Perioperative Pain, Risk Stratification and Multimodal Analgesia

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Outline

- **Acute Postoperative Pain**
- **Chronic Pain After Surgery**
- **Opioids in Acute and Chronic Pain**
- **Multimodal Analgesia**
- **Perioperative Pain Management**

Disclosure

None

Nothing at all

Postoperative Pain

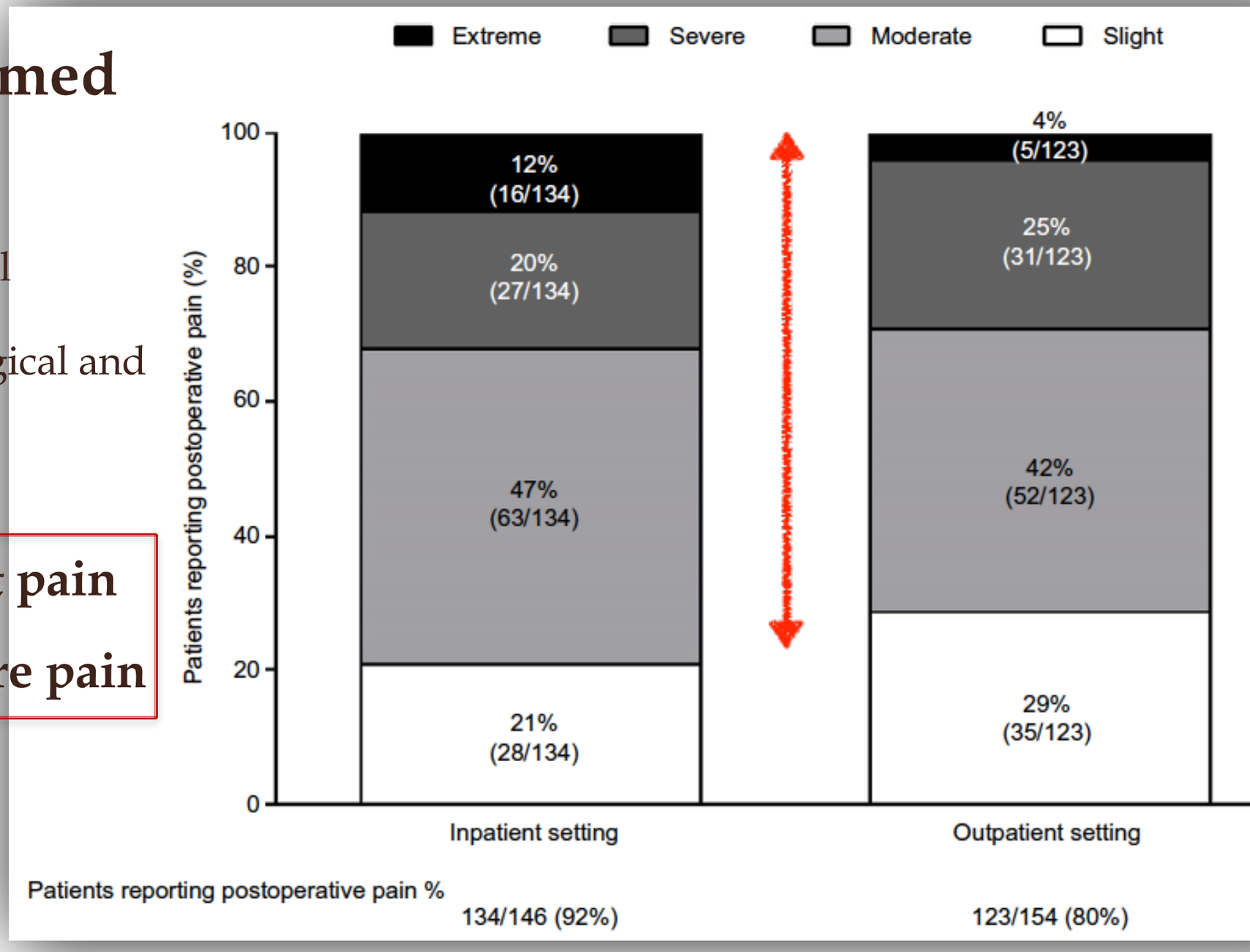
Procedures performed

- **28 mil. inpatient** surgical
- **48 mil. ambulatory** surgical and non-surgical

cdc.gov

- **~ 86% of patients report pain**

  ~ 75% with mod-severe pain



Gan TJ et al. CMRO 2014

British Journal of Anaesthesia 89 (3): 409–23 (2002)

Effectiveness of acute postoperative pain management: I. Evidence from published data

High levels of postoperative pain

pulmonary and cardiovascular complications
delayed hospital discharge
unexpected hospital (re)admissions
increased cost of care
impaired function and quality of life
prolonged opioid use
chronic pain after surgery

- patient satisfaction
[one of most feared surgery related side effects among patients]

Anesthesiology 2009; 111:657–77

Predictors of Postoperative Pain and Analgesic Consumption

A Qualitative Systematic Review

Hui Yun Vivian Ip, M.B.Ch.B., M.R.C.P., F.R.C.A.,* Amir Abrishami, M.D.,† Philip W. H. Peng, M.B.B.S., F.R.C.P.C.,‡

Type of surgical procedure (ortho, thoracic, open abdominal, OB, trauma, emergency… but also minor procedures)

Analgesic protocols

Preoperative pain, chronic pain

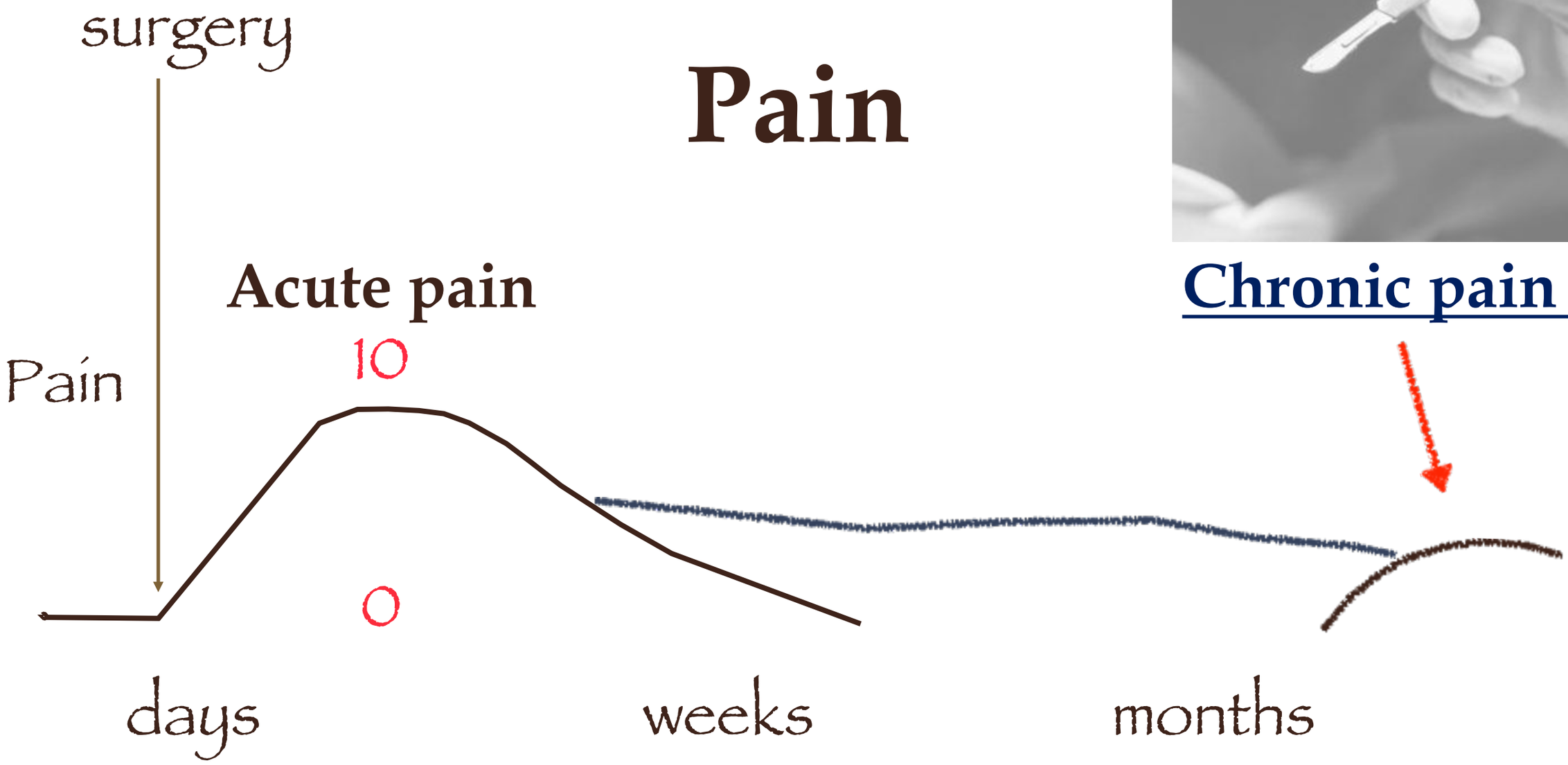
Anxiety, catastrophizing

Preoperative opioid use

which can affect wound healing[3] and cardiopulmonary

sion," "diagnostic model," "analysis of variance." The

Postoperative Pain

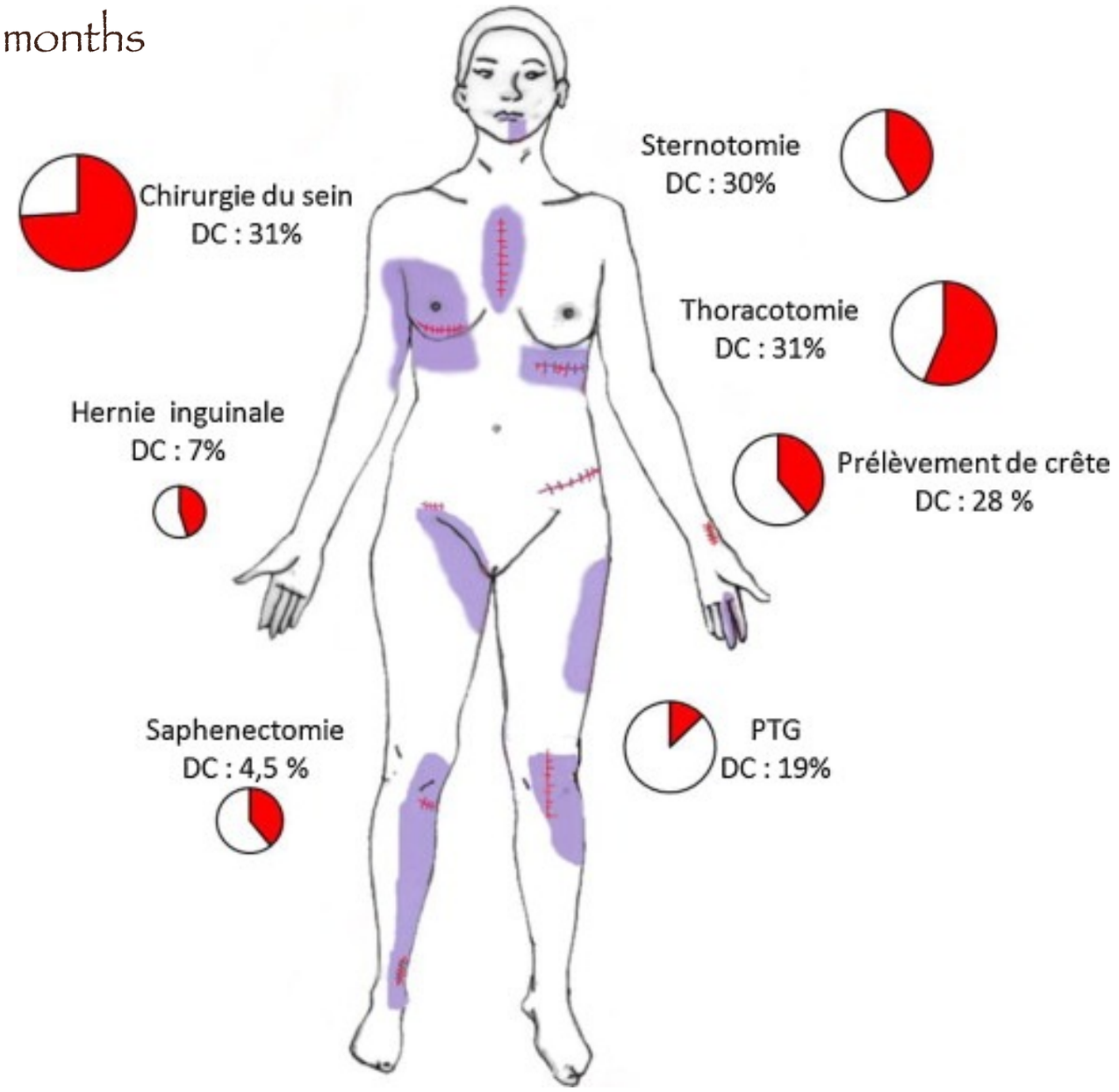


1) continuation of acute
2) delayed onset after asymptomatic time

The incidence of chronic pain after surgical procedures

surgery	%
amputation	30-85
thoracotomy	5-67
mastectomy	11-57
ing. hernia repair	0-63
sternotomy	28-56
cholecystectomy	3-56
knee arthroplasty	19-43
prostatectomy	35
gynecological laparotomy	32
iliac crest bone graft harvest	30

> 2 months



V. Martinez et al. Annales Francaises d'Anesthesie et de Reanimation 2013

E.J. Visser. Acute Pain 2006

Predictors for Chronic Postoperative Pain

Type of surgery, duration, repeat

Intensity/duration of acute post-op pain

Depression, anxiety, catastrophizing

Preexisting pain condition

Genetics, pain sensitivity, CPM

Kehltet H. et al. Lancet 2006
Fletcher D. et al. Eur J Anesth 2015

Rhodin et al. Molecular Brain 2013, 6:8
http://www.molecularbrain.com/content/6/1/8

Molecular Brain

RESEARCH Open Access

Combined analysis of circulating β-endorphin with gene polymorphisms in OPRM1, CACNAD2 and ABCB1 reveals correlation with pain, opioid sensitivity and opioid-related side effects

Annica Rhodin[1,4], Alfhild Grönbladh[2], Harumi Ginya[3], Kent W Nilsson[4], Andreas Rosenblad[4], Qin Zhou[2], Mats Enlund[1,4], Mathias Hallberg[2], Torsten Gordh[1] and Fred Nyberg[2*]

Abstract

Background: Opioids are associated with wide inter-individual variability in the analgesic response and a narrow therapeutic index. This may be partly explained by the presence of single nucleotide polymorphisms (SNPs) in genes encoding molecular entities involved in opioid metabolism and receptor activation. This paper describes the investigation of SNPs in three genes that have a functional impact on the opioid response: OPRM1, which codes for the μ-opioid receptor; ABCB1 for the ATP-binding cassette B1 transporter enzyme; and the calcium channel complex subunit CACNA2D2. The genotyping was combined with an analysis of plasma levels of the opioid peptide β-endorphin in 80 well-defined patients with chronic low back pain scheduled for spinal fusion surgery, and with differential sensitivity to the opioid analgesic remifentanil. This patient group was compared with 56 healthy controls.

Results: The plasma β-endorphin levels were significantly higher in controls than in pain patients. A higher incidence of opioid-related side effects and sex differences was found in carriers of the minor allele of the ABCB1 gene. Further, a correlation between opioid sensitivity and the minor allele of OPRM1 was also confirmed. A tendency of a relationship between opioid sensitivity and the minor allele of OPRM1 was also found.

Conclusions: Although the sample cohort in this study was relatively small, it was possible to observe significant correlations between genetic variations, pain sensitivity, opioid sensitivity and opioid response. Of particular interest was the finding of a correlation between pain sensitivity and the major CACNA2D2 allele. These findings may be important for the individualized treatment of chronic pain with opioids.

Keywords: Chronic pain, Opioid sensitivity, Genetic polymorphisms, μ-opioid receptor (OPRM1), Calcium channel subunit 2 (CACNA2D2), ATP-binding cassette B1 (ABCB1)

GENETICS

Single Nucleotide Polymorphisms (SNPs)

COMT, GCH1, ABCB1
CACNAD2, OPRM1, SCN9A

opioid metabolism
opioid receptor activity

- pain sensitivity and modulation
- opioid sensitivity
- opioid-related side effects

Research

JAMA Surgery | Original Investigation

New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults

Chad M. Brummett, MD; Jennifer F. Waljee, MD, MPH, MS; Jenna Goesling, PhD; Stephanie [illegible], PhD; Paul Lin, MS; Michael J. Englesbe, MD; Amy S. B. Bohnert, PhD, MHS; Sachin Kheterpal, MD; Brahmajee K. Nallamothu, MD, MPH

IMPORTANCE Despite increased focus on reducing opioid prescribing for long- is known regarding the incidence and risk factors for persistent opioid use afte

OBJECTIVE To determine the incidence of new persistent opioid use after min surgical procedures.

DESIGN, SETTING, AND PARTICIPANTS Using a nationwide insurance claims dat

surgery, parathyroidectomy, and carpal tunnel) and major surgical procedures incisional hernia repair, colectomy, reflux surgery, bariatric surgery, and hyster then assessed data for patient-level predictors of persistent opioid use.

MAIN OUTCOMES AND MEASURES The primary outcome was defined a priori p extraction. The primary outcome was new persistent opioid use, which was de opioid prescription fulfillment between 90 and 180 days after the surgical pro

RESULTS minor sur mean (SD (26 091 [7 ranging fr was only included p and substance abuse disorders (aOR, 1.34; 95% CI, 1.05-1.72), mood disorders CI, 1.01-1.30), anxiety (aOR, 1.25; 95% CI, 1.10-1.42), and preoperative pain disc pain: aOR, 1.57; 95% CI, 1.42-1.75; neck pain: aOR, 1.22; 95% CI, 1.07-1.39; arthr 95% CI, 1.40-1.73; and centralized pain: aOR, 1.39; 95% CI, 1.26-1.54).

CONCLUSIONS AND RELEVANCE New persistent opioid use after surgery is com

Great majority of acute postoperative pain management is based on opioids

SPECIAL SERIES

Chronic Opioid Usage in Surgical Patients in a Large Academic Center

Xueying Jiang, MD, PhD,† Margaret Orton, BS,† Rui Feng, PhD,‡ Erik Hossain, BS,§ Neil R. Malhotra, MD,|| Eric L. Zager, MD,|| and Renyu Liu, MD, PhD†*

is high, and that significant disparities may exist among different surgical populations.

Methods: Data of opioid usage in outpatients among different surgical services were extracted from the electronic medical record database. Patient demographics, clinical characteristics of sex, age, race, body mass index (BMI), specialty visited, duration of opioid use, and opioid type were collected. Chronic opioid users were defined as patients who had been recorded as taking opioids for at least 90 days determined by the first and last visit dates under opioid usage during the investigation.

Results: There were 79,123 patients included in this study. The average prevalence is 9.2%, ranging from 4.4% to 23.8% among various specialties

to reduce chronic opioid usage in surgical patients.

Keywords: chronic, opioids, prevalence, risk factor, surgical patients

(*Ann Surg* 2017;265:722–727)

6-9% opioid naive patients still on opioids 3 months post op

During the last decade, the use of opioids for pain management has dramatically increased. Sales and distribution of opioids in the United States have increased nearly 4-fold between 1997 and

Opioid depend- as high as 26% 00 deaths in the he total cost of ted to be $53.4 ds clinician and government action.

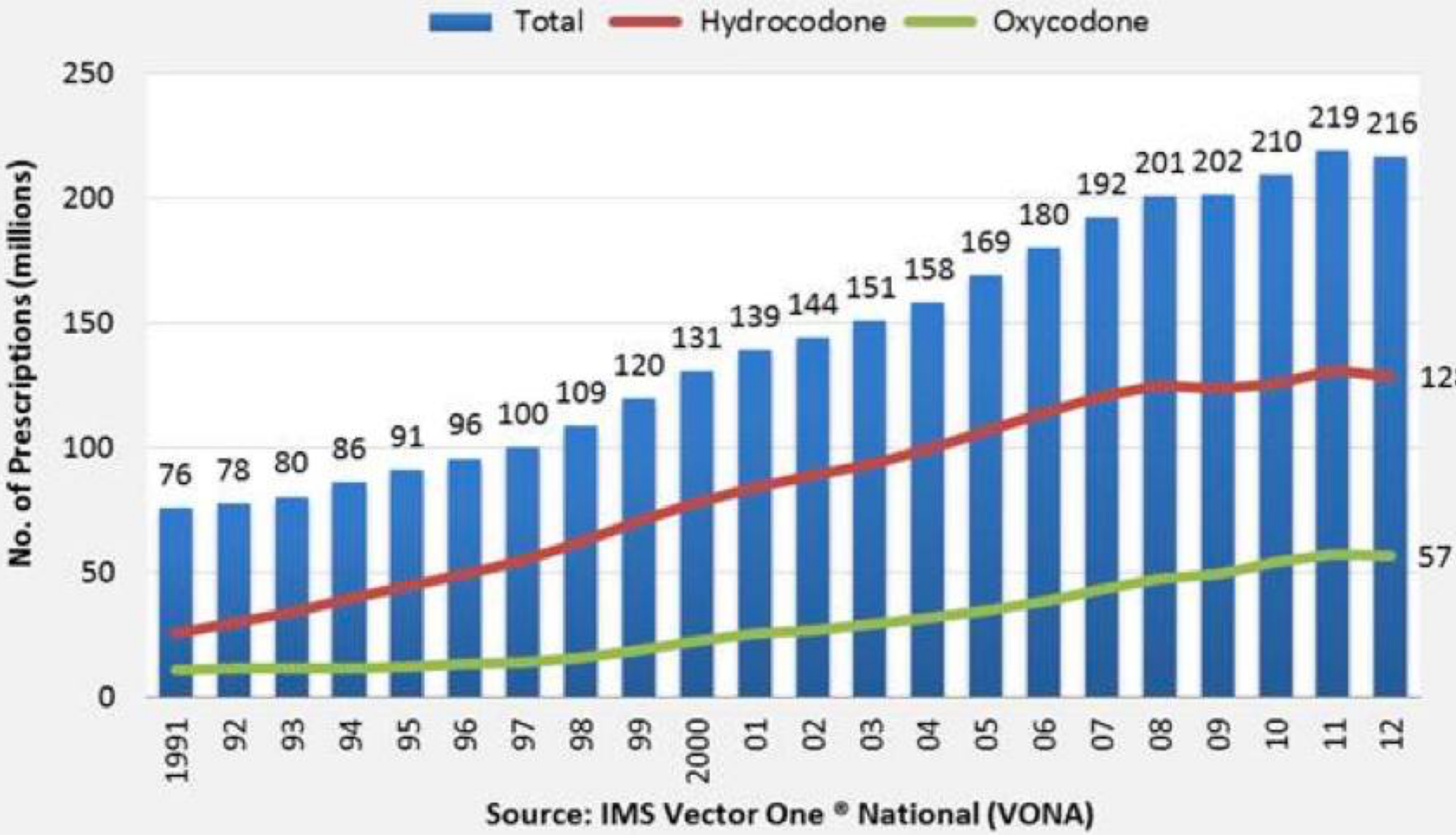
Over 100 million surgical procedures are performed annually in the United States. In 2010, 51.4 million inpatient procedures were performed in the United States;[5] another 53.3 million procedures were performed during ambulatory surgical visits.[6] Approximately 98.6% of these surgical patients received opioids during hospitalization.[7] The occurrence of chronic postsurgical pain varied from 10% to 50% depending on the type of operation.[8] A recent Canadian study demonstrated that 7.7% of opioid-naive elderly patients were still on opioids a year subsequent to surgery.[9] The clinical epidemiology of chronic opioid usage in surgical patients is not well characterized. As operative period and many are suffering with pain, we ronic opioid usage in surgical ors may be identified through ns of our study are to deter- s of chronic opioid usage in n a large medical center.

S

This investigation protocol was approved and the written informed consent was waived by the Institutional Review Board of the University of Pennsylvania.

In this retrospective cross-sectional study, data from surgical patients' electronic medical records were extracted out of Clarity, an Epic analytical reporting database, using an SQL-driven crystal report at the University of Pennsylvania Health system. Data were cleaned using R statistical software. The inclusion criteria consisted

Figure 4. Opioid Prescriptions Dispensed by US Retail Pharmacies



Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 1
March 18, 2016

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Opioids are not first line therapy

Establish goals for pain and function

Discuss risks/benefits

Start with immediate release opioids

Lowest effective dose

Short duration Rx for acute pain

Evaluate benefits and harm

Tolerance

Dependance

Immunosupression

Addiction

Neurotoxicity

Opioid induced hyperalgesia

Constipation

Respiratory depression

Urinary retention

Mood and sleep disturbance

Sedation confusion

Hormonal changes

Postoperative Care Goals

Minimize Pain
Enhance Recovery
Improve Function
Shorten Hospital Stay
Improve Patient Satisfaction
Decrease Opioid Use

Multimodal Analgesia

Pharmacological intervention along pain pathways

Opioids, APAP, Clonidine, Ketamine, Gabapentin, Tricyclics

5. Perception

6. CNS responses

Muscle relaxants, Beta blockers

1. Transduction

NSAIDS, COX-2 Inhibitors, Anti-Histamines, Topical local anesthetics

4. Modulation

Opioids, Clonidine APAP, COX-2 Inhibitors, Ketamine Gabapentin

2. Conduction

Peripheral nerve block local anesthetics

3. Transmission

Epidural block local anesthetics

A. Chandrakantan, P.S.A Glass. BJA 2011, with permission from R. Sinatra MD

Perioperative Period

peripheral sensitization

Pre operative → **Intra operative** → **Post operative**

ACUTE PAIN → CHRONIC PAIN

central sensitization

Preventive analgesia

(completely block any pain and afferent signals from the surgical wound

from the incision time until final wound healing

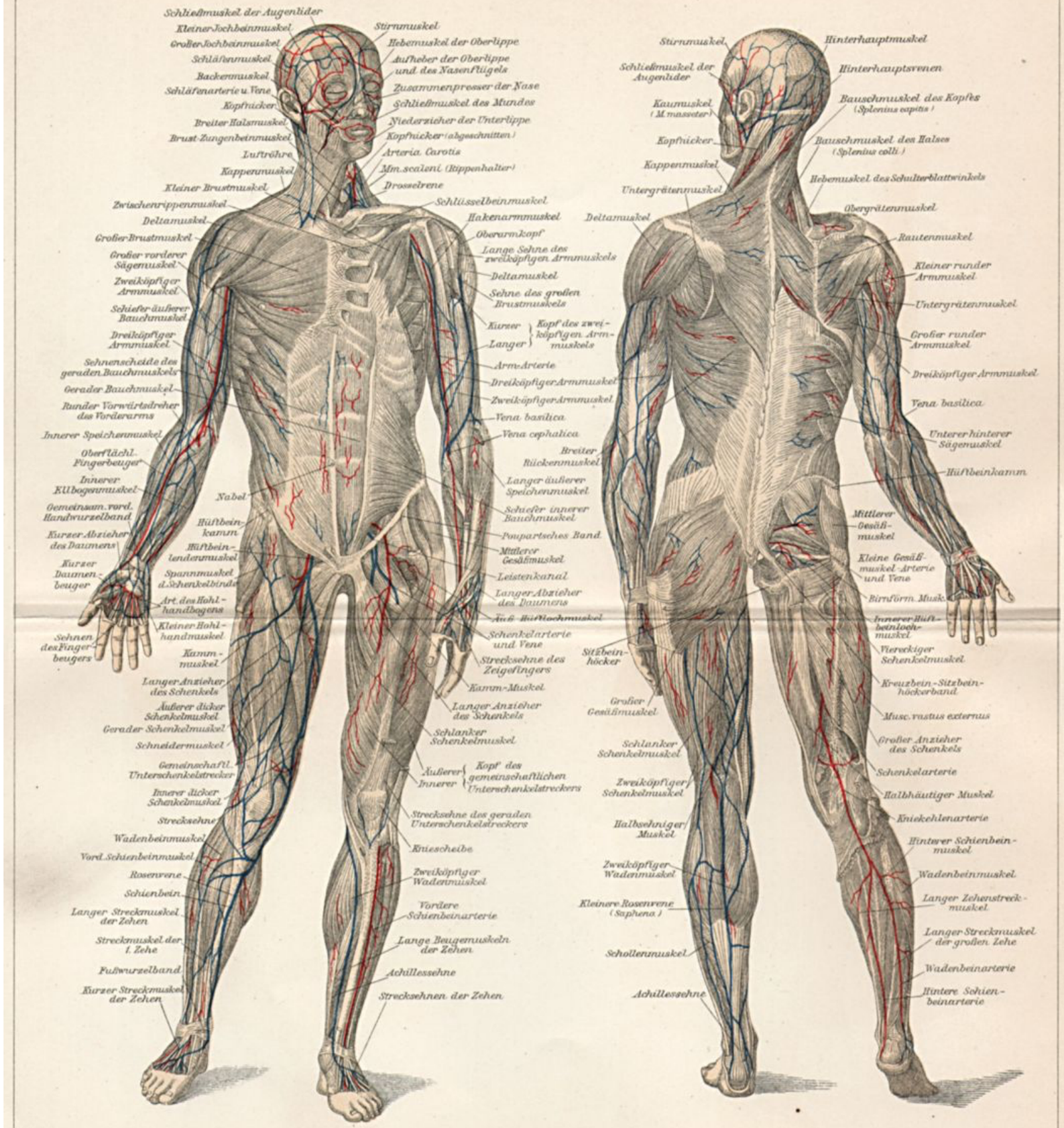


Fig. 1. Vorderansicht.

Auf der linken Körperhälfte sind am Halse, der Schulter, dem Unterarm und Oberschenkel die oberflächlichen Muskeln abgetragen worden.

Fig. 2. Rückenansicht.

Auf der rechten Körperhälfte sind die oberflächlichen Muskeln teilweise abgetragen worden, dadurch tritt die Schenkelarterie in ihrem ganzen Verlauf zum Vorschein.

Die roten Linien bezeichnen die Arterien, die blauen die Venen (vgl. Tafel „Blutgefäße").

Interscalene

Supraclavicular

Axillary

PECs

Serratus

Femoral

Adductor canal

Ankle

Intercostal

Rectus sheath

TAP

Paravertebral

orthopedic

vascular

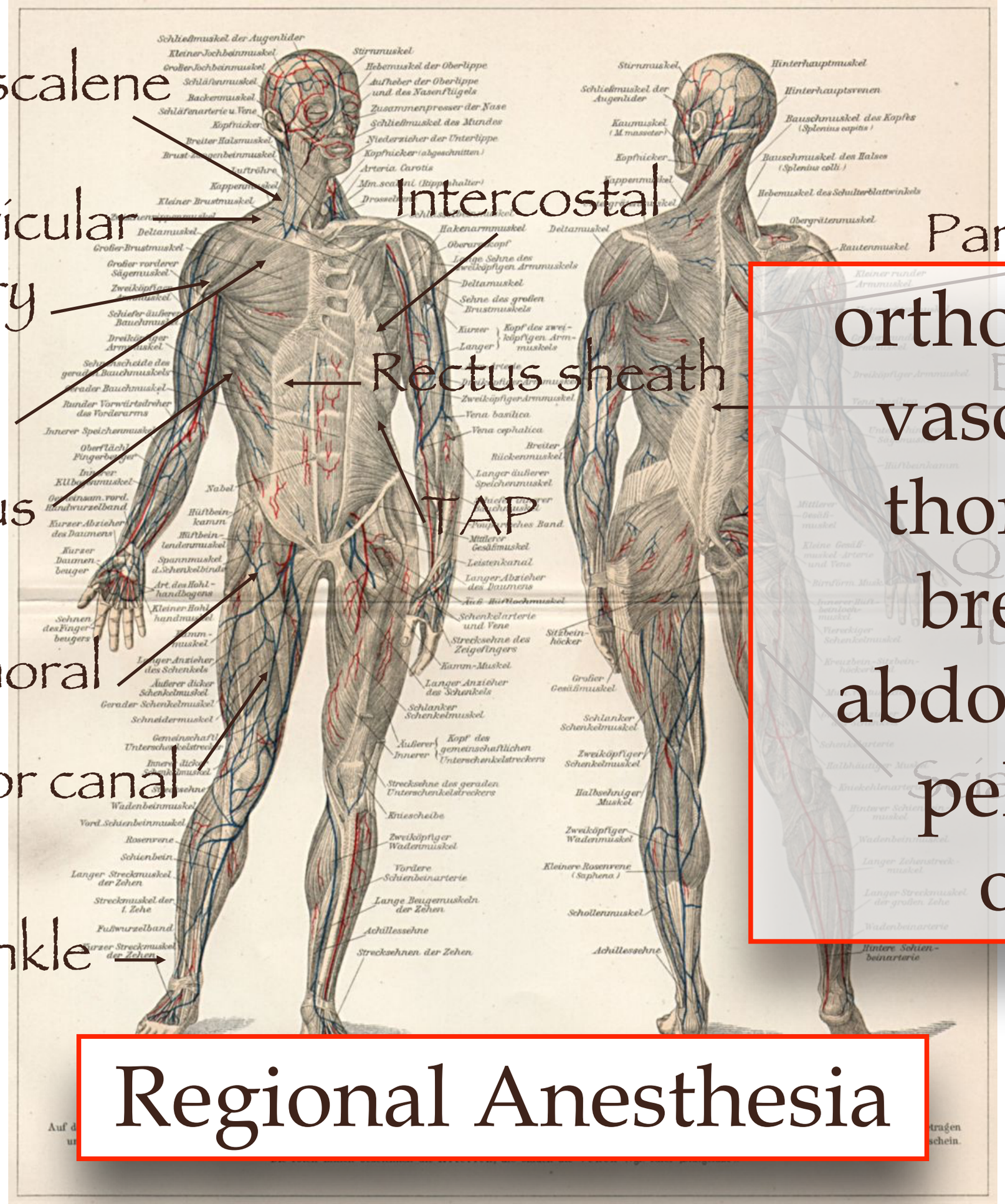
thoracic

breast

abdominal

pelvic

ob



Regional Anesthesia

Multimodal Analgesia

Agent	Mode	Effect
NSAIDS	prostglnd. antiinflam, central	↓ pain, opioid use
Acetaminophen	central nocicept. ihibit.	pain, opioid use
Dexamethasone	antiinflam, antinocicept.	pain, opioid use, LA duration*
Dexmedetomidine	Alpha-2 agonist	pain, opioid use, LA duration*
Ketamine	NMDA antag.	pain,opioid use, tolerance
Gabapentinoids	Dcr. excit. NTs	pain, opioid use
Lidocaine	Na+ chan., NMDA	pain, opioid use, ileus
Duloxetine, Venlafaxine	SNRI, desc. inhib.	decreased neuropathic pain
TCA	SN, NMDA, Na+	unclear
Esmolol	excit. pain signaling	opioid use

Multimodal Analgesia

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Patient and procedure specific analgesic planning

Perioperative Pain Management

Identify **high risk patients** (surgery type, risk factors)

Pre-operative pain management **evaluation**, patient **education** and psychological **counseling**

Expand the timing/duration and **modality** of preventive analgesia

Perioperative Pain Management

Pain management protocols utilizing multimodal analgesia (procedure specific)

Postoperative pain service evaluation and follow up

prospect

procedure specific postoperative pain management

PROCEDURES:

- Abdominal Hysterectomy
- C-Section
- Colonic Resection
- Haemorrhoid Surgery
- Herniorraphy
- Laparoscopic Cholecystectomy Update
- Non-cosmetic Breast Surgery
- Radical Prostatectomy
- Thoracotomy
- Total Hip Arthroplasty
- Total Knee Arthroplasty
- PROSPECT Methodology

Archive

AFFILIATES:

State of the Art Safety Standards in RA
THE EUROPEAN SOCIETY OF REGIONAL ANAESTHESIA & PAIN THERAPY

CHANGE PAIN®
Taking care of pain

WHY PROSPECT?

There is growing evidence that the efficacy of analgesic agents differs between surgical procedures[1]

Current analgesic information is often derived by pooling data from a variety of surgical procedures (e.g. numbers needed to treat or harm: NNT or NNH[1]

Evidence shows that current postoperative pain management is not optimal – See Evidence

Therefore, postoperative pain management protocols may be optimised by examining procedure-specific outcomes[1]

1. Gray A, Kehlet H, Bonnet F, Rawal N. Predicting postoperative analgesic outcomes: NNT league tables or procedure-specific evidence? Br J Anaesth 2005; 94 (6): 710–14. Abstract

WHY PROCEDURE-SPECIFIC RECOMMENDATIONS?

THANK YOU

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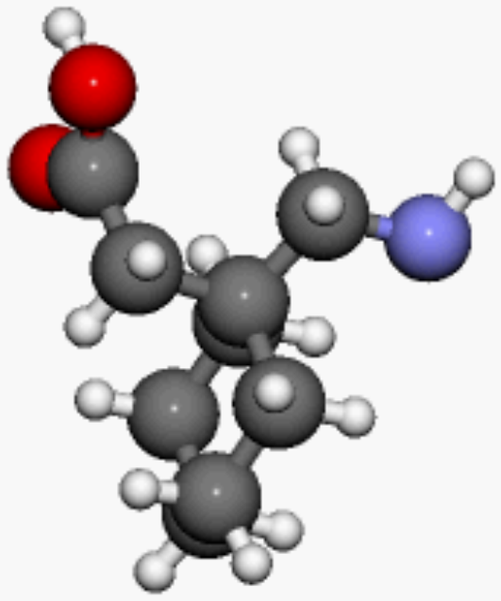

Gabapentin, Pregabalin

structural **GABA analogs**
(chronic) neuropathic pain agents

selective inhibition of voltage dependent Ca++ channels in activated neuron

decrease glutamate, norepinephrine and substance P release

interact/enhance descending inhibitory noradrenergic pathways

modulate **NMDA** receptors

CME

Preventive Analgesia by Local Anesthetics: The Reduction of Postoperative Pain by Peripheral Nerve Blocks and Intravenous Drugs

Antje Barreveld, MD,* Jürgen Witte, MD,† Harkirat Chahal, MD,* Marcel E. Durieux, MD, PhD,† and Gary Strichartz, PhD*

The use of local anesthetics to reduce acute postoperative pain has a long history, but recent reports have not been systematically reviewed. In addition, the need to include only those clinical studies that meet minimum standards for randomization and blinding must be adhered to. In this review, we have applied stringent clinical study design standards to identify publications on the use of perioperative local anesthetics. We first examined several types of peripheral nerve blocks, covering a variety of surgical procedures, and second, we examined the effects of intentionally administered IV local anesthetic (lidocaine) for suppression of postoperative pain. Thirdly, we have examined publications in which vascular concentrations of local anesthetics were measured at different times after peripheral nerve block procedures, noting the incidence when those levels reached ones achieved during intentional IV administration. Importantly, the very large number of studies using neuraxial blockade techniques (epidural, spinal) has not been included in this review but will be dealt with separately in a later review. The overall results showed a strongly positive effect of local anesthetics, by either route, for suppressing postoperative pain scores and analgesic (opiate) consumption. In only a few situations were the effects equivocal. Enhanced effectiveness with the addition of adjuvants was not uniformly apparent. The differential benefits between drug delivery before, during, or immediately after a surgical procedure are not obvious, and a general conclusion is that the significant antihyperalgesic effects occur when the local anesthetic is present during the acute postoperative period, and its presence during surgery is not essential for this action. (Anesth Analg 2013;116:1141–61)

AA 2013

- **Nerve blocks by local anesthetics improve postoperative analgesia compared with placebo or PCA and decrease opioid requirements**
- **Significant antihyperalgesic effects occur when the local anesthetic is present during the acute postoperative period**

and hospital discharge, decreases acute morbidity, and may well reduce the probability of developing chronic

publications for a complete collection, keeping in mind the importance of inclusion criteria for discerning among

PPS Pain Mechanisms

- Ectopic nerve discharge (neuroma)
- Peripheral nociceptive sensitization at the site of injury
- Central neuronal sensitization at spinal/supraspinal sites
- CNS inflammatory changes triggered by injury-induced proliferation of immunologically active microglia and astrocytes
- Reactive/compensatory MSK changes after surgery
- Impaired nociceptive inhibitory modulation
- Enhanced nociceptive facilitory modulation

I. Gilron, H. Kehlet. Can J Anesth 2014