How Regional Anesthesia

and Multimodal Analgesia Can Aid in the Opioid Epidemic

Aaron Relic, D.O., M.B.A
Program Director, OSU Anesthesiology Residency
Assistant Clinical Professor of Surgery-Anesthesiology

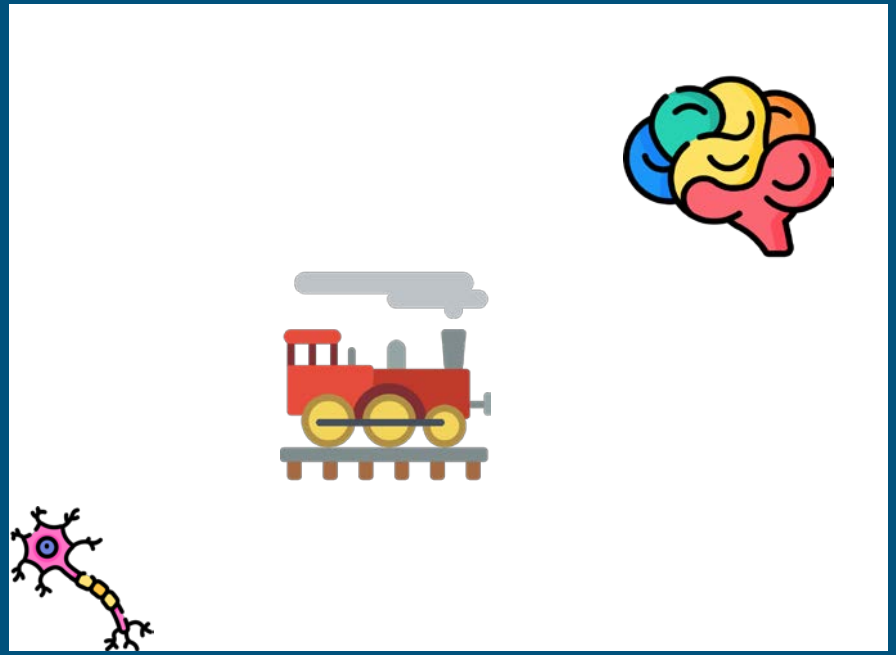
Disclosures

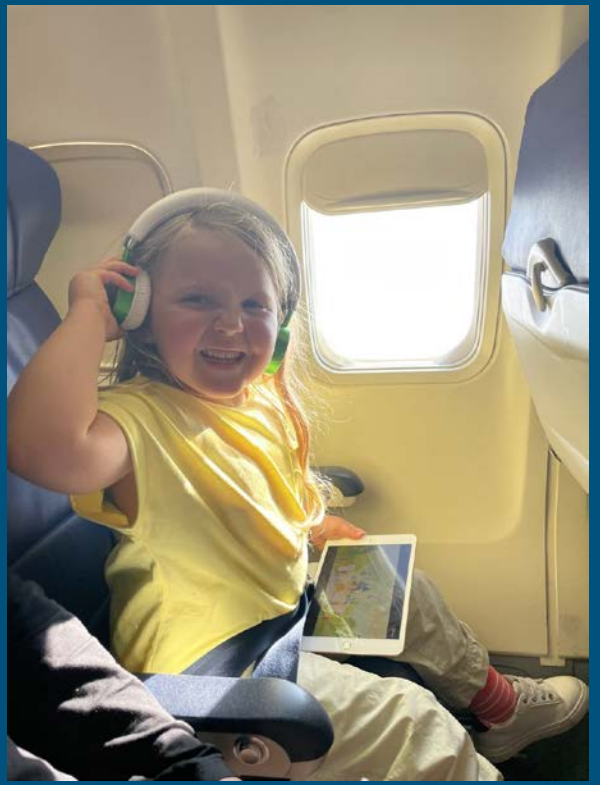
- None

Objectives

- Provide an introduction to regional anesthesia for non-anesthesiologists
- Describe situations where regional anesthesia is beneficial, especially outside of the OR
- Describe a multimodal analgesic approach to
  - reduce opioid use and its undesired effects
  - improve patient pain control and satisfaction
  - decrease hospital length of stay

Pain





Gate Theory of Pain

- Pain can be modulated at several points through several mechanisms
- Nociception occurs secondary to tissue damage or inflammation
  - potassium, histamine, bradykinin, prostaglandins, ATP
- Pain signals transmitted
  - A-delta and C fibers
  - Dorsal horn of spinal cord
  - Brainstem and cerebral cortex
- Enhancement, modulation and inhibition can occur
  - Direct nerve activation
  - Sympathetic regulation, etc

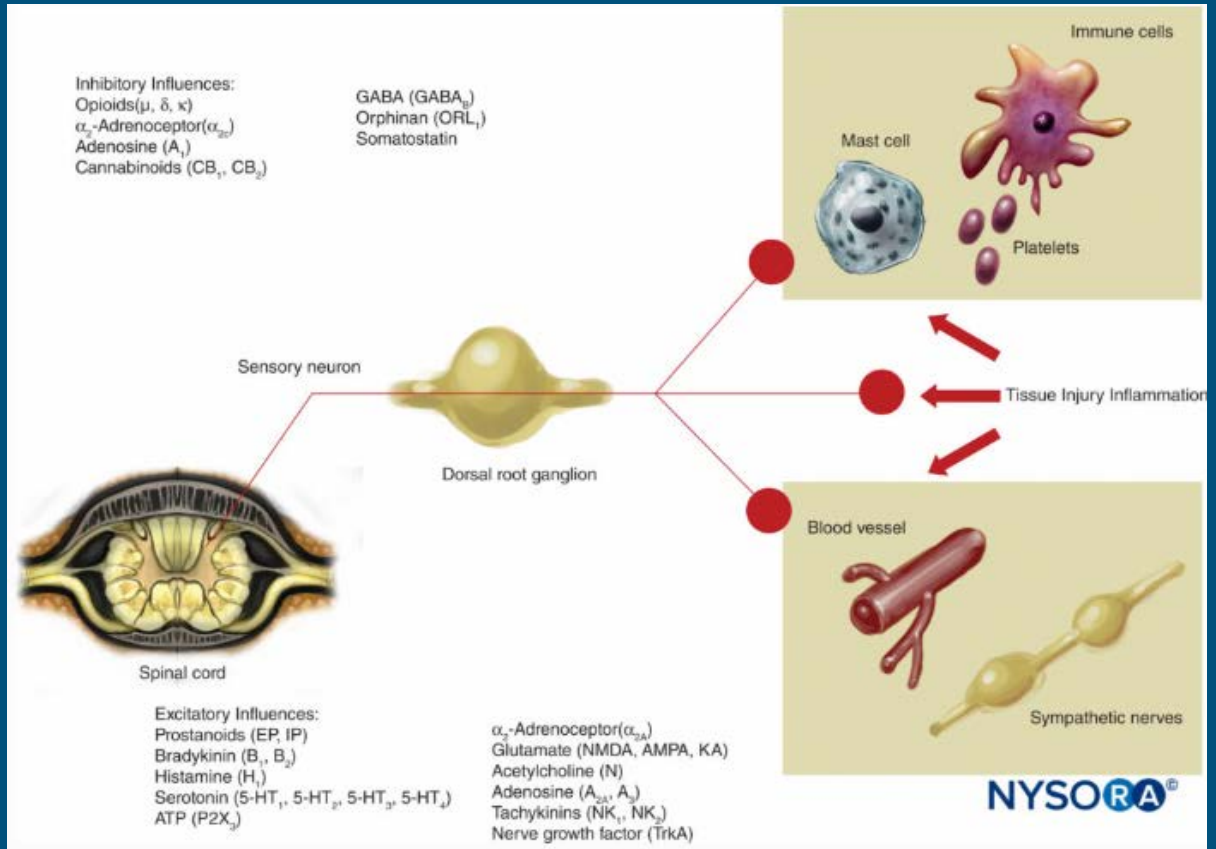


FIGURE 3. Excitatory and inhibitory influences on peripheral nerve activity by mediators released by tissue injury and inflammation and by a variety of agents acting on neuroreceptors. AMPA = α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid; KA = kainic acid; NMDA = N-methyl-d-aspartate; NK = neurokinin; TrkA = Tropomyosin receptor kinase A.

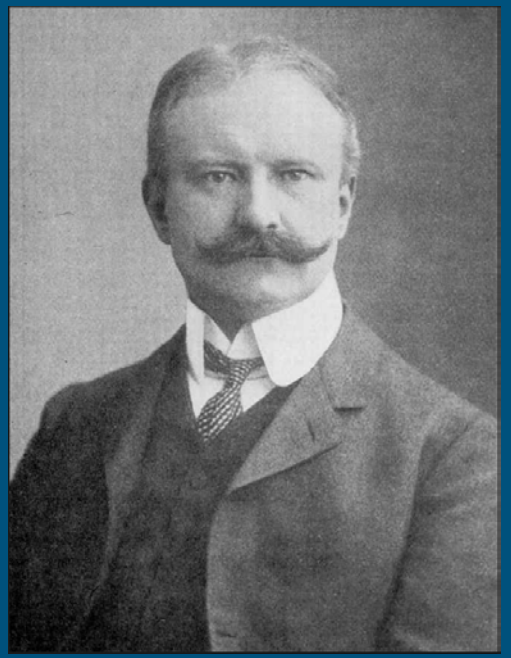
Types of Pain

- Nociceptive
  - Activation of nociceptors through actual or potential tissue damage
  - Throbbing, aching, pressure
  - Inflammatory component
- Neuropathic
  - Damage to the peripheral nervous system
  - Burning, stinging, electric
- Nociplastic
  - Abnormal processing or modulation of pain signals

Different types of pain require different treatments

History of Regional Anesthesia

- August Bier performed the first spinal anesthetic in 1898 “cocainization of the spinal cord”
- Local infiltration (1892) and brachial plexus block (1911) came later.
- In 1908, Bier later described IV regional anesthesia, or the “Bier Block”

