

MESTRADO INTEGRADO  
MEDICINA

# **The influence of locoregional anesthesia on perioperative outcomes: a review.**

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## **The influence of locoregional anesthesia on perioperative outcomes: a review.**

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## **DECLARAÇÃO DE INTEGRIDADE CIENTÍFICA**

Eu, Ana Carolina Eirado Pontes, declaro solenemente que esta dissertação, intitulada " The influence of locoregional anesthesia on perioperative outcomes: a review.", é um trabalho original e genuíno. Durante o seu processo de investigação e elaboração, segui estritamente os princípios éticos e as normas académicas estabelecidas pela comunidade científica. Assumo total responsabilidade pelo conteúdo desta dissertação e estou ciente das possíveis consequências de qualquer violação dos princípios de integridade científica.

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Ao Professor Doutor Humberto Machado e à Dra. Neusa Lages pela orientação e acompanhamento.

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A concretização deste sonho faz de mim melhor pessoa,  
melhor filha, melhor namorada e melhor amiga.

Obrigada.

## RESUMO

### Introdução

O controlo inadequado da dor no período perioperatório é comum e continua a ser, nos dias de hoje, um problema frequentemente sem solução que está associada à diminuição da satisfação do paciente, ao aumento da incidência de complicações pulmonares e cardíacas, ao aumento de tempo até a mobilização pós-operatória do doente, ao desenvolvimento de dor crónica e ao aumento da mortalidade. A administração de opioides para controlar a dor pós-operatória está relacionada a efeitos adversos como obstipação, náuseas e vómitos, risco de dependência e risco de desenvolvimento de hiperalgesia induzida por opióides. Para atenuar estes efeitos, técnicas anestésicas complexas estão a ser utilizadas com mais frequência para reduzir a dor pós-operatória e acelerar a reabilitação. Atualmente, acredita-se que a anestesia sem opióides seria apropriada quando baseada em técnicas de bloqueio regional contínuo ou de ação prolongada. O uso generalizado da anestesia regional associada, ou não, à anestesia geral tem contribuído para a melhoria da dor pós-operatória tanto em cirurgias de ambulatorios como em pacientes internados.

O conceito de analgesia preventiva sugere que a dor pós-operatória pode ser atenuada se a transmissão da mesma for bloqueada antes da ocorrência dos estímulos nocivos. Lesões teciduais, como **ocorrem** durante a cirurgia, aumentam o nível de mediadores inflamatórios no campo cirúrgico, levando ao desenvolvimento de sensibilização periférica. As fibras nervosas que transmitem sinais de dor, na medula espinhal, podem tornar-se hipersensíveis e reagir até mesmo a estímulos comuns, resultando em hiperalgesia. A anestesia local preventiva diminui a sensibilização periférica e central através da inibição da libertação de mediadores inflamatórios e do bloqueio de nociceptores e terminações nervosas, reduzindo a dor pós-operatória e inibindo o desenvolvimento de dor neuropática. Adicionalmente, um regime analgésico multimodal equilibrado auxilia na redução de recurso a fármacos opióides aos mínimos necessários durante o menor período possível, permitindo atenuar os seus efeitos adversos.

### Objetivos

Esta revisão da literatura visa estudar e analisar os avanços na anestesia regional nos últimos vinte anos e evidenciar seu impacto clínico na recuperação funcional, morbidade e mortalidade do paciente.

## **Métodologia**

Foi efetuada uma pesquisa estruturada através de plataformas digitais de publicação científica como PubMed, Google Scholar e Medline que incluiu revisões, meta-análises, ensaios clínicos randomizados e estudos prospectivos selecionados e considerados para avaliação do texto completo.

## **Resultados**

A prevenção da dor pós-operatória crônica é um objetivo clínico importante, apoiado por um número crescente de pesquisas. A anestesia locorregional perioperatória é a estrela da abordagem analgésica multimodal, opondo-se às alterações neuronais induzidas pela cirurgia e pelo recurso a fármacos opióides. O uso de anestesia locorregional permite bloquear a ativação neuronal induzida pela lesão tecidual e a consequente sensibilização do sistema nervoso periférico e central. O conhecimento sobre os diferentes tipos de dor, as técnicas de anestesia locorregional e o uso de adjuvantes anestésicos locais para anestesia locorregional é a chave para desenvolver melhores resultados e melhorar a satisfação do paciente.

A anestesia locorregional apresenta melhores resultados como menor tempo de internamento hospitalar, menos recorrência e menor tempo de internamento em Unidades de Cuidados Intensivos e menor necessidade de opióides no pós operatório. No entanto, esta não apresenta diferenças significativas nas taxas de mortalidade e morbidade.

## **Conclusão**

Embora inúmeros estudos que comparam a anestesia geral com a anestesia locorregional tenham considerado a anestesia locorregional uma alternativa mais segura e com menos complicações, essas conclusões apresentam resultados muito diferentes de acordo com o tipo de cirurgia realizada.

Sobre a dor crônica não há evidências suficientes de que os anestésicos locais possam reduzir o risco de desenvolver dor crônica pós-cirúrgica, mas os estudos realizados permitem ao cirurgião e ao anesthesiologista colocar esta opção em cima da mesa e escolher de acordo com as condições e avaliação do estado de saúde dos doentes.

**Palavras-chave:** “anestesia locorregional preventiva”; “anestesia regional”; “bloqueio de nervos periféricos”; “analgesia opioid-free”; “analgesia multimodal”.

## **ABSTRACT**

### **Background**

Inadequate pain management in the perioperative period is common and remains an unsolved problem. It has been associated with decreased patient satisfaction, an increased incidence of pulmonary and cardiac complications, delayed postoperative mobilization, the development of chronic pain and increased mortality. The administration of opioids to control postoperative pain has been related to adverse effects such as constipation, nausea and vomiting, risk of dependence and opioid-induced hyperalgesia [15].

To mitigate such effects, complex anesthesia is being used more often to reduce postoperative pain and accelerate rehabilitation. There is currently a belief that opioid-free anesthesia would be appropriate when based on long-acting or continuous regional block techniques. The widespread use of regional anesthesia whether or not associated to general anesthesia has contributed to the improvement of postoperative pain in both ambulatory surgery and inpatients.

The preemptive analgesia concept suggests that postoperative pain may be attenuated if the transmission of pain is blocked before the occurrence of noxious stimuli. Tissue injuries, as occurs during surgery, increase the level of inflammatory mediators within the operative field, leading to development of peripheral sensitization. Nerve fibers that transmit pain signals, in the spinal cord, may become hypersensitive and react even to common stimuli, resulting in hyperalgesia. Preemptive local anesthesia decreases the peripheral and central sensitization through inhibition of inflammatory mediator generation and blocking nociceptors and nerve endings reducing postoperative pain and inhibit neuropathic pain. Additionally, a balanced multimodal analgesic regimen assists the reduction of opioids to necessary minimums for the shortest period possible while mitigating their adverse effects.

### **Objectives**

This literature revision aims to acknowledge advances in regional anesthesia over the last twenty years and evidence its clinical impact in management of patient functional recovery, morbidity and mortality.

### **Methods**

A structured search through digital scientific publication platforms as PubMed, Google Scholar and Medline that included reviews, meta-analyses, randomized controlled trials and prospective studies selected and considered for full-text assessment.

## **Results**

The prevention of chronic postoperative pain is an important clinical goal, supported by a growing body of research. Perioperative locoregional anesthesia remains a pivot of the multimodal analgesic approach opposing the neuronal changes induced by surgery and opioids. The use of locoregional anesthesia allows block injury-induced activation and sensitization of both the peripheral and central nervous system. Knowledge about the different types of pain, locoregional anesthesia techniques and the use of local anesthetic adjuvants for locoregional anesthesia is the key to a develop better outcomes and patient satisfaction.

Locoregional anesthesia has search based support with better outcomes such as shorter hospital length of stay, ICU rates of utilization and opioids need after surgery but no significant differences in the rates of mortality and morbidity.

## **Conclusion**

Although numerous studies comparing general anesthesia to locoregional anesthesia found locoregional anesthesia a safer alternative with fewer complications, these conclusions have very different results according to the type of surgery performed.

About chronic pain there is not enough evidence that local anesthetics may reduce the risk of developing chronic postsurgical pain, but the performed studies allow the surgeon and the anesthesiologist to put this option on the table and choose according to patients conditions health status assessment.

## **Keywords**

Preemptive locoregional anesthesia; Perioperative period; Regional anesthesia; Peripheral nerve block, Opioid-Free, Multimodal Analgesia

## **LIST OF ABBREVIATIONS**

CEA – carotid endarterectomy

CPSP – Chronic Postsurgical Pain

EVAR – endovascular aortic aneurysm repair

GA – general anesthesia

ICU – intensive care units

LA – locoregional anesthesia

LOS – length of stay

NMDA – Nmethyl-D-aspartic acid

TEVAR – Thoracic Endovascular Aortic Repair

## TABLE OF CONTENTS

Agradecimientos.....	i
Resumo.....	ii
Abstract .....	iv
List of abbreviations.....	vi
Table of contents.....	vii
List of tables.....	viii
Introduction.....	1
Methods .....	4
Discussion.....	5
Conclusion .....	12
Appendix .....	13
References.....	16

## **LIST OF TABLES**

Table I – Pain types definitions and mechanisms

Table II – Outcomes of TEVAR by type of anesthesia

Table III - Outcomes of patients undergoing open inguinal herniorrhaphy by type of anesthesia

Table IV - Anesthesia locoregional versus conventional analgesia outcomes

## **INTRODUCTION**

### **Preemptive analgesia**

Preemptive analgesia is defined as an analgesic intervention given before the onset of a noxious stimulus to prevent the development of central sensitization, incisional and inflammatory injuries, and it has been shown to be more effective than the same intervention given after surgery. By preventing sensitization of the central nervous system induced by painful stimuli, appropriate interventions alleviate the response to future nociceptive input and decrease the degree of central nervous system sensitization to allow normally painful stimuli to be experienced as painless. By decreasing the altered central sensory processing and inflammation, induced by the release of cytokines and prostaglandins, preemptive analgesia is thought consequently to decrease the incidence of postoperative hyperalgesia and allodynia <sup>[10]</sup>.

In the preemptive approach, it is possible to use different analgesics and techniques, including preemptive epidural anesthesia, local wound infiltration, opioids, Nmethyl-D-aspartic acid (NMDA) receptor antagonists, nonsteroidal anti-inflammatory drugs (NSAIDs), and preemptive multimodal analgesia <sup>[11]</sup>.

### **Acute pain vs Chronic pain**

Acute pain has a biological significance by its protective role for the organism. The acute pain leads to avoidance of harmful stimulus encouraging healing of damaged tissue and it's evoked via direct activation and sensitization of nociceptors by inflammatory mediators <sup>[3, 7]</sup>.

On the other side, chronic pain is a maladaptive response with no biological significance characterized by a pain state that continues beyond normal healing time. According to the International Classification of Diseases (ICD), chronic pain is defined as pain that persists or recurs for more than three months [2]. Chronic pain is characterized by spontaneous pain (e.g., burning) as well as evoked pain in response to noxious (hyperalgesia) or non-noxious (allodynia) stimuli. It is well understood in the pain research community that neuronal and synaptic plasticity, i.e. neural plasticity in pain coding pathways and circuits results in chronic pain. Neuronal plasticity occurs in primary sensory neurons of dorsal root ganglia (DRG) and trigeminal ganglia (peripheral sensitization) as well as in pain-processing neurons in the spinal cord and brain (central sensitization) <sup>[2, 4]</sup>.

## **Chronic Postsurgical Pain (CPSP)**

Chronic postoperative pain is defined as pain persisting for at least 3 months after surgery, which was either not present before or differs from pre-operative pain, and which is localized to the surgical site, and without other obvious cause [8].

The pathophysiology of pain involves complex nervous system interactions after initial noxious stimuli. When stimuli persist, biochemical and structural changes occur in the nociceptive pathways of the central and peripheral nervous systems, leading to pain sensitization. Peripheral and central sensitization are key in the transition from acute to chronic pain. This development of chronic pain is particularly common following various surgical procedures, with many postsurgical patients experiencing persistent pain for significant periods [4,5].

Chronic postoperative pain has been recognized as a common and severe adverse outcome of many different types of surgery. The presence of some degree of post-operative pain is expected after various procedures; however, many patients develop continuous and persistent pain that is severe enough to affect their quality of life years after their initial surgery [5]. Preventing this pain is tantamount to improving patient outcomes.

A variety of operative, anesthetic, and patient factors have been observed to correlate with the increased risk for development of chronic postsurgical pain. These factors include several biomedical, psychological, and social predictors such as genetic factors, psychosocial factors and pain cognition, preoperative pain, operative factors, anesthesia technique and postoperative pain.

Preventative strategies involved in chronic postsurgical pain development include preventative analgesia and a multimodal approach.

**Preventive analgesia** should aim to limit and prevent primary afferent stimulation and long-term changes in CNS functions allowing to reduce nociceptive stimulation and inflammation that leads to primary and secondary sensitization and playing an important role in reducing chronic pain development. The mainstay of preventative analgesia includes local anesthetic infiltration of the surgical field and judicious titration of opioids to maintain adequate pain control, but now there is an increasing emphasis on multimodal analgesic plans beyond opioids. The development of an effective preventative approach to CPSP—as opposed to treatment after pain is already established—depends on further study of such multimodal techniques.

**Multimodal analgesia** targets the various levels of nociceptive pathways and is vital in CPSP prevention and treatment. These techniques work in tandem to reduce the excitability of neurons involved in these nociceptive pathways both centrally with preventative analgesia and peripherally with neuraxial, regional, and local anesthesia <sup>[5]</sup>. Multimodal analgesia combines the use of local anesthetics in the surgical field with locoregional anesthetic techniques and in aggressive pain approach it can add other analgesic medication during the preoperative, intraoperative, and postoperative periods.

## **METHODS**

For this review a bibliographic research was performed in medical and scientific databases such as PubMed, Google Scholar and Medline including reviews, meta-analyses, randomized controlled trials and prospective studies published to March 2024. It was conducted a hand search in reference lists of included studies, review articles and conference abstracts.

Search terms included “chronic postoperative pain”; “multimodal analgesia”; “opioid-free analgesia”; “regional anesthesia”; “locoregional anesthesia”; “general anesthesia”; “acute pain”; “chronic pain”; “locoregional anesthesia outcomes”; “general versus local anesthesia”. In addition, the reference lists of retrieved articles were searched for other relevant articles.

Articles selected for inclusion were manuscripts whit relevant evidence about locoregional anesthesia outcomes and the multimodal analgesia approach.

Only studies available in English and Portuguese languages were considered.

## **DISCUSSION**

The prevention of chronic postoperative pain is an important clinical goal, supported by a growing body of research. Perioperative locoregional anesthesia remains a pivot of the multimodal analgesic approach as opposed to the neuronal changes induced by surgery and opioids. The use of locoregional anesthesia blocks injury-induced activation and sensitization of both the peripheral and central nervous system <sup>[7]</sup>.

### **Nociceptive, inflammatory and neuropathic pain** <sup>[1, 7, 13]</sup>

Several distinct mechanistic pain types have been identified and defined as contributing to both acute and chronic pain after surgery (Table I).

Nociceptive pain is based on a perception of a noxious stimulus and involves activation of mostly unmyelinated C-fibers and some myelinated A $\delta$ -fibers within peripheral sensory neurons (nociceptors) in response to mechanical, chemical or noxious stimuli of non-neuronal tissue.

Inflammatory pain results from the release of inflammatory mediators and cytokines primarily by non-neuronal cells which are called to the area after tissue injury.

Neuropathic pain is caused by injury of a neuron - leading to a spontaneous firing of action potentials (ectopic activity) by the injured and surrounding neurons (A $\beta$ , A $\delta$  and C fibers) - , activation of NMDA receptors - leading to 'wind-up' phenomenon - , induction of central sensitization and heightened pain sensitivity.

A surgical incision may involve all three (nociceptive, inflammatory and neuropathic) types of pain to varying degrees.

Peripheral sensitization is a reduction in the nociceptors activation threshold, that innervate inflamed tissue. Central sensitization, in contrast to peripheral sensitization, is an increase in excitability of neurons in the central nervous system.

### **Locoregional anesthesia techniques**

Locoregional anesthesia involves the injection of local anesthetic agents around nerves, in the peripheral nervous system or central nervous system, blocking the generation and propagation of

electrical impulses in a reversible manner. These techniques result in loss of sensory, motor and autonomic function in the corresponding innervated tissues.

Locoregional anesthesia can be divided into peripheral nerve blocks (injection of local anesthetic agents around nerves in the peripheral nervous system to achieve reversible numbing of pain conduction in the corresponding innervated tissue), or neuraxial anesthesia such as epidural anesthesia (local anesthetics with or without opioids and alpha-adrenergic agonists are injected into the epidural space and act on the spinal nerve roots. Epidural anesthesia blocks several nerve roots around the site of injection and barely affects the function of the nerve roots above and below - segmental anesthesia) and spinal anesthesia (local anesthetics with or without opioids and alpha-adrenergic agonists are injected into the cerebrospinal fluid in the lumbar spine and act directly on the spinal cord. Combined spinal and epidural anesthesia (CSE) combines the advantages of spinal anesthesia (rapid action, motoric block) with the advantages of epidural anesthesia (favorable post-operative pain management via an epidural catheter) playing a major role in obstetrics and orthopedics) <sup>[12]</sup>.

### **Mechanism of action for locoregional anesthetics**

The pharmacological mechanism of local anesthetics arises from the interaction with specific ionic channels, receptors and, possibly, from their more general effects on biological membranes <sup>[13]</sup>.

#### Ion channels

Voltage-gated channels conduct specific ions across membranes and are essential for the generation and propagation of action potentials as well as for transmitter release and postsynaptic responsiveness. The voltage-gated channels include Na<sup>+</sup> channels, K<sup>+</sup> channels, Ca<sup>2+</sup> channels and HCN channels (hyperpolarization-activated cyclic nucleotide-gated channels).

Locoregional anesthetics act by blocking the voltage-gated sodium channels thus preventing the generation of action potentials, and by inhibiting K<sup>+</sup> channels that slows repolarization and keeps the membrane depolarized for a longer time during the AP. Inhibition of voltage-gated potassium channels potentiates the impulse blocking action that occurs via the blockade of voltage-gated sodium channels.

LA Acts on the TRP channels by first opening the channel, at one “gating” site, and secondarily, in the channel’s pore, passing through it, although at slower rate than Na<sup>+</sup>.

### G Protein–Coupled Receptors

Synaptic cellular communication and hormonal modulation result from the activation of G protein–coupled receptors that release into the cytoplasm small “G proteins” resulting in the activation of a wide variety of signaling pathways. LA inhibits the synaptic transmission, essential for pain responses after injury.

### Intracellular Pathways

Locoregional anesthesia acts at several locations of intracellular signaling pathways. It inhibits cytoplasmic signaling that can release Ca<sup>2+</sup> from intracellular stores and starts pain signaling pathways.

### Membrane properties: fluidity and phase differences

The local anesthesia drugs interaction and absorption through the lipid bilayer membranes can modify the membrane’s surface electrical charge and can affect lipid dynamics, without a direct binding of the LA molecules to the proteins. This interaction results in increasing fluidity of the membranes.

### **Local anesthetic adjuvants for locoregional anesthesia**

Despite the improvement in analgesia brought by locoregional anesthesia, one drawback of single-shot peripheral nerve blockade is its limited duration of action <sup>[14]</sup>.

Continuous peripheral nerve blockade is defined as the percutaneous insertion of a catheter adjacent to a peripheral nerve, plexus or fascial plane, followed by the administration of local anesthetic through the catheter. This modality has been associated with decreased rebound pain and improved postoperative analgesia, relative to single-shot peripheral nerve blockade <sup>[16]</sup>. Due to catheter migration, obstruction or shearing, fluid leakage and infusion pump malfunction, the rate of secondary block failure has been reported to be as high as 20–50% <sup>[17]</sup>. Other complications include inaccurate placement of the catheter tip, knotting, catheter-related mechanical nerve irritation, inflammation at the insertion site, bacterial colonization, and local anesthetic systemic toxicity <sup>[18]</sup>. Given these outcomes the use of adjuvants is considered as a viable practice.

The administration of local anesthetic adjuvants is defined as the simultaneous administration of one or more pharmacological agents by intravenous injection or perineural injection (around a peripheral nerve, plexus or fascial plane) to extend and potentiate the benefits of peripheral nerve block beyond the conventional maximum of 8–14 hours.

Used anesthetic adjuvants include adrenaline, commonly administered with local anesthetics in peripheral nerve blockade, due to its vasoconstrictor action that allows the increase of analgesia mean duration and prolong the motor component of the block <sup>[19]</sup>. Adrenaline has been found to delay the systemic absorption of local anesthetic with the resultant possibility of decreasing the risk of local anesthetic systemic toxicity <sup>[20]</sup>. The decrease in blood flow to the peripheral nerve when perineural adrenaline is administered, should be modified in patients with acquired peripheral neuropathy by eliminating or reducing the concentration of adjuvant <sup>[21]</sup>.

Buprenorphine is an opioid receptor agonist also used as anesthetic adjuvant that acts blocking voltage-gated sodium channels, inhibiting the generation of action potentials [18], and interacting with opioid receptors on the axons of unmyelinated C fibers, increasing analgesia and motor block duration <sup>[22]</sup>.

Clonidine is another agent used as an adjuvant in locoregional anesthesia blocking the restore of the neuron resting potential in the refractory phase of the action potential, delaying the resumption of functional activity. This and its localized vasoconstriction action increase the mean duration of analgesia, sensory block and motor block <sup>[23]</sup>.

Magnesium is an N-methyl-D-aspartate (NMDA) receptor antagonist that has been demonstrated to increase neuron excitation. Its co-administration with anesthetic substances increases the duration of analgesia, sensory block and motor block.

Dexmedetomidine and dexamethasone have been extensively investigated as novel local anesthetic adjuncts. Dexmedetomidine mechanism of action after perineural administration is likely to be similar to clonidine, although it is not thought to mediate localized vasoconstriction, unlike the latter. Dexmedetomidine can produce a differential sensorimotor effect, extending the sensory block without prolonging the motor block.

Dexamethasone has a mechanism of action after perineural administration that is likely to be due to stimulation of glucocorticoid receptors located on the neuronal membrane, increasing the expression of inhibitory potassium channels and hence decreasing the excitability of unmyelinated C fibers. It could further work by inducing localized vasoconstriction or through systemic anti-inflammatory processes following vascular absorption. Its co-administration increased the mean duration of analgesia. Dexamethasone can induce an increase in the postoperative blood glucose concentration, subsequent to either perineural or intravenous administration.

Any of the local anesthetic adjuncts referred to, either administered intravenously or perineural, are a promising and technically simple alternative to other strategies for extending the beneficial effects of peripheral nerve block.

### **Anesthesia locoregional versus conventional analgesia**

Based on all the referred knowledge, this review aims to compare locoregional and conventional anesthesia's perioperative outcomes and its influence in the development of chronic pain.

A meta-analysis comparing local or regional anesthesia versus conventional analgesia with a pain outcome beyond three months after elective surgery concludes that there is moderate-quality evidence that regional anesthesia may reduce the risk of developing CPSP 3 to 18 months after thoracotomy (7 RCTs; 499 participants) and 3 to 12 months after cesarean section (4 RCTs; 551 participants). There is low-quality evidence that regional anesthesia may reduce the risk of developing CPSP 3 to 12 months after breast cancer surgery (18 RCTs; 1297 participants). There is moderate evidence that intravenous infusion of local anesthetics may reduce the risk of developing CPSP 3 to 6 months after breast cancer surgery (2 RCTs; 97 participants) <sup>[9]</sup>. This meta-analysis conclusions may be considerably weakened by performance bias, shortcomings in allocation concealment, considerable attrition and incomplete outcome data and conclusions cannot be extended to other surgical interventions or regional anesthesia techniques. For example, we cannot conclude that paravertebral block reduces the risk of chronic pain after thoracotomy.

A study with 1028 patients comparing 30-day postoperative outcomes as mortality, morbidity and hospital length of stay, between general and locoregional anesthesia groups in Thoracic Endovascular Aortic Repair (TEVAR), shows that locoregional anesthesia is significantly associated with shorter postoperative hospital length of stay, without showing any significant additional postoperative morbidities compared to general anesthesia. Locoregional anesthesia is a safe alternative to general anesthesia for TEVAR with reduced total hospital length of stay, especially in select elective cases with unruptured thoracic aneurysms (Table II) <sup>[24]</sup>.

Another systematic review with nineteen studies aimed to establish the efficacy and the safety of locoregional anesthesia in the pain management after breast surgery. Including 1058 patients who underwent lumpectomy/mastectomy, 142 for breast augmentation and 79 for breast reduction, the review shows that locoregional anesthesia provides effective anesthesia and analgesia in the periopera-

tive setting. However, no statistically significant difference emerged when compared to other techniques. For mastectomy only, the use of locoregional techniques reduces pain in the first hour after the end of the surgery if compared to other procedures. Other potentially beneficial effects of locoregional anesthesia include decreased need for opioids, decreased postoperative nausea and vomiting, fewer complications and increased patient satisfaction. All these benefits allow to improve postoperative recovery and shortens hospital LOS. In none of these cases, locoregional anesthesia was statistically superior to other techniques <sup>[25]</sup>.

Another study with two groups of 3027 patients demonstrated that elective endovascular aortic aneurysm repair (EVAR) patients repaired under LR are associated with shorter hospital stays and a reduced need for ICU admission, with ICU admission being highly reliant on the hospital center performing the procedure. There is no difference in postoperative outcomes or mortality. These findings highlight the ability of LR to be used as a safe anesthetic alternative to GA and highlight the potential of decreased hospital resource utilization based on an association with reduced hospital stays and reduced ICU utilization <sup>[26]</sup>.

Based on a systematic review and meta-analysis the RCT performed including 1969 patients in the general anesthesia cohort and 1987 patients in the local anesthesia cohort, there are no significant differences between the outcomes of the two groups. When nonrandomized data with much larger sample sizes also were considered, small but significant differences were demonstrated that favored LA where patients who underwent surgery with general anesthesia were slightly more likely to experience postoperative myocardial infarction and required longer periods of hospitalization than the other group <sup>[27]</sup>.

Another study with a total of 25213 patients, where two equivalent groups (n = 8623) were created, analyses open inguinal herniorrhaphy performed under locoregional versus general anesthesia. Studied outcomes were anesthesia and operative times, postoperative admission, and 30-day morbidity.

When compared by anesthetic choice, those undergoing locoregional anesthesia have shorter operative and anesthetic time as well as fewer postoperative admissions to a hospital despite increased preoperative risk factors. Post-operative admission to a hospital, as well as 30-day morbidity, is significantly increased after general anesthesia. After propensity matching for perioperative risk, we confirm the safety and efficacy of locoregional anesthetic as a safe and effective alternative to general anesthesia for initial, open inguinal herniorrhaphy (Table III) <sup>[28]</sup>.

Table IV - Anesthesia locoregional versus conventional analgesia outcomes

Author, year	Questions and groups analyzed	Main findings
Weinstein et al., 2018	Compare local or regional anesthesia versus conventional analgesia with a pain outcome beyond three months after elective surgery.	The meta-analysis has weak results and conclusions cannot be extended to other surgical interventions or regional anesthesia techniques.
Panossian et al., 2022	Analyze postoperative outcomes between general and locoregional anesthesia groups in TEVAR.	Locoregional anesthesia results in significantly lower postoperative hospital LOS with similar postoperative mortality and morbidity compared to general anesthesia in patients undergoing TEVAR.
Sansone et al., 2020	Establish the efficacy and the safety of locoregional anesthesia in the pain management after breast surgery.	Locoregional anesthesia decreased need for opioids, postoperative nausea and vomiting increasing patient satisfaction but in none of these cases, locoregional anesthesia was statistically superior to other techniques.
Zottola et al., 2022	Compare postoperative outcomes between locoregional and general anesthesia in the setting of elective EVAR.	Patients repaired under LR are associated with shorter hospital stays and a reduced need for ICU admission and there is no difference noticed in postoperative outcomes or mortality.
Harky et al., 2019	Studies and compares the effects of general anesthesia and locoregional anesthesia on carotid endarterectomy outcomes.	There are no significant differences in the rates of mortality and cardiac complications in patients after undergoing carotid endarterectomy with local anesthesia or general anesthesia.
Bhattacharya et al., 2012	Analyses open inguinal herniorrhaphy performed under locoregional anesthesia versus general anesthesia.	Patients undergoing locoregional anesthesia have shorter operative and anesthetic time as well as fewer postoperative admissions to a hospital. Post-operative admission to a hospital, as well as 30-day morbidity, are also significantly decreased after locoregional anesthesia.

## **CONCLUSION**

The practice of regional anesthesia has advanced rapidly. There are well-defined benefits such as reducing pain, reduced opioid consumption and improved quality of early recovery. The current challenges include extending the impact beyond the immediate postoperative period, improving access for patients and defining the long-term effects mainly when we consider chronic postsurgical pain.

Local anesthetic adjuncts, either administered intravenously or perineural, are a promising and technically simple alternative to other strategies for extending the beneficial effects of peripheral nerve blockade. Locoregional anesthetic modalities are thus a safe alternative, avoiding endotracheal intubation, mechanical ventilation, and the possible risks and complications of general anesthesia, which would ultimately increase morbidity and mortality, delay discharge, and increase the cost of care.

Numerous studies, comparing general and locoregional anesthesia, found locoregional anesthesia a safer alternative with fewer complications, when compared to general anesthesia in a variety of surgeries. These conclusions mainly focus on hospital length of stay, UCI utilization and opioids need and have very different results according to the type of surgery performed.

Regarding chronic pain, there is not enough evidence suggesting that local anesthetics may reduce the risk of developing CPSP, although the performed studies allow anesthesiologists to consider this option as an alternative to stop the morbidity that chronic pain represents.

## APPENDIX

Table I – Pain types, definitions and mechanisms [7]

Pain classification	Definition	Example	Evolutionary response	Evolutionary plasticity	Sensitisation
Nociceptive	Activation of high threshold peripheral sensory neurons in response to potential or actual injury to non-neuronal tissue	Surgical incision of innervated tissue	Adaptive	Reversible	Peripheral
Inflammatory	Activation of local or infiltrating immune or stromal cells, release of inflammatory mediators in response to nonneuronal injury	Heat, pain, redness and swelling in the area of a surgical wound	Adaptive	Generally reversible	Peripheral and central
Neuropathic	Injury to neuronal structures	Cutting, electrocautery or devascularisation of a nerve in surgical field	Maladaptive	Variably reversible	Peripheral and central

Table II – Outcomes of TEVAR by type of anesthesia [24]

Outcomes	General Anesthesia (n = 889)	Locoregional Anesthesia (n = 139)	P value
30-day mortality	70 (7.9 %)	5 (3.6 %)	0.071
30-day morbidity	220 (24.8 %)	26 (18.7 %)	0.121
Wound complications	16 (1.8 %)	3 (2.2 %)	0.734
Pulmonary complications	110 (12.4 %)	10 (7.2 %)	0.077
Venous thromboembolic events	17 (1.9 %)	1 (0.7 %)	0.494
Urinary tract infection	31 (3.5 %)	3 (2.2 %)	0.609
Progressive renal insufficiency	5 (0.6 %)	1 (0.7 %)	0.583
Acute renal failure	11 (1.2 %)	4 (2.9 %)	0.133
Myocardial infarction	5 (0.6 %)	3 (2.2 %)	0.081
Intraoperative or postoperative cardiac arrest requiring CPR	30 (3.4 %)	4 (2.9 %)	0.999
Return to the operating room	77 (8.7 %)	12 (8.6 %)	0.991
Sepsis	26 (2.9 %)	3 (2.2 %)	0.787
Septic shock	16 (1.8 %)	1 (0.7 %)	0.717
Median length of stay (days)	5 (3-10)	4 (2-7 %)	0.002

Table III - Outcomes of patients undergoing open inguinal herniorrhaphy by type of anesthesia <sup>[28]</sup>

Outcomes	General Anesthesia (n = 8623)	Locoregional Anesthesia (n = 8623)	P value
Overall anesthesia/operative time	95.2 ± 35.7 min	85.3 ± 27.8 min	<0.0001
Anesthesia only time	38.0 ± 21.3 min	32.0 ± 14.7 min	<0.0001
Operative time	57.2 ± 24.9 min	53.3 ± 20.9 min	<0.0001
Postoperative admission	940 (10.9%)	506 (5.9%)	<0.0001
30-day morbidity	108 (1.3%)	80 (0.9%)	0.047

Table IV - Anesthesia locoregional versus conventional analgesia outcomes

Author, year	Questions and groups analyzed	Main findings
Weinstein et al., 2018	Compare local or regional anesthesia versus conventional analgesia with a pain outcome beyond three months after elective surgery.	The meta-analysis has weak results and conclusions cannot be extended to other surgical interventions or regional anesthesia techniques.
Panossian et al., 2022	Analyze postoperative outcomes between general and locoregional anesthesia groups in TEVAR.	Locoregional anesthesia results in significantly lower postoperative hospital LOS with similar postoperative mortality and morbidity compared to general anesthesia in patients undergoing TEVAR.
Sansone et al., 2020	Establish the efficacy and the safety of locoregional anesthesia in the pain management after breast surgery.	Locoregional anesthesia decreased need for opioids, postoperative nausea and vomiting increasing patient satisfaction but in none of these cases, locoregional anesthesia was statistically superior to other techniques.
Zottola et al., 2022	Compare postoperative outcomes between locoregional and general anesthesia in the setting of elective EVAR.	Patients repaired under LR are associated with shorter hospital stays and a reduced need for ICU admission and there is no difference noticed in postoperative outcomes or mortality.
Harky et al., 2019	Studies and compares the effects of general anesthesia and locoregional anesthesia on carotid endarterectomy outcomes.	There are no significant differences in the rates of mortality and cardiac complications in patients after undergoing carotid endarterectomy with local anesthesia or general anesthesia.
Bhattacharya et al., 2012	Analyses open inguinal herniorrhaphy performed under locoregional anesthesia versus general anesthesia.	Patients undergoing locoregional anesthesia have shorter operative and anesthetic time as well as fewer postoperative admissions to a hospital. Post-operative admission to a hospital, as well as 30-day morbidity, are also significantly decreased after locoregional anesthesia.

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