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REVIEW

Chronic Postsurgical Pain in Children and Adolescents: A Call for Action

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Abstract: Chronic postsurgical pain (CPSP) affects a significant proportion of children and adolescents after major surgery and is a detriment to both short- and long-term recovery outcomes. While clinical characteristics and psychosocial risk factors for developing CPSP in children and adults are well established in the literature, there has been little progress on the prevention and management of CPSP after pediatric surgery. Limited evidence to support current pharmacologic approaches suggests a fundamentally new paradigm must be considered by clinicians to both conceptualize and address this adverse complication. This narrative review provides a comprehensive evaluation of both the known and emerging mechanisms that support our current understanding of CPSP. Additionally, we discuss the importance of optimizing perioperative analgesic strategies to mitigate CPSP based on individual patient risks. We highlight the importance of postoperative pain trajectories to identify those most at risk for developing CPSP, the early referral to multi-disciplinary pain clinics for comprehensive evaluation and treatment of CPSP, and additional work needed to differentiate CPSP characteristics from other chronic pain syndromes in children. Finally, we recognize ongoing challenges associated with the universal implementation of available knowledge about pediatric CPSP into practically useful care plans for clinicians.

Keywords: chronic postsurgical pain, pediatrics, perioperative care, pain management, secondary pain

Introduction

Chronic postsurgical pain (CPSP) is defined as pain that develops or increases in intensity after a surgical procedure, in the area of the surgery, persisting beyond the normal period of healing (>3 months) that cannot be explained by any other cause. This distinct pain syndrome has been recognized in the latest version of the *International Classification of Diseases (ICD-11)*.[1] CPSP is recognized as a major complication after surgery in both children and adults.[2–4] Estimated median prevalence rates vary based on surgery type, but CPSP is reported to affect 20–40% of children, adolescents, and young adults at 12 months after surgery.[5] While clinical characteristics, surgical, and psychosocial risk factors associated with the transition from acute to chronic pain have been identified and are well described in the literature, there remains a considerable knowledge deficit around the mechanisms, prevention, and optimal treatment of CPSP in pediatric patients.[5–14]

The purpose of this narrative review is to provide clinicians with a comprehensive evaluation of the existing and emerging evidence that supports our current understanding of the mechanisms associated with the development of CPSP in children and adolescents. We will also discuss the role of pharmacologic perioperative analgesic strategies and the role of perioperative analgesic protocols in the mitigation of CPSP. Finally, we will highlight the importance of identifying acute postoperative pain trajectories as a precision-based approach to anticipating the development of persistent pain after surgery and the need for early individualized treatment plans in children and adolescents. This review serves as a call to

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action for clinicians to implement available knowledge about pediatric CPSP into their routine practice and work towards eliminating system-driven barriers to comprehensive pain care for pediatric surgical patients.

Development of CPSP

Known Risks Factors

Risk factors for the development of pediatric CPSP have been extensively described in multiple comprehensive literature reviews and prospective observational studies and will be concisely summarized here.[5,6,8–10,15–17] These risk factors can be understood within perioperative context and are shown in Table 1. Clinical descriptors (age, BMI), psychosocial behaviors, pre-existing and postsurgical pain intensity, functional disability prior to surgery, type of surgery as well as parental factors have all been identified as potential risks in the development of persistent postoperative pain in children and adolescents.

Psychosocial: Preoperative patient psychosocial factors have long been recognized as a risk for pediatric CPSP and numerous high-quality observational studies continue to support this principle.[3,9,15,17–19,26,27,32,33] However, the extent to which individual psychosocial factors contribute to both the development and maintenance of CPSP remains to be determined. Most studies agree that baseline anxiety, depressive symptoms, sleep quality, and pain catastrophizing (parental and patient) are strongly associated with persistent postoperative pain.[3,9,15,16,18–20,24,26,27,32–34] More recently, two longitudinal studies revealed that pain catastrophizing is a dynamic trait, which does not remain stable, and thus, could be considered a potential target for intervention, in contrast to anxiety levels which remained consistent throughout the perioperative period.[14,21] The identification and routine reassessment of "malleable" psychosocial distress-related contributors to CPSP could be of clinical importance to improving patient outcomes by constructing and delivering appropriate behavioral therapies before, during, and after the surgery.

