



Dolore persistente e cronico post-operatorio

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Anestesia e Rianimazione

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Narrative Review

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The IASP classification of chronic pain for ICD-11: chronic postsurgical or posttraumatic pain

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Abstract

Chronic pain after tissue trauma is frequent and may have a lasting impact on the functioning and quality of life of the affected person. Despite this, chronic postsurgical and posttraumatic pain is underrecognised and, consequently, undertreated. It is not represented in the current International Classification of Diseases (ICD-10). This article describes the new classification of chronic postsurgical and posttraumatic pain for ICD-11. Chronic postsurgical or posttraumatic pain is defined as chronic pain that develops or increases in intensity after a surgical procedure or a tissue injury and persists beyond the healing process, i.e. at least 3 months after the surgery or tissue trauma. In the classification, it is distinguished between tissue trauma arising from a controlled procedure in the delivery of health care (surgery) and forms of uncontrolled accidental damage (other traumas). In both sections, the most frequent conditions are included. This provides diagnostic codes for chronic pain conditions that persist after the initial tissue trauma has healed and that require specific treatment and management. It is expected that the representation of chronic postsurgical and posttraumatic pain in ICD-11 furthers identification, diagnosis, and treatment of these pain states. Even more importantly, it will make the diagnosis of chronic postsurgical or posttraumatic pain statistically visible and, it is hoped, stimulate research into these pain syndromes.

Keywords: Classification, ICD-11, Chronic pain, Postsurgical pain, Posttraumatic pain, Injury, Trauma, Surgery, Thoracotomy, Herniotomy, Mastectomy, Breast surgery, Hysterectomy, Arthroplasty, Whiplash, Burns, Amputation

1. Background on chronic postsurgical or posttraumatic pain

The risk for the development of chronic pain after surgery or trauma has been underestimated in the past.²³ Regarding postsurgical pain, data suggest an incidence, varying with the type of operation, from 5% to 85%.²⁴ Severe chronic postsurgical pain that negatively affects the patient's quality of life is in the range of 2% to 15%.²⁵ The high prevalence has been confirmed in a population-based study, in which 18% of patients who had surgery in the last 3 years reported pain in the area of surgery, of whom 10.5% reported pain even if all participants were excluded

who had the same pain before, and still 6.2% were left after excluding any pain before surgery.²⁴ The proportion of neuropathic pain is variable but can be very high in operations such as amputation, hernia repair, and mastectomy.^{22,26} (Table 1). There is also a high prevalence of chronic pain after trauma, in particular multitrauma,^{27,28} specifically with spinal cord injury,²⁹ brachial plexus injury, and other nerve injuries³⁰ and burns injury.³¹ In conclusion, chronic pain after surgery and trauma is common, still widely unrecognised and underdiagnosed and often poorly treated.

2. The need for a classification system

To improve the quality of life and functioning, recognition of surgery and trauma as causes of chronic pain, a proper diagnosis of its type, and initiation of appropriate treatment approaches are essential. Currently, no adequate classification system is available. The International Classification of Diseases (ICD), 10th revision (ICD-10), does not offer appropriate diagnostic categories for the classification of many chronic pain conditions, including postsurgical and posttraumatic pain.^{32,33} This hinders the identification, the diagnosis, and, in the end, the treatment of patients with these pain states. Even worse, thereby such cases fail to appear in health statistics, with all its consequences for research and health policies.

3. The IASP Task Force ICD Initiative

To improve the representation of chronic pain in general (including that of chronic postsurgical and posttraumatic pain), the International Association for the Study of Pain (IASP) formed a taskforce that worked in close co-operation with

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S.A. Schug, P. Lavand'homme, A. Barke contributed equally to the manuscript. W. Rief, R. D. Treede contributed equally.

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CPSP

Dolore cronico che si sviluppa o aumenta dopo un intervento chirurgico e persiste oltre il processo di guarigione (almeno 3 mesi dopo l'intervento).

Dolore localizzato al campo chirurgico, proiettato al territorio di innervazione di un nervo situato in quest'area, o riferito a un dermatomero.

Non è spiegabile da altre cause di dolore (infezioni, neoplasie, condizioni di dolore preesistente)

Ha spesso una componente neuropatica

L'inclusione della CPSP nell'ICD-11 identifica una condizione di malattia piuttosto che semplice sintomo
Se ne risalta quindi la necessità di un trattamento e di una gestione specifici.

CPSP e PPP: le dimensioni del problema

- Epidemia crescente che negli USA stima 100 milioni di adulti che soffrono di dolore cronico da lieve a debilitante
- Il numero di americani che soffrono di dolore cronico supera il totale degli americani affetti da malattie cardiache, cancro e diabete messi insieme
- Il dolore persistente post-operatorio è una delle principali cause di dolore cronico che si manifesta nei pazienti post-operati e negli anni successivi all'intervento
- PPP principale preoccupazione per la salute pubblica perché il costo totale sostenuto dalla società americana per numero di pazienti che soffrono di dolore cronico intrattabile post-chirurgico può contribuire all'attuale epidemia da oppioidi



CPSP

- La prevalenza del CPSP varia dal 5% all'85% a seconda della procedura, con incidenze elevate dopo interventi di toracotomia, mastectomia, e amputazione
- Circa il 10% dei pazienti manifesta CPSP con intensità moderata o grave, portando a svantaggi funzionali significativi
- Toracotomia, mastectomia, amputazioni e interventi ortopedici: alto rischio di CPSP (incidenza 50%)
- Condizione multifattoriale (fattori di rischio)
- Misure preventive (adeguata analgesia, anestesia regionale, supporto psicoeducativo)
- Approccio multidisciplinare al paziente

Chronic post-surgical pain – update on incidence, risk factors and preventive treatment options

D.C. Rosenberger and E.M. Pogatzki-Zahn*

Table 1 Incidences of CPSP for different types of surgery. Data adapted from several studies.^{1,3,5,6,12} Severe CPSP is defined as pain ratings of ≥ 5 on a scale from 0 (no pain) to 10 (worst possible pain).^{1,11} CPSP, chronic post-surgical pain; NP, neuropathic pain.