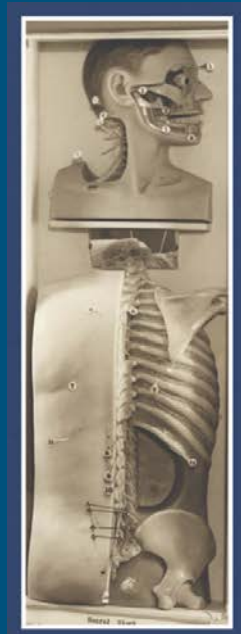


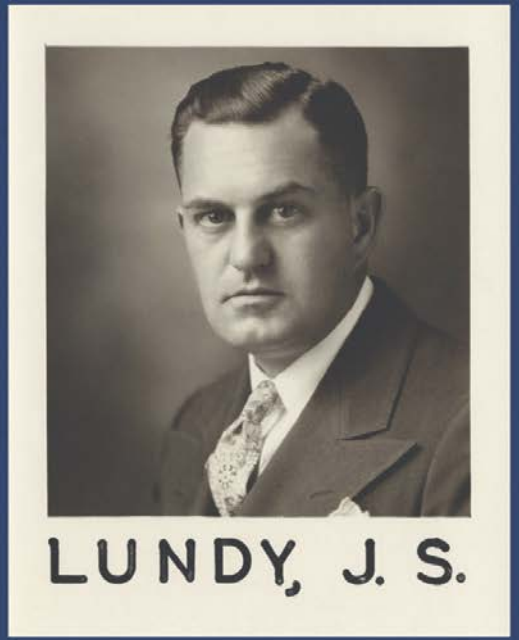
History of Regional Anesthesia

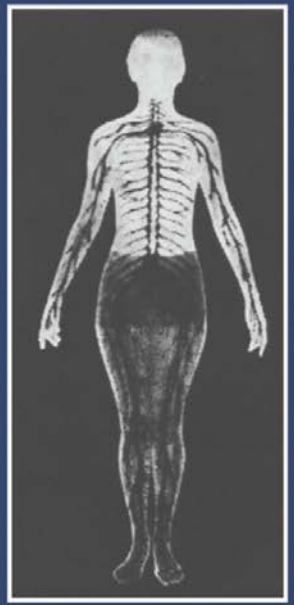
- Hallstead and Hall later described injection of cocaine near peripheral nerves.
- In 1920, French surgeon Gaston Labat was invited by Charles Mayo to teach regional anesthesia at the Mayo Clinic.
- Regional anesthesia allowed for specific blockade of peripheral nerves based on the area of pain, operation, and desired length of block

History of Regional Anesthesia

John Silas Lundy, MD

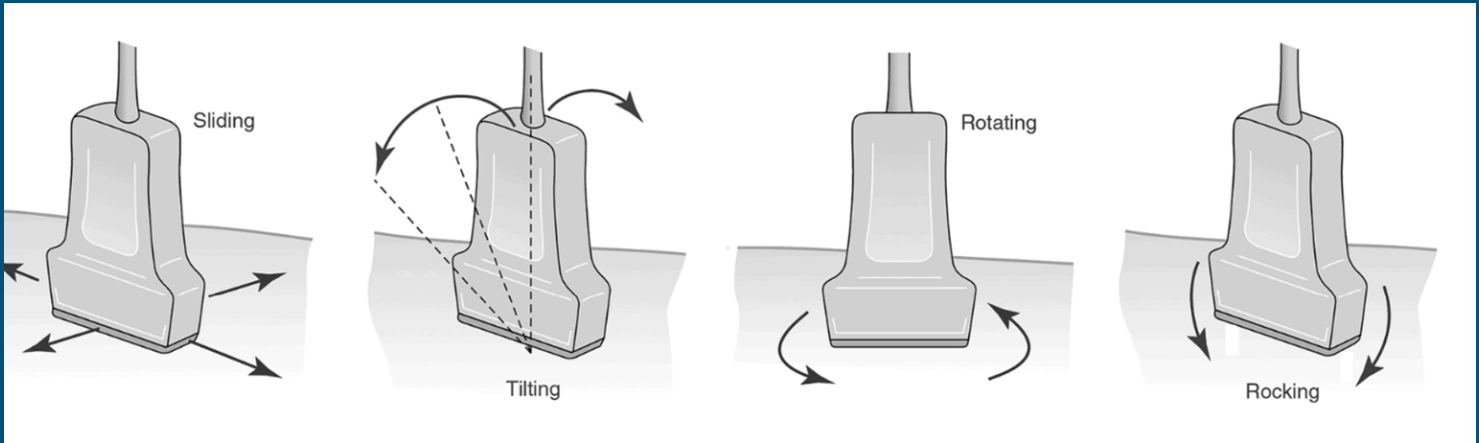






Techniques for Nerve Localization

- Landmark + Paresthesia
- Peripheral Nerve Stimulation
- Ultrasound-Guided



Regional Anesthesia

- Decreases pain
- Decreases need for opioids
- Decreases incidence of nausea and vomiting
- Shortens PACU time
- Increases patient satisfaction

Types of Regional Anesthesia

- Location
  - Neuraxial
    - Spinal/Epidural
  - Blockade of specific peripheral nerves
    - Brachial plexus block (interscalene, supraclavicular, infraclavicular axillary)
    - Femoral nerve block
    - Sciatic nerve block
  - Planar blocks of multiple peripheral nerves
    - TAP, QL, PECs, etc.
- Single-shot vs. continuous infusion

Local Anesthetics

- Block the transmission of the action potential by inhibition of voltage-gated sodium ion channels.
- Decrease the rate of depolarization in response to excitation
- Factors affecting blockade
  - pH: relative proportion of charged and uncharged local anesthetic molecules
  - Lipid solubility
  - Protein binding: affects duration of blockade
  - Nerve fiber diameter and myelination

First Local Anesthetic

Common Local Anesthetics

Table 11-1 Comparative Pharmacology and Common Current Use of Local Anesthetics

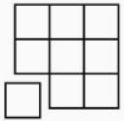
Classification and Compounds	pK_a	% Nonionized at pH 7.4	Potency*	Max. Dose (mg) for Infiltration†	Duration after Infiltration (min)	Topical	Local	IV	Periph	Epi	Spinal
Esters											
Procaine	8.9	3	1	500	45-60	No	Yes	No	Yes	No	Yes
Chloroprocaine	8.7	5	2	600	30-60	No	Yes	Yes	Yes	Yes	Yes‡
Tetracaine	8.5	7	8			Yes	Yes§	No	No	No	Yes
Amides											
Lidocaine	7.9	24	2	300	60-120	Yes	Yes	Yes	Yes	Yes	Yes‡
Mepivacaine	7.6	39	2	300	90-180	No	Yes	No	Yes	Yes	Yes‡
Prilocaine	7.9	24	2	400	60-120	Yes¶	Yes	Yes	Yes	Yes	Yes‡
Bupivacaine, levobupivacaine	8.1	17	8	150	240-480	No	Yes	No	Yes	Yes	Yes
Ropivacaine	8.1	17	6	200	240-480	No	Yes	No	Yes	Yes	Yes

Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia

Systematic review and meta-analysis of 9 randomized trials

- Trials compared liposomal with nonliposomal bupivacaine for peripheral nerve (not field or plane) blockade
- **Primary outcome:** difference in AUC of the pooled 24- to 72-h rest pain severity scores

- **24- to 72-h AUC pain scores:** statistically but not clinically significantly lower after liposomal bupivacaine
- **After removal of 1 industry-funded trial:** difference was not significant statistically nor clinically



No significant differences in:

- Pain severity at individual time points
- Opioid consumption
- Time to first analgesic request
- Opioid-related side effects

- Patient satisfaction
- Length of stay
- Functional recovery

High-quality evidence does not support use of liposomal bupivacaine over nonliposomal bupivacaine for peripheral nerve blocks

Hussain N, *et al.* Anesthesiology. February 2021.

Interscalene Brachial Plexus Block with Liposomal Bupivacaine *versus* Standard Bupivacaine with Perineural Dexamethasone: A Noninferiority Trial

David H. Kim, M.D.; Jiabin Liu, M.D., Ph.D.; Jonathan C. Beathe, M.D.; Yi Lin, M.D., Ph.D.; Douglas S. Wetmore, M.D.; Sang J. Kim, M.D.; Stephen C. Haskins, M.D.; Sean Garvin, M.D.; Joseph A. Oxendine, M.D.; Michael C. Ho, M.D.; ... Show more

What This Article Tells Us That Is New

- Interscalene nerve blocks using bupivacaine plus dexamethasone were compared with blocks using liposomal bupivacaine for shoulder surgery
- These alternative blocks provided very similar levels and durations of analgesia, and no differences in opioid consumption were identified
- The interscalene injection of bupivacaine plus dexamethasone and liposomal bupivacaine provide similar clinical benefits for shoulder surgery

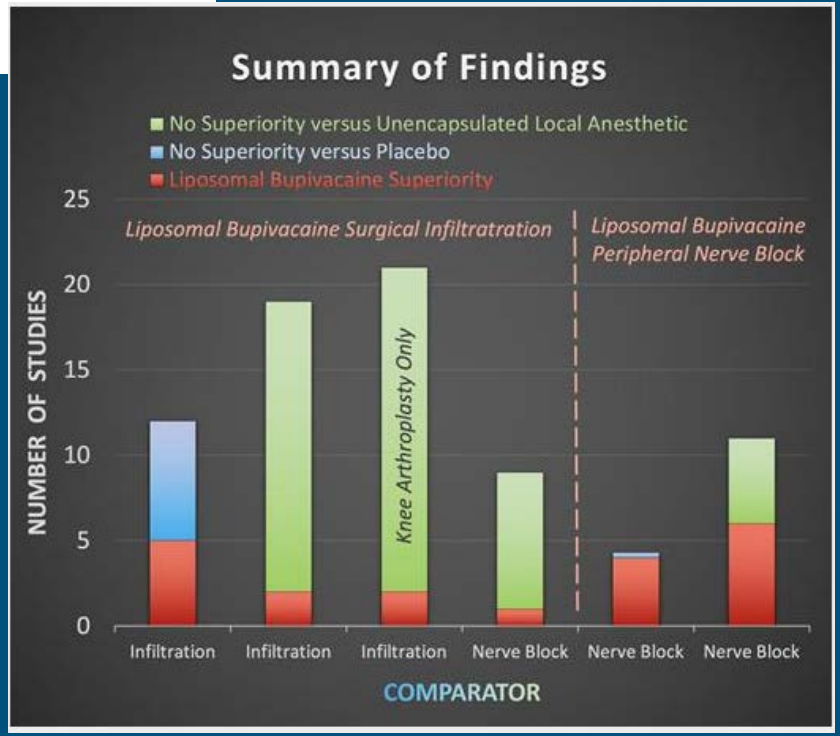
Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review

Brian M. Ilfeld, M.D., M.S.; James C. Eisenach, M.D.; Rodney A. Gabriel, M.D., M.S.