Type of Surgery: The prevalence of CPSP has also been found to be associated with surgery type. Prospective, longitudinal observational cohort studies in children and adolescents undergoing major musculoskeletal surgery report higher rates of CPSP than smaller retrospective cross-sectional studies.[9,22,23,25,26,32,35] Within each surgery type, the development of CPSP has been theorized to be age-dependent with older age groups experiencing more persistent pain.[25,29,35]

Mechanisms

Understanding the proposed mechanisms that underly the transition from acute to chronic pain states is necessary to identify potential targets to prevent or minimize persistent pain.[30,31] There are a number of relevant publications that

Table 1 Reported Psychological and Perioperative Clinical Risk Factors for the Development of Chronic Post-Surgical Pain (CPSP)

Pediatric Psychological Risks Factors	Pediatric Perioperative Clinical Risk Factors	
• Anxiety sensitivity[9,18–22] • Perception of pain unpleasantness[17,19,21] • Fear of pain[23] • Fear of re-injury[23] • Poor coping strategies[24] • Depressive symptoms[15,25] • Tendency to catastrophize[3,16,18–20,24,26] • Sleep quality[15,23]	**Preoperative**	• Age (12–18 years old)[3,10] • Pre-existent pain (>1-month, Visual analog scale (VAS) > 30)[9,10,18,26] • Pre-existing functional disability[17] • Intensity of recent pain (<1-month, VAS > 30)[8,9] • Parent factors (pain anxiety, pain catastrophizing)[16] • Greater body mass index (BMI)[27]
	Intraoperative	• Surgery Type a. General Orthopedic[3,11,15,28] (2–54% prevalence) b. Spinal Fusion[9,18] (11–54% prevalence) c. Thoracotomy[29,30] (2–28% prevalence) d. Inguinal Hernia[28,31] (2–9% prevalence) e. Urologic[28] • Hypospadias (5% prevalence) • Orchiopexy (2% prevalence)
	Postoperative	• Acute postsurgical pain[15,17,18,32,33] • Scar size (>3 cm)[10] • Postoperative opioid consumption[17,18] • Parents' tendency for pain catastrophizing and anxiety regarding patient's pain[16,18]

describe the known pathophysiology associated with persistent postoperative pain and the transition from acute to chronic pain after surgery (Figure 1).[28,31,36] However, as we review in this section, there are substantial knowledge deficits in our mechanistic understanding of CPSP in children.

Proteins: There is increasing evidence that chronic pain is a neuroinflammatory disorder with pathophysiology involving a complex interplay between the nervous and immune systems.[37] Proteins, including neurotransmitters, receptors, and cytokines, have an integral role in the generation and maintenance of pain. In the context of CPSP, pre-clinical and translational investigations have identified nociceptive pathways from the periphery to the brain that mediate pain that endures beyond the expected period of recovery. These postsurgical alternations are a result of both peripheral and central sensitization and include 1) local inflammatory responses (interleukin 1β and the chemokine ligand which contribute to long-term alterations in sensitivity in the area of surgery; 2) gene expression of local factors (neurotrophin-3 nerve growth factor, artemin) which influence nerve regrowth, affect tissue remodeling and are important factors in persistent incisional and scar pain; 3) changes in ionotropic channel expression in sensory neurons; and 4) synaptic plasticity in the spinal cord with resultant increased excitatory signaling and reduced descending inhibition.[38–46]

Numerous studies have quantified inflammatory indices such as the neutrophil-to-lymphocyte ratio (NLR), mean platelet volume (MPV), and C-reactive protein (CRP) as a potential biomarker in patients with fibromyalgia and chronic multisite pain.[47–49] Interestingly, more recent studies report that the preoperative NLR itself or the change ratio from postoperative to preoperative significantly correlate with the development of CPSP.[50–52] It is hypothesized that the higher NLR may represent a heightened preoperative state of systemic inflammation and/or inflammatory dysregulation within the central nervous system promoting central sensitization and subsequently a state of hyperalgesia. On the other hand, a recent landmark study suggests that the inflammatory response via neutrophil activation and up-regulation was protective against chronic pain development in adult patients with low back pain and temporomandibular joint pain.[37] The disruption of the acute inflammatory pathway through the use of non-steroid anti-inflammatories (NSAIDs) after injury was associated with an elevated risk of pain persistence.