Type of surgery	Incidence of all CPSP (%)	Incidence of severe CPSP ($>5/10$)	Chronic pain up to 12 months	Proportion of NP
Abdominal surgery (bowel and colorectal)	17–21	Not reported	Not reported	Not reported
Amputation	30–85	5–10%	75% (lower limbs)	80%
Caesarean section	6–55	5–10%	Not reported	50%
Cholecystectomy	3–56	Not reported	Not reported	Not reported
Craniotomy	7–65	25%	Not reported	Not reported
Dental surgery	5–13	Not reported	Not reported	Not reported
Hip arthroplasty	7–23	6%	28%	1–2%
Inguinal herniotomy	5–63	2–4%	30%	80%
Knee arthroplasty	13–44	15%	18%	6%
Mastectomy	11–57	5–10%	43–56% (breast cancer surgery)	65%
Sternotomy	7–50	5–10%	27%	13%
Thoracotomy	5–71	10%	41%	45%
Vasectomy	0–37	Not reported	Not reported	Not reported

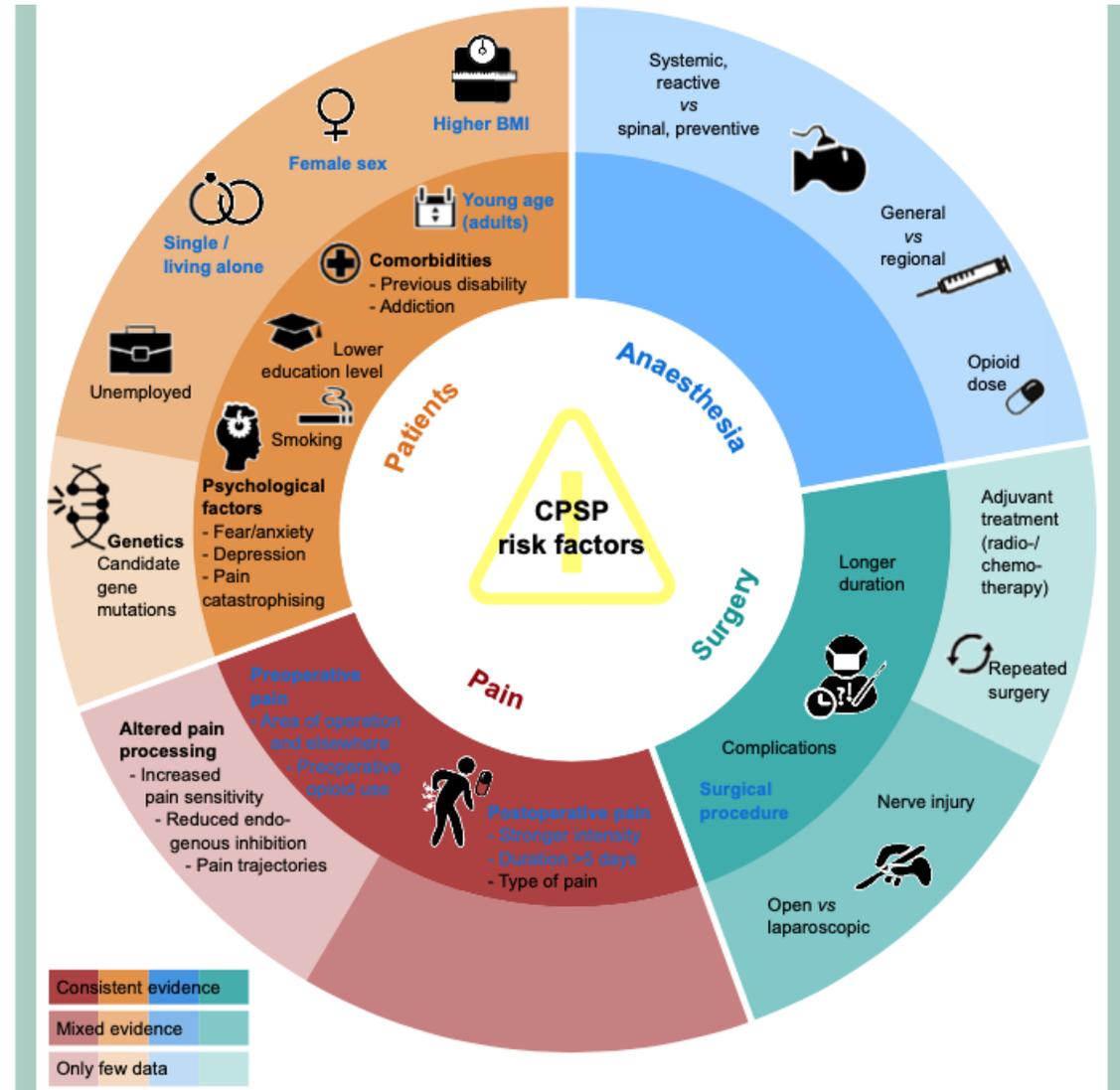
Postoperative pain management and opioids 1



Transition from acute to chronic pain after surgery

Paul Glare, Karin R Aubrey, Paul S Myles

Strumenti predittivi basati su fattori clinici e psicosociali possono aiutare a identificare i pazienti a rischio, permettendo interventi preventivi personalizzati. Sono necessari studi standardizzati per migliorare l'efficacia delle strategie preventive e ridurre l'impatto del CPSP



Fattori di rischio biomedici

- Tipo di intervento
- Tecnica chirurgica
- Controllo del dolore perioperatorio

60-70% dei pazienti sottoposti ad amputazione, mastectomia o toracotomia soffre di dolore cronico per mesi dopo l'intervento

Fondamentale evitare tecniche chirurgiche potenzialmente in grado di causare danni nervosi

ES linfonodo sentinella nella chirurgia mammaria

Ottimizzare la gestione del dolore pre e intra-operatorio



Prevention and Treatment of Chronic Postsurgical Pain: A Narrative Review

Arnand Steyaert¹ · Patricia Lavand'homme¹

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Abstract Chronic postsurgical pain affects between 5 and 75% of patients, often with an adverse impact on quality of life. While the transition of acute to chronic pain is a complex process—involving multiple mechanisms at different levels—the current strategies for prevention have primarily been restricted to perioperative pharmacological interventions. In the present paper, we first present an up-to-date narrative literature review of these interventions. In the second section, we develop several ways by which we could overcome the limitations of the current approaches and enhance the outcome of our surgical patients, including the better identification of individual risk factors, tailoring treatment to individual patients, and improved acute and subacute pain evaluation and management. The third and final section covers the treatment of established CPSP. Given that evidence for the current therapeutic options is limited, we need high-quality trials studying multimodal interventions matched to pain characteristics.