+ Author and Article Information

Anesthesiology February 2021, Vol. 134, 283–344.

https://doi.org/10.1097/ALN.0000000000003630



Should we use liposomal bupivacaine?

Regional Anesthesia Outside the OR

Case #1

- A 90 year-old female nursing home resident presents to the ER s/p ground level fall.
  - PMH of dementia, HTN, COPD
  - Imaging reveals a mid-shaft femoral fracture
  - Orthopedic Surgery has been consulted, will proceed with ORIF the following day
- Pain management prior to surgery?

Pain control options

- Multimodal, opioid sparing approach utilizing regional anesthesia
- Options include femoral nerve block, PENG block, fascia iliaca block
- Early regional blockade leads to
  - Improved pain control
  - Decreased opioid use
  - Decreased delirium

Fascia Iliaca Block

- Indications are anterior thigh or hip pain or surgery
- Performed with patient supine
- Provides block for femoral nerve, lateral femoral cutaneous, and sometimes obturator
- Can be performed supra- or infra-inguinal
- 20-40 mL of local anesthetic deposited deep to the fascia iliaca-overlying the iliopsoas or iliacus muscle
- Success depends on spread of local anesthetic- “volume-dependent”

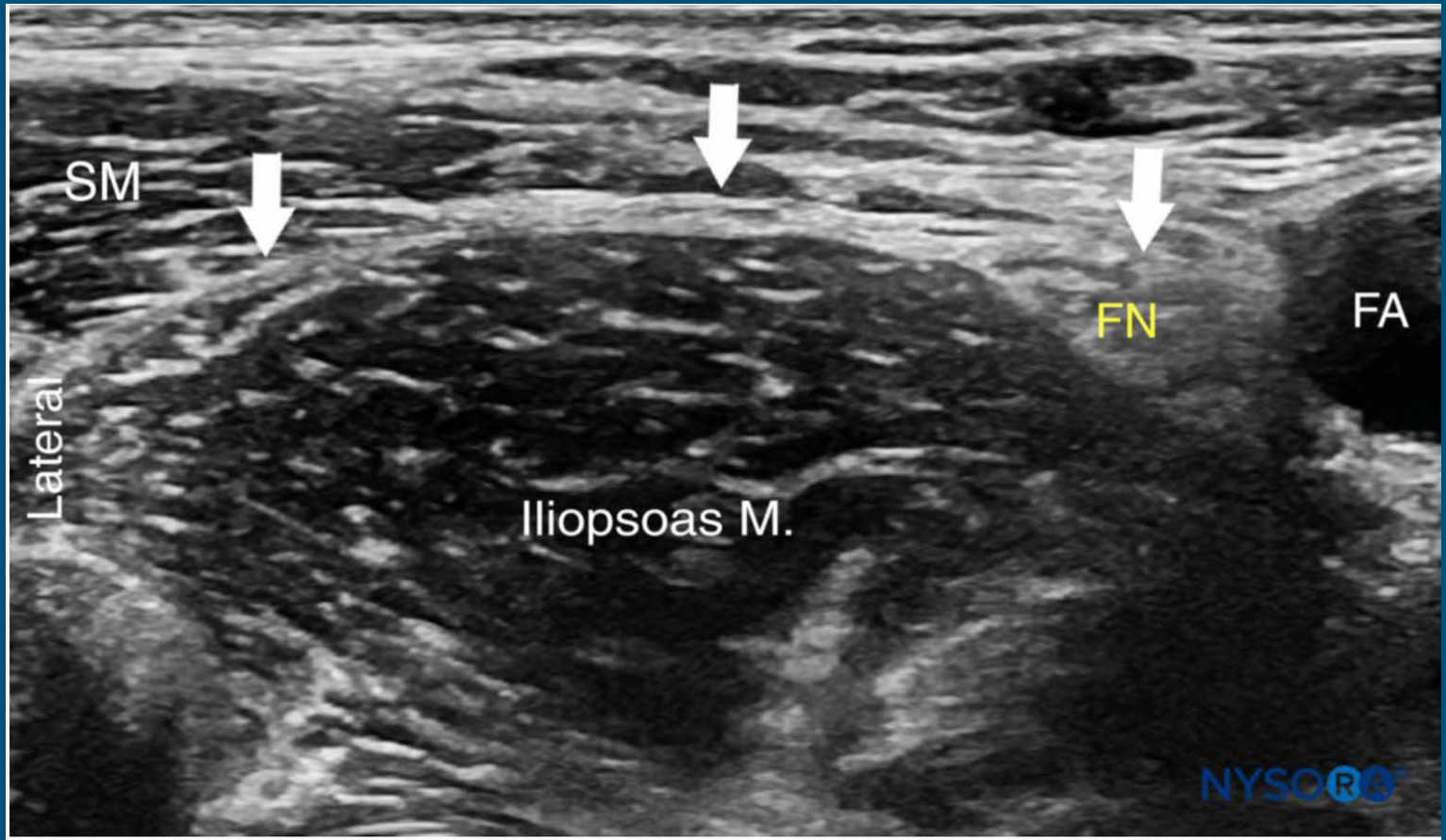
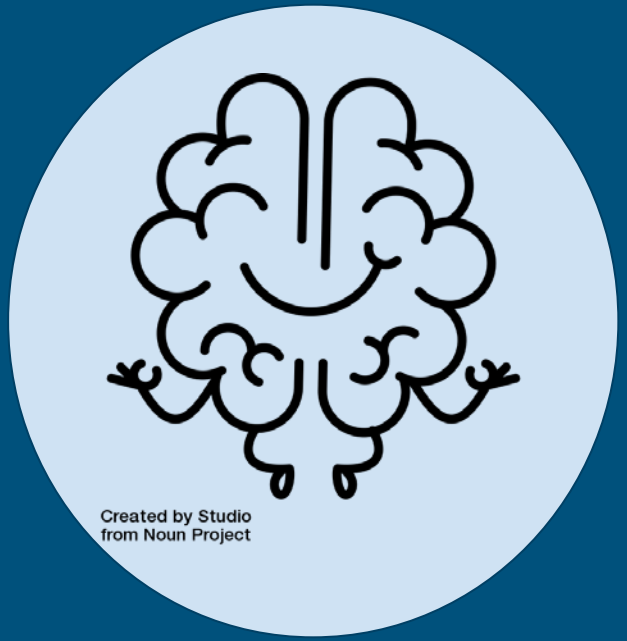


FIGURE 4. Ultrasound image of the fascia iliaca (white line and arrows) at the level of the inguinal ligament. The femoral nerve (FN) and femoral artery (FA) are visualized on the medial side and the sartorious muscle (SM) on the lateral side.

Perioperative Brain Health Initiative Recommendations

- Education and training
- Cognitive Screening
- Delirium Screening
- Non-pharmacologic Interventions
- Pain Control
- Avoid Antipsychotics and Anxiolytics

Perioperative
Brain Health Initiative
American Society of **Anesthesiologists**™



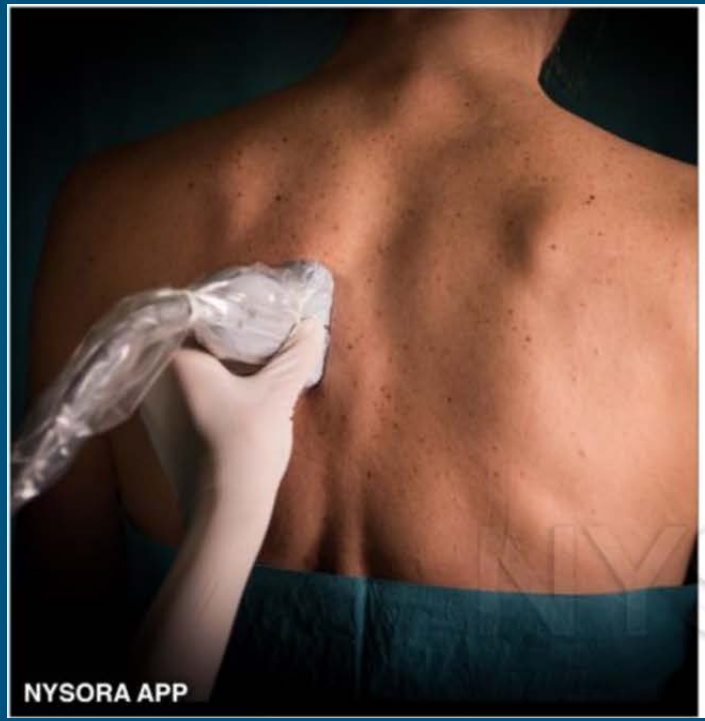
Case #2

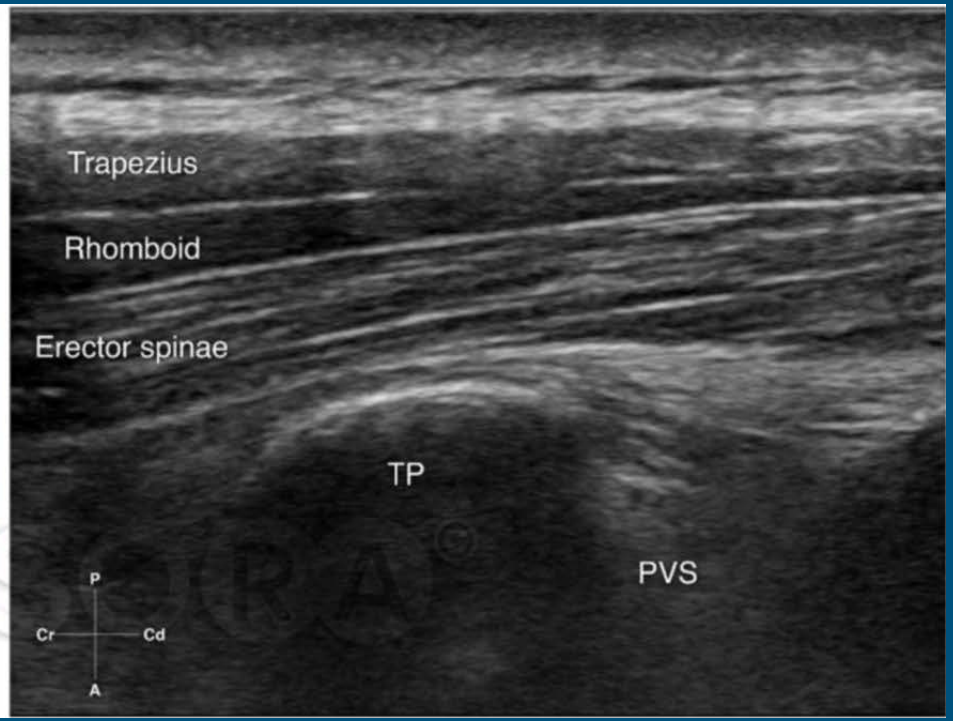
- A 25 year-old male is admitted to the med-surg unit for pain control after being bucked off a horse in a rodeo. He was found to have displaced fractures of ribs 4-7 which the Thoracic Surgeon has determined to be non-operative. He is receiving multimodal analgesia with ketorolac, acetaminophen, and hydromorphone, but he still rates his pain as 8/10 and is requiring supplemental oxygen secondary to splinting. He is currently unable to be discharged from the hospital.
- What options are available for additional pain control?

