First Aid Perioperative Ultrasound

Acute Pain Manual for Surgical Procedures

Jinlei Li · Wei Jiang
Nalini Vadivelu *Editors*

Springer

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ISBN 978-3-031-21290-1 ISBN 978-3-031-21291-8 (eBook)
https://doi.org/10.1007/978-3-031-21291-8

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

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Part I

Ultrasound Guided High-Yield Perioperative Regional Anesthesia

Safe Practice of Ultrasound Guided Regional Anesthesia

Tae S. Lee and Yan H. Lai

Case Stem As a regional anesthesiology fellow, you are meeting your first patient of the day in the preoperative holding area. Patient is a 61-year-old man with a BMI of 18 (weight of 45 kg) presenting for elective total shoulder arthroplasty (TSA) for treatment of his primary osteoarthritis. His past medical history includes hypertension, diabetes, coronary artery disease with a drug-eluting stent placed 1 year earlier, Wolf-Parkinson-White syndrome, and emphysema secondary to a 30-pack year smoking history. He also has a history of polysubstance abuse, and successfully tapered off of methadone completely just this past year. His medications include Aspirin 81 mg, Clopidogrel (which he had stopped 7 days ago), Atorvastatin, Amlodipine, Metformin, Insulin, Carvedilol, and Albuterol. His electrocardiogram was notable for left anterior hemiblock and pathologic Q waves in the anterior distribution. A recent stress echocardiogram demonstrated left ventricular hypertrophy, moderate pulmonary hypertension, an ejection fraction of 35%, and multiple areas of reversible ischemia. On exam, patient was noted to have a mallampati III airway, small mouth opening, and limited cervical exten-

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_1

sion. He is interested in regional anesthesia in order to avoid opioids given his history of substance abuse. You are also made aware of the fact that he will not be expected to participate in physical therapy until postoperative day 1.

Key Question 1

What peripheral nerve blocks (PNBs) can be performed for this patient? Compare and contrast single-shot versus continuous methods. Which technique do you believe is best suited for this patient?

PNBs can generally be administered by one of two possible techniques: a one-time injection (i.e. "single-shot" or SSPNB) of local anesthetic (LA), or a continuous infusion of LA via a percutaneously placed catheter (CPNB). Each technique has distinct advantages and disadvantages that should be carefully considered and thoroughly discussed with both the patient and the perioperative team.

CPNBs involve infusion of LA to a target nerve or nerve plexus in an attempt to extend the benefits of SSPNB. CPNBs offer several distinct advantages, particularly in the postoperative period. Advantages of CPNBs are summarized in Table 1 based on a plethora of research validating CPNBs in various surgical models, particularly those related to orthopedics [1–3].

Despite these many advantages, CPNBs are also associated with some drawbacks that have prevented them from being used routinely. Catheter specific complications include [4–6]:

- Dislodgement (up to 15% of all catheters, 5% with ISB catheters) [4]
- Infections

Table 1 Advantages of continuous peripheral nerve blocks (CPNBs) relative to single-shot peripheral nerve block

• Superior and prolonged postoperative analgesia
• Reduced supplemental opioid consumption and opioid related adverse effects
• Improved postoperative rehabilitation/ambulation
• Reduced length of hospital stay and expedited discharge to home
• Improved patient satisfaction

- Local anesthetic systemic toxicity (LAST), and LA induced myo- and neurotoxicity
- Increased incidence of falls (with femoral CPNB due to resultant quadricep muscle weakness [7])

Indications for CPNB tend to vary between different institutions, but generally include palliative management (i.e., non-operative femoral neck fractures) and circumstances in which systemic opioids should be minimized or avoided entirely (i.e., substance abuse, opioid-induced hyperalgesia). Our patient has a longstanding history of opioid abuse and it would undoubtedly be in his best interest to minimize systemic opioids in the perioperative period with CPNB. CPNBs can also provide adequate pain control to ensure that patient can tolerate aggressive physical therapy (PT) on postoperative day 1 (POD1).

Case Stem At the end of your preoperative discussion with the patient, you collectively agree to perform an ultrasound-guided interscalene nerve catheter (US-ISB). After obtaining informed consent, you set up an ultrasound machine at the bedside. You recall and confirm that the patient is having a right-sided procedure, and so you place the ultrasound machine on the left side of the patient's stretcher.

Key Question 2
During your preparation for the US-ISB catheter, a visiting medical student asks you what equipment/medications he/she could help gather?

A principal means of delivering safe and effective local and regional anesthesia involves maintaining a practice aimed at avoiding adverse outcomes and preventing known complications. Achieving this goal generally requires consistency on the part of the anesthesiologist when it comes to preparation and basic setup for every case.

Standard American Society of Anesthesiologist (ASA) monitors, such as pulse oximetry, electrocardiography, and noninvasive blood pressure measurement should be utilized for any

type of anesthetic, and regional anesthesia (RA) is no exception. These monitors are crucial given that neuraxial and peripheral nerve blocks are generally performed in patients who have received some degree of sedation, both for improved procedural conditions as well as for patient comfort. Over sedation and its undesirable sequelae, including hypoventilation, airway obstruction, and hypoxemia, can be easily avoided with steadfast monitoring of oxygenation and ventilation.

Patient sedation while performing PNB has been shown to be beneficial for numerous reasons. Sedation reduces procedural pain and recall of the procedure, which in turn has resulted in increased patient satisfaction during block performance and greater tolerance of nerve blocks [8]. Furthermore, sedation with benzodiazepines or propofol increases the seizure threshold, thereby potentially reducing the risk for neurotoxic sequelae associated with systemic toxicity [9]. Table 2 outlines a number of medications that are frequently used for sedation in regional anesthesia. Doses are titrated to patient comfort while ensuring that patients maintain levels of consciousness that are necessary for communication and cooperation.

Although the use of ultrasound has significantly mitigated the risk of severe LAST by allowing direct visualization of vascular structures and injectate, the risk has not been completely elimi-

Table 2 Sedatives for regional anesthesia

Drug	Onset (min)	General IV drug dose range	Benefits and complications
Midazolam	1–2	1–4 mg	Significant anxiolysis, anterograde amnesia. Synergistic with opioids in causing respiratory depression
Fentanyl	3–5	25–100 micrograms	Significant analgesia, respiratory depression
Ketamine	Variable	5–20 mg	Significant analgesia with minimal respiratory depression
Propofol	<1	10–50 mg	Hypnosis with significant respiratory depression

nated [10]. Therefore, emergency drugs and resuscitation equipment should always be readily available when administering any regional anesthetic to obtain timely control of the airway, stabilize vital signs, and treat both cardiotoxic and neurotoxic effects of LAST. Resuscitation equipment and emergency medications are shown in Table 3.

All PNBs require some mode of nerve localization to ensure that the injectate/catheter is deposited in the correct location adjacent to the target nerve. SSPNB are performed with insulated needles (to conduct electrical stimulus for nerve stimulation) or echogenic needles (for ultrasound guidance) of different lengths and diameters (see Fig. 1). Shorter, larger-diameter needles allow for better handling and manipulation, whereas longer, smaller-diameter needles offer less control and are more easily distorted when traversing different layers of tissues (muscles, subcutaneous tissues, fascial layers, etc.); however, these longer, smaller-diameter needles are often required simply to perform deeper blocks that would otherwise be out of reach.

Case Stem You summarize the patient's pertinent medical history and airway exam to the medical student. You show the medical student the equipment you have gathered thus far, including 18-gauge continuous block needle system, chlorhexidine prepara-

Table 3 Resuscitation equipment and emergency medications for regional anesthesia

Resuscitation equipment	Emergency medications
• Self-inflating bag-mask ventilation device (i.e., Ambu bag) • Suction • Oxygen-supply with face mask • Endotracheal tube(s), oral airways, nasal airways • Laryngoscopes (Macintosh and Miller blades) • Defibrillator	• Induction agent (i.e., Propofol should be avoided in LAST) • Succinylcholine • Atropine • Ephedrine vs. Phenylephrine • Glycopyrrolate • 20% Intralipid (ideally, together with LAST protocol for use and necessary equipment to draw up the medication)

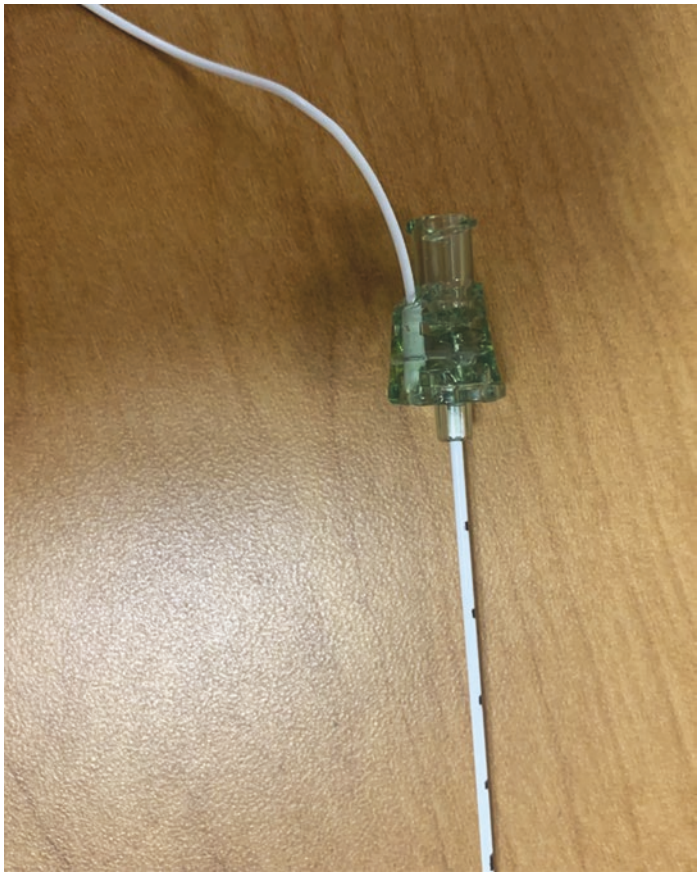

Fig. 1 18-gauge insulated CPNB needle with stimulation wire

tion, sterile drape, skin adhesive (i.e., Dermabond), transparent dressing, sterile ultrasound transducer covers, and sterile ultrasound gel (see Fig. 2).

Key Question 3

The medical student states that he has never seen a PNB performed before, and asks how the ultrasound machine is able to produce accurate and clinically useful images.

Fig. 2 CPNB supplies: (Upper left counterclockwise) PNB tray (sterile drape, syringes, etc.…), chloroprep impregnated tegaderm, dermabond sealant, small tegaderm, sterile gloves, CPNB needle kit with catheter, sterile ultrasound cover

UG is used in conjunction with anatomic landmarks to locate targeted nerves. Ultrasound imaging enables direct visualization of:

- Needle and its relation to muscles, bones, blood vessels, and other nerves
- LA distribution during and after injection.

Ultrasound waves are a type of acoustic energy that are generated when piezoelectric crystals within an ultrasound transducer vibrate at high frequency in response to an alternating current. When placed in contact with skin via a conductive gel, the transducer transmits the rapid vibrations that then propagate sound waves longitudinally into the body, reflect off tissue interfaces, and back to the receiver part of the same transducer. When ultrasound waves return to the transducer, the piezoelectric crys-

tals will vibrate again, thereby transforming acoustic energy into electrical energy and generating a clinically useful ultrasound image [11].

When passing through any given medium, an ultrasound wave is subject to several interactions at tissue interfaces including reflection, refraction, and attenuation [11]:

- Reflection: Acoustic impedance (resistance to passing of ultrasound waves) between the two media account for degree of reflection
- Refraction: sound waves change direction with different acoustic velocities
- Attenuation: acoustic energy is progressively lost as sound waves travel deeper into tissue. Attenuation can degrade image quality to the point where performing a nerve block would be impractical, or even unsafe
- Certain functions the ultrasound machine, such as increasing gain, can artificially increasing the signal intensity from a specific or all points in the field.
- Resolution is the ability to distinguish between two separate objects

Case Stem Shortly before you begin the block, you discover that the ultrasound machine is not functional and so you opt to perform the interscalene nerve catheter using peripheral nerve stimulation.

Key Question 4: What Is Peripheral Nerve Stimulation (PNS) and How Does It Assist in Nerve Localization?

PNS is a nerve localization technique that uses an insulated block needle to deliver low-intensity (up to 5 mA), short-duration (0.05–1 ms) electrical stimuli to elicit predefined responses (i.e., twitch in a specific muscle or muscle groups vs. sensory responses in the form of paresthesias within certain dermatomes) in order to locate a target nerve/plexus prior to injecting local anesthetic [12]. The overall goal of this technique is to approximate the needle (and thus, LA delivery) and nerve as much as possible without

violating essential neural structures (such as intraneural fascicles). Both needle trauma and LA toxicity caused by intraneural injections could potentially be associated with transient and/or permanent nerve damage. Successful use of PNS is dependent on a strong foundational knowledge in anatomy and a comprehensive understanding of electrophysiology.

PNS incorporates several different principles of electrophysiology. Stimulation of nerve fibers occurs when a delivered charge to a nerve result in a change in transmembrane voltage (i.e., difference between intracellular and extracellular voltage) that is greater than the threshold to generate an action potential or series of action potentials along the nerve fiber. The peripheral nervous system consists of various types of nerve fibers, each of which can be distinguished by its diameter, as well as by its degree of myelination. In general, the speed of impulse propagation of action potentials is greater/threshold of excitability is lower in myelinated, large-diameter fibers (i.e., Aα motor fibers), whereas the speed of impulse propagation of action potentials is lower/threshold of excitability is higher in non-myelinated, small-diameter fibers (i.e., C fibers) [13].

When operating the nerve stimulator, the starting amplitude/current that is used depends on the projected depth of the target nerve. An initial amplitude of 1 mA is appropriate for superficial nerves (i.e., upper extremity nerves), whereas amplitudes of 1.5–3.0 mA may be required for deeper nerves (i.e., paravertebral or lower extremity nerves). After the intended muscle response is observed, current is gradually decreased while simultaneously advancing the block needle until the observed motor response is elicited with a current of 0.2–0.5 mA at 0.1 ms stimulus duration. At this point, 1–2 mL of local anesthetic is injected as a test dose to observe for timely termination of the muscle twitch, followed by injection of the remaining volume of local anesthetic [13].

Case Stem As you begin positioning the patient to perform the block, the surgeon pulls you aside and quietly requests something "long acting" for the patient because he anticipates that the proce-

dure may take slightly longer than usual and that the patient may be in a significant amount of pain.

Key Question 5: What Factors Are Involved When Choosing LA to Administer for Any Peripheral Nerve Block?

When performing regional anesthesia, the anesthesiologist must decide on not only the specific LA agent to be used, but also the volume, concentration, and dose to be administered. These decisions are generally based on the desired outcomes of block onset, duration, density and degree of motor blockade, and adverse effects. In turn, the desired characteristics of specific LA agents is dependent on clinical circumstances. For example, motor blockade is beneficial when a peripheral nerve bock serves as a sole surgical anesthetic or when prolonged postoperative analgesia is needed. However, motor blockade would be unattractive when a patient is expected to participate in PT in the early postoperative period or if adequate neurological exam/sensory assessment recovery is immediately following the conclusion of surgery [14].

- Onset dependent on proximity to nerve (likely most important factor). Other factors include total LA dose (not LA volume or concentration), as well as the hydrophobicity of specific LA used [14].
- Potency dependent on lipophilicity of LA, which facilitates LA penetration through the axon [14].
- Duration of action influenced primarily by rate of clearance of LA. Other factors include hydrophobicity (hydrophobic LA have longer duration) and the total LA dose (larger LA doses produce longer blocks) [14].
- General guidelines for maximum LA doses are shown in Table 4 [14].