Promoting research on the relationship between pro-inflammatory state after surgery and the development of CPSP in children is of utmost importance. Currently, there have been no studies evaluating this specific relationship in pediatric patients, and this represents a significant gap in our understanding of CPSP in children. Further research in this area may provide valuable insights into targeted interventions allowing for personalized treatment approaches to improve the quality of life for children who experience CPSP.

Genetics: In addition to the neuroinflammatory changes described above, it has been recognized that chronic pain susceptibility may be heritable.[53–56] Similarly, the large variability in CPSP risk and/or severity among patients

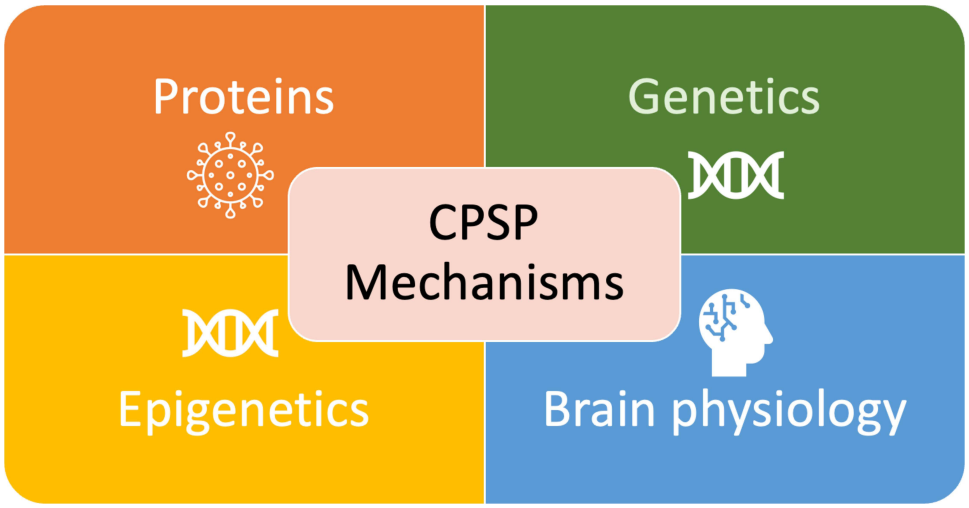

Figure 1 Schematic diagram illustrating the mechanistic factors thought to be associated with the development of chronic postsurgical pain (CPSP). Proteins: regulation of inflammation through neurotransmitters, receptors, and cytokines; Genomics (genetics/epigenetics): heritable genes and modification of gene expression; Brain physiology: structural and functional brain changes associated with the chronification of pain.

undergoing similar surgeries suggests that genetic determinants are significant contributors to individual differences in pain outcomes.[57–59] In fact, heritability estimates suggest that about half of the variance in CPSP levels is attributable to genetic variation.[60,61] Subsequently, there has been a substantial effort to identify genomic factors that are relevant to the development of CPSP.[60–63] Pre-clinical animal models offer the opportunity to identify CPSP-relevant candidate genes through genome-wide analysis. Despite the plethora of hypothesis driven gene approaches and genome-wide studies evaluating genetic influences on CPSP, finding a genetic explanation to individual CPSP phenotypes has largely remained elusive.[57,59] Specifically in the pediatric pre-clinical literature, gene enrichment, gene editing, reverse translational approaches, and the inclusion of CPSP endophenotypes in large-scale biobanks have been proposed as suggested frameworks for future targeted genetic profiling of CPSP risk.[57,58] While these methods are widely available and reliable, their application to pediatric CPSP has trailed behind their application to other forms of chronic pain. Of the CPSP-genetics associated studies in humans, only one clinical investigation included pediatric patients that assessed pain intensity using long-term outcomes.[64]