Regional Anesthesia for Rib Fracture

- Thoracic Epidural
  - Gold standard
  - Deep block, concerns with anticoagulation
  - Continuous infusion required, often with increased monitoring
- Paravertebral Block
  - Also considered deep block
  - Multiple injections required
- Erector Spinae Block +/- Serratus Anterior Block
  - Not considered deep blocks
  - Easy to perform with good efficacy

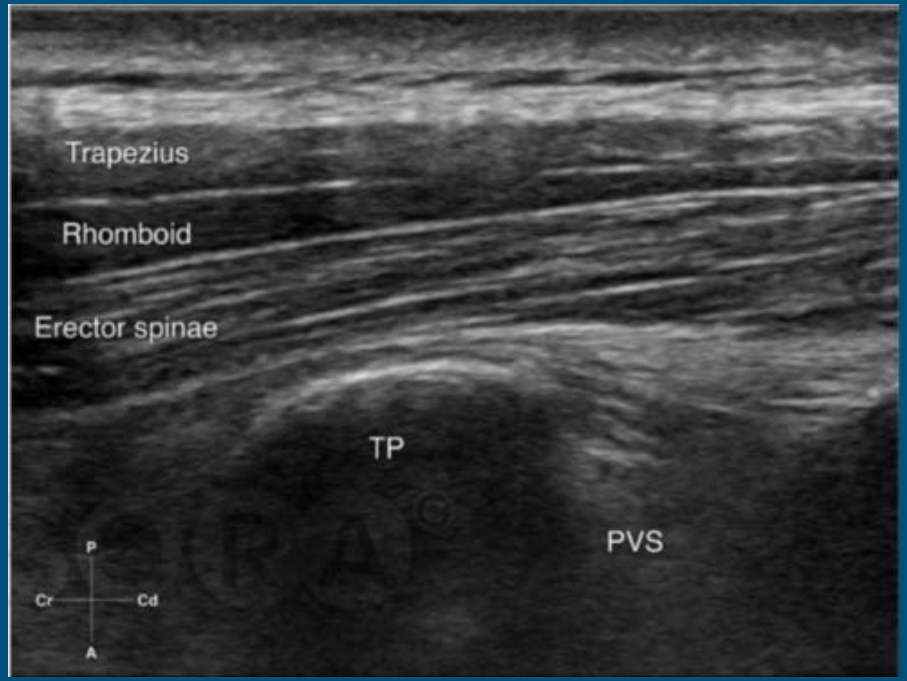
Erector Spinae Plane Block



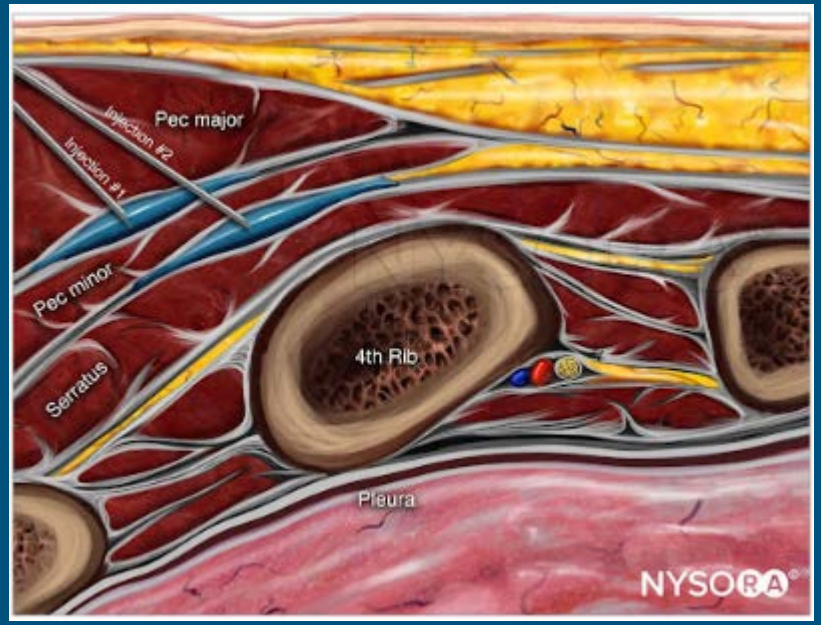


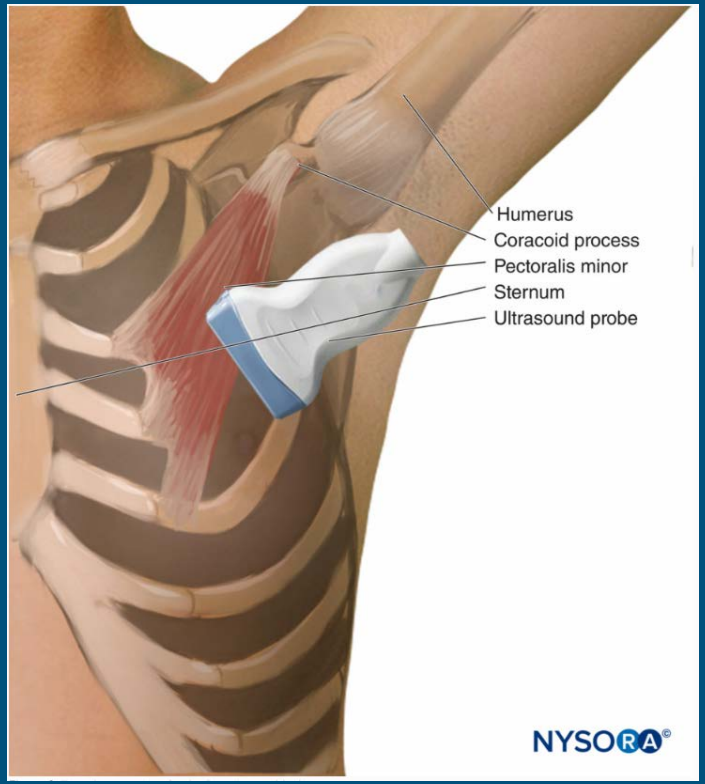
Erector Spinae Plane Block

- First described in 2016
- Indications are rib fractures, chest wall surgery, or abdominal surgery
- Performed with patient sitting, lateral, or prone
- 20-40 mL of local anesthetic deposited deep to erector spinae muscles and superficial to transverse process
- Also a “volume-dependent” block

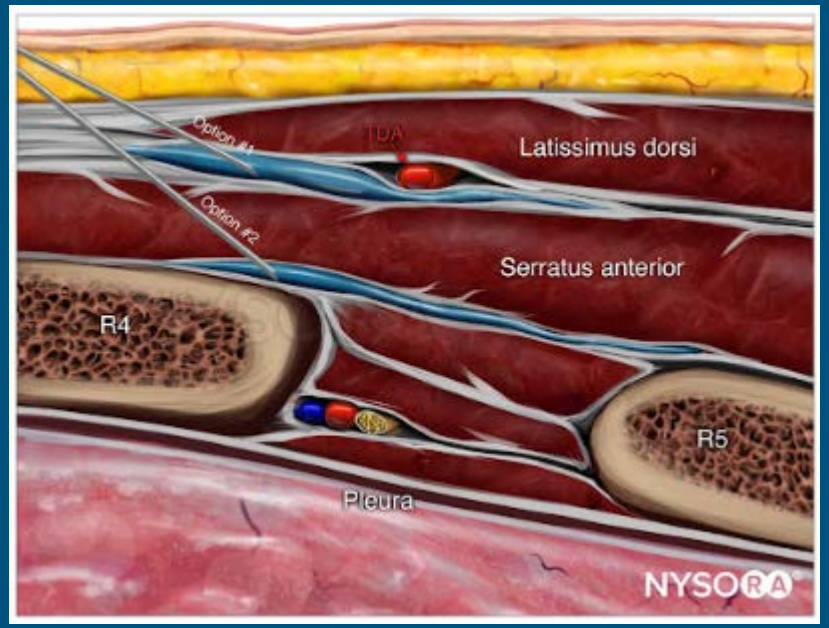


Serratus Plane Block





Serratus Plane Block



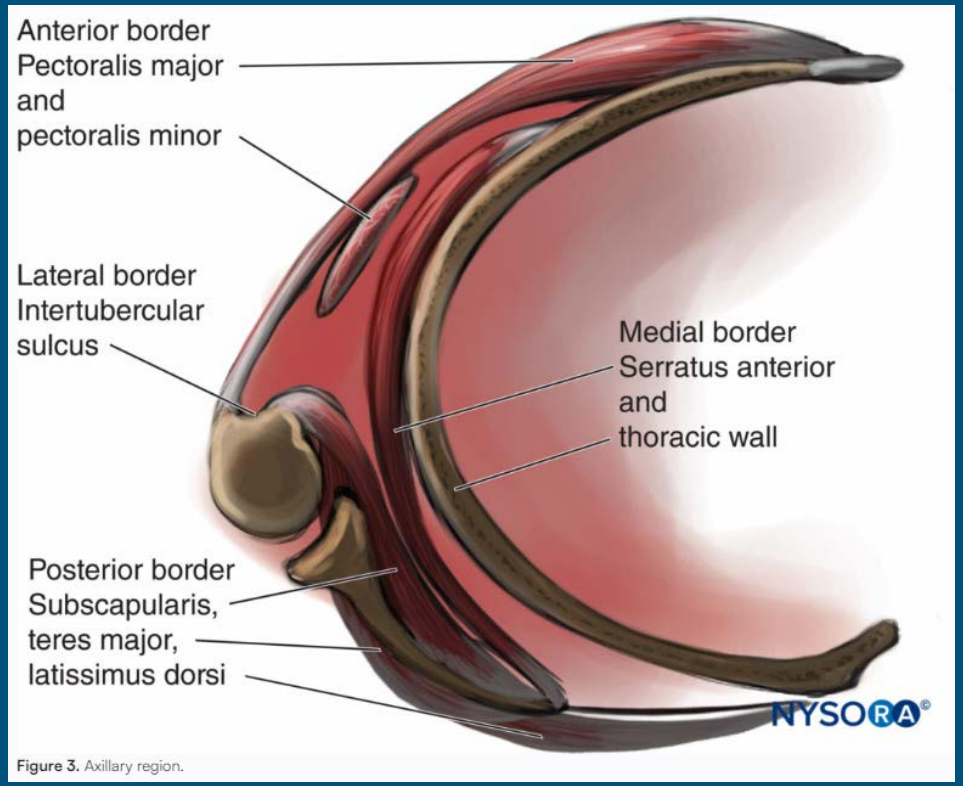


Figure 3. Axillary region.