Key Points

The transition from acute to chronic postsurgical pain is a complex process, involving multiple mechanisms at different levels. Despite this understanding, current preventive strategies have primarily been restricted to perioperative pharmacological interventions.

Perioperative ketamine is the most studied drug and shows preventive effects. Small trials have shown a preventive effect for thoracic epidural analgesia, remifentanyl, intravenous lidocaine, and nefopam. A potential preventive effect of opioid-free anesthesia should be investigated.

To achieve more efficient prevention strategies, we need to better identify patients at risk and tailor interventions to their risk factors.

As both under- and over-treatment of subacute postsurgical pain can have negative consequences, we should set up dedicated structures to manage our patients beyond the immediate postsurgical period.

The results of the available randomized trials on CPSP treatments are not encouraging. High-quality trials of multimodal interventions matched to pain characteristics are needed to improve CPSP management.

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Psychosocial risk factors

Psychological risk factors, such as psychological distress, anxiety, catastrophizing, reduced ability to cope with pain, depression and hypervigilance, increase the risk of CPSP (Fig. 1) and long-term opioid use.^{7,16} A recent meta-analysis highlights state anxiety as the main psychological risk factor for CPSP (and to a lesser degree depression, catastrophizing, kinesiophobia and impaired self-efficacy).¹⁷

Psychological and psychosocial predictors of chronic postsurgical pain: a systematic review and meta-analysis

Emanuele M. Giusti^{1,2,3*}, Marco Lacerenza², Gian Mauro Manzoni², Gianluca Castelnovo^{4,5}

Abstract
Knowledge about psychological and psychosocial predictors of chronic postsurgical pain is important to identify patients at risk for poor outcomes. The objective of this systematic review with meta-analysis was to assess the effect of such predictors. A comprehensive search of the available literature on this topic was performed using the electronic databases PubMed, Scopus, Embase, and PsycInfo. Estimates of the effect of each predictor were extracted, and both a narrative synthesis and a quantitative synthesis of these estimates were performed. Multiple imputation was used to take into account the effect of nonsignificant estimates in case they were not reported by original studies. From a sample of 8322 records, 83 articles were included in the narrative synthesis and 41 studies were used to perform the meta-analysis. The narrative synthesis showed that evidence about the effect of psychological predictors is heterogeneous, with few expected predictors, such as optimism, state anxiety and psychological distress, consistently associated with chronic postsurgical pain. By contrast, the meta-analysis showed that state anxiety, trait anxiety, mental health, depression, catastrophizing and, to a lesser extent, kinesiophobia and self-efficacy have a weak but significant association with chronic postsurgical pain. In conclusion, this study showed that psychological predictors have a significant association with chronic postsurgical pain and that state anxiety is the most explicative one.

Keywords: Postsurgical pain, Predictors, Catastrophizing, Depression, Psychological risk factors

1. Introduction

The past 2 decades have shown a constant growth in studies on chronic postsurgical pain.¹⁷ The importance of identification of its modifiable predictors has led to an increasing interest in psychological and psychosocial factors, which are hypothesized to increase its incidence by interacting with the physiological underpinnings of pain, by shaping its perception, and by influencing pain behaviors.¹⁸ However, although the strength of the association between these factors and pain has been clearly established in patients with various chronic diseases,^{19–21} studies focusing on postsurgical pain report conflicting results, with estimates ranging from moderate values²² to weaker or absent ones.¹⁷

A first review of 50 studies retrieved from an initial search of 800 articles from 1980 to 2008 tried to collect in a narrative manner the available evidence on this topic and found that depression,

psychological vulnerability, stress, and late return to work were weak predictors of chronic postsurgical pain, whereas the role of anxiety was uncertain.¹⁷ However, it was impossible to provide a quantitative synthesis of the results due to variability among the studies in terms of assessment of predictors and outcomes and the inclusion of studies on both cancer and noncancer conditions. This led to uncertain results. A previous attempt to use meta-analytic methods was performed by Jackson et al.¹⁸ in a review of 47 studies ($n = 6207$), based on an initial search of 1934 records on acute and chronic pain due to both cancer and noncancer conditions. The authors found a weak correlation between emotional distress and postsurgical pain (Pearson's $r = 0.25$, 95% CI = 0.20–0.29). However, the estimate was the result of pooling data from studies focusing on both acute and chronic pain, on both cancer and noncancer conditions, and on a heterogeneous set of predictors, merged under the category of "emotional distress."¹⁸ This category includes predictors such as anxiety, depression, aversive mood states (eg, anger, fear, and guilt), cognitions (eg, catastrophizing), and coping strategies. Because the effects of each predictor computed by the authors through a moderation analysis included both acute and chronic pain and cancer and noncancer condition, the differential role of each predictor on chronic postsurgical pain needs to be studied in more detail. Theunissen et al.²³ studied the role of anxiety and catastrophizing on the incidence of chronic postsurgical pain by performing a systematic review of 29 cohort studies, case-control studies, and randomized controlled trials on both cancer and noncancer operations ($n = 4628$, based on an initial search of 812 records). The authors estimated that these predictors have an overall effect of weak to strong (odds ratios between 1.55 and 2.18). An additional meta-analysis focusing on predictors of total