Epigenetics: Epigenetic modifications alter gene expression through a variety of pathways, including DNA methylation, regulation of chromatin by histones, and noncoding microribonucleic acids, without changing the DNA sequence.[65,66] It has been hypothesized that epigenetic differences prior to surgery may predispose individuals to greater risk of CPSP.[67] For example, DNA methylation at the promoter region of the mu-opioid receptor gene (OPRM1) that codes for mu-opioid receptor has been well studied and is important in opioid pain pathways.[68] In children undergoing spine fusion, blood DNA methylation in an active regulatory region of OPRM1 gene was associated with CPSP.[69] However, despite the potential role of epigenetic modifications in the development of CPSP, additional work characterizing the complex relationship between genetic, epigenetic, and heritable transcriptomic variation is needed to determine innovative targets and CPSP mitigation strategies, particularly in pediatric patients.[59]

Brain Physiology: Changes in brain physiology associated with chronic pain states may be detected with neuroimaging, particularly when imaging is combined with machine-learning approaches. Neuroimaging studies, using structural, functional and diffusion magnetic resonance imaging (MRI), may offer image-based markers to predict or evaluate the chronification of pain.[70,71] Brain MRI allows for the assessment of functional connectivity, white matter tractography and diffusion imaging, and pattern responses to nociceptive stimuli.[72] With respect to the transition from acute to chronic pain, a comprehensive trial (Acute to Chronic Signatures Program, A2CSP) is investigating the biomarkers and signatures of CPSP in adults undergoing surgery and will employ brain imaging before surgery and during the recovery period to correlate changes in brain physiology to the development of persistent pain.[72] There are currently no studies in children characterizing image-based structural and functional changes in the central nerve system before and after surgery. This represents another future area of study.

To summarize, multiple mechanisms have been identified that may influence the development of CPSP in children including neuroinflammation, genetics, epigenetics, and structural and functional changes in brain physiology. However, the data is limited in children, and no mechanistic biomarkers have been described with sufficient precision and reliability to be useful in clinical scenarios.

Perioperative Pharmacologic Analgesic Strategies

From a perioperative standpoint, broad recommendations include the use of multimodal analgesia, and when applicable, the use of neuraxial or regional anesthesia. However, perioperative analgesic studies in children are often in heterogenous populations, and the outcomes associated with specific pharmacologic therapies are often conflicting, even for the management of acute postsurgical pain.[73,74] Available perioperative interventional analgesic pediatric studies rarely assess pain beyond the early postoperative period, limiting our understanding of their utility for preventing CPSP.[73–79]

Additionally, perioperative analgesic strategies have become increasingly protocolized through the use of surgery-specific enhanced recovery after surgery (ERAS) pathways in contrast with precision-based patient care models that account for inter-individual differences. This is relevant to long-term pain recovery as there is substantial evidence demonstrating that postsurgical pain severity and duration are predominantly defined by patient factors.[18,80–86] As ERAS protocols often fail to allow for risk adjustment to patient-specific phenotypes,[87] it is essential that as clinicians, we prioritize the care of patients as individuals, including their previous pain experience and baseline characteristics, to

determine an appropriate analgesic approach, particularly for those at higher risk of having more severe and prolonged pain after surgery. A regional anesthetic, for example, may be offered based on anatomical considerations of surgery type and the estimated severity of postoperative pain. However, regional anesthesia use could be more strongly considered in a child or adolescent with multiple risk factors, even for less extensive surgery, to improve early postoperative pain and potentially mitigate CPSP.[18,81,85,88] Personalization of the perioperative analgesic approach could represent a valid path forward for individualized care, particularly for those patients who are phenotypically at an increased risk for persistent postoperative pain after a surgical insult.

In addition to standardized protocols being largely procedure-specific, there is great variation in the implementation of analgesic ERAS approaches across institutions. In pediatrics, published protocols for idiopathic spinal fusion surgery, a procedure with high incidence of CPSP, are highly variable in their use of opioids, regional anesthesia, and adjuvant analgesic medications including gabapentinoids, muscle relaxants, ketamine, subcutaneous local anesthetic infusions, and dexmedetomidine.[89–96] At this time, there is little evidence to support the use of one perioperative analgesic protocol over another for acute pain in pediatric patients undergoing major musculoskeletal surgery, and no evidence to support any specific pharmacologic approach to prevent the transition to CPSP. Thus, we propose that operative protocols and institutional "best practice" should incorporate universal screening of each child or adolescent undergoing surgery to determine their risk level for developing CPSP.