Case Stem With US not functioning, you decided it would be safer to place a US-ISB SSPNB using the nerve stimulator with 30 mL of 0.5% Ropivacaine and a 22-gauge insulated block needle. As you are manipulating the block needle, the patient

Table 4 Local anesthetic properties [14]

Anesthetic	Onset (minutes)	Duration of Action (hours)	Maximum Dose Without Epi (mg/kg)	Maximum Dose with Epi (mg/kg)
2% lidocaine	10–20	2–8	4.5	7
1.5% mepivacaine	10–20	2–10	5	7
0.2% ropivacaine	15–30	5–15	3	3.5
0.5% ropivacaine	15–30	4–24	3	3.5
0.25% bupivacaine	15–30	5–25	2.5	3
0.5% bupivacaine	15–30	5–30	2.5	3

suddenly complains of shooting pain down his arm. You immediately reposition the needle until the intended muscle response is elicited with a current of 0.3 mA. You confirm that the patient's paresthesias have subsided, and inject the LA. Following block placement, TSA is completed by the surgeon without event, and you transfer the patient to the recovery room. During your routine postoperative phone call with the patient the following day, he endorses slightly decreased sensation in the extremity.

Key Question 6: What Are the Complications Associated with Peripheral Nerve Blocks?

Fortunately, serious complications of PNBs are exceedingly rare when proper techniques and equipment are utilized; however, when they do occur, these complications can be potentially devastating for both patient and provider. Therefore, it is imperative that patients be presented with the necessary information to fully comprehend the risks associated with peripheral nerve blocks and to participate in informed decision making. Serious complications of PNBs that should be discussed prior to procedure include bleeding, catheter infection, nerve injury, and LAST.

- Inadvertent puncture of neighboring vascular structures during PNB can result in perineural hematoma formation. Hematomas can cause compression of nerves and lead to neurologic sequelae.
- Bleeding in non-compressible areas (especially with deeper blocks) can rarely occur, sometimes requiring surgical decompression. As such, it is often wise to avoid performing peripheral nerve blocks in non-compressible areas for patients with abnormal coagulation profiles. Anticoagulation guidelines for PNBs do exist but extend beyond the scope of this discussion.
- Infection risk for SS PNBs is minimal whereas bacterial colonization of CPNB is higher-ranging between 7.5 and 57%. Nevertheless, colonization rarely leads to systemic infection, with overall risk of infection ranging between 0 and 3.2% [15]. Femoral and axillary nerve catheters are associated with the highest rates of colonization, while rates of colonization of popliteal catheters are low [15]. Other independent risk factors for PNC infection include intensive care unit (ICU) admission, trauma, immunocompromised states (i.e., diabetes), indwelling catheters for >48h, male sex, and the absence of antibiotics.
- Nerve injury:
  - Rare occurrence with exact incidence that remains controversial and highly variable across studies.
  - Persistent symptoms of nerve injury (i.e., pain, tingling, or paresthesia) can be as high as 8–10% in the days following the block [16].
  - Majority of symptoms are transient (days to less than 6 months). Permanent symptoms range between 0.015 and 0.09% [17].
  - Historically associated with intraneural injection but controversial evidence
- LAST:
  - Can be caused by inadvertent injection of LA into blood vessels or delayed uptake of LA by small veins (via indwelling CPNBs or catheter migration, for example) [18].

- Highly variable clinical presentation:
  Mild: tinnitus, perioral numbness, metallic taste
  Severe: Seizure, coma, respiratory depression, and cardiovascular collapse (i.e. hypertension vs. hypotension, tachycardia vs. bradycardia, arrhythmias, and arrest).
- Guidelines for prevention and treatment of LAST will be discussed in later chapters.

1 Summary

- PNB may be performed as SS PNB or infusion of LA via perineural catheters (CPNB)
- CPNBs allows prolonged analgesia and have been successfully used in numerous settings
- Emergency drugs and resuscitation equipment should always be readily available when administering any regional anesthetic in the event of acute complications
- Peripheral nerve localization techniques include direct visualization via ultrasound guidance and/or electrical nerve stimulation to observe for motor responses
- Thorough understanding of ultrasound physics and technique is necessary to prevent serious adverse effects, such as hemorrhagic/infectious complications and LAST.

Common Pitfalls

- Failure to adequately explain the indications/risks/benefits/alternatives of PNB may limit patients' ability to make informed decisions.
- Failure to follow-up with ambulatory patients discharged with CPNBs may cause delays in diagnosis/treatment of complications.
- Failure to consider all perioperative circumstances when selecting LA for a given procedure may lead to block failure or other unexpected complications.

Clinical Pearls

- Although the use of ultrasound has significantly reduced the risk of complications, this risk has not been completely eliminated.
- Under the appropriate clinical circumstances, CPNBs can be an effective way to extend analgesia, facilitate earlier and dynamic PT, and reduce overall hospital costs.
- When utilizing ultrasound guidance, it is imperative to select the appropriate transducer and settings for a given procedure.
- While peripheral nerve stimulation can be an alternative to ultrasound for nerve-localization, it can also be used to confirm ultrasound findings.

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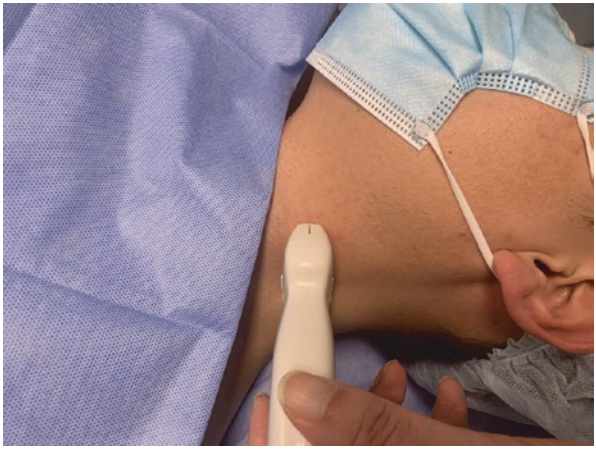
Sonographic Image of Head and Neck Regional Anesthesia

Shenyuan Zhou and Wei Jiang

1 Ultrasound Image of Superficial Cervical Plexus

1.1 High Frequency Probe; Short-Axis



Probe position: transverse over the midpoint of the sternocleidomastoid muscle

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
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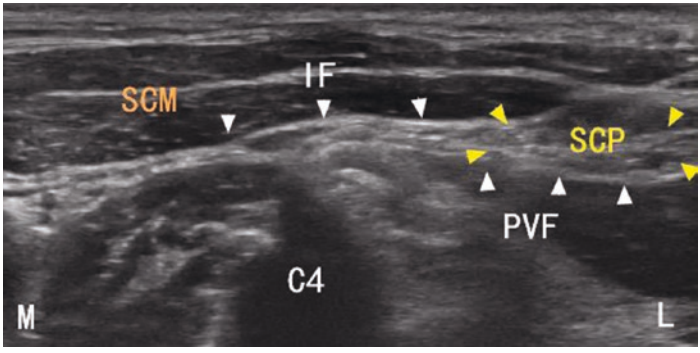
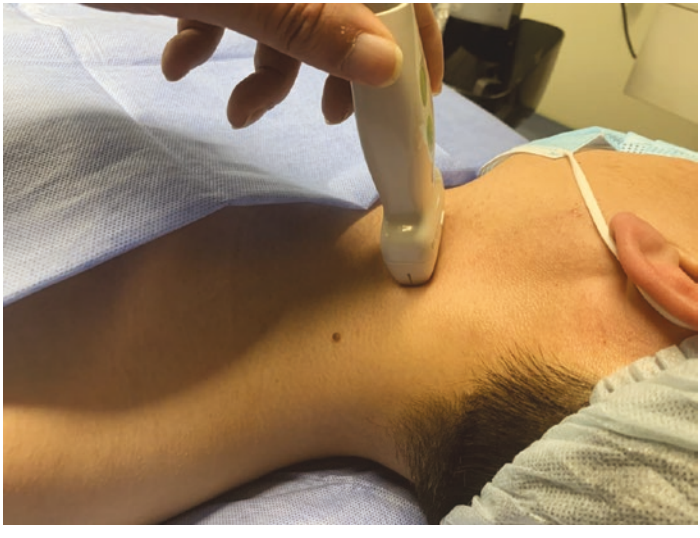


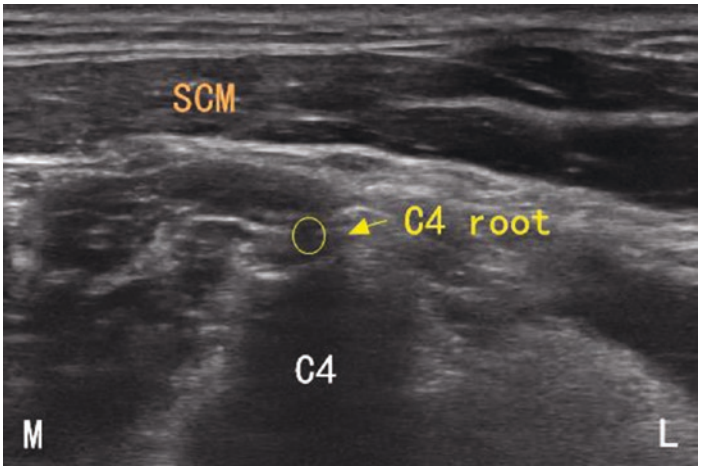
SCM: sternocleidomastoid muscle; IF: investing fascia; PVF: prevertebral fascia; SCP: superior cervical plexus; M:medial; L:lateral

2 Ultrasound Image of Cervical Root

2.1 High Frequency Probe; Short-Axis

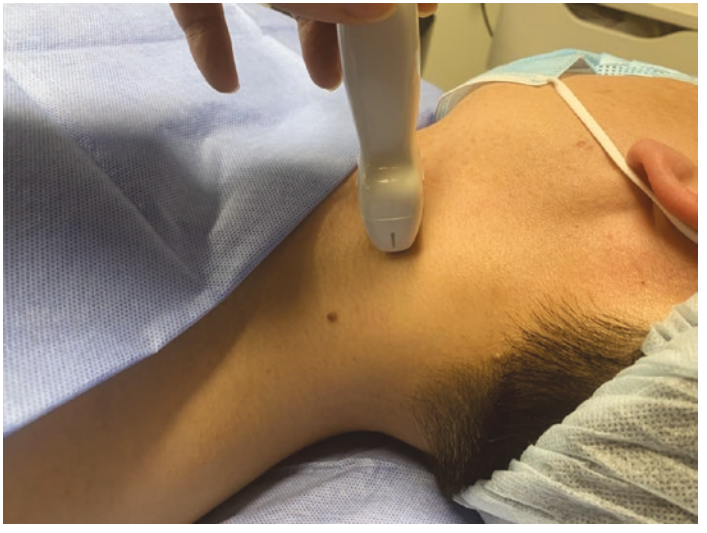


Probe position: horizontal plane, transverse on neck, superior to clavicle

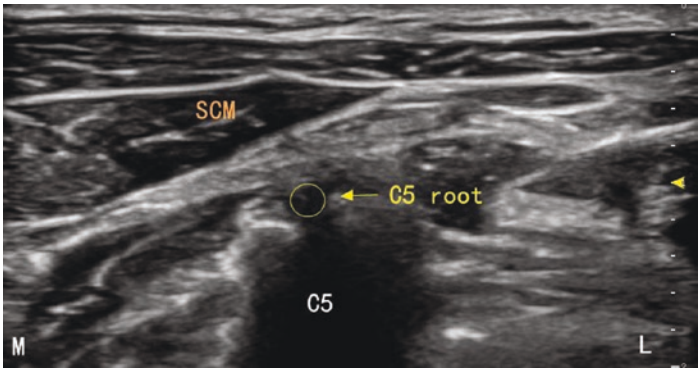


SCM: sternocleidomastoid muscle; M: medial; L: lateral

2.2 High Frequency Probe; Short-Axis

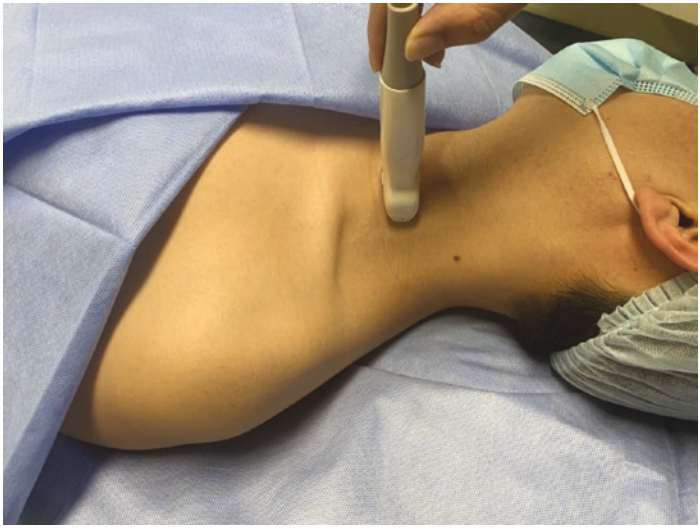


Probe position: horizontal plane, transverse on neck, superior to clavicle

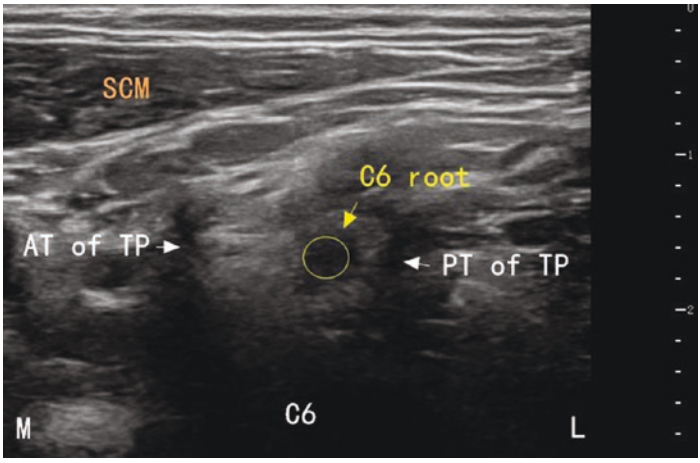


SCM: sternocleidomastoid muscle; M:medial; L:lateral

2.3 High Frequency Probe; Short-Axis

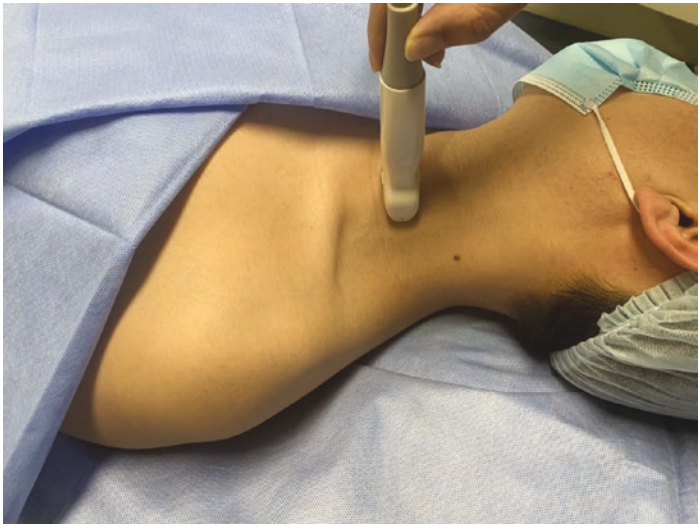


Probe position: horizontal plane, transverse on neck, superior to clavicle

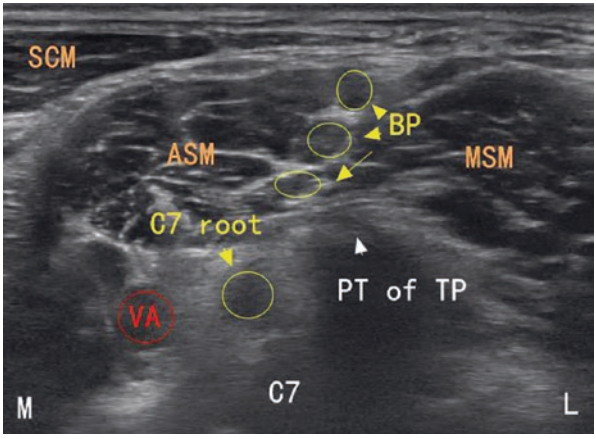


SCM: sternocleidomastoid muscle; AT of TP: anterior tubercle of transverse process; PT of TP: posterior tubercle of transverse process; M:medial; L:lateral