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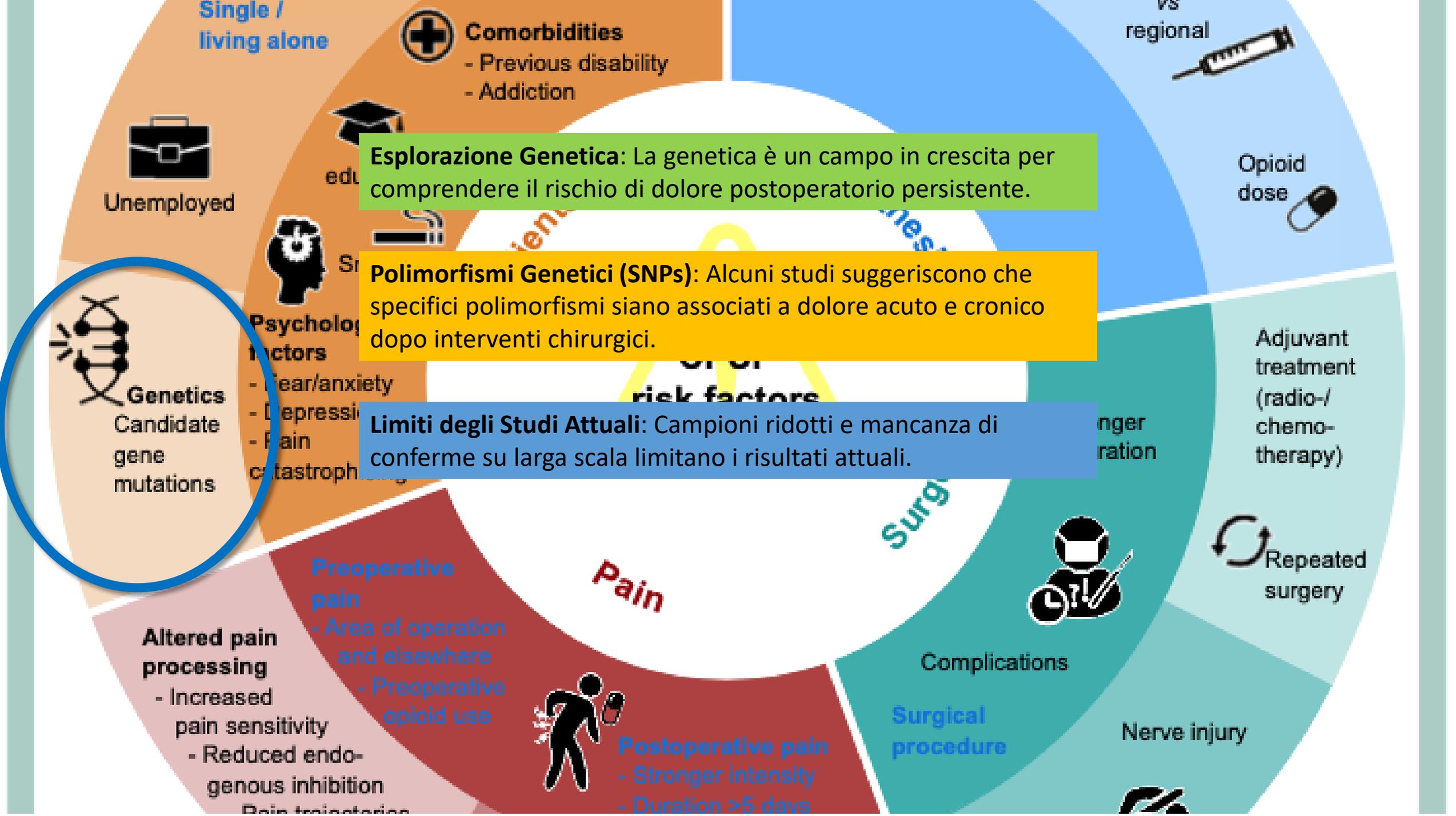
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PAIN®



Single /
living alone



Comorbidities
- Previous disability
- Addiction



Unemployed



edu



St



Psychological factors

- Fear/anxiety
- Depression
- Pain catastrophizing



Genetics
Candidate gene mutations

Esplorazione Genetica: La genetica è un campo in crescita per comprendere il rischio di dolore postoperatorio persistente.

Polimorfismi Genetici (SNPs): Alcuni studi suggeriscono che specifici polimorfismi siano associati a dolore acuto e cronico dopo interventi chirurgici.

Limiti degli Studi Attuali: Campioni ridotti e mancanza di conferme su larga scala limitano i risultati attuali.

vs regional



Opioid dose



Adjuvant treatment (radio-/chemotherapy)

nger
ration



Repeated surgery

Complications

Surgical procedure

Nerve injury

Pain

Preoperative pain

- Area of operation and elsewhere
- Preoperative opioid use

Altered pain processing

- Increased pain sensitivity
- Reduced endogenous inhibition



Postoperative pain
- Stronger intensity
- Duration >5 days

Previsione della CPSP

Prevenzione Individualizzata del CPSP:

Identificare sottogruppi di pazienti che potrebbero beneficiare di interventi preventivi, mirando alla prevenzione personalizzata del CPSP.

Series

Postoperative pain management and opioids 1

Transition from acute to chronic pain after surgery

Paul Clare, Karin R Aubrey, Paul S Myles

Over the past decade there has been an increasing reliance on strong opioids to treat acute and chronic pain, which has been associated with a rising epidemic of prescription opioid misuse, abuse, and overdose-related deaths. Death from prescription opioids have more than quadrupled in the USA since 1999, and this pattern is now occurring globally. Inappropriate opioid prescribing after surgery, particularly after discharge, is a major cause of this problem. Chronic postoperative pain, occurring in approximately 10% of patients who have surgery, typically begins as acute postoperative pain that is difficult to control, but soon transitions into a persistent pain condition with neuropathic features that are unresponsive to opioids. Research into how and why this transition occurs has led to a stronger appreciation of opioid-induced hyperalgesia, use of more effective and safer opioid-sparing analgesic regimens, and non-pharmacological interventions for pain management. This Series provides an overview of the epidemiology and societal effect, basic science, and current recommendations for managing persistent postsurgical pain. We discuss the advances in the prevention of this transitional pain state, with the aim to promote safer analgesic regimens to better manage patients with acute and chronic pain.

Introduction

Acute pain is almost ubiquitous after surgery. Fortunately, it can be controlled and mostly resolves within 1 week. It should not cause distress or limit postoperative recovery.¹ However, for some patients acute postoperative pain persists beyond the usual time of tissue healing and transitions into a chronic pain state.^{2,3}

The prevalence of chronic postoperative pain (CPSP), which is bad enough to cause substantial functional impairment, is approximately 10% after all surgeries (table 1).⁴ Globally, more than 320 million people have surgery each year, which represents a vast potential for CPSP.⁵ As a result, CPSP is increasingly recognised as a public health problem, not only because of the discomfort, distress, and disability it causes, but also because past approaches to managing it have contributed substantially to the current opioid crisis.⁶ The use of opioids for patients who have surgery presents a particularly challenging problem requiring clinicians to balance two competing interests: managing acute pain in the immediate postoperative period and minimising the risks of persistent opioid use after surgery. Finding ways to minimise this risk is particularly salient in light of a growing literature suggesting that patients who have had surgery are at increased risk of chronic opioid use.⁷ As a result, in 2016, the Joint Commission in the USA began a project to revise its pain standards and address the opioid epidemic.⁸ In January 2018, the Commission added an emphasis on the need to actively engage medical staff and hospital leaders to include strategies to decrease opioid use. This included the use of at least one of non-pharmacological modality for pain treatment and access to prescription drug monitoring programmes. There was also a stronger focus on pain assessments of how the pain affects patients' physical function.⁹

Postoperative pain is a paradigm for understanding and studying other pain that is also itrogenic.^{10,11} Because

CPSP occurs from a planned incision at a specified point in time, it has the potential to be prevented and better controlled. However, there are many factors that contribute to the development and persistence of CPSP, and only some of these are related to the surgery. As with non-surgical chronic pain, psychological and social factors have an important influence. All clinicians—not just surgeons and anaesthetists—should have some knowledge on CPSP and how to manage established cases, which can persist for months or years after the procedure. As with many other chronic conditions, early intervention is likely to improve outcomes and so identifying patients at risk is crucial.

