative parameters as well as the need to assess early postoperative pain characteristics i.e. presence of neuropathic components<sup>35</sup>.

The presence of a neuropathic component is frequently incriminated in CPSP<sup>17,18</sup> and always associated to more severe pain and higher impact on the quality of life as functional impairment and sleep disturbances are often reported<sup>16</sup>. Neuropathic pain characteristics may vary with time<sup>37</sup>. A neuropathic component in postoperative pain may develop as early as 48h after surgery with a high predictive value of persistence at 2 months and later 38. It may also develop after a free interval as demonstrated after various surgical procedures including thoracic surgery<sup>37</sup>.

The recent model of van Driel et al<sup>36</sup> however suffers some limitations including the fact that psychological factors were not taken into account. Psychological vulnerability has been incriminated in the risk to present with severe acute postoperative pain and to develop CPSP. A recent meta-analysis has pointed the association of several psychological predictors like anxiety, depression, catastrophizing and kinesiophobia with

CPSP<sup>39</sup>. Peoples who present for surgery with a pre-existing chronic pain condition, a well known risk factor of CPSP, often also present with a greater psychological vulnerability. Pain catastrophizing, an exaggerated negative mindset during or after an anticipated painful experience, is one of the most robust psychosocial predictors of surgical outcomes. In elderly patients after hip fracture repair, pain catastrophizing in the immediate postoperative period and at 4 weeks after surgery (subacute phase) was predictive of CPSP<sup>7</sup>. Also interesting to note, preoperative parental pain catastrophizing but not child catastrophizing is a risk factor of CPSP after major surgical procedures in children<sup>19</sup>. The later point highlights the major role played by the patient's environment and the importance to take into account the bio-psycho-social model of pain in the context of CPSP.

### The need for better preventive treatments in clinical practice

The unchanged incidence of CPSP over the last 20 years also questions the efficacy of current preventive strategies. The conclusions of an updated systematic review and meta-analysis about systemic drugs for the prevention of CPSP in adults concluded that “extremely little progress has been made despite agreement that CPSP is an important topic”<sup>40</sup>. The authors hypothesized that failure may

be due on study designs being insufficient to address the complexities of this multifactorial problem. Similar observations have been made regarding the benefits of regional anesthesia<sup>41,2,4</sup>. The relative effectiveness of the different strategies has been summarized in a table (see Table IV) according to very recent meta-analyses and systematic reviews. Both systemic drugs administration<sup>40,43</sup> and regional anesthesia techniques<sup>44-47</sup> have been taken into account. It is important to note that the results are at best of moderate quality evidence and that the risks of bias are important as stated in the conclusions of the meta-analyses and systematic reviews.

The failures of preventive treatments should encourage clinicians to reconsider their perioperative use. In example, a better stratification of patients e.g. high-pain responders might help to target patients who will most benefit of these preventive treatments not only in the perioperative period but also at longer term<sup>48</sup>. More, preventive strategies might impact the character of CPSP rather than its incidence. By example, sub-group analyses have questioned the protective effect of paravertebral block in breast cancer surgery on the development of neuropathic CPSP. In this context, Harkouk et al<sup>46</sup> (n=7 pooled RCTs) found a reduced relative risk of 0.51 (95% CI:0.31-0.85) while Lim et al<sup>45</sup> (n=3 pooled RCTs) reported no significant benefit (RR 0.55, 95%CI: 0.24-1.31). Finally, whether therapeutic treatments applied

**Table IV.** — Reported effectiveness of different perioperative treatments to prevent the development of CPSP at 3 months and later according to recent meta-analyses and systematic reviews.

Preventive treatment	Surgical procedure	Number of RCTs (n)	Relative Risk of CPSP when compared to placebo
<b>Systemic treatments</b>			
Intravenous ketamine <sup>40</sup>	Mixed	27	0.51 (95% CI: 0.16-1.58)
Oral pregabalin <sup>40</sup>	Mixed	26	0.47 (95% CI: 0.33-0.68)
Oral pregabalin <sup>43</sup>	Mixed (including unpublished trials)	18	0.87 (95% CI: 0.66-1.14)
Oral gabapentin <sup>40</sup>	Mixed	17	0.96 (95% CI: 0.75-1.24)
Intravenous lidocaine <sup>40</sup>	Mixed	10	0.41 (95% CI: 0.13-1.27)
Intravenous lidocaine <sup>44</sup>	Breast cancer	2	0.43 (95% CI: 0.28-0.68)*
NSAIDs/COX-2 inhibitors <sup>40</sup>	Mixed	9	0.69 (95% CI: 0.34-1.37)
Intravenous corticosteroids <sup>40</sup>	Mixed	6	1.47 (95% CI: 1.05-2.06)
<b>Regional Anesthesia</b>			
Epidural <sup>44</sup>	Thoracotomy	7	0.52 (95% CI: 0.32-0.84)*
Epidural <sup>45</sup>	Thoracotomy	10	0.94 (95% CI: 0.75-1.18)
Parietal block (TAP) <sup>44</sup>	Cesarean section	4	0.46 (95% CI: 0.28-0.78)*
Paravertebral block <sup>47</sup>	Breast cancer	9	0.54 (95% CI: 0.24-0.88)*
Paravertebral block <sup>46</sup>	Breast cancer	12	0.82 (95% CI: 0.62-1.08)
Paravertebral block <sup>45</sup>	Breast cancer	10	0.73 (95% CI: 0.50-1.05)
*Statistically significant preventive effect as reported in the meta-analysis. Recent meta-analyses and systematic reviews included: Carley et al (2021) <sup>40</sup> , Martinez et al (2017) <sup>43</sup> , Weinstein et al (2018) <sup>44</sup> , Hussain et al (2018) <sup>47</sup> , Harkouk et al (2021) <sup>46</sup> , Lim et al (2022) <sup>45</sup> .			

in the sub-acute pain period will have higher preventive effect on the development of CPSP than early perioperative treatments still remain to be demonstrated.

## Conclusion

Chronic post-surgical pain stands as an important individual and socio-economic health issue. The unchanged incidence over the last two decades underlines both the failure of predictive models developed until now and the lack of efficacy of common “preventive” strategies (pharmacotherapy and regional analgesic techniques) applied in current clinical practice. New clinical directions based on the resolution of postoperative pain and supported by individual pain trajectories argue for both predictive models and preventive strategies extended to the subacute pain period i.e. after hospital discharge. Future well designed studies are mandatory to support these findings and improve CPSP management.

*Conflict of interest:* None.

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