Preoperative Screening and Optimization

The Pediatric Pain Screening Tool (PPST) is a concise, self-report questionnaire comprising nine items which may be used to identify patients with greater risk for poor functional outcomes and CPSP in a pediatric cohort.[97] Divided into physical and psychosocial subscales, the tool assesses factors such as widespread pain, functional ability, and psychosocial constructs, providing a total score and subscale scores that range from 0 to 9. A recent study investigated PPST applicability to preoperative risk stratification for the development of CPSP.[98] Individuals were categorized into two groups: those with PPST scores <2 were identified as having a medium risk for CPSP (23%), while those with PPST scores ≥2 were characterized as having a high risk for CPSP (49%). This screening construct provides a foundation for personalized presurgical interventions to manage both the type and severity of identified individual patient risk factors.

Optimization strategies that have been used in clinical practice are highlighted in Table 2. Approaches include pain education, pharmacologic and non-pharmacologic physical treatments (acupuncture, TENS, massage) as appropriate,

Table 2 Recommended Preoperative Interventions Based on Chronic Postsurgical Pain Risk Stratification from Pediatric Pain Screening Tool (PPST)

Category	Questions	Prep Interventions for Moderate Risk Group (Total Score < 2)	Preop Interventions for High Risk (Physical OR Psychosocial Score ≥ 2)
Physical Factors	1. My pain is in more than one body part	- Pain education - Scan for surgical risk factors - Preventative pain management strategies - Close follow up and early referral	- Sleep hygiene - Physical therapy - Massage therapy - TENS - Acupuncture - Pharmacological treatment - Preop pain clinic referral
	2. I can only walk a short distance because of my pain		
	3. It is difficult for me to be at school all day		
	4. It is difficult for me to fall asleep and stay asleep at night		
Psychosocial Factors	5. It's not really safe for me to be physically active		- Cognitive behavioral therapy - Coping strategies - Relaxation therapy - Hypnosis - Biofeedback - Anxiolytics - Sleep hygiene - Preop behavioral medicine consult
	6. I worry about my pain a lot		
	7. I feel that my pain is terrible and it's never going to get any better		
	8. In general, I do not have as much fun as I used to		
	9. Overall, how much has pain been a problem in the last 2 weeks?		

Notes: Adapted from Narayanasamy S et al: Pediatric Pain Screening Tool: A Simple 9-Item Questionnaire Predicts Functional and Chronic Postsurgical Pain Outcomes After Major Musculoskeletal Surgeries. J Pain 2022; 23: 98–111.

preoperative pain referrals, sleep hygiene, and the development of coping strategies through relaxation, cognitive-behavioral therapy, and biofeedback. The impact of a comprehensive cognitive-behavioral intervention during the one-month period before and after surgery is currently being studied in a large multicenter trial in adolescents undergoing major surgery.[99] This research will provide additional insight on the effects of a preemptive approach towards mitigating CPSP before surgery.

Postoperative Pain Trajectories

There has been important work to define postsurgical pain trajectories, which has led to a better understanding of the impact of inter-individual pain responses on the development of CPSP. Pain trajectory analyses examine the rate of change in pain intensity at numerous time points after surgery. Longitudinal data collection allows for the evaluation of the pain experience as a dynamic process to discern different phenotypic recovery pathways. Sieberg et al and Ocay et al defined five and four pain trajectories, respectively, using the Scoliosis Research Scale-30 (SRS-30) whereas other studies have distinguished two main trajectories using numerical rating scales (NRS).[3,17,81,83,85] Despite the heterogeneity in measurements and number of trajectories identified, the finding of distinct pain recovery pathways has been replicated in many pediatric and adult studies.[18,80,100,101]