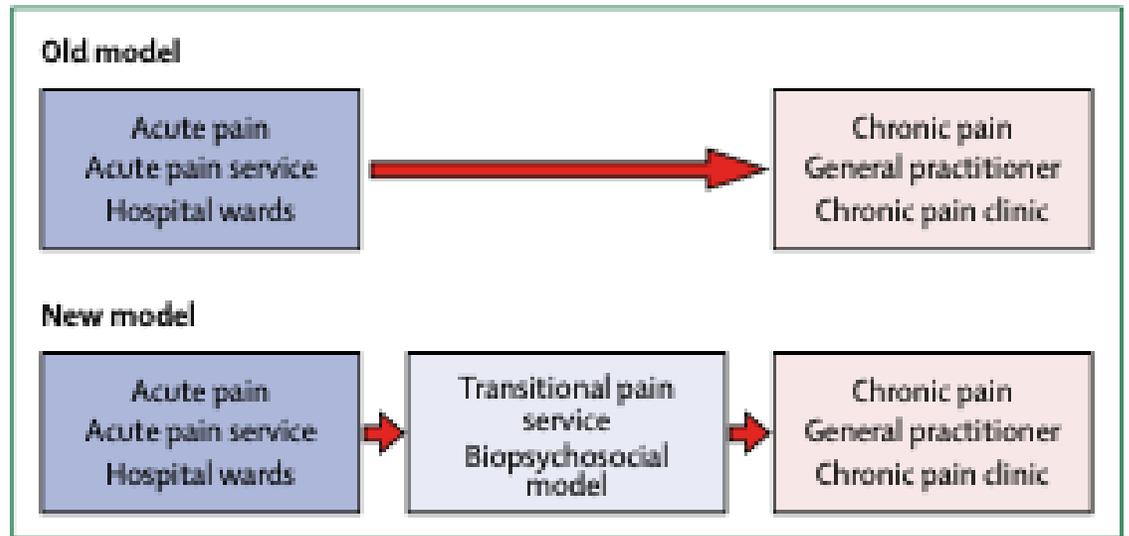
Definition

CPSP is pain that occurs at the site of the incision or related areas of the surgery and persists a month longer than it takes for most injured tissues to fully heal. Consequently, the time of onset has mostly been set between 3 and 6 months.^{10,11} Definitions of CPSP also vary as to whether or not other causes of pain, such as disease recurrence after surgery or presence of a pre-existing pain syndrome, are included under the CPSP rubric.¹² For example, chronic pain after lumbar spine surgery, also known as failed back surgery syndrome, refers to chronic back or leg pain that continues or recurs following spinal surgery, and affects more than 20% of patients.^{13,14} The 11th revision of the International Classification of Diseases defines CPSP as pain developing or increasing in intensity after a surgical procedure, in the area of the surgery, persisting beyond the healing process (ie, at least 3 months) and not better explained by another cause such as infection, malignancy, or a pre-existing pain condition.¹⁵

Clinical features

The nature of CPSP is often poorly characterised in clinical studies,¹⁶ but aching is the most commonly chosen sensory descriptor of persistent pain after a range

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This is the first in a Series of three papers about postoperative pain management and opioids
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Non-opioid analgesics for the prevention of chronic postsurgical pain: a systematic review and network meta-analysis

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Abstract

Background: Chronic postsurgical pain is common after surgery. Identification of non-opioid analgesics with potential for preventing chronic postsurgical pain is important, although trials are often underpowered. Network meta-analysis offers an opportunity to improve power and to identify the most promising therapy for clinical use and future studies. **Methods:** We conducted a PRISMA-NMA-compliant systematic review and network meta-analysis of randomised controlled trials of non-opioid analgesics for chronic postsurgical pain. Outcomes included incidence and severity of chronic postsurgical pain, serious adverse events, and chronic opioid use.

Results: We included 132 randomised controlled trials with 23 902 participants. In order of efficacy, i.v. lidocaine (odds ratio [OR] 0.32; 95% credible interval [CrI] 0.17–0.58), ketamine (OR 0.64; 95% CrI 0.44–0.92), gabapentinoids (OR 0.67; 95% CrI 0.47–0.92), and possibly dexmedetomidine (OR 0.36; 95% CrI 0.12–1.00) reduced the incidence of chronic postsurgical pain at ≤6 months. There was little available evidence for chronic postsurgical pain at >6 months, combinations agents, chronic opioid use, and serious adverse events. Variable baseline risk was identified as a potential violation to the network meta-analysis transitivity assumption, so results are reported from a fixed value of this, with analgesics more effective at higher baseline risk. The confidence in these findings was low because of problems with risk of bias and imprecision.

Conclusions: Lidocaine (most effective), ketamine, and gabapentinoids could be effective in reducing chronic postsurgical pain ≤6 months although confidence is low. Moreover, variable baseline risk might violate transitivity in network meta-analysis of analgesics; this recommends use of our methods in future network meta-analyses.

Systematic review protocol: PROSPERO CRD42021269642.

Keywords: chronic postsurgical pain; multimodal analgesia; network meta-analysis; non-opioid analgesia; systematic review

Editor's key points

- Chronic postsurgical pain is common after surgery, so identification of non-opioid analgesics with potential for preventing chronic postsurgical pain is important.

- A systematic review and network meta-analysis of randomised controlled trials of non-opioid analgesics was performed analysing effects on the incidence and severity of chronic postsurgical pain, serious adverse events, and chronic opioid use.