Serratus Plane Block

- Indications are analgesia after breast, lateral thoracic wall surgery, or pain in these areas
- Performed with the patient in the supine, lateral, or prone position (for posterior approach deep to latissimus dorsi)
- 10-30 mL of local anesthetic

Regional Anesthesia for Cesarean Sections

SOAP Enhanced Recovery After Cesarean

6) Initiate multimodal analgesia	Neuraxial long-acting opioid Example: • IT morphine 50–150 µg or • Epidural morphine 1–3 mg Nonopioid analgesia started in OR unless contraindicated: 1. Ketorolac 15–30 mg IV after peritoneum closed 2. APAP IV after delivery or orally, per os before or after delivery Consider local anesthetic wound infiltration or regional blocks such as TAP or QLB if neuraxial morphine is not administered	• Use neuraxial doses consistent with SOAP Center of Excellence criteria Link: bit.ly/2Ii8GBe • Nonopioid analgesia is ideally started before the onset of pain • Rectal APAP may be an alternative but has lower bioavailability • The role of wound infiltration and other regional blocks for postcesarean pain should be considered in select cases, for example, in women who could not receive neuraxial morphine, or other multimodal analgesia regimen components, or patients at risk for severe pain	Class I Data to support preemptive analgesia in cesarean delivery are limited	Level A

Quadratus Lumborum Block

- While a transverse abdominis plane (TAP) block has become common for abdominal surgery, it is limited to somatic analgesia
- Quadratus Lumborum (QL) blocks
  - More consistent somatic analgesia
  - May provide visceral analgesia

Quadratus Lumborum Block

- Indications are analgesia for abdominal surgery
- Performed with the patient in the supine, supine with bump under hip, lateral, or prone position
- 15-30 mL of local anesthetic

Quadratus Lumborum Block

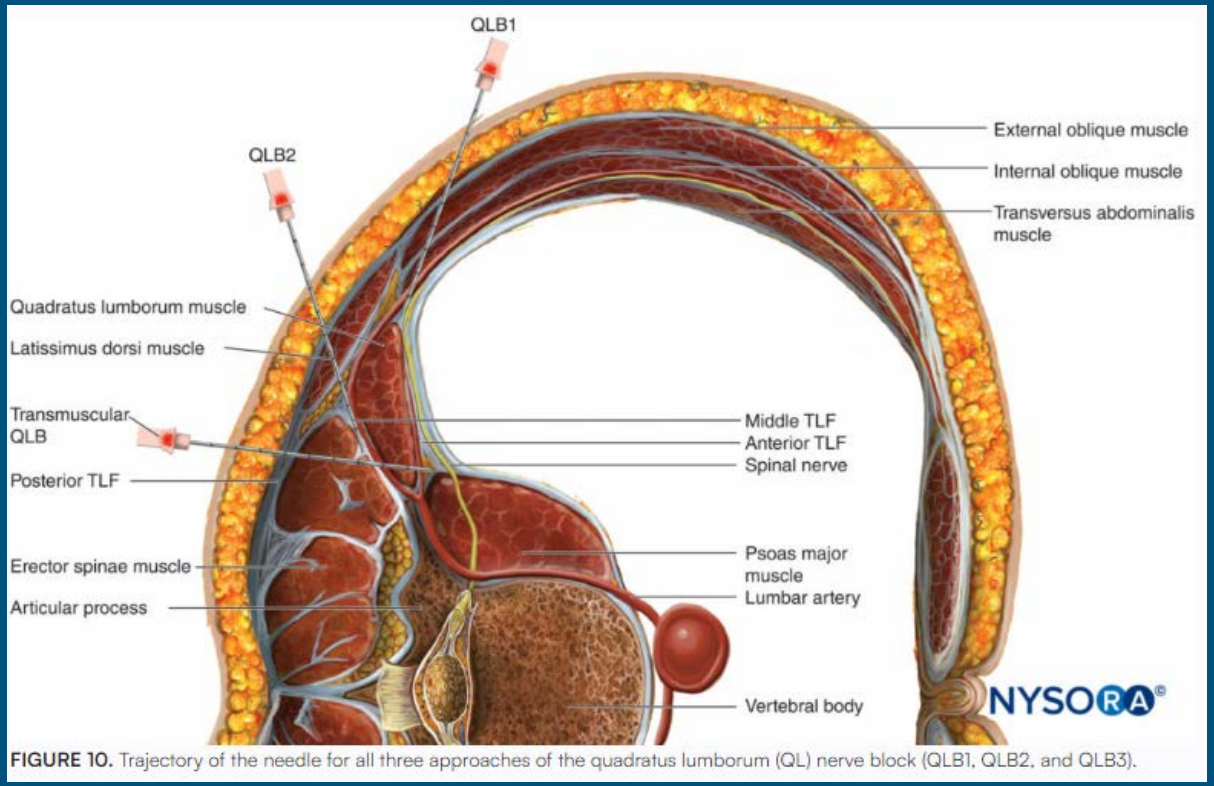


FIGURE 10. Trajectory of the needle for all three approaches of the quadratus lumborum (QL) nerve block (QLB1, QLB2, and QLB3).

Quadratus Lumborum Block

- QL1
- QL 2
- Transmuscular QL

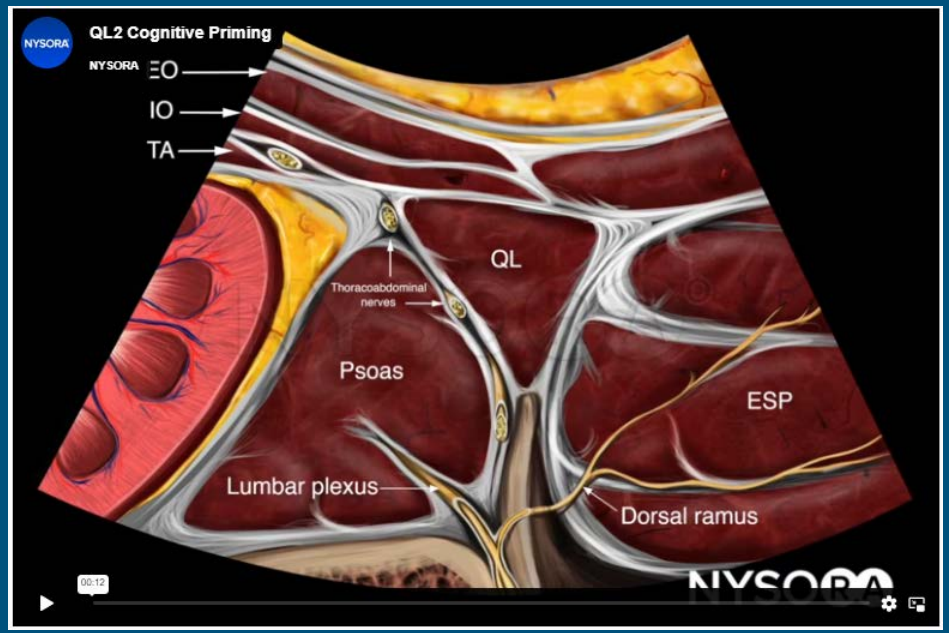


TABLE 1. Main features of QL nerve blocks.

	QLB1	QLB2	TQLB
Clinical indications	Abdominal surgery below the umbilicus.	Abdominal surgery either above or below the umbilicus (any type of operation that requires intra-abdominal visceral pain coverage and abdominal wall incisions as high as T6)	Abdominal surgery either above or below the umbilicus (any type of operation that requires intra-abdominal visceral pain coverage and abdominal wall incisions as high as T6)
Dermatomes covered	L1	T4 to T12-L1; blocks the anterior and the lateral cutaneous branches of the nerves	T4 to T12-L1; blocks the anterior and the lateral cutaneous branches of the nerves
Lower extremity weakness	Not reported	Not reported	Potential
Spread to lumbar plexus	Not reported	Not reported	Potential
Needle entry and approach	Lateral abdomen near the posterior axillary line, below the costal margin and above the iliac crest and inserting the needle inplane with the curved array probe oriented axially.	Lateral abdomen near the posterior axillary line, below the costal margin and above the iliac crest and inserting the needle inplane with the curved array probe oriented axially.	Lateral abdomen near the posterior axillary line, below the costal margin and above the iliac crest and inserting the needle inplane with the curved array probe oriented axially.
Potential complications	Complications are related to the lack of anatomical understanding and needle expertise. It is possible to puncture intra-abdominal structures such as the kidney, liver, and spleen.	Complications are related to the lack of anatomical understanding and needle expertise. It is possible to puncture intra-abdominal structures such as the kidney, liver, and spleen.	Complications are related to the lack of anatomical understanding and needle expertise. It is possible to puncture intra-abdominal structures such as the kidney, liver, and spleen.
Injection site	Potential space medial to the abdominal wall muscles and lateral to QL muscle, anterolateral border of the QL muscle, at the junction with the transversalis fascia, outside the anterior layer of the TLF and fascia transversalis	Posterior to the QL muscle, outside the middle layer of the TLF	Anterior to the QL muscle, between the QL and the psoas major muscles, outside the anterior layer of the TLF and fascia transversalis, close to the intervertebral foramen
Level of difficulty	Intermediate	Intermediate	Advanced

Adjuvants to Regional Anesthesia

- Medications can be added to augment the local anesthetic through several routes
  - Perineural
  - Intravenous
  - Intra-articular
  - Local infiltration
- These can increase the efficacy or duration of regional blockade

Perineural Adjuvants

- Dexamethasone
- Alpha-2 Agonists
  - Dexmedetomidine
  - Clonidine
- Opioids
- Epinephrine (for neuraxial)

Adverse Effects of Regional Anesthesia

- Bleeding (especially if anticoagulated)
- Infection
- Nerve damage
- Allergic reaction
- Local tissue injury
  - Pneumothorax
  - Viscus perforation
- Local Anesthetic Systemic Toxicity (LAST)
  - Cardiovascular and Central Nervous System Toxicity

Local Anesthetic Systemic Toxicity Checklist

ASRA

- Call for help
- Get LAST rescue kit
- Consider cardiopulmonary bypass team

\+ Consider administering LIPID EMULSION early

LIPID EMULSION 20%

The order of administration (bolus or infusion) and method of infusion (manually, iv roller clamp, or pump) are not critical

over 70 kg

- Bolus ~100 mL over 2-3 min
- Infuse ~250 mL over 15-20 min

IF PATIENT REMAINS UNSTABLE:
- Repeat bolus
- Double infusion

under 70 kg

- Bolus ~1.5 mL/kg over 2-3 min
- Infuse ~0.25 mL/kg/min (consider using a pump if <40 kg)

IF PATIENT REMAINS UNSTABLE:
- Repeat bolus
- Double infusion

Seizure?

- Ensure adequate airway
- Benzodiazepine preferred
- If only propofol available, use low dose, e.g., 20 mg increments

Arrhythmia or Hypotension?

BEWARE
LAST Resuscitation is DIFFERENT from Standard ACLS

EPINEPHRINE

- Smaller than normal dose preferred
- Start with ≤1 mcg/kg

AVOID

- Local anesthetics
- Beta-blockers
- Calcium channel blockers
- Vasopressin

Stable?

- Continue lipid emulsion ≥15 min once hemodynamically stable
- Maximum lipid dose: 12 mL/kg

Once Stable, OBSERVE

- 2 hrs after seizure
- 4-6 hrs after cardiovascular instability
- As appropriate after cardiac arrest

ASRA PAIN MEDICINE EDUCATION RESEARCH

Graphic: Erin Jane Neal

Special situations for multimodal analgesia

Medical Marijuana

Table 1 Cannabis terminology*

Term	Description
Cannabis	All plant materials, components, and derivative products of the cannabis plant, including flowers, leaves, seeds, stalks, and other materials and cannabis resins, extractions, and other derivative products. Cannabis is listed in Schedule 1 of the Controlled Substances Act in the USA.
Marijuana, marihuana	Historical slang with Mexican roots adopted in the 1930s during the American prohibition efforts. Marijuana continues to be used interchangeably with cannabis in reference to plant strains containing high THC. Given the racial stigma, the word marijuana is becoming less used in favor of cannabis.
Hemp	Describes a collection of cannabis cultivars with specific properties, namely high production of fiber and seeds with minimal production of THC.
Cultivars (varieties, strains)	Distinct cultivars of the cannabis plant having unique genetic signature and expressing distinct chemical composition. Colloquially referred to as strains.
Cannabis extracts	Highly concentrated preparations of cannabis which are produced via a variety of manufacturing techniques.
Terpenes	Aromatic compounds that exist in unique profiles in different strains and may provide some therapeutic benefits.
Cannabinoid-based medicines	A general term used to describe therapeutic cannabis or cannabinoid-based products in which cannabinoids are the primary active pharmaceutical ingredient. This term is applied regardless of origin as plant-derived or synthetic cannabinoids.
Pharmaceutical or prescription cannabinoids	Cannabinoid-based treatments that have been approved as medical treatments for specific indications. Examples include nabilone (Cesamet), dronabinol (Marinol), cannabidiol (CBD; epidiolex), and nabiximols (1:1 preparation of THC:CBD, eg, Sativex, not available in the USA).
Medical cannabis	Cannabis-based treatments that are not approved medical treatments but have been legalized and regulated for patient access. Medical cannabis is differentiated from non-medical cannabis by a unique access program and a required medical authorization.
Recreational cannabis use	Non-medical use for pleasure or leisure
Recent cannabis use	Use within the past 30 days
Heavy cannabis use	Daily or near-daily use
Endocannabinoids	Endogenous cannabinoids produced by the body and active at cannabinoid receptors. The most well-known endocannabinoids are anandamide and 2-arachidonolyglycerol
Phytocannabinoids	Cannabinoids that are produced by the cannabis plant, primarily in the female flower. More than 100 unique cannabinoids have been identified. Common phytocannabinoids include Δ9-THC, CBD, cannabinol, and cannabigerol.
Δ9-THC	THC is the primary cannabinoid in almost all varietals of cannabis. THC is the primary psychoactive agent and contributes the most therapeutic effects as well as adverse effects and intoxication of cannabis.
CBD	CBD is usually the other well-characterized cannabinoid found in cannabis. It has potential analgesic, anti-epileptic, anxiolytic, and anti-inflammatory properties, which inspired the selective breeding of cannabis strains with high concentrations of CBD and minimal THC concentration.

*Information extracted from references 307 308.
CBD, cannabidiol; Δ9-THC, Δ9-tetrahydrocannabinol.

USPSTF methodology for grading evidence and recommendations used (A, B, C, D, or I)

Grade A — Universal screening for cannabinoids should be performed prior to surgery: product type, amount and frequency, time and route of last consumption.

Grade A — We recommend that the frequent, heavy cannabis user be counseled on the potentially negative effects on postoperative pain control. Low-dose, medically supervised use likely has a lower risk of negative effects.

Grade A — We recommend postponing elective surgery in patients who have altered mental status or impairment of decision-making capacity due to acute cannabis intoxication.

Grade A — Pregnant patients should be educated about the risks of maternal cannabis use on the fetus/neonate.

Grade B — Cannabis use during pregnancy and immediate postpartum period should be discouraged.

Grade B — Patients should be counseled on the potential risks of continued perioperative cannabinoids.

Grade C — We recommend utilizing multimodal analgesia incorporating regional analgesia if appropriate and using opioids as rescue medication.

Grade C — Postoperatively, patients who consume cannabis frequently should be monitored for cannabis withdrawal symptoms.

Grade C — We recommend delaying non-emergent surgery for a minimum of 2 hours after cannabis smoking because of increased perioperative risk of acute MI.

(There is a lack of published data with other routes of administration.)

Grade C — Consideration should be given to adjusting induction and maintenance doses of anesthetic agents based on clinical presentation and timing of the last consumption of cannabis in surgical and procedural patients.

Grade C — A cannabinoid agonist such as dronabinol* at a low dose is the best choice to treat severe cannabis withdrawal symptoms postoperatively.

* Off-label use in the United States

Grade D — Universal toxicology screening is not currently indicated based on insufficient evidence.

Grade I — We cannot recommend for or against the routine tapering of cannabis and cannabinoids in the perioperative period.

Shah S, Schwenk ES, Sondekoppam RV, Clarke H, Zakowski M, Rzasa-Lynn RS, Yeung B, Nicholson K, Schwartz G, Hooten MW, Wallace M, Viscusi ER, Narouze S. ASRA Pain Medicine Consensus Guidelines on the management of the perioperative patient on cannabis and cannabinoids. *Reg Anesth Pain Med* 2022; https://doi.org/xxxxx.

Artwork by Jim Snively.

Opioid Use Disorder

Table 4

Opioid use disorder (OUD) medications[39–43 47]

	Methadone (dolophine, methadose)	Buprenorphine±naloxone (Subutex buprenorphine sublingual tablets; Suboxone buprenorphine/naloxone sublingual film for sublingual or buccal use)	Naltrexone (ReVia tablets, Vivitrol injection)
Mu-opioid receptor activity	• Synthetic, full agonist	• Buprenorphine: partial agonist with high-affinity binding • Naloxone: non-selective and competitive opioid receptor antagonist with the high affinity for the mu receptors	• Pure, full competitive opioid antagonist with the highest affinity for the mu receptors
Other receptor considerations	• Some agonist action at the kappa receptor • Weak antagonist action at N-methyl-D-aspartate receptor • Possible antagonist action at the delta receptor	• Buprenorphine: partial kappa receptor agonist or functional antagonist (possibly with antidepressant effects) • Weak delta antagonist	• Modifies the hypothalamic-pituitary-adrenal axis to suppress alcohol consumption
Clinical considerations	• Stimulation of the mu receptor causes euphoria, analgesia, constipation, and respiratory depression	• Due to buprenorphine being a partial agonist, there is a ceiling effect for the binding of mu receptors, which causes decreased euphoric feelings and respiratory depression • Due to high-affinity binding, buprenorphine can displace full agonists from the mu receptor and cause withdrawal symptoms • The addition of naloxone to buprenorphine is to help decrease injection misuse. Buprenorphine monotherapy is reserved for patients who are pregnant or have a documented severe reaction to naloxone	• Due to naltrexone being a high-affinity opioid antagonist, it blocks the euphoric effects if other opioids are used

Table 4

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	Methadone (dolophine, methadose)	Buprenorphine±naloxone (Subutex buprenorphine sublingual tablets; Suboxone buprenorphine/naloxone sublingual film for sublingual or buccal use)	Naltrexone (ReVia tablets, Vivitrol injection)

Pharmacokinetics	• Oral bioavailability: 36%–100%
	• Onset of action:
	  ◦ Oral: 0.5–1 hours
	  ◦ Intravenous: 10–20 min
	  ◦ Metabolized in the liver by CYP2B6 (major), CYP3A4 (major), CYP2D6 (minor), CYP2C19 (minor), and CYP2C9 (minor)
	• Half-life:
	  ◦ Children: 19.2+13.6 hours
	  ◦ Adults: 8–59 hours
	• Excreted as metabolites by the kidneys and in the bile
		• Bioavailability
		• Buccal film: 46%–65%
		• Intramuscular: 70%
		• SL tablet: 29%
		• Transdermal patch: 15%
		• Onset of action: intramuscular >15 min
		• Metabolized in the liver by CYP3A4 to norbuprenorphine (active metabolite), which then undergoes glucuronidation by UGT1A3 or to a lesser extent is metabolized by glucuronidation by UGT1A1 and UGT2B7 to buprenorphine-3-glucuronide
		• Half-life adults
		  ◦ Buccal film: 27.6+11.2 hours
		  ◦ SL tablet: 37 hours
		  ◦ Transdermal patch: 26 hours
		• Excreted in the feces and urine
			• Oral bioavailability: 5%–40%
			• Duration of action:
			  ◦ Oral 50 mg: 24 hours
			  ◦ Oral 100 mg: 48 hours
			  ◦ Oral 150 mg: 72 hours
			  ◦ Intramuscular: 4 weeks
			• Metabolized by non-cytochrome-mediated dehydrogenase conversion to 6-beta-naltrexol (primary metabolite) and minor metabolites and glucuronide conjugates
			• Half-life adults:
			  ◦ Oral: 4 hours
			  ◦ Intramuscular: 5–10 days
			• Excreted in the urine

Table 5

FDA-approved buprenorphine formulations for MOUD and analgesia[50]

Milligram formulations of MOUD	
Buprenorphine+naloxone	Buprenorphine
Sublingual tablets (Zubsolv)	Sublingual tablets
Sublingual film (Suboxone)	ER solution for injection (Sublocade, Brixadi*)
Buccal film (Bunavail)	
Microgram formulations for analgesia†	
Transdermal patch (Butrans) weekly application	
Buccal film (Belbuca)	

- *Tentative approval from FDA (not eligible for marketing in the USA. Date to be determined (TBD).
- †Low abuse potential.[146 147]
- ER, extended release; FDA, Food and Drug Administration; MOUD, medication treatment of opioid use disorder.

Recommendations for Postoperative Management

Clinical Pearl: Buprenorphine home dose should not be routinely discontinued or tapered perioperatively

All surgery types (elective, urgent, emergent)

Buprenorphine Management

Mild/Moderate Pain:

- Home bupre-norphine dose can be split into two times per day/three times per day dosing to provide an analgesic effect.

Severe Pain:

- Home buprenorphine dose can be split into three times per day dosing to provide improved analgesic effect.
- Consider increasing dose of buprenorphine to 24-32 mg given in divided doses or using buprenorphine intravenous 0.3 mg every 6 hours prn
- Consider close monitoring if increasing or adding opiate for pain

Acute Pain with Other Opioids

- Maximize non-opioid strategies
- Treat acute pain with high affinity additional opioids as indicated in patients with OUD, avoid the opioid of past misuse
- Fentanyl derivatives and hydromorphone likely to be most effective due to high receptor affinity
- Consider close monitoring if increasing or adding opiate for pain

Nonopioid Pharmacological Management

- Regional anesthesia (Epidural catheter, Transversus Abdominus Plane block, peripheral nerve blocks with or without catheters including but not limited to erector spinae plane blocks, paravertebral block, femoral/adductor canal block, etc)
- Local infiltration by surgical team
- Intraoperative or postoperative ketamine/lidocaine/magnesium infusions
- Consider Dexmedetomidine if intravenous sedation used postoperatively
- Topical agents (e.g. ice, lidocaine ointment or patches)
- NSAIDs when indicated (e.g. ketorolac, ibuprofen, etc)
- Intravenous vs. oral acetaminophen when indicated
- Antineuropathic agents when indicated or if comorbid anxiety (e.g. gabapentinoids, antidepressants such as TCAs, SNRIs, etc)
- Muscle relaxants as indicated (e.g. baclofen, tizanidine, cyclobenzaprine; avoid benzodiazepines or carisoprodol)

Non-Pharmacological Management

- Ice to surgical site
- Position change
- Relaxation strategies and mindfulness techniques for pain (e.g. guided "apps" such as the free app "Calm")
- Peer recovery support
- Distraction aligned with interests (e.g. reading, music, family and social support, etc)

Postoperative Disposition

- Post anesthesia care unit
- Discharge home if satisfactory pain control, coordinate buprenorphine dosing plan with prescriber
- Inpatient floor admission as applicable
- Consider ICU admission if uncontrolled pain and respiratory concerns

Multimodal Analgesia

- “Multimodal techniques for pain management include the administration of two or more drugs that act by different mechanisms for providing analgesia.”
- Benefit of multimodal analgesia is improved pain scores, reduced opioid use, and/or reduced nausea and vomiting.

V. Multimodal Techniques for Pain Management

- Whenever possible, anesthesiologists should use multimodal pain management therapy.
  - Unless contraindicated, patients should receive an around-the-clock regimen of NSAIDs, COXIBs, or acetaminophen.
  - Regional blockade with local anesthetics should be considered.
- Dosing regimens should be administered to optimize efficacy while minimizing the risk of adverse events.
- The choice of medication, dose, route, and duration of therapy should be individualized.

Ketamine

- Phencyclidine analog and dissociative anesthetic first used for GA in the 1960s
- Thought to reverse central sensitization and improve descending modulatory pathways
- N-methyl-D-aspartate (NMDA) antagonist
    - Also has activity at mu-opioid, GABA, muscarinic, and other receptors

Ketamine for which patients?

- Patients undergoing surgery where postop pain will be severe
  - Upper abdominal and thoracic (greatest opioid reduction), lower abdominal, orthopedic (limb and spine).
- Opioid tolerant or dependent patients undergoing surgery
  - Spine surgery has been specifically shown to have reduced opioid consumption with ketamine use
- Opioid tolerant or dependent patients experiencing an acute exacerbation of chronic pain
  - Sickle Cell Crisis has been shown to be helped in smaller studies, though no RCTs have been done
- Patients at increased risk for opioid-related respiratory depression
  - Opioids increase severity of OSA after surgery
  - Ketamine has been demonstrated to reduce opioid consumption

What is a subanesthetic dose of Ketamine?

- Maximum bolus doses of 0.35 mg/kg and infusions of 1 mg/kg/hr without intensive monitoring
  - Adverse effects may prevent tolerance of higher doses
  - Adverse effects can include risk for aspiration, cardiovascular, and psychomimetic effects.
  - Anxiolytics to reduce risk of adverse psych effects
    - Midazolam, lorazepam, dexmedetomidine, clonidine patch

Contraindications for Ketamine Infusions?

- Avoid in poorly controlled cardiovascular disease, pregnancy, active psychosis, severe hepatic disease, elevated intracranial or intraocular pressure.
- Used with caution in moderate hepatic disease

TABLE 4. A Summary of Results of Systematic Reviews and Meta-Analyses on the Role of Ketamine as an Adjunct for Perioperative Analgesia

Authors and Year	No. RCTs Included	Goal of Study	Conclusions	Comments
Laskowski et al[2] (2011)	70	Determine the effect of IV ketamine on postoperative analgesia	Ketamine reduced pain scores and opioid consumption; greatest efficacy in thoracic, upper abdominal, major orthopedic surgeries	Effect independent of type of intraoperative opioid, dose, or timing of ketamine Hallucinations and nightmares more common with ketamine
Jouguelet-Lacoste et al[41] (2015)*	39	Determine the effect of an IV single dose or infusion of ketamine on postoperative analgesia	Ketamine reduced pain scores and opioid consumption for the first 48 postoperative hours	Evaluated a low-dose infusion rate of less than 1.2 mg/kg per hour with or without bolus dose of 1 mg/kg
Wang et al[42] (2016)	36	Determine the effect of IV ketamine added to opioid IV-PCA	Ketamine reduced pain scores, opioid consumption, and PONV in the first 72 postoperative hours	Adverse events of ketamine were probably underreported
Assouline et al.[43] (2016)	19	Determine the effect of ketamine added to an opioid IV-PCA in surgical patients	Ketamine reduced pain scores, opioid consumption and PONV at 24 hours.	No significant change in the incidence of hallucinations. Data insufficient to draw conclusions on respiratory adverse events or a dose-response relationship.
Pendi et al[35] (2018)	14	Determine the effect of ketamine on analgesia after spine surgery	Ketamine reduced pain scores and opioid consumption for the first 24 postoperative hours	No increase in adverse effects with ketamine

TABLE 6. Summary of ASRA/AAPM Recommendations for Subanesthetic Ketamine in Acute Pain

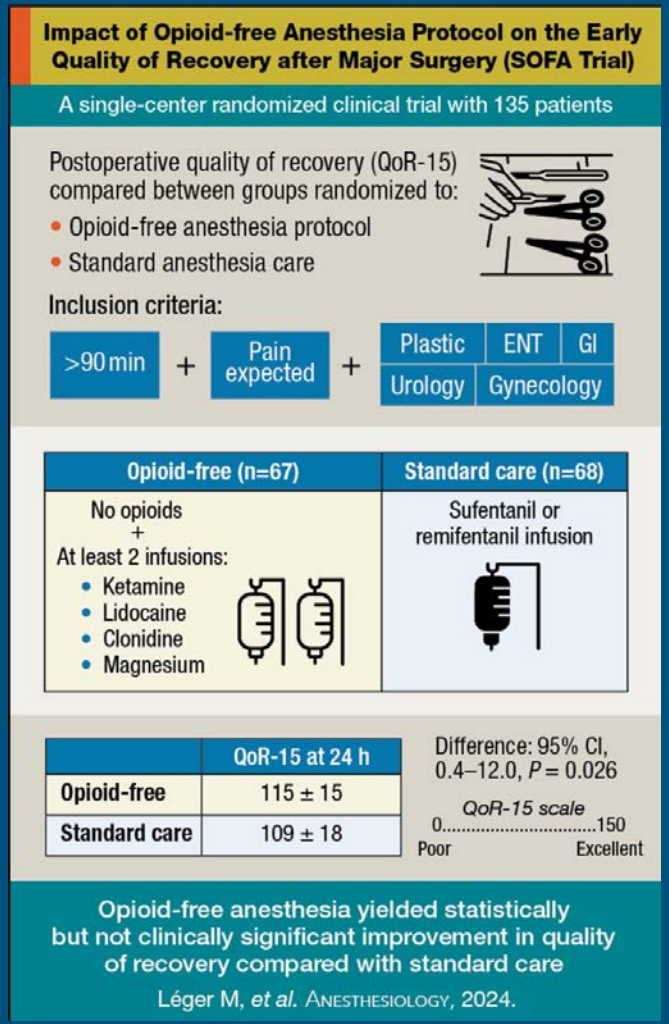
Recommendation Category	Recommendation	Level of Evidence*
Indications for use	(1) Perioperative use in surgery with moderate to severe postoperative pain (2) Perioperative use in patients with opioid tolerance (3) As analgesic adjunct in opioid-tolerant patients with sickle cell crisis (4) As analgesic adjunct in patients with OSA	(1) Grade B, moderate certainty (2) Grade B, low certainty (3) Grade C, low certainty (4) Grade C, low certainty
Dosing range	Bolus: up to 0.35 mg/kg Infusion: up to 1 mg/kg per hour	Grade C, moderate certainty
Relative contraindications	(1) Poorly controlled cardiovascular disease (2) Pregnancy, psychosis (3) Severe hepatic disease, ie, cirrhosis (avoid), moderate hepatic disease (caution) (4) Elevated intracranial pressure, elevated intraocular pressure	(1) Grade C, moderate certainty (2) Grade B, moderate (3) Grade C, low certainty (4) Grade C, low certainty
Personnel	Supervising clinician: a physician experienced with ketamine (anesthesiologist, critical care physician, pain physician, emergency medicine physician) who is ACLS certified and trained in administering moderate sedation Administering clinician: registered nurse or physician assistant who has completed formal training in safe administration of moderate sedation and is ACLS certified	Grade A, low certainty (see Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain from ASRA, AAPM, and ASA)[35]

*Evidence was evaluated according to the USPSTF grading of evidence, which defined levels of evidence based on magnitude and certainty of benefit.[5]

Psychedelics for Pain?

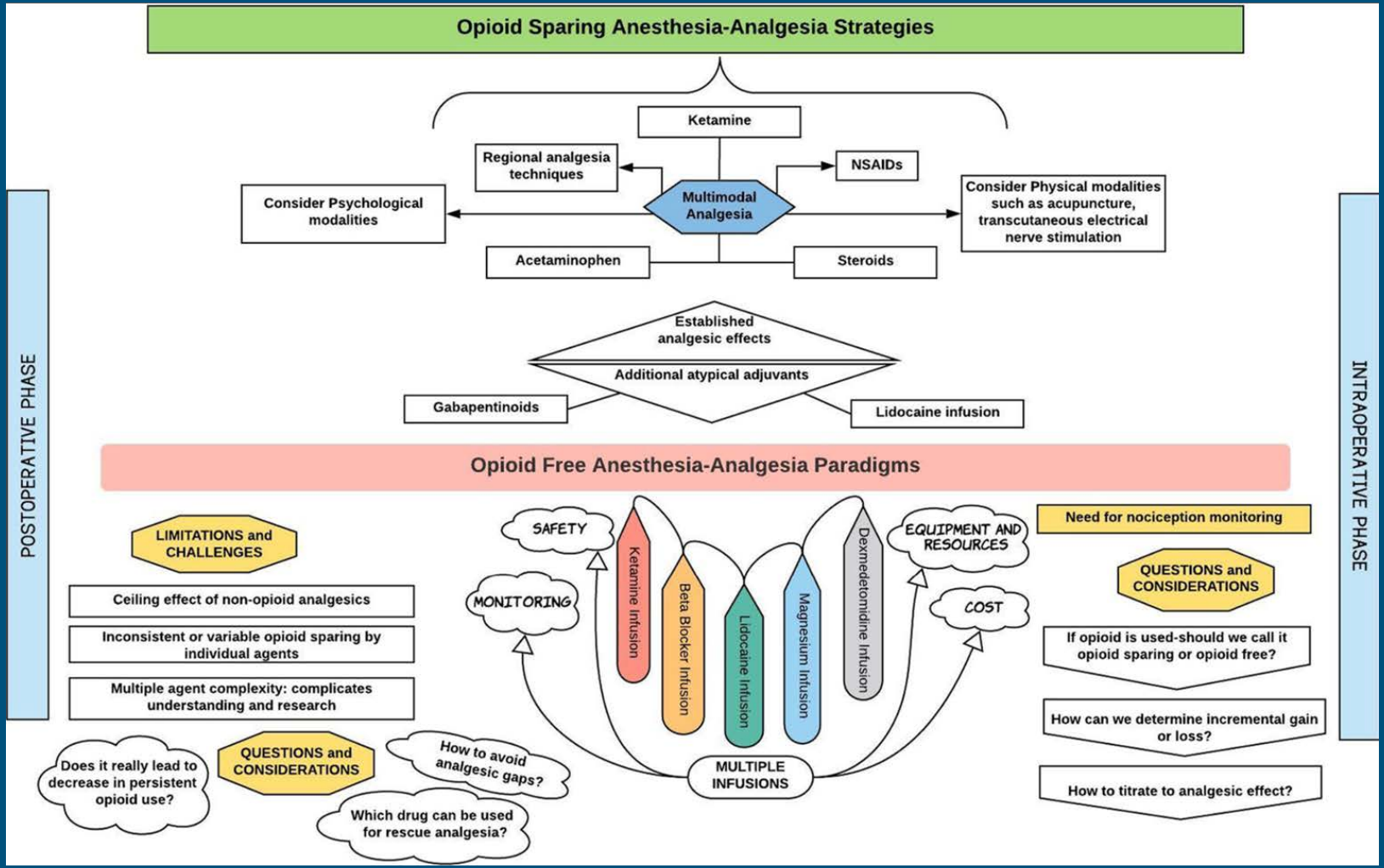
- In general, psychedelics showed efficacy as treatment and prophylactic therapy for headaches by increasing remission times.
- Microdoses of lysergic acid diethylamide (less than 50 µg) and macrodoses of psilocybin (2 to 3 g) significantly reduce phantom limb pain
- For cancer pain, Kast and Collins (n = 50) demonstrated that 100 µg lysergic acid diethylamide-25 provided more persistent pain relief compared to hydromorphone and meperidine.

Opioid Free Anesthesia?



In this single-center, randomized controlled clinical trial, patients received a combination of at least two drugs including ketamine, lidocaine, clonidine, and magnesium sulfate without opioids for anesthesia or a standard approach that included opioids

Opioid-free anesthesia, compared to the standard approach, resulted in a small improvement in a validated measure of quality of recovery at 24, 48, and 72 h after surgery, but these differences did not completely reach the threshold for clinical significance


Opioid Sparing Anesthesia-Analgesia Strategies
Ketamine
Regional analgesia techniques
NSAIDs
Consider Psychological modalities
Multimodal Analgesia
Consider Physical modalities such as acupuncture, transcutaneous electrical nerve stimulation
Acetaminophen
Steroids
Established analgesic effects
Additional atypical adjuvants
Gabapentinoids
Lidocaine infusion
POSTOPERATIVE PHASE
INTRAOPERATIVE PHASE
Opioid Free Anesthesia-Analgesia Paradigms
LIMITATIONS and CHALLENGES
Ceiling effect of non-opioid analgesics
Inconsistent or variable opioid sparing by individual agents
Multiple agent complexity: complicates understanding and research
QUESTIONS and CONSIDERATIONS
Does it really lead to decrease in persistent opioid use?
How to avoid analgesic gaps?
Which drug can be used for rescue analgesia?
SAFETY
MONITORING
EQUIPMENT AND RESOURCES
COST
Ketamine Infusion
Beta Blocker Infusion
Lidocaine Infusion
Magnesium Infusion
Dexmedetomidine Infusion
MULTIPLE INFUSIONS
Need for nociception monitoring
QUESTIONS and CONSIDERATIONS
If opioid is used-should we call it opioid sparing or opioid free?
How can we determine incremental gain or loss?
How to titrate to analgesic effect?

Opioid Free Laparoscopic Cholecystectomy

- “Bakan et al. report an 80-patient trial in which all patients had multimodal analgesia, with the opioid-free anesthesia group having a combination of lidocaine plus dexmedetomidine and propofol infusion during surgery compared with remifentanil and fentanyl in the standard group. The primary outcome of opioid consumption within 6 h after extubation was not significantly different between the two groups. There was actually a significant increase in the discharge time from recovery in the opioid-free anesthesia group.”

Nonpharmacologic Pain Management

- Physical modalities include transcutaneous electrical nerve stimulation, acupuncture, massage, yoga, continuous passive movement, and cryotherapy.
- Psychological modalities can be grouped into four categories: information provision, stress reduction, attentional strategies, and cognitive–behavioral interventions.

- Several preoperative (patient) factors have been recognized to play a role in postoperative pain control, persistent opioid use, persistent postsurgical pain, and overall recovery.
    - Anxiety, depression, catastrophizing-coping, preexisting opioid use, chronic pain, smoking, and frailty are risk factors.
- Patients should be active participants in their clinical process, but at the same time, managing anticipation of pain, decreasing opioid use, and optimizing non-opioids for pain control is important.

- Do Opioid-free Strategies Have Benefits above and beyond Opioid-sparing Strategies?
  - No. To date, there is no evidence.
- Is Complete Opioid Sparing Possible in the Context of Existing Multimodal Opioid-sparing Strategies?
  - Yes, but only in some contexts and procedures.
- Do Opioid-free Anesthesia Strategies Prevent Persistent Opioid Use or Overprescription?
  - No.
  - Postoperative prescriptions more relevant for postoperative OUD
    - As little as a 5 day prescription can increase risk

Enhanced Recovery After Surgery (ERAS) Considerations

Preoperative Management-Personal Preferences

- Acetaminophen 1 g PO
  - Hold for liver disease, reduce dose for low body mass
- Celecoxib 200-400 mg PO
  - Hold for moderate-severe coronary disease, moderate chronic kidney disease, or surgical bleeding risk
- Pregabalin 75 mg or Gabapentin 300-600 mg PO
  - Hold for greater age or frailty

Intraoperative Management-Personal Preferences

- Regional Anesthesia as able
- Limit opioids, use shorter-acting opioids
- Redose NSAID/Acetaminophen after 6-8 hours
- 1st line adjunct: Dexmedetomidine 0.5 mg/kg total
- 2nd line adjunct: Ketamine
- Consider lidocaine infusion or magnesium IV up to 2g

Postoperative Management-Personal Preferences

- Scheduled NSAID/acetaminophen
- PRN shorter-acting opioid that does not contain acetaminophen
  - Oxycodone
- Consider scheduled gabapentinoid
- Repeat regional anesthesia as needed or use a continuous regional anesthetic technique
- Opioid PCA with Fentanyl or Hydromorphone for opioid tolerant patients with higher pain surgeries
  - No basal rate

Takeaways

- Multimodal analgesia is a vital tool to reduce opioid consumption, improve patient pain and satisfaction, and improve outcomes
- Multimodal analgesia should especially be utilized in certain patient populations such as those with Opioid Use Disorder, frequent cannabis use, and those with chronic pain
- Regional anesthesia is a powerful tool within multimodal analgesia
- Your local anesthesiologists can help with acute pain needs

Questions?

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