Prospective studies examining acute and chronic postoperative pain trajectories have shown that the majority of children undergo normal recovery with decreasing surgical pain over time. However, there is a subset of patients classified into cohorts with high or severe pain that persists or increases over time. Results from trajectory analyses indicate that the incidence of high persistent pain phenotypes are present in 11–60% of patients based on both the definition (average vs maximum pain) and pain intensity rating scale used (NRS vs SRS-30).[101] Characteristics include both nociceptive and neuropathic pain.[102] Predictors of this persistent pain phenotype include 1) prolonged and intense postoperative pain with NRS $\geq$ 3 at 2 weeks after scoliosis surgery and NRS $\geq$ 3 one month after general surgery, 2) pre-existing pain in the 3 months before surgery, and 3) psychosocial factors.[10,18,29,32,102] Opioid consumption in the acute postoperative period, which is often used as a surrogate for pain intensity, has not been shown to be definitely predictive of CPSP based on a prospective longitudinal study.[103] Given that pain trajectories diverge as early as 2 weeks after major surgery, patients with persistent pain at 2 weeks postoperatively should be referred for multi-disciplinary care to establish a comprehensive treatment plan (Figure 2).

Brief Summary of Pharmacologic and Non-Pharmacologic Treatment Modalities for CPSP

No studies have examined the efficacy and safety of long-term pharmacologic treatments for pediatric CPSP. There has been only one systematic review, published in 2017, that summarizes specific pharmacological treatments used in the management of both adult and pediatric CPSP.[104] The efficacy of analgesics and treatment modalities, including gabapentin and pregabalin, topical neuropathic agents such as capsaicin and lidocaine patches, epidural injections, local anesthetics, neurotoxins, and NMDA receptor antagonists, were largely studied in isolation. The ultimate conclusion of this comprehensive investigation suggests that the current evidence available for single interventions was insufficient to make formal recommendations. Thus, at this point, a robust treatment plan incorporates multimodal analgesia, with the diminishing use of opioids in CPSP management due to their ineffectiveness for long-term pain relief and the escalating misuse observed among adolescents later in life.[105] In addition to higher-quality studies evaluating pharmacologic agents, the effectiveness of regional nerve blocks to treat CPSP should be further investigated in pediatrics, as they are increasingly utilized in practice for CPSP for pain that is localized to a targetable nerve or fascial plane. The use of interventional procedures was associated with return to normal function, reduction in pain intensity, and reduction in pain medications in almost three-quarters of patients included in a multidisciplinary pain treatment program.[106] Although non-pharmacological modalities like cognitive-behavioral therapy (CBT), mindfulness, hypnosis, mental imagery, and acupuncture are well established for treating acute and chronic primary pain, research specifically addressing their utility for CPSP is also currently lacking.[104]