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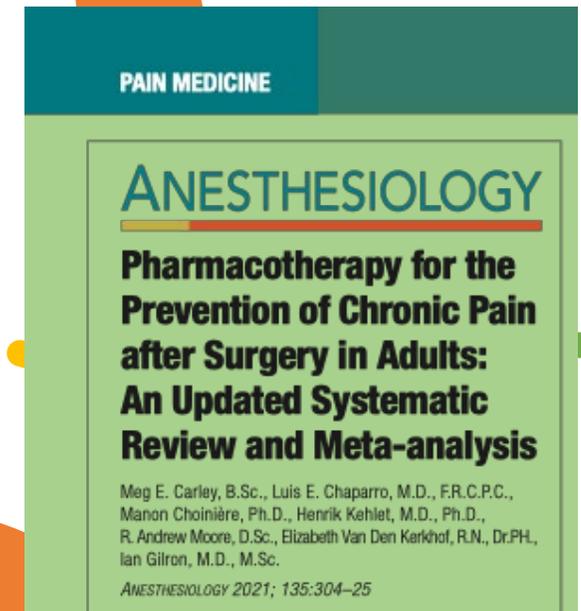
- Anestesia Regionale:** Epidurale e blocchi paravertebrali, riducono il CPSP in chirurgia toracica e mammaria, mentre l'infiltrazione continua della ferita può ridurre il dolore cronico post-cesareo.

Prevenzione e Gestione del CPSP

- **Strategie farmacologiche** : Ketamina e gabapentinoidi hanno effetti limitati nella prevenzione del CPSP; la riduzione dell'uso di oppioidi e l'adozione dell'anestesia regionale sembrano efficaci

Riduzione dell'Uso di Oppioidi: L'uso preoperatorio di oppioidi è un fattore di rischio per il CPSP. Riduzioni di oltre il 50% nel consumo preoperatorio possono migliorare i risultati fino a 6-12 mesi dopo l'intervento, in particolare se accompagnate da analgesia multimodale e anestesia regionale.

- **Interventi non farmacologici** : L'approccio multidisciplinare, con supporto psicologico e fisioterapico, è promettente per la prevenzione della cronicizzazione del dolore
- **Monitoraggio della Nocicezione:** L'uso di monitor di nocicezione intraoperatoria, come l'indice di variabilità della frequenza cardiaca e l'indice di nocicezione, può aiutare a ridurre l'esposizione agli oppioidi, sebbene sia necessaria più evidenza sull'efficacia di questi strumenti.



Practical strategies for the prevention and management of chronic postsurgical pain

Bo Rim Kim¹, Soo-Hyuk Yoon², and Ho-Jin Lee^{2,3}

12 months after surgery [58]. In a randomized controlled trial on phantom limb pain, the incidence of CPSP was significantly reduced by using intravenous or epidural analgesia starting 48 hours before surgery [59]. Recently, a meta-analysis reported that preemptive epidural analgesia before surgical incision reduced the incidence of CPSP after thoracotomy compared to epidural analgesia after incision [60]. Proper pain management at the right time during the perioperative period may lead to better outcomes for preventing CPSP.

(months)

Limb amputation

Bach, 1988 [37]

Epidural

Preincision, continuous vs control

Morphine

Pain/no pain

12 mo

Preoperative lumbar epidural blockade with bupivacaine and morphine reduced the incidence of phantom limb pain in the first year postoperatively compared to controls treated with conventional methods

Katsuly-Liapis [33]

Epidural

Pre vs intra vs postoperative vs none

None

Pain/no pain

VRS

12 mo

Perioperative analgesia using regional anesthesia techniques can be advantageous in decreasing acute phantom limb pain and PPP in patients who have undergone limb amputation

Karanikolas, 2011 [40]

Epidural

Pre vs intra vs postoperative vs all vs control

Intravenous PCA

Pain/no pain

VAS, phantom pain frequency, McGill

6 mo

Perioperative epidural analgesia and/or intravenous PCA reduced phantom limb pain intensity, prevalence, and frequency 6 months post amputation

Ong, 2006 [38]

Epidural spinal

Preincision vs continuous, pre vs postoperative vs control

None

Pain/no pain Phantom sensation/pain Stump pain

VRS

14 mo

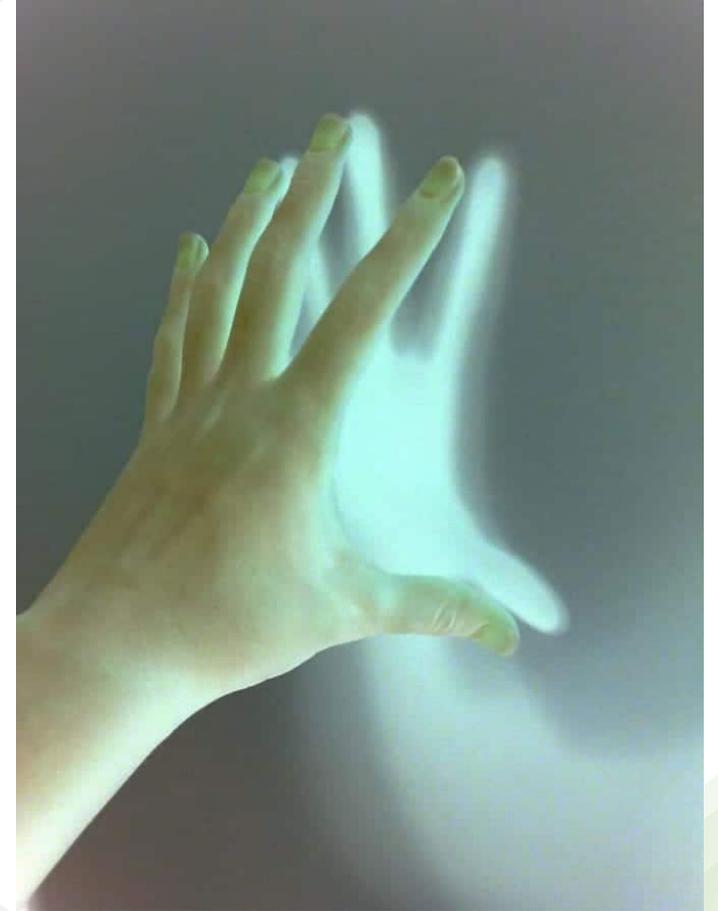
Epidural anesthesia and PNB aid in pain reduction during the first week postsurgery by preventing central sensitization, a major contributor to chronic postoperative pain