2.4 High Frequency Probe; Short-Axis



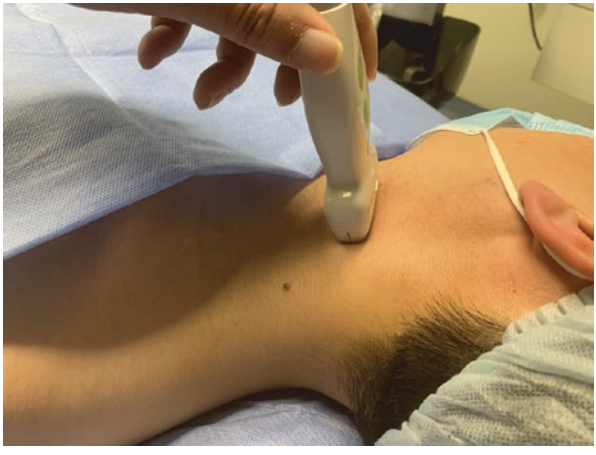
Probe position: horizontal plane, transverse on neck, superior to clavicle



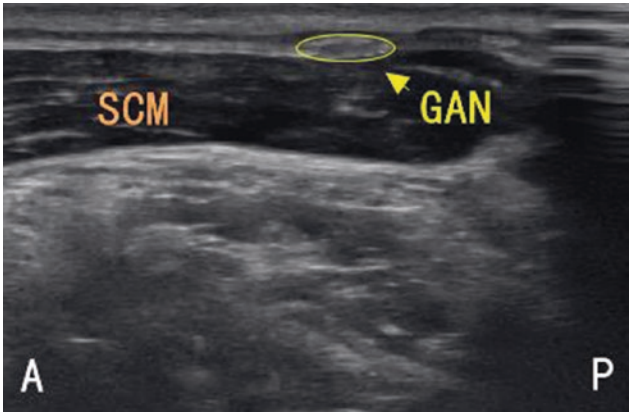
SCM: sternocleidomastoid muscle; ASM: anterior scalene muscle; PT of TP: posterior tubercle of transverse process; M:medial; L:lateral

3 Ultrasound Image of Great Auricular Nerve

3.1 High Frequency Probe; Short-Axis



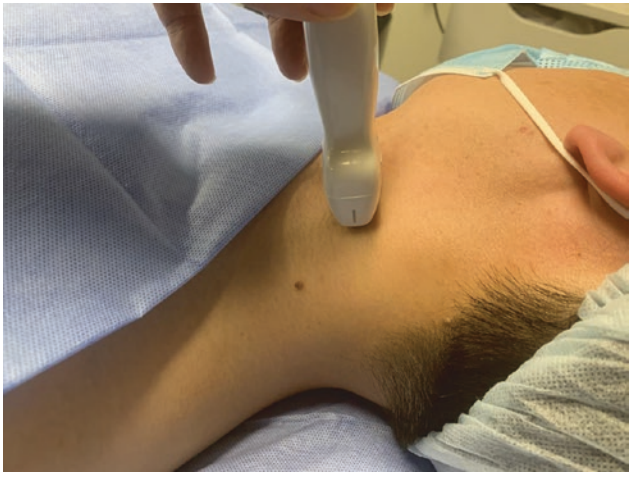
Probe position: horizontal plane, transverse on neck, superior to clavicle



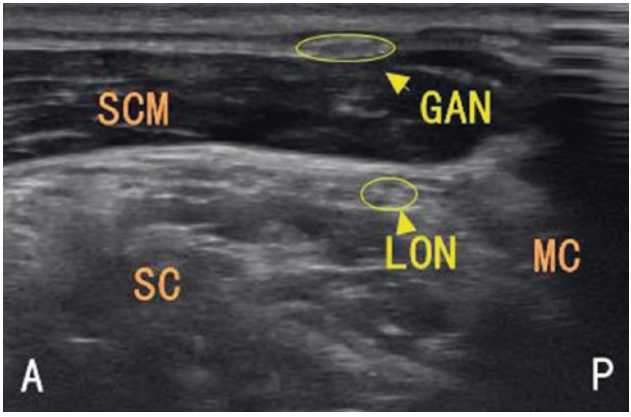
SCM: sternocleidomastoid muscle; GAN: great auricular nerve; A: anterior; P: posterior

4 Ultrasound Image of Lesser Occipital Nerve

4.1 High Frequency Probe; Short-Axis



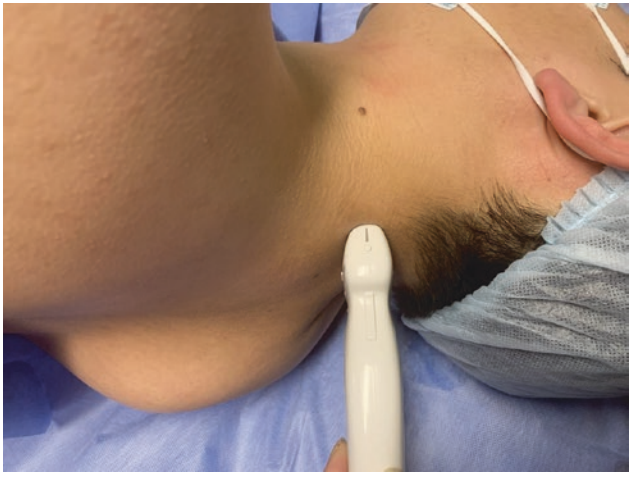
Probe position: horizontal plane, transverse on neck, superior to clavicle



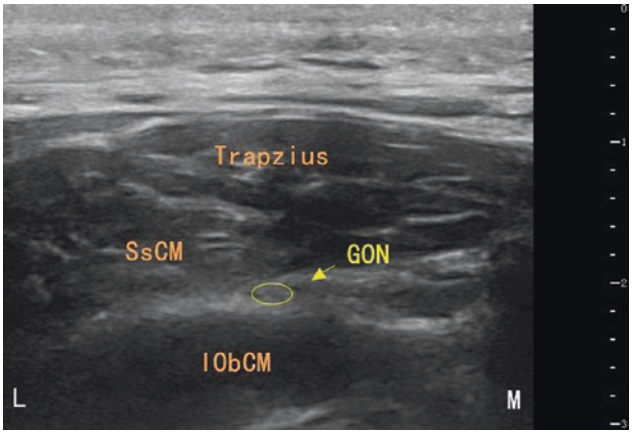
SCM: sternocleidomastoid muscle; SC: splenius cervicis; MC: musculus capitis; GAN: great auricular nerve; A:anterior; P:posterior

5 Ultrasound Image of Greater Occipital Nerve

5.1 High Frequency Probe; Short-Axis



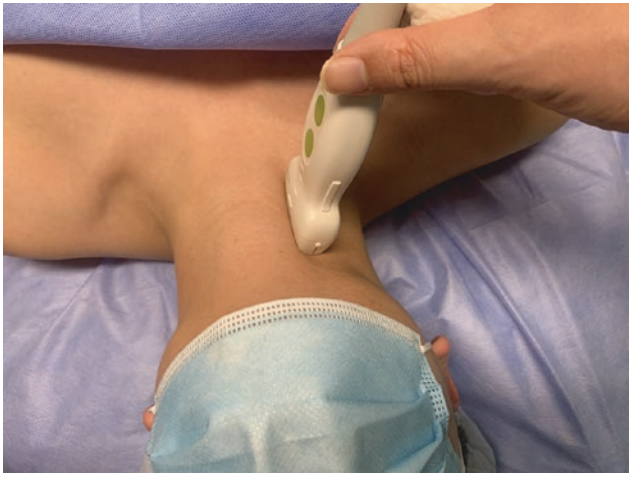
Probe position: horizontal plane, transverse just inferior to the hairline



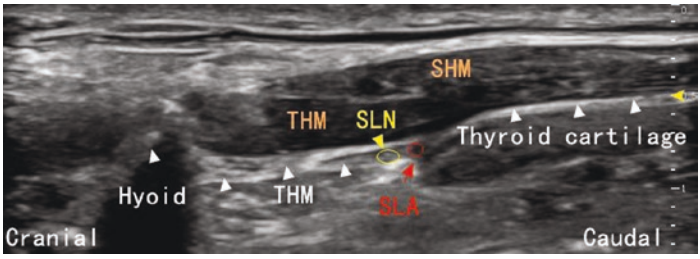
SsCM: semispinalis capitis; IObCM: obligus capitis inferior muscle; GON: greater occipital nerve; L:lateral; M:medial

6 Ultrasound Image of Superior Laryngeal Nerve

6.1 High Frequency Probe; Long-Axis



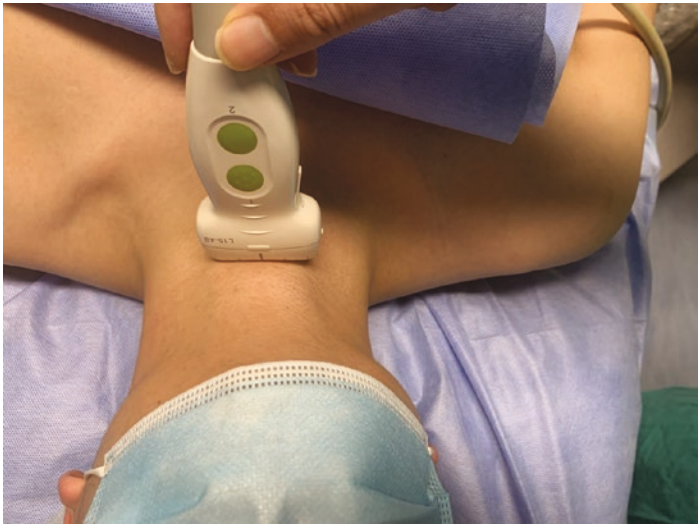
Probe position: parasagittal plane, longitudinal just inferior to the mandibula



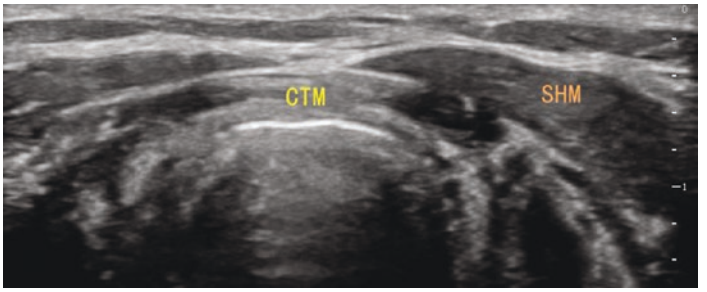
SHM: sternohyoid muscle; THM: thyrohyoid muscle; THM: thyrohyoid membrane; SLN: superior laryngeal nerve; SLA: superiro laryngeal artery

7 Ultrasound Image of Cricothyroid Membrane

7.1 High Frequency Probe; Short-Axis



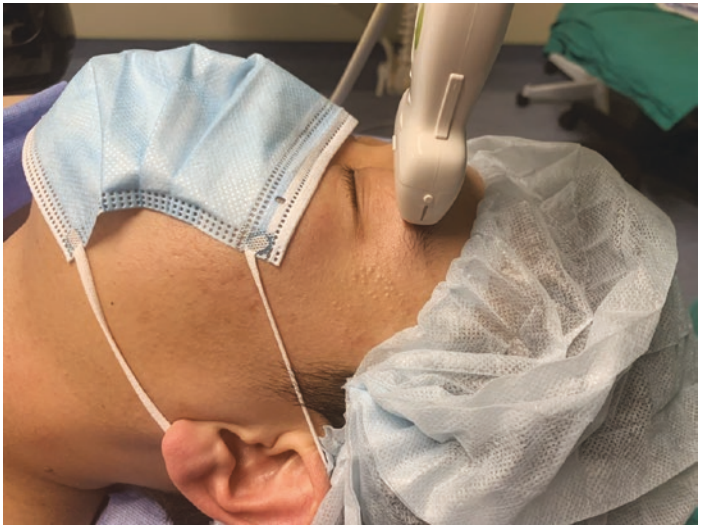
Probe position: horizontal plane, transverse on middle aspect of neck



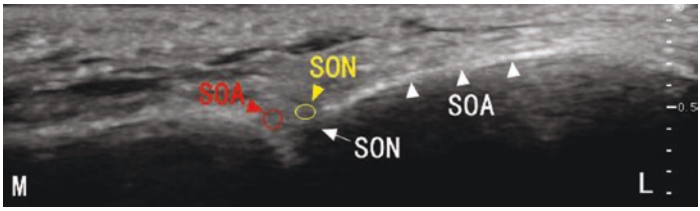
SHM: sternohyoid muscle; CTM: cricothyroid membrane

8 Ultrasound Image of Supraorbital Nerve

8.1 High Frequency Probe; Short-Axis



Probe position: horizontal plane, transverse on the supraorbital margin

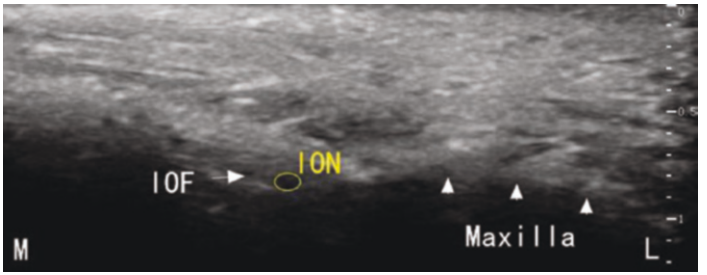


SOA: supraorbital notch; SON: supraorbital arch; SON: supraorbital nerve; SOA: supraorbital artery; M:medial; L:lateral

9 Ultrasound Image of Infraorbital Nerve

9.1 High Frequency Probe; Short-Axis

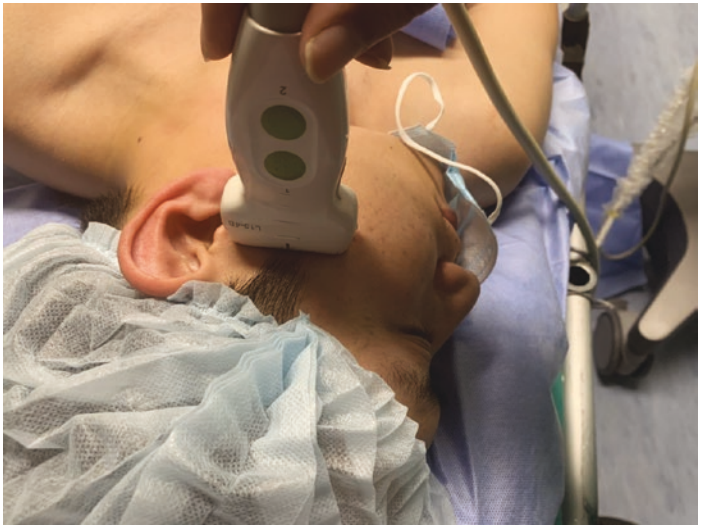
Probe position: horizontal plane, transverse on the infraorbital margin