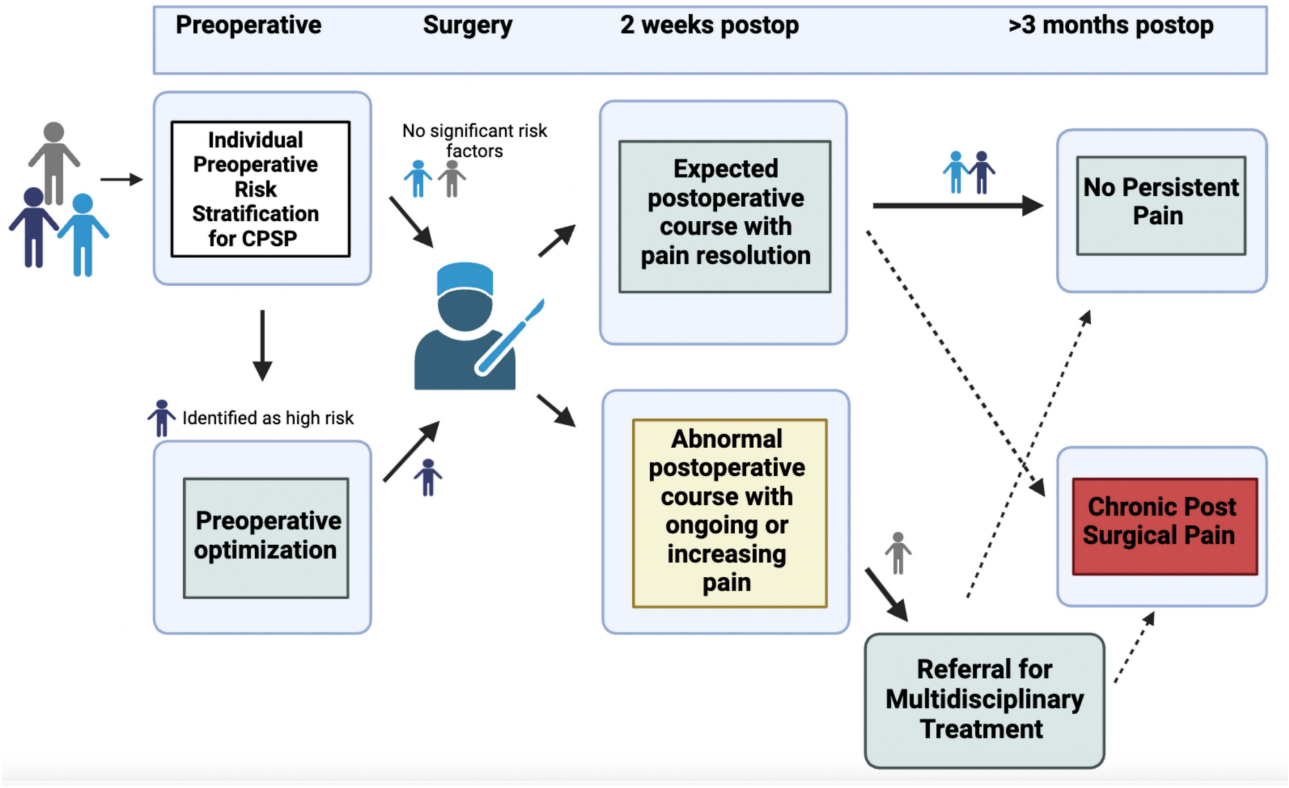

Figure 2 Algorithmic Approach and Timeline for Chronic Postsurgical Pain (CPSP) Evaluation. Icons represent examples of pediatric pain trajectories, pathways, and outcomes. Green boxes represent the optimal pathway towards favorable pain recovery outcomes. Grey icon represents a patient without significant preoperative risk factors. This patient experienced ongoing or increasing pain at 2 weeks postoperatively and was appropriately referred for multidisciplinary treatment. This patient will either recover or develop chronic postsurgical pain. Blue icon represents a patient without significant preoperative risk factors and expected postoperative pain recovery. Navy icon represents a patient identified as high risk during preoperative risk stratification. This patient received appropriate preoperative optimization followed by expected postoperative pain recovery and appropriate pain resolution.

The scarcity of data regarding the efficacy and safety profiles of pharmacologic treatments for non-oncological chronic pain in adolescents has prompted the search for new therapeutic models.[107] Recent studies suggested that personalized treatment approaches to various pediatric chronic pain conditions in general, and in pediatric neuropathic pain in particular, can be developed based on the individual nociceptive phenotypes as determined by the use of Quantitative Sensory Testing and conditioned pain modulation evaluation (QST/CPM).[108–110] QST/CPM testing appears to provide more targeted therapeutic options, resulting in less polypharmacotherapy and the use of interventional treatments, while still being at least as effective as standard treatment protocols. However, further studies are needed to examine the potential benefits of pain phenotyping and to confirm these hypotheses.

To summarize, current data supporting the use of analgesic medications to treat pediatric CPSP are very limited. Interventional procedures via regional nerve blocks for localized pain and non-pharmacologic modalities focused on functional outcomes may be effective strategies but require further study. Pain phenotyping with QST/CPM may provide targeted therapeutic options in the future. Given the lack of evidence to support available treatment options, we again emphasize that early identification of those at high risk to transition from acute to chronic pain is of utmost importance to mitigate the risk of CPSP-related comorbidities.[107,111]

CPSP vs Other Chronic Pain Syndromes in Children and Adolescents

It is important to differentiate pediatric CPSP from other chronic pain syndromes in children. For example, chronic primary pain (CPP) and CPSP represent distinct syndromes along the spectrum of complex pain conditions. These diagnoses in individual patients may be characterized by nociceptive and/or neuropathic pain or nociplastic pain.

Nociplastic pain, as characterized by the International Association for the Study of Pain (IASP), stems from altered nociception without clear evidence of actual or threatened tissue damage.[112] A recent study investigated pediatric patients meeting the criteria for nociplastic pain, revealing significant distinctions in their biopsychosocial factors and clinical outcomes compared to those without nociplastic pain.[31] Notably, adolescents meeting the criteria for nociplastic pain were more prone to hyperalgesia and hypersensitivity to mechanical and thermal stimuli. These patients also exhibited higher rates of psychiatric comorbidities, including panic disorder and social phobias, poor sleep quality, along with compromised functional status, as evidenced by less meaningful outcomes achieved after completing treatment.[113] Similar work should be completed for patients with CPSP. To that end, a brief QST protocol in two cohorts of youth with post-surgical and post-traumatic pain was recently published.[114] The study demonstrated the feasibility, tolerability, and reliability of this protocol, which will be an important tool in future research in the CPSP patient population, along with the implementation of nine patient-reported core outcome domains recently identified for inclusion in all pediatric chronic pain clinical trials.[115] Ultimately, further investigation into the differences between CPSP and other chronic pain syndromes is imperative to identify gaps in our understanding of the mechanisms contributing to long-term analgesic outcomes, and to further distinguish the risk factors, pain trajectories, and functional outcomes between these conditions. This will help inform advances in optimal treatment approaches for children suffering from CPSP and other types of chronic pain.

Barriers to Implementation

We recognize that clinicians may experience system level or institutionally driven barriers that may make the implementation of available knowledge on pediatric CPSP challenging. First, despite recommendations, screening for risk factors associated with the development of CPSP is not common before surgery. The lack of routine screening prevents opportunities to facilitate the comprehensive coordination of care for patients undergoing high-risk surgeries or have patient-related factors placing them at high risk for CPSP. Second, there is minimal communication across specialties at any stage of perioperative care. Medical teams often work in silos, and universal education about this common postsurgical condition is not provided. Recognition of CPSP is largely dependent on surgical practitioners who may or may not consider ongoing pain at two to four weeks after surgery as a "red flag" during the early follow-up period. As previously discussed, this is the critical window in which modifiable risk factors for CPSP can be mitigated through pharmacologic and non-pharmacologic approaches. Additionally, we are missing evidence-based data on whether the use of specific perioperative analgesic medications or clusters of medications may be associated with lower rates of CPSP for individual patients. Furthermore, accessibility to specialized centers for complex pain is limited, and thus, children and adolescents may arrive to clinic very late in their pain course which makes treatment more challenging. Finally, stigmas around those with pre-existing mental health conditions may result in patients at high risk for CPSP being more likely to not receive services. It is important for clinicians to systematically identify the impact of these barriers in their own practice with the goal to implement multidisciplinary quality improvement that prioritizes comprehensive, effective, timely, patient-centered, equitable, and coordinated care.

Conclusion

In this review, we described what is known about the clinical and mechanistic factors influencing the development of CPSP in children and adolescents. We also highlighted four specific areas that are needed to improve the care of the pediatric surgical patient in clinical practice. First, universal screening can be implemented preoperatively to identify and stratify patients at high risk of CPSP to allow for better presurgical optimization. Second, standardized perioperative analgesic protocols can be refined to allow for more flexibility and personalization of perioperative management in high-risk patients. Third, patients with ongoing pain at two weeks after surgery can be expeditiously referred for additional treatment, including personalized multidimensional interventions and interventional procedures. Finally, treatment can be based on individual patient physical and psychosocial phenotypes as determined by validated assessments and somatosensory testing. While more work remains to complete our understanding of pediatric CPSP, as clinicians, we have the opportunity to put into practice the knowledge that is currently available. This call to action serves as a reminder that the individual patients can benefit from the proactive implementation of CPSP-mitigating strategies. Identifying and

removing system-level or institutionally driven barriers is paramount towards ensuring that these approaches can be routinely incorporated into pediatric perioperative care.

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Disclosure

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