Study ID	Regional technique	Timing of intervention	Adjuvants	Outcomes	Continuous	Follow-up (months)	Primary outcomes
Sahin, 2011 [39]	Epidural Spinal peripheral nerve block	Preincision vs continuous vs single shot, pre vs postoperative vs control	None	Pain/no pain Phantom pain Stump pain	NRS	17 mo	Epidural anesthesia or PNB lead to significantly less pain in the first week after surgery. No difference in phantom limb pain, phantom sensation, or stump pain at 14 to 17 months post amputation
Breast surgery							
Albi-Feldzer, 2013 [52]	Infiltration and intervertebral block	Postincision, single shot vs placebo	None	Pain/no pain	Brief Pain Index	12 mo	Multimodal block was found to promote a reduced risk of PPP after breast cancer surgery
Baudry, 2008 [55]	Local infiltration	Single shot, postincision vs control	None	Pain/no pain	McGill results not reported	18 mo	Local infiltration was found to promote a reduced risk of PPP after breast cancer surgery
Basic, 2014 [58]	Local infiltration	Postincision, continuous postop vs control	None	Pain/no pain	None	3 mo	Local infiltration was found to promote a reduced risk of PPP after breast cancer surgery
Fassoulaki, 2000 [54]	Topical application	Preincision, continuous postop vs placebo	Propoxyphene	Pain/no pain	Verbal Intensity Scale	3 mo	Local infiltration was found to promote a reduced risk of PPP after breast cancer surgery
Fassoulaki, 2001 [57]	Brachial plexus block	Postincision, single shot vs placebo	Mexiletine, propoxyphene	Pain/no pain	VAS	3 mo	Local infiltration was found to promote a reduced risk of PPP after breast cancer surgery
Fassoulaki, 2005 [50]	Topical application	Postincision, continuous postop vs control	Gabapentin	Pain/no pain	Analgesic consumption	6 mo	Local infiltration was found to promote a reduced risk of PPP after breast cancer surgery

Study ID	Regional technique	Timing of intervention	Adjuvants	Outcomes	Continuous	Follow-up (months)	Primary outcomes
O'Neill, 2005 [84]	Local infiltration (bupivacaine)	Postincision, single shot vs control	None	Pain/no pain	Short form-12 mental and physical component scores, EuroQol-5D, and Oswestry Disability Index, satisfaction	5 mo	A single local administration of bupivacaine at the iliac crest graft harvest site during posterior spine fusion surgery results in improved overall outcomes and pain scores in the acute and long-term settings
Singh, 2013 [86]	Wound irrigation	Postincision, continuous postoperative vs control	None	Pain/no pain	VAS, pain frequency, functional activity score, overall satisfaction	56 mo	0.5% Marcaine via a continuous infusion catheter placed at the IBGH harvest site showed a statistically significant decrease in graft site pain score ($P < 0.05$), significantly improved overall postoperative function and patient satisfaction at a 4-year follow-up ($P < 0.05$), and significantly reduced chronic dysesthesias ($P < 0.05$)
Laparotomy S. M. M. M., 2005 [88]	Epidural	Preincision, continuous postoperative vs control	Ketamine, clonidine	Pain/no pain	Mental Health Inventory	12 mo	Intraoperative epidural anesthesia in combination with ketamine provides effective preventive pain management after laparotomy. Administration of an intraoperative epidural was shown to have a greater effect on residual pain in a 1-year follow-up

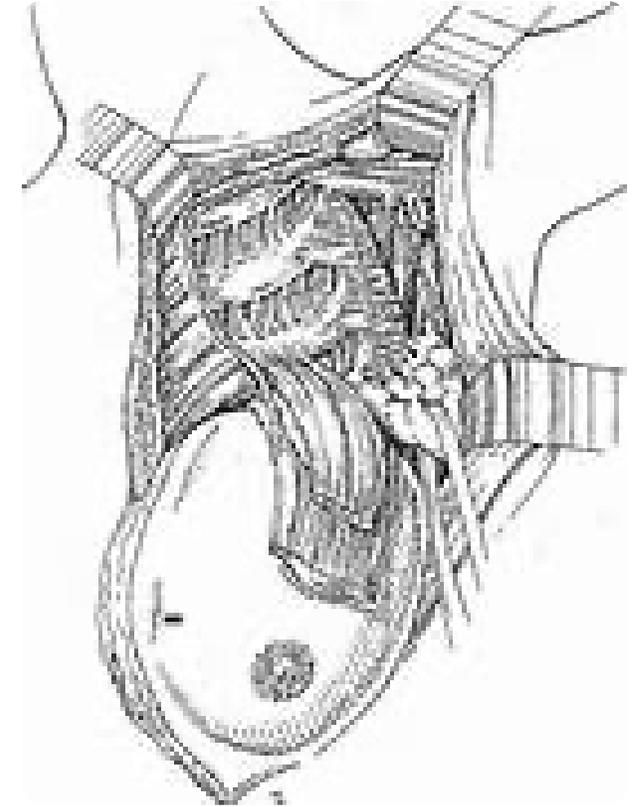
Arto fantasma

- Anestesia neurassiale e PNB attenuano e prevengono il dolore da arto fantasma
- Blocco epidurale lombare preoperatorio con AL e morfina ha ridotto l'incidenza del dolore da arto fantasma nel primo anno post-operatorio rispetto ai controlli trattati con metodi convenzionali