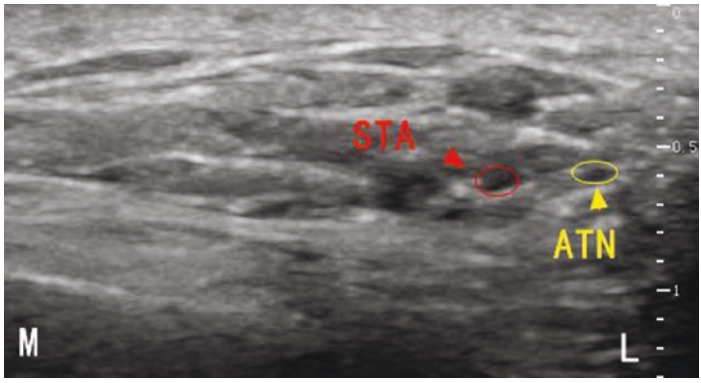
IOF: infraorbital foramen; ION: infraorbital nerve; M:medial; L:lateral

10 Ultrasound Image of Auriculotemporal Nerve

10.1 High Frequency Probe; Short-Axis



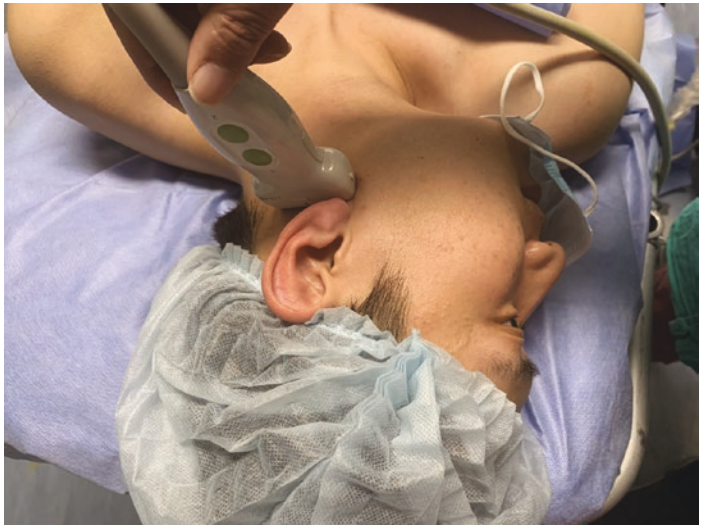
Probe position: horizontal plane, transverse on the anterior margin of tragus



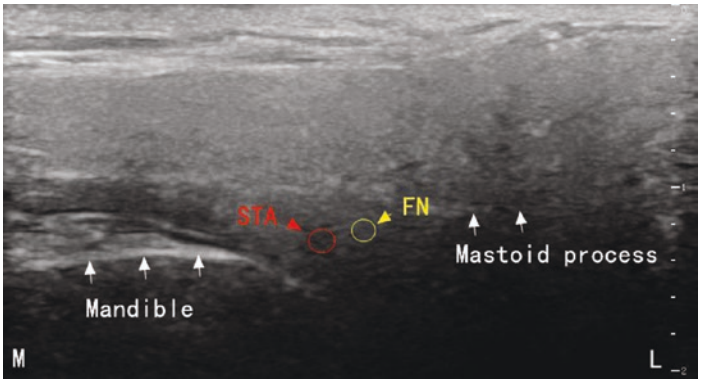
ATN: auriculotemporal nerve; STA: superficial temporal artery; M: medial; L: lateral

11 Ultrasound Image of Facial Nerve

11.1 High Frequency Probe; Short-Axis



Probe position: horizontal plane, transverse between the mastoid process and rami mandibulae



FN: facial nerve; STA: superficial temporal artery; M: medial; L: lateral

Sonographic Image of Upper Extremity Regional Anesthesia

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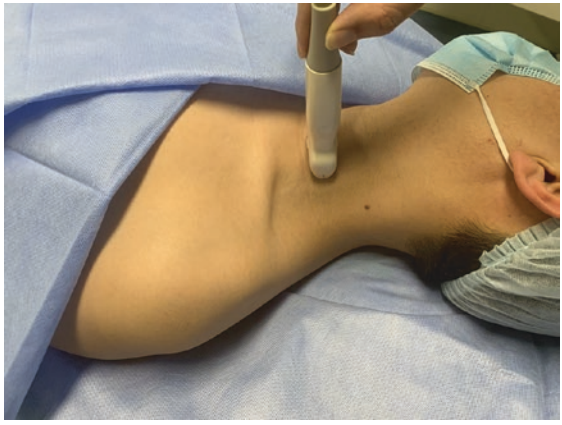
J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_3

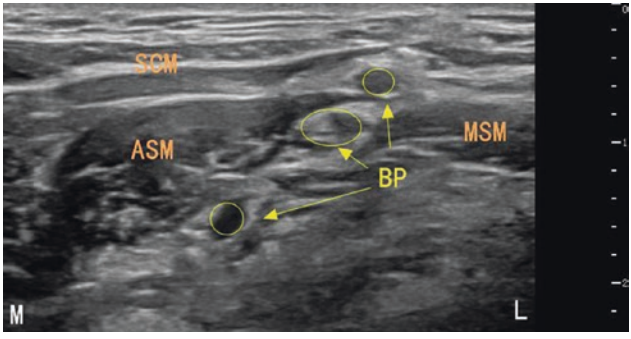
1 Ultrasound Image of Brachial Plexus

1.1 Ultrasound Image of Interscalene Brachial Plexus

1.1.1 High Frequency Probe; Short-Axis



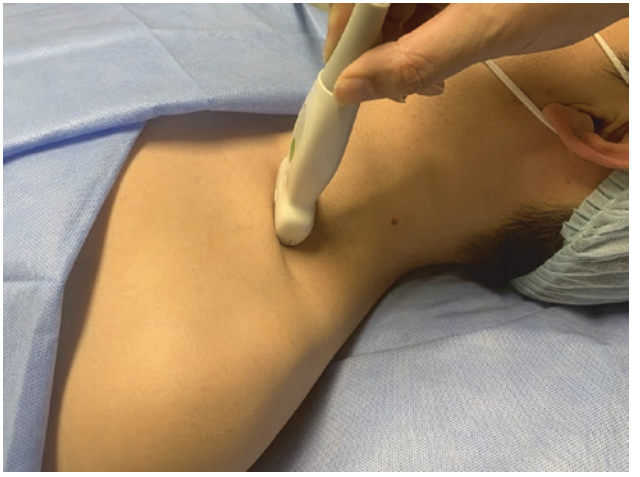
Probe position: horizontal plane, transverse on neck, 3–5 cm superior to clavicle, over external jugular vein



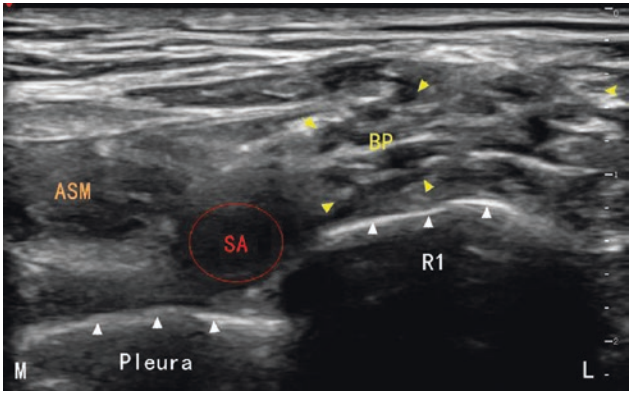
SCM: sternocleidomastoid muscle; ASM: anterior scalene muscle; MCM: middle scalene muscle; BP: brachial plexus; M: medial; L: lateral

1.2 Ultrasound Image of Supraclavicular Brachial Plexus

1.2.1 High Frequency Probe; Short-Axis



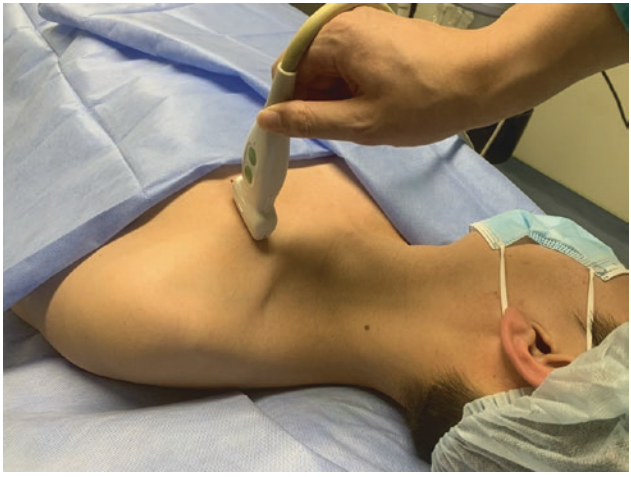
Probe position: horizontal plane, transverse on neck, just superior to the clavicle at midpoint



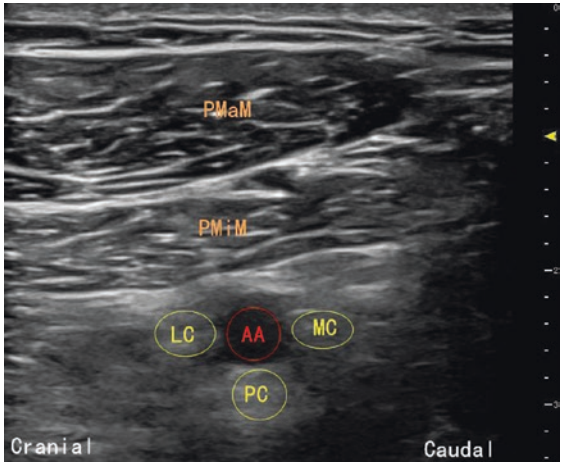
BP: brachial plexus; SA: subclavian artery; R1: first rib; P: pleura; M: medial; L: lateral

1.3 Ultrasound Image of Infraclavicular Brachial Plexus

1.3.1 High Frequency Probe; Short-Axis



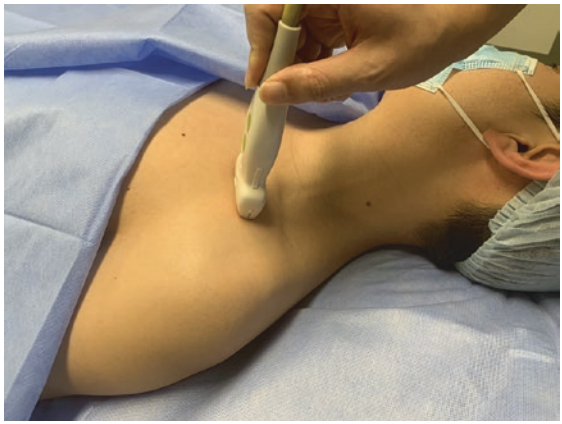
Probe position: parasagittal plane, medial to coracoid process, inferior to clavicle



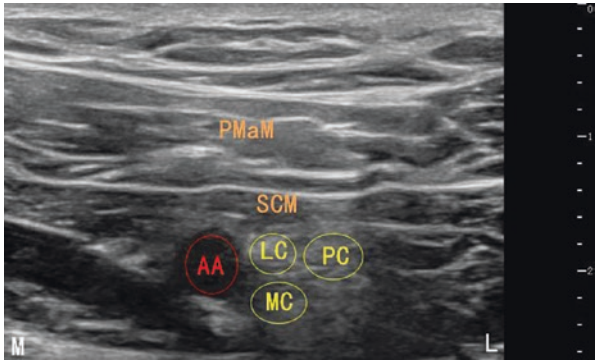
PMaM: pectoralis major muscle; PMiM: pectoralis minor muscle; LC: lateral cord; MC: medial cord; PC: posterior cord; AA: axillary artery

1.4 Ultrasound Image of Costoclavicular Brachial Plexus

1.4.1 High Frequency Probe; Short-Axis



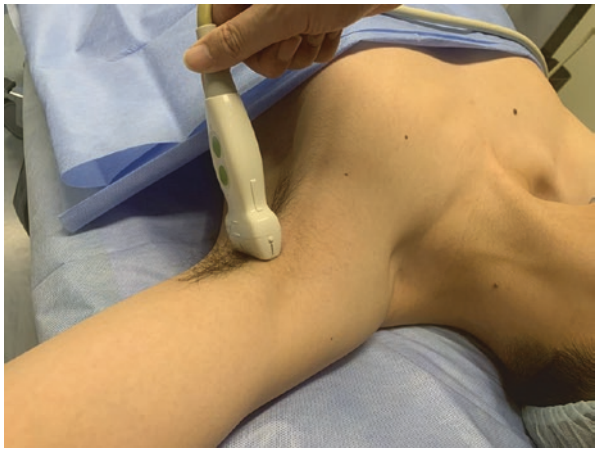
Probe position: horizontal plane, transverse on anterior chest wall, just inferior to the clavicle



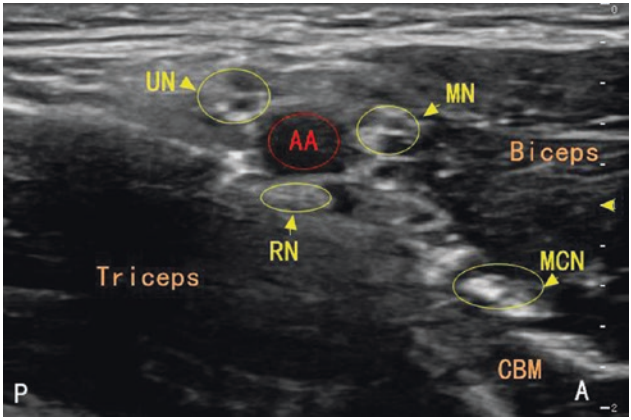
PMaM: pectoralis major muscle; BP: brachial plexus; AA: axillary artery; M: medial; L: lateral

1.5 Ultrasound Image of Axillary Brachial Plexus

1.5.1 High Frequency Probe; Short-Axis



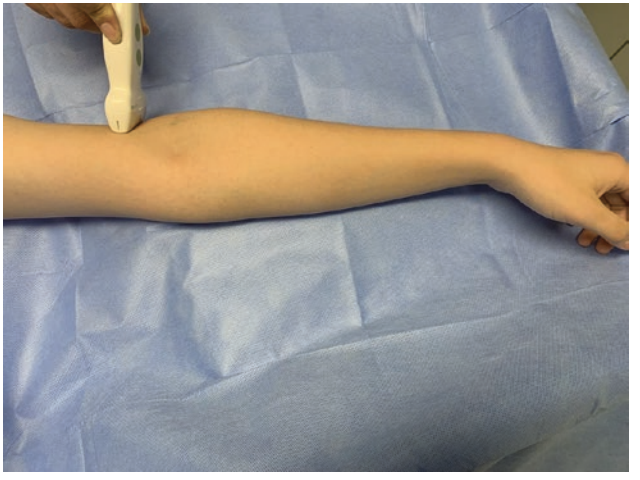
Probe position: short axis to arm, just distal to pectoralis major insertion



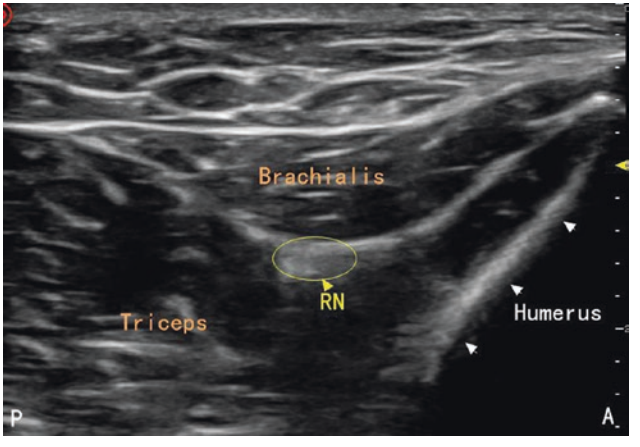
CBM: coracobrachialis muscle; MN: medial nerve; UN: ulnar nerve; RN: radial nerve; AA: axillary artery; P: posterior; A: anterior

2 Ultrasound Image of Radial Nerve

2.1 High Frequency Probe; Short-Axis

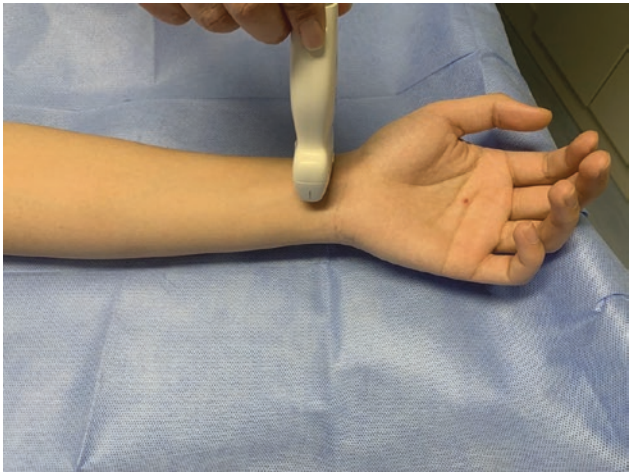


Probe position: short axis to the upper limb, transverse on the arm

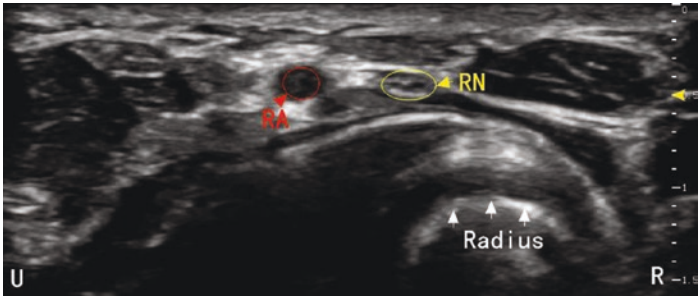


RN: radial nerve; P: posterior; A: anterior

2.2 High Frequency Probe; Short-Axis



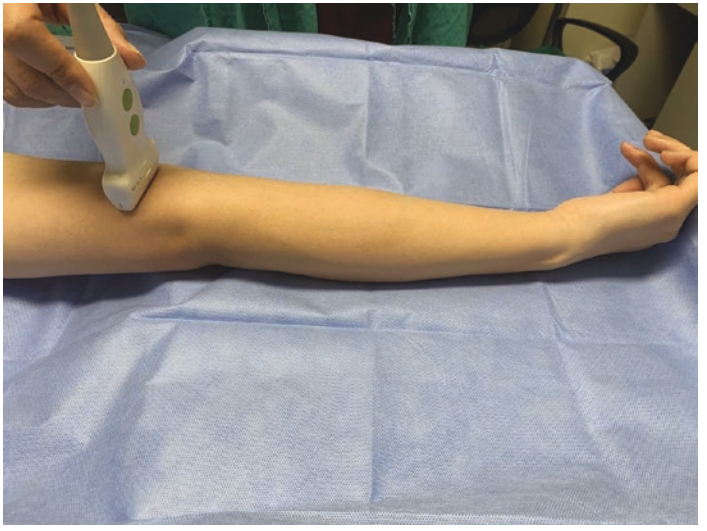
Probe position: short axis to the upper limb, transverse on the wrist



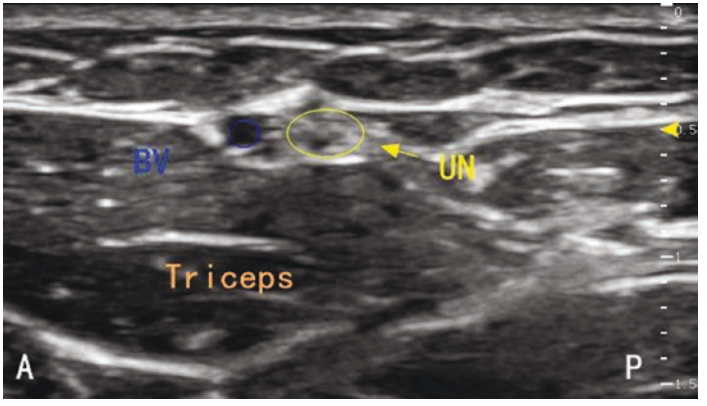
RN: radial nerve; RA: radial artery; U: ulnar; R: radialis

3 Ultrasound Image of Ulnar Nerve

3.1 High Frequency Probe; Short-Axis

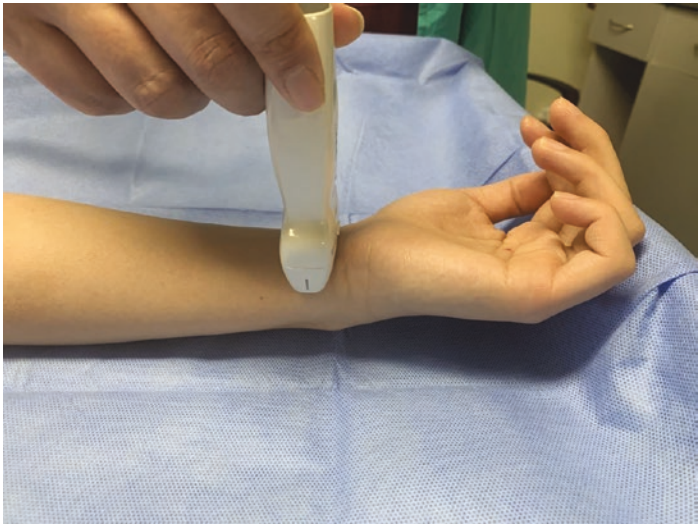


Probe position: short axis to the upper limb, transverse on the arm

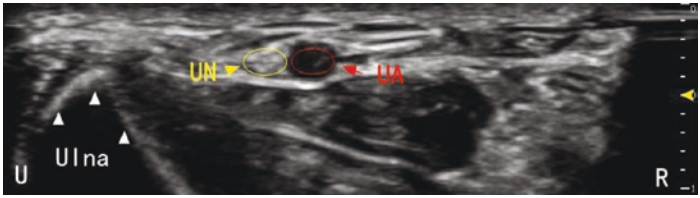


UN: ulnar nerve; BV: basilic vein; A: anterior; P: posterior

3.2 High Frequency Probe; Short-Axis



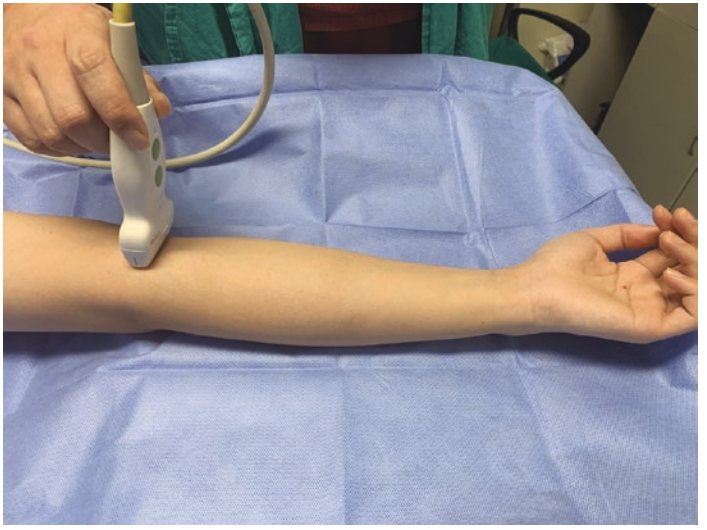
Probe position: short axis to the upper limb, transverse on the wrist



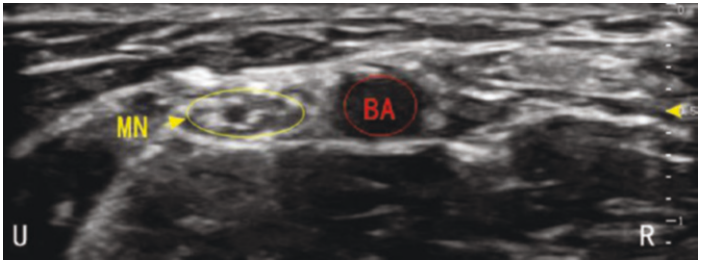
UN: ulnar nerve; UA: ulnar artery; U: ulnar; R: radialis

4 Ultrasound Image of Medial Nerve

4.1 High Frequency Probe; Short-Axis

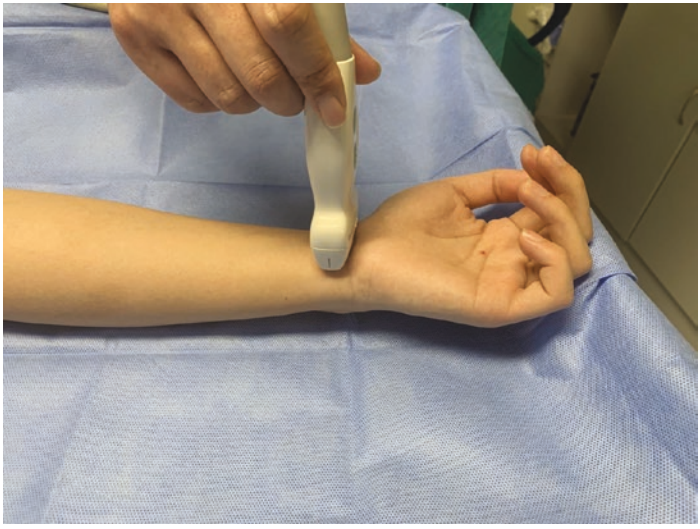


Probe position: short axis to the upper limb, transverse on the arm

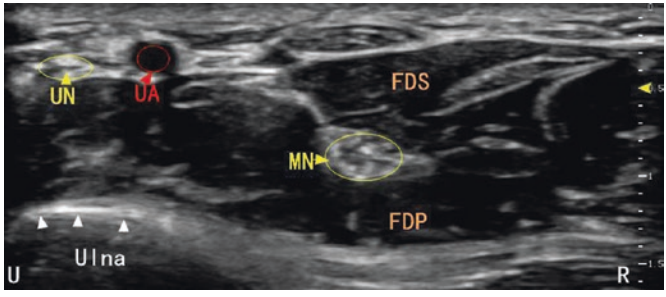


MN: medial nerve; BA: brachial artery; U: ulnar; R: radialis

4.2 High Frequency Probe; Short-Axis



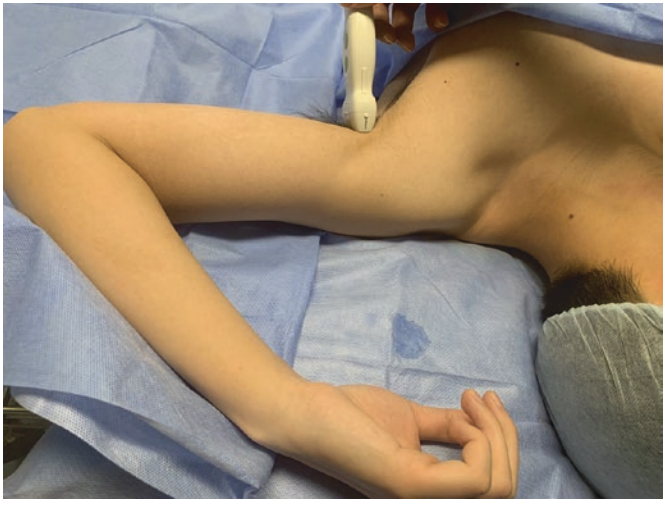
Probe position: short axis to the upper limb, transverse on the wrist



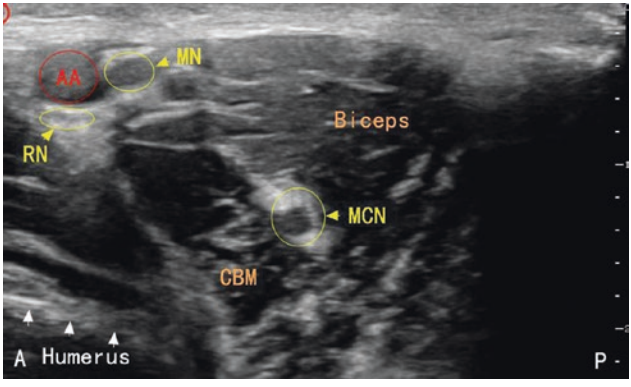
MN: medial nerve; UN: ulnar nerve; UA: ulnar artery; FDS: flexor digitorum superficialis; FDP: flexor digitorum progundus; U: ulnar; R: radialis

5 Ultrasound Image of Musculocutaneous Nerve

5.1 High Frequency Probe; Short-Axis



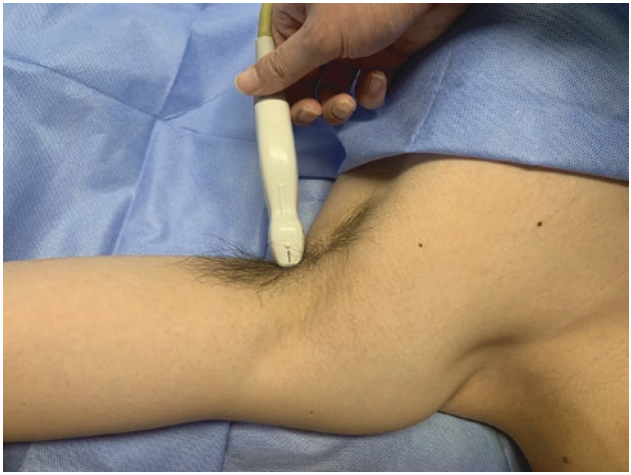
Probe position: short axis to arm, just distal to pectoralis major insertion



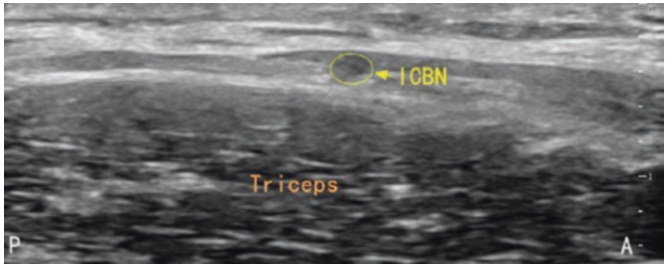
CBM: coracobrachial muscle; MCN: musculocutaneous nerve; MN: medial nerve; RN: radial nerve; AA: axillary artery; A: anterior; P: posterior

6 Ultrasound Image of Intercostobrachial Nerve

6.1 High Frequency Probe; Short-Axis

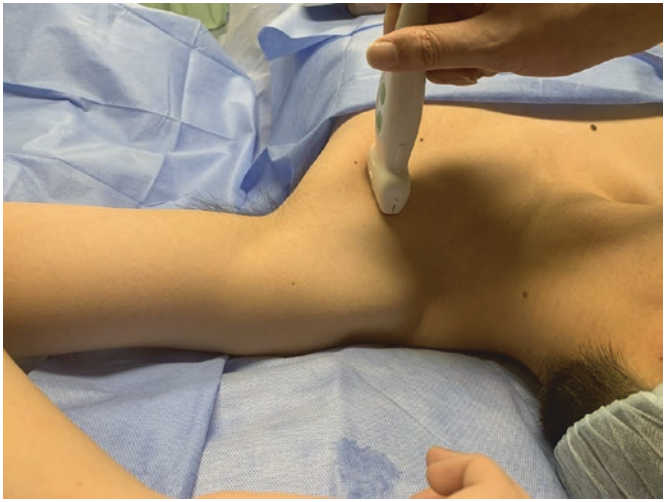


Probe position: horizontal plane, transverse on the proximal arm, just inferior to the axillary fossa

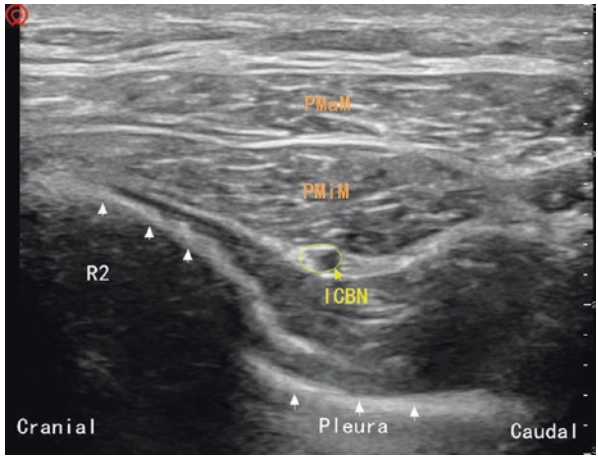


ICBN: intercostalbrachial nerve; P: posterior; A: anterior

6.2 High Frequency Probe; Short-Axis



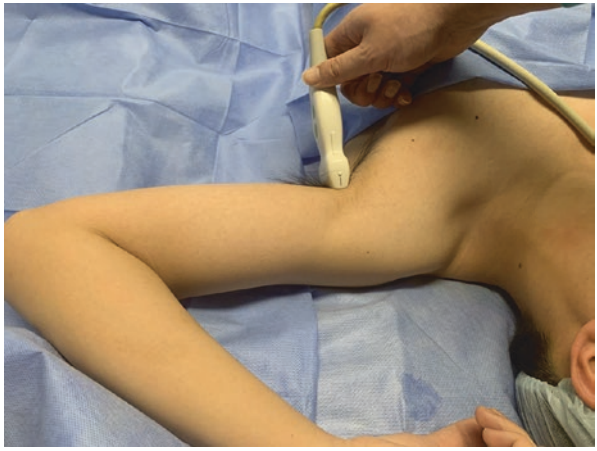
Probe position: parasagittal plane, just inferior to the clavicle, vertical to the second rib



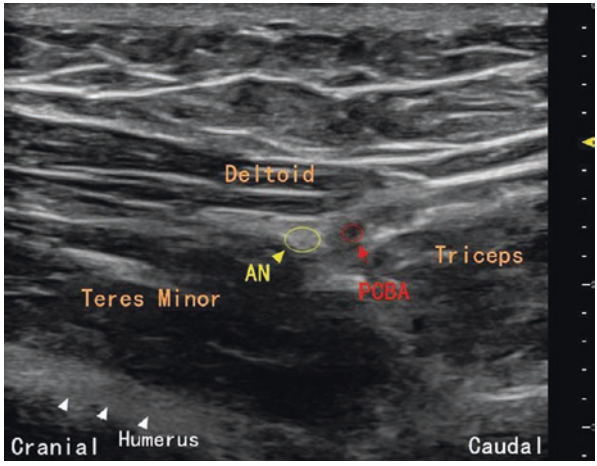
PMaM: pectoralis major muscle; PMiM: pectoralis minor muscle; ICBN: intercostalbrachial nerve; R2: second rib

7 Ultrasound Image of Axillary Nerve

7.1 High Frequency Probe; Short-Axis

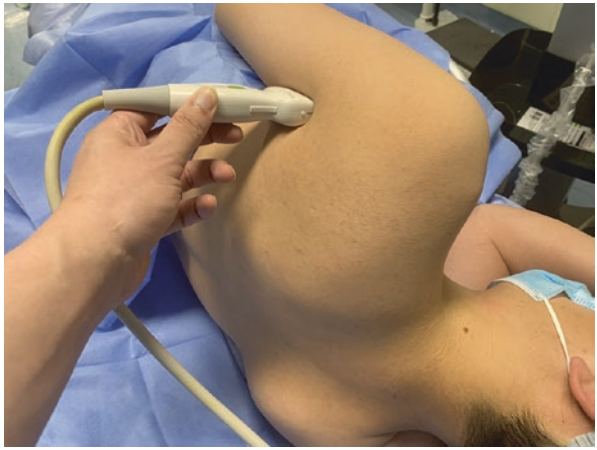


Probe position: long axis to arm, longitudinal on the back side of arm, just inferior to the axillary fossa

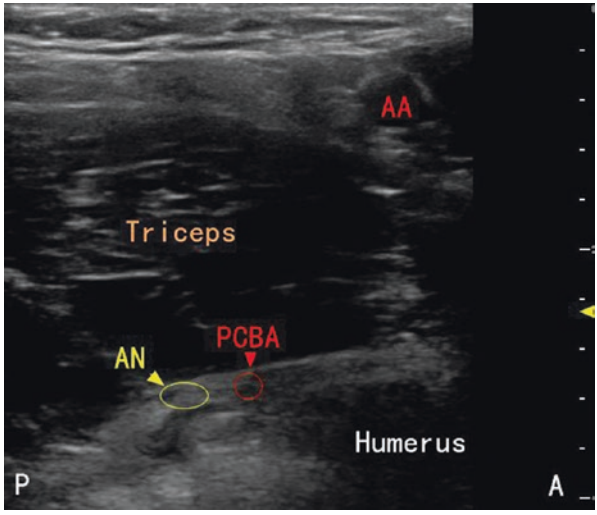


AN: axillary nerve; PCBA: posterior circumflex brachial artery

7.2 High Frequency Probe; Short-Axis



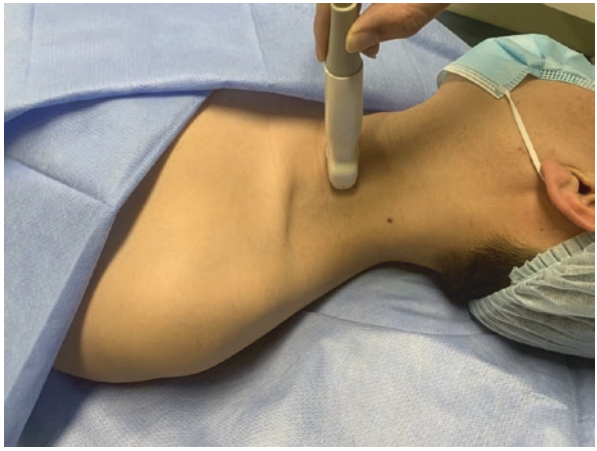
Probe position: short axis to arm, just distal to pectoralis major insertion



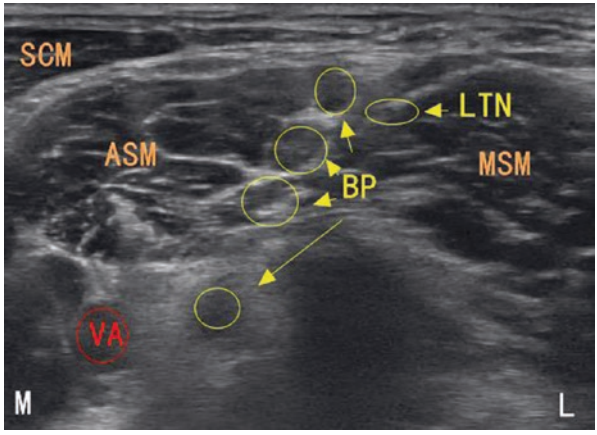
AN: axillary nerve; PCBA: posterior circumflex brachial artery, AA: axillary artery

8 Ultrasound Image of Long Thoracic Nerve

8.1 High Frequency Probe; Short-Axis

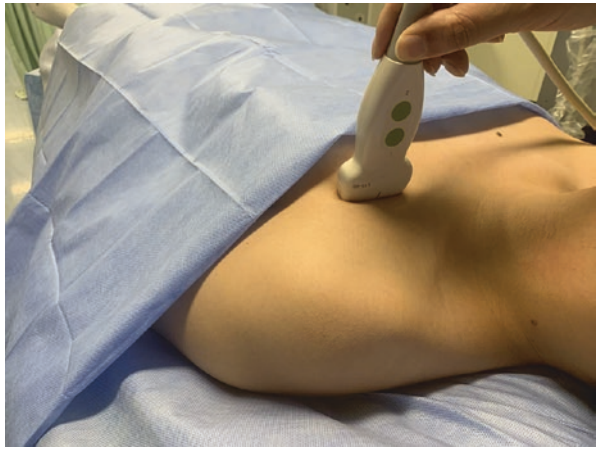


Probe position: horizontal plane, transverse on neck, 3–5 cm superior to clavicle, over external jugular vein

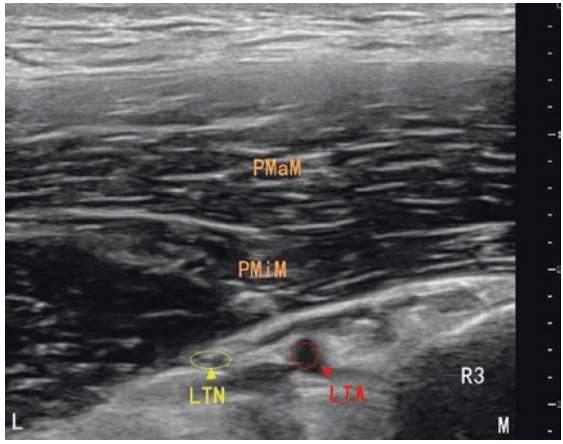


ASM: anterior scalene muscle; MSM: middle scalene muscle; BP: brachial plexus; LTN: long thoracic nerve; VA: vertebral artery; M: medial; L: lateral

8.2 High Frequency Probe; Short-Axis



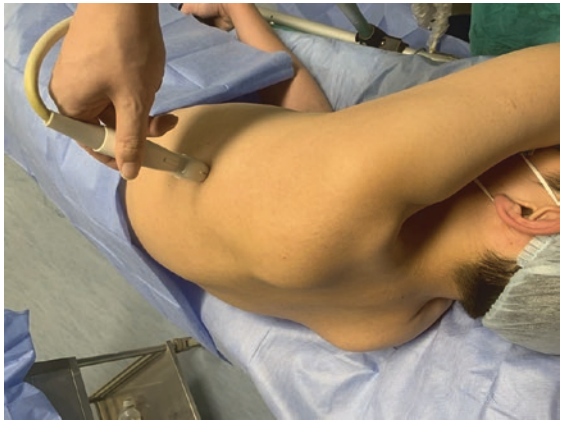
Probe position: horizontal plane, transverse on wall chest, medial to the anterior axillary line, at the third rib level



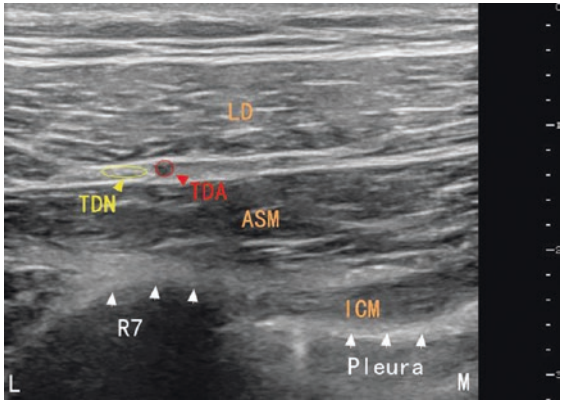
PMaM: pectoralis major muscle; PMiM: pectoralis minor muscle; LTN: long thoracic nerve; LTA: long thoracic artery; R3: third rib; L: lateral; M: medial

9 Ultrasound Image of Thoracodorsal Nerve

9.1 High Frequency Probe; Short-Axis



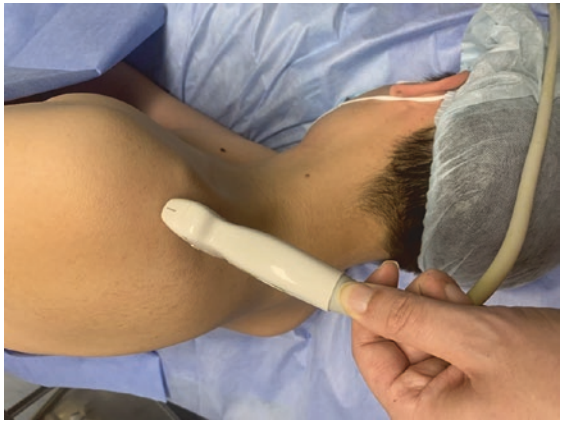
Probe position: coronal plane, longitudinal on the middle axillary line, just inferior to the scapula



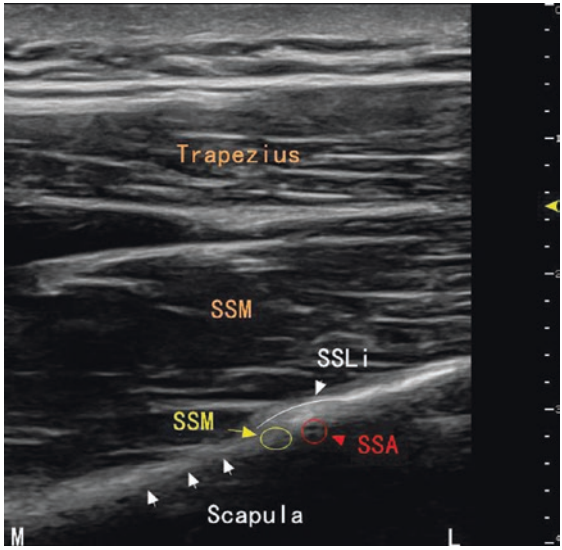
LD: latissimus dorsi; ASM: anterior serratus muscle; ICM: intercostal muscle; TDN: thoracodorsal nerve; TDA: thoracodorsal artery; R7: seventh rib; L: lateral; M: medial

10 Ultrasound Image of Suprascapular Nerve

10.1 High Frequency Probe; Short-Axis

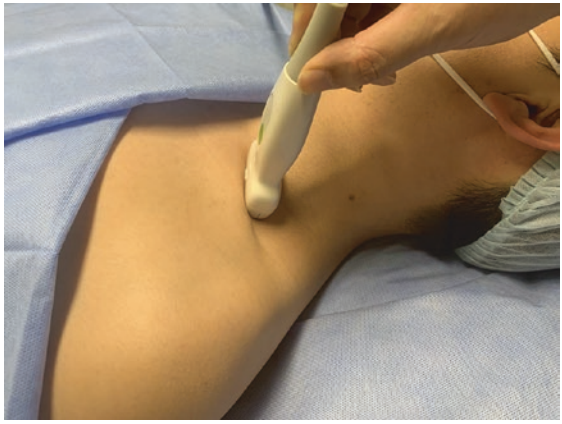


Probe position: transverse on superior margin of scapula

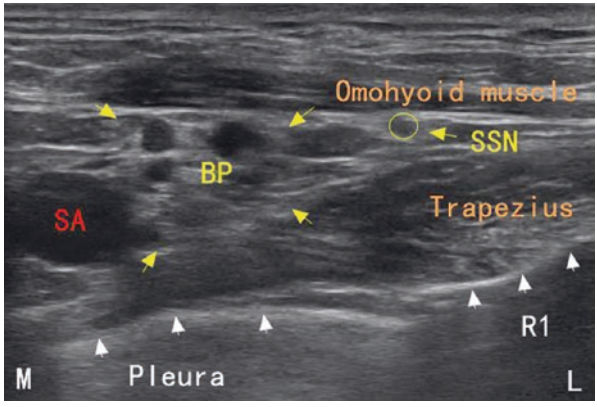


SSM: supraspinatus muscle; SSLi: suprascapular ligament; SSM: suprascapular nerve; SSA: suprascapular artery; M: medial; L: lateral

10.2 High Frequency Probe; Short-Axis



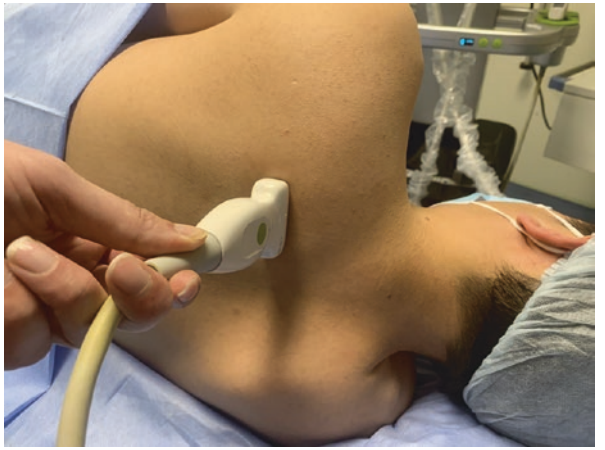
Probe position: horizontal plane, transverse on neck, just superior to the clavicle at midpoint



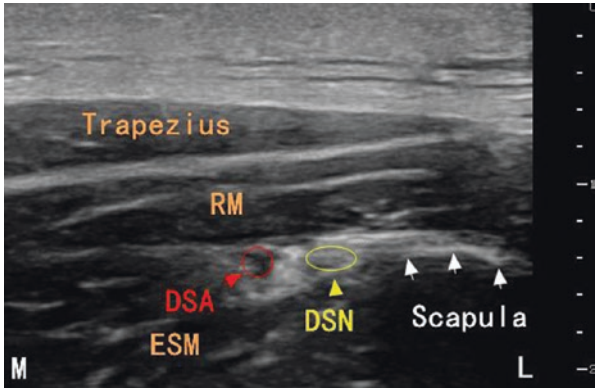
BP: brachial plexus; SSN: suprascapular nerve; SA: subclavian artery; R1: first rib; M: medial; L: lateral

11 Ultrasound Image of Dorsal Scapular Nerve

11.1 High Frequency Probe; Short-Axis



Probe position: horizontal plane, transverse on back, between the scapula and spine



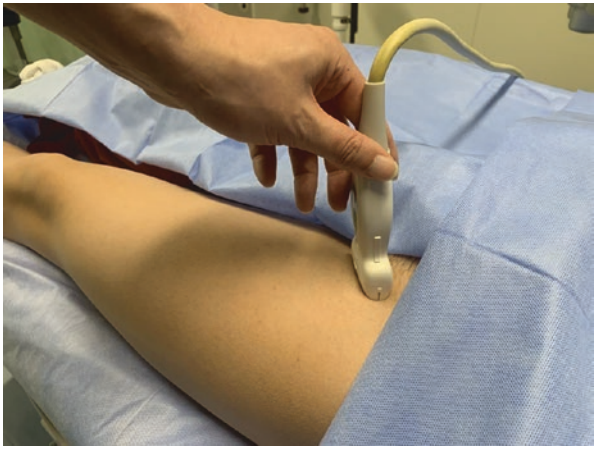
RM: rhomboid muscle; ESM: erector spinae muscle; DSA: dorsal scapular artery; DSN: dorsal scapular nerve; M: medial; L: lateral

Sonographic Image of Lower Extremity Regional Anesthesia

Shenyuan Zhou and Wei Jiang

1 Ultrasound Image of Femoral Nerve

1.1 High Frequency Probe; Short-Axis



Probe position: horizontal plane, middle aspect of thigh, transverse on the iliofemoral crease

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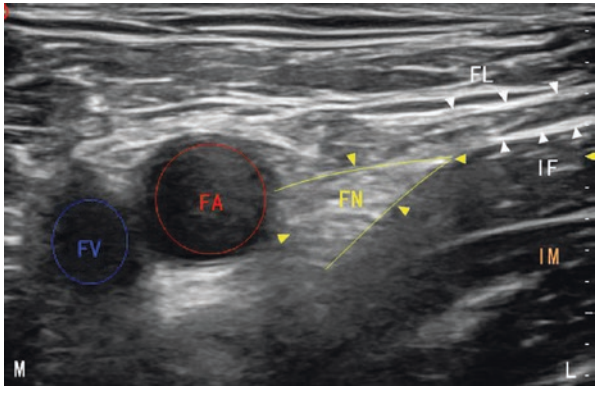
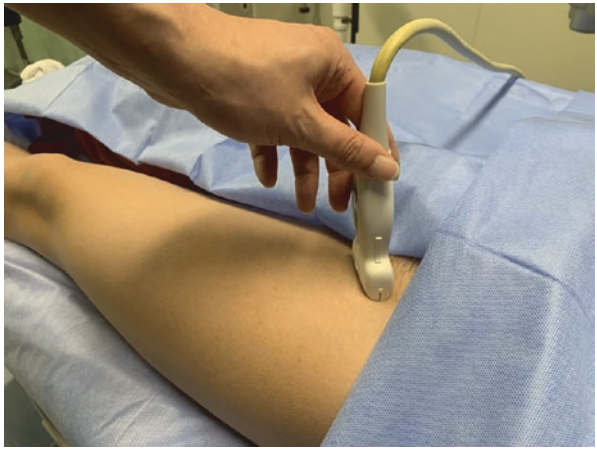
J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_4



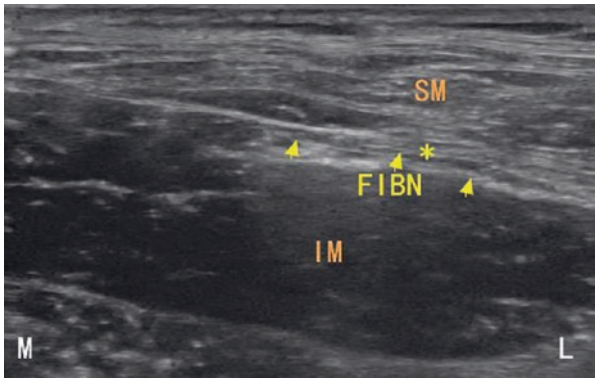
IM iliac muscle, *IF* iliac fascia, *FL* fascia lata, *FN* femoral nerve, *FA* femoral artery, *FV* femoral vein, *M* medial, *L* lateral

2 Ultrasound Image of Fascia Iliaca Block

2.1 High Frequency Probe; Short-Axis



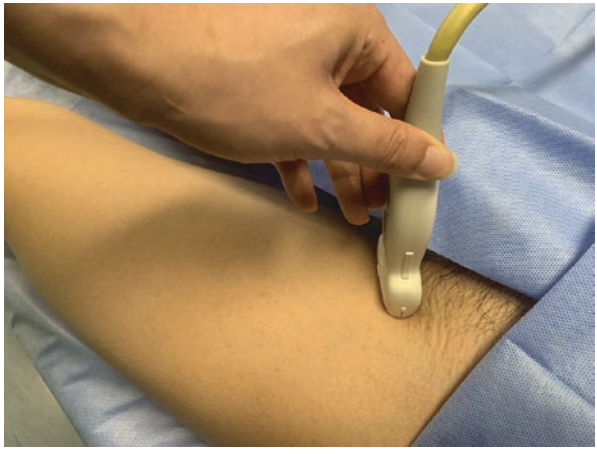
Probe position: horizontal plane, lateral aspect of thigh, transverse on the iliofemoral crease



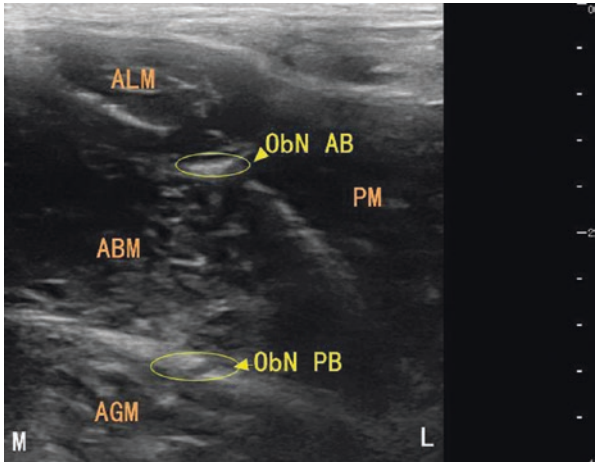
SM sartorius muscle, *MTFL* tensor fascia lata muscle, *IM* iliac muscle, *FIBN* fascia iliaca block, *M* medial, *L* lateral

3 Ultrasound Image of Obturator Nerve

3.1 High Frequency Probe; Short-Axis

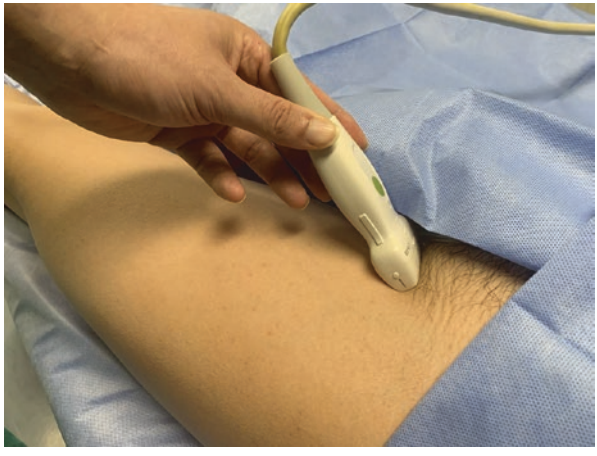


Probe position: horizontal plane, medial aspect of thigh, transverse on the iliofemoral crease

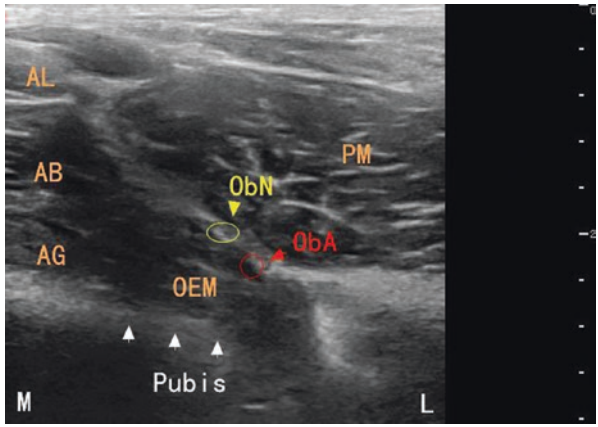


PM pectineus muscle, *ALM* adductor longus, *ABM* adductor brevis, *AGM* adductor magnus, *ObN AB* anterior branch of obturator nerve, *ObN PB* posterior branch of obturator nerve, *M* medial, *L* lateral

3.2 High Frequency Probe; Short-Axis



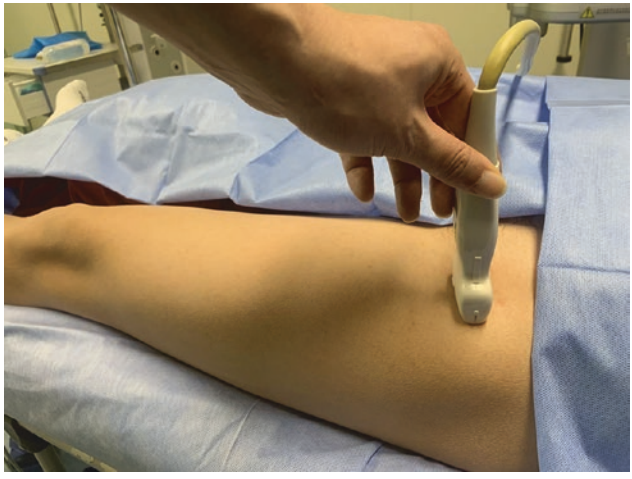
Probe position: horizontal plane, medial aspect of thigh, transverse on the iliofemoral crease



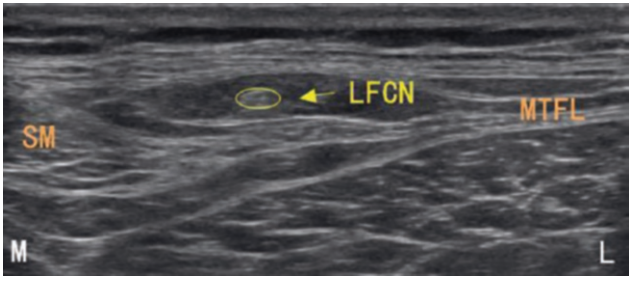
PM pectineus muscle, *ALM* adductor longus, *ABM* adductor brevis, *AGM* adductor magnus, *OEM* obturator externus muscle, *ObN* obturator nerve; *ObA* obturator artery, *M* medial, *L* lateral

4 Ultrasound Image of Lateral Femoral Cutaneous Nerve

4.1 High Frequency Probe; Short-Axis



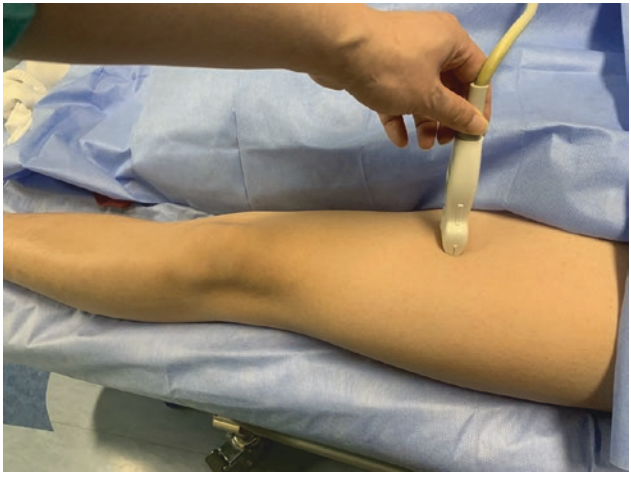
Probe position: horizontal plane, transverse on the proximal lateral thigh



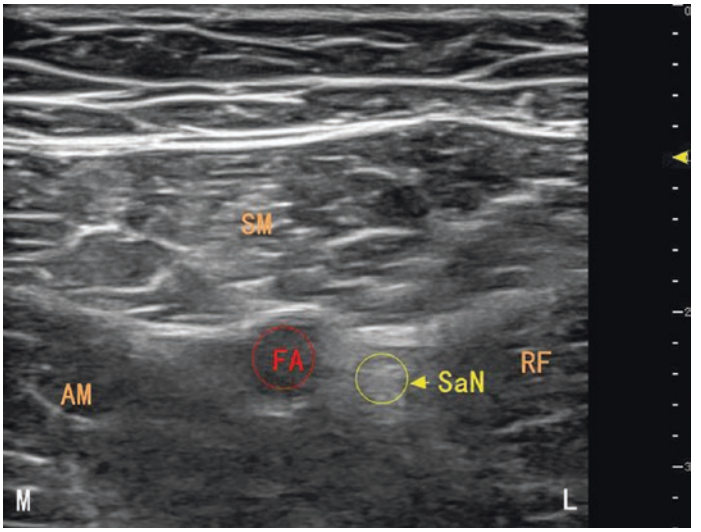
SM sartorius muscle, *MTFL* tensor fascia lata muscle, *LFCM* lateral femoral cutaneous nerve, *M* medial; *L* lateral

5 Ultrasound Image of Saphenous Nerve

5.1 High Frequency Probe; Short-Axis



Probe position: horizontal plane, transverse on anteromedial mid thigh

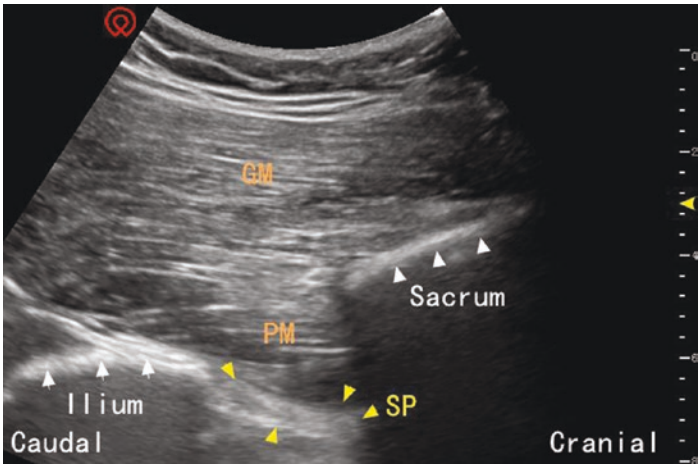


SM sartorius muscle, *RF* rectus femoris, *AM* adductor magnus, *FA* femoral artery, *SaN* saphenous nerve, *M* medial, *L* lateral

6 Ultrasound Image of Sacral Plexus

6.1 Low Frequency Probe; Long-Axis

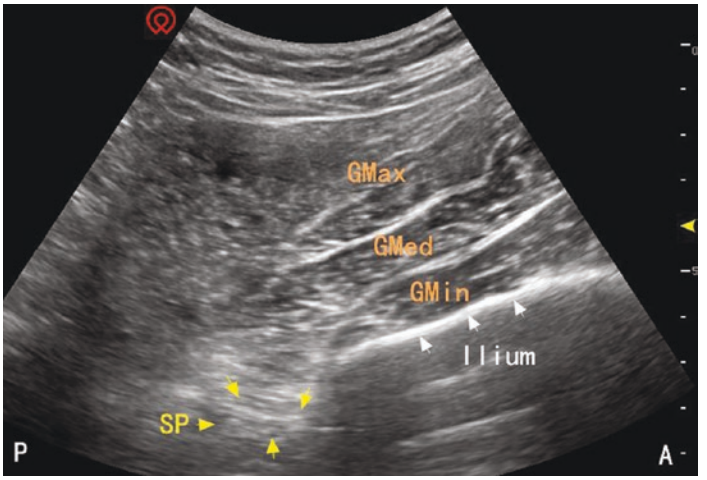
Probe position: transverse on the posterior buttock, between the posterior superior iliac spine and greater trochanter.



GM gluteus maximus, *PM* piriformis muscle, *SP* sacral plexus

6.2 Low Frequency Probe; Short-Axis

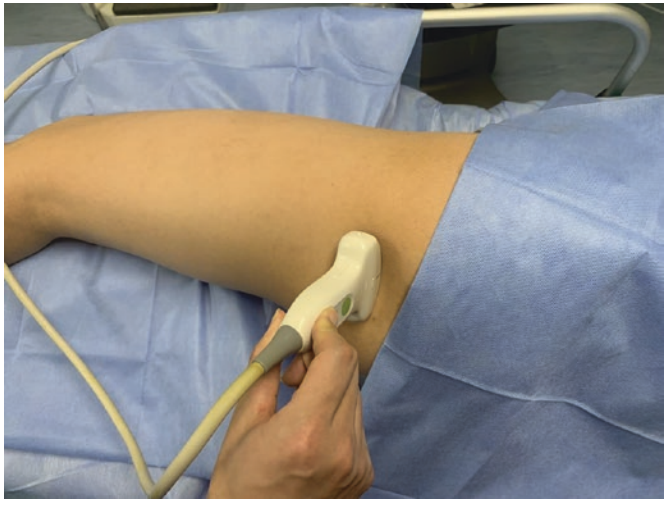
Probe position: horizontal plane, transverse on the proximal lateral aspect of thigh.



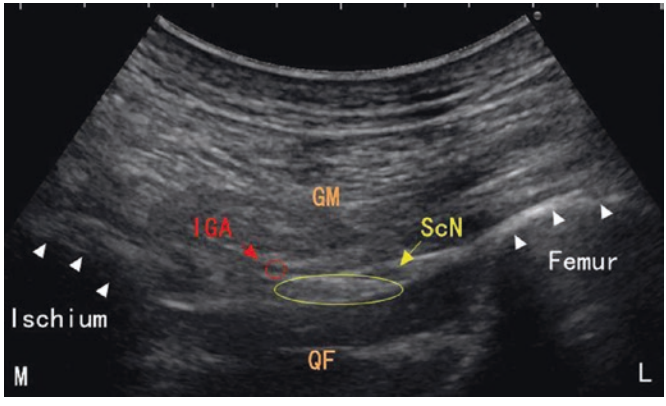
GMax gluteus maximus, *GMed* gluteus mediums, *GMin* gluteus miniums, *SP* sacral plexus, *P* posterior, *A* anterior

7 Ultrasound Image of Sciatic Nerve

7.1 Low Frequency Probe; Short-Axis

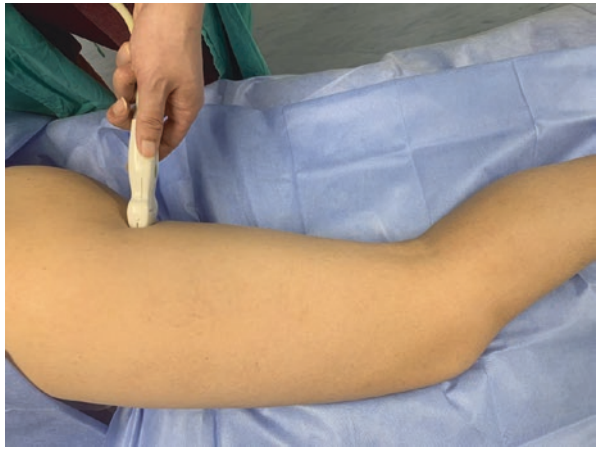


Probe position: horizontal plane, transverse on the posterior buttock, between the ischial tuberosity and greater trochanter

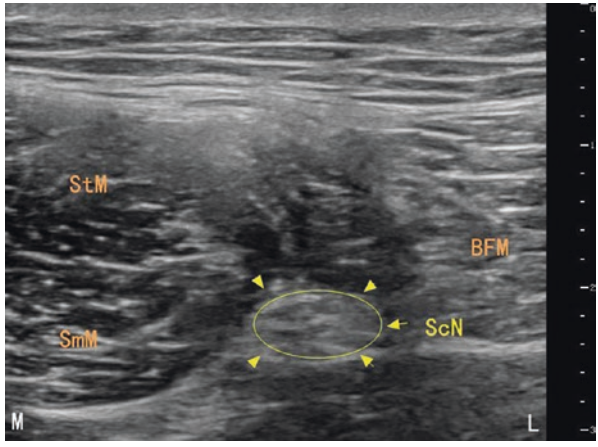


GM gluteus maximus, *QF* quadratus femoris, *ScN* sciatic nerve, *IGA* inferior gluteal artery, *M* medial, *L* lateral

7.2 High Frequency Probe; Short-Axis

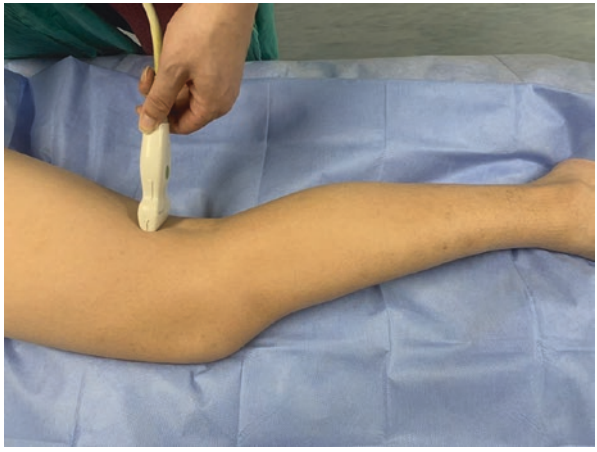


Probe position: horizontal plane, transverse on the proximal posto-lateral aspect of thigh

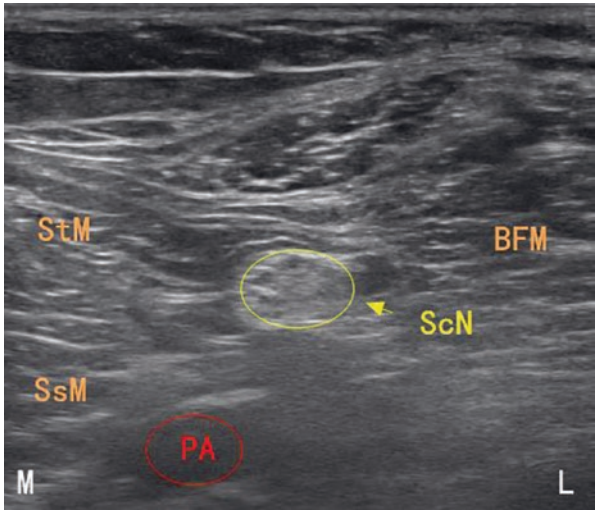


BFM biceps femoris muscle, *StM* semitendinosus muscle, *SmM* semimembranosus muscle, *ScN* sciatic nerve, *M* medial, *L* lateral

7.3 High Frequency Probe; Short-Axis



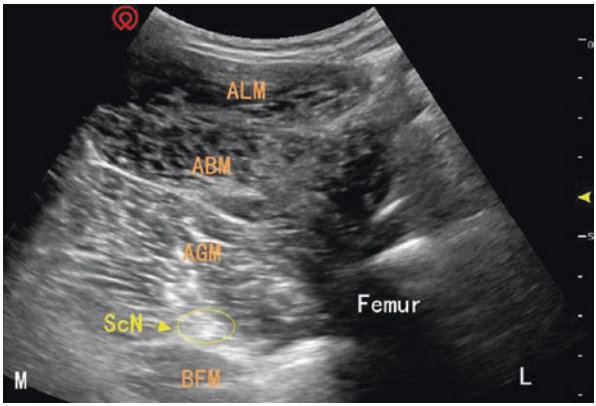
Probe position: horizontal plane, transverse on the thigh, 4–5 cm over popliteal fossa



BFM biceps femoris muscle, *StM* semitendinosus muscle, *SmM* semimembranosus muscle, *ScN* sciatic nerve, *PA* popliteal artery, *M* medial, *L* lateral

7.4 Low Frequency Probe; Short-Axis

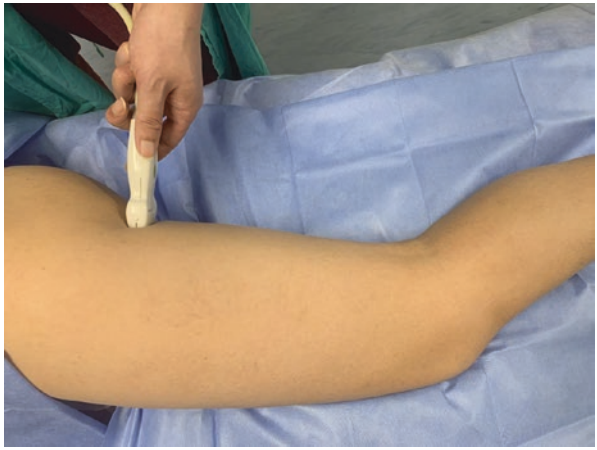
Probe position: horizontal plane, transverse on the proximal medial thigh.



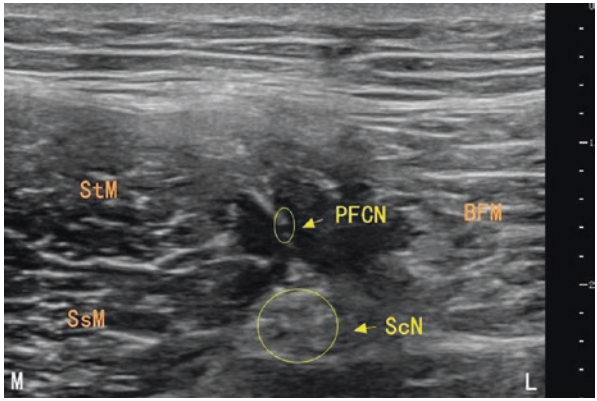
ALM adductor longus, *ABM* adductor brevis, *AGM* adductor magnus, *BF* biceps femoris, *ScN* sciatic nerve, *M* medial, *L* lateral

8 Ultrasound Image of Posterior Femoral Cutaneous Nerve

8.1 High Frequency Probe; Short-Axis



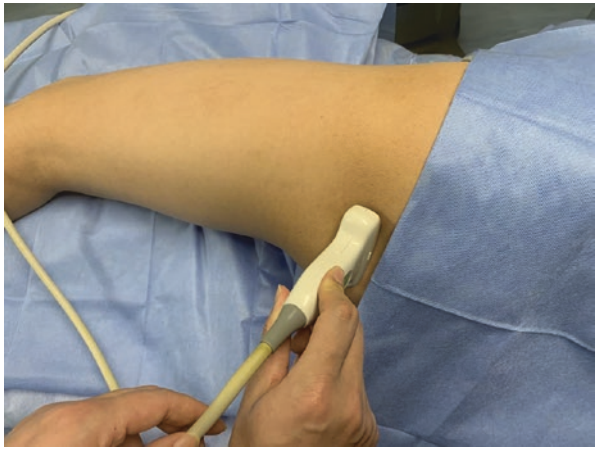
Probe position: horizontal plane, transverse on the proximal posto-lateral aspect of thigh



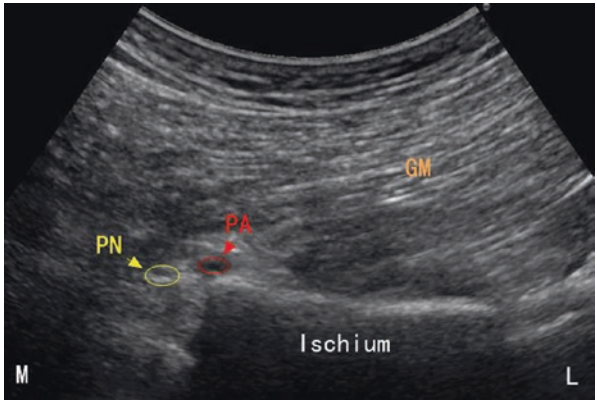
BFM biceps femoris muscle, *StM* semitendinosus muscle, *SmM* semimembranosus muscle, *ScN* sciatic nerve, *PFCN* posterior femoral cutaneous nerve, *M* medial, *L* lateral

9 Ultrasound Image of Pudendal Nerve

9.1 Low Frequency Probe; Short-Axis



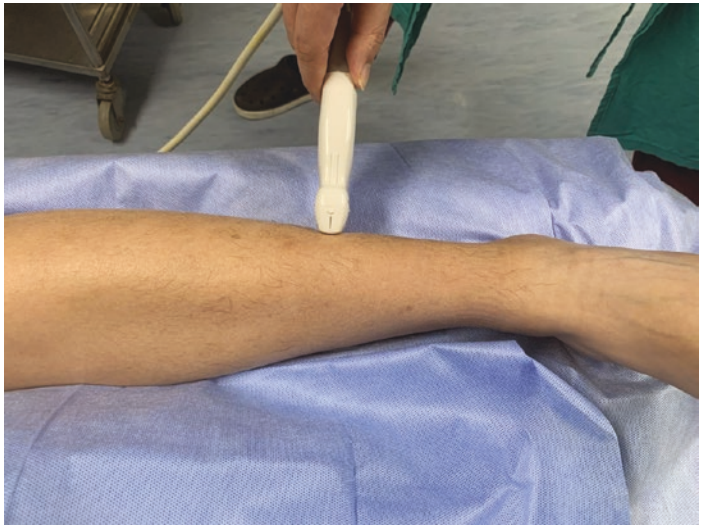
Probe position: horizontal plane, transverse on the posterior buttock



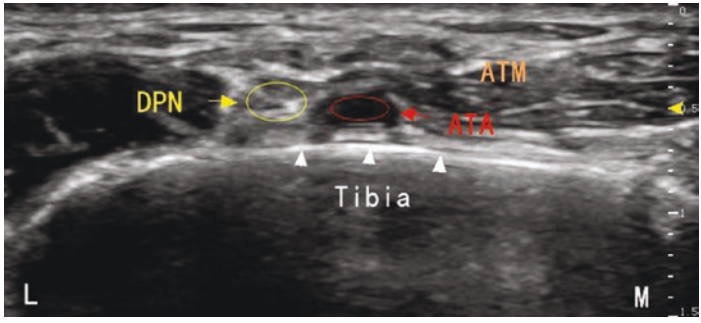
GM gluteus maximus, *PN* pudendal nerve, *ScN* sciatic nerve, *PA* pudendal artery, *M* medial, *L* lateral

10 