Chirurgia mammaria

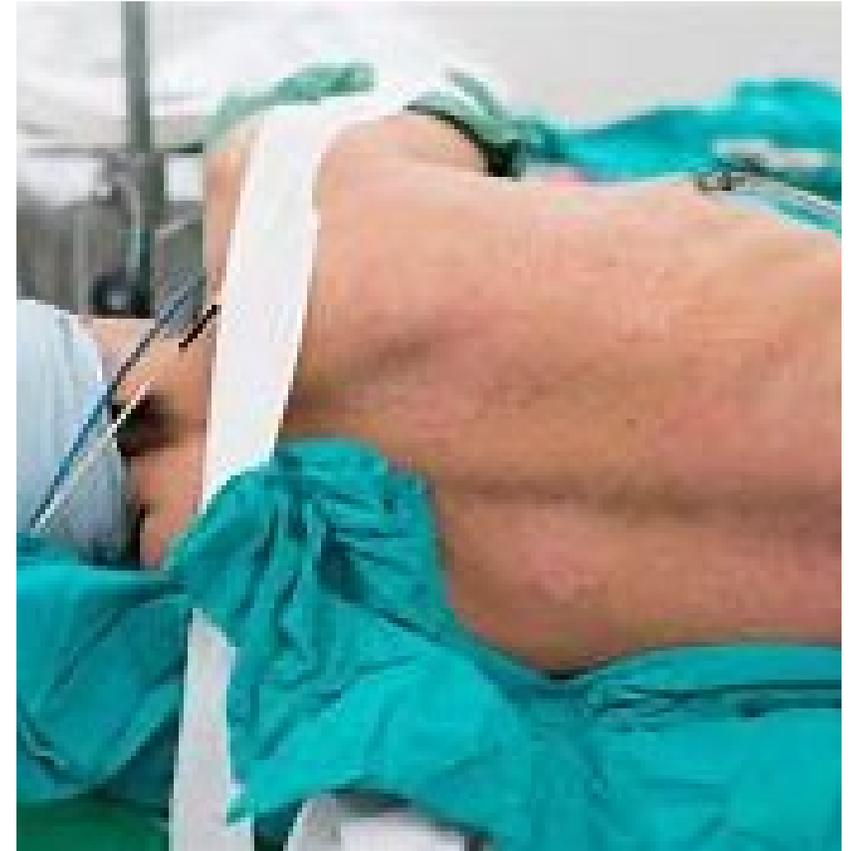
Il blocco paravertebrale è risultato essere la tecnica di anestesia regionale superiore e preferita rispetto ai metodi convenzionali per la prevenzione del dolore cronico in questa popolazione di pazienti

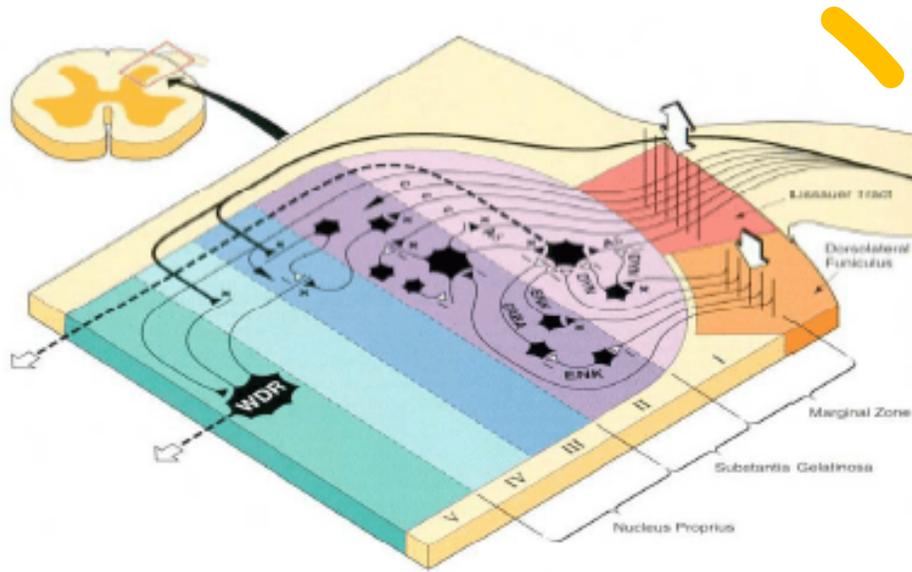


Toracotomia

Peridurale gold standard

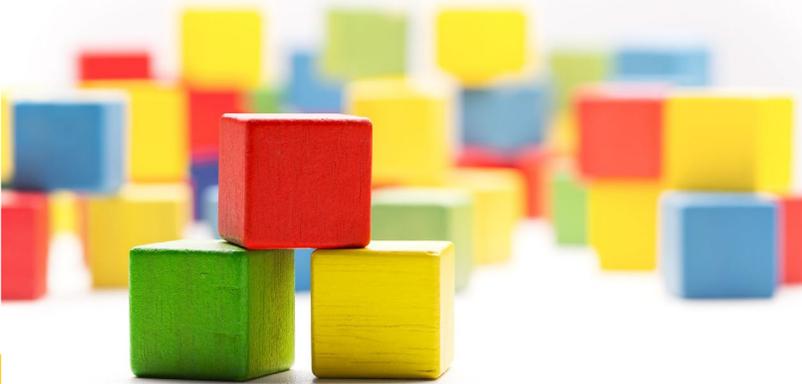
- Obata et al: blocco peridurale continuo preoperatorio riduce significativamente l'incidenza di dolore persistente e CPSP rispetto alla sola infusione post-operatoria
- Ju et al: Epidurale toracica Vs crioanalgesia– sviluppo di dolore cronico significativamente più grave che interferisce con la vita quotidiana nel gruppo crio
- Liu et al: infusione continua della ferita con ropivacaina Vs PCA con sufentanyl. Migliori risultati con AL





Anestesia regionale e prevenzione del CPSP

- L'anestesia locoregionale crea un blocco della trasmissione del segnale nocicettivo
- Previene quindi il meccanismo di sensibilizzazione centrale che è alla base dello sviluppo del dolore cronico.



Trattamento della CPSP accertata

- **Approccio Graduato:**
- Scala analgesica dell'OMS modificata per il dolore cronico non oncologico:
 - Partenza con analgesici non oppioidi.
 - Gli oppioidi forti usati con cautela solo in casi selezionati.
- **Trattamenti per il Dolore Neuropatico:**
- Prima linea: antidepressivi triciclici, SNRI, gabapentinoidi, topici, transdermici.
- Seconda linea: tramadolo e tapentadolo.
- **Tecniche di Neuromodulazione:**
- Neuromodulazione o termoablazione con radiofrequenza e stimolazione midollare come opzioni per pazienti non responsivi ai farmaci.



In conclusione

La CPSP è un problema crescente con l'invecchiamento della popolazione e l'aumento degli interventi chirurgici

Il dolore acuto post-operatorio, se non ben controllato, può essere alla base della CPSP e i farmaci attualmente utilizzati non sono efficaci nel prevenirlo

È stato dimostrato il ruolo dell'anestesia regionale nella prevenzione della CPSP in ambito perioperatorio

Dolore persistente e CPSP possono essere prevenuti in un paziente su quattro con l'applicazione di tecniche di ALR

Numerosi studi dimostrano il ruolo chiave dell'anestesia locoregionale nella prevenzione della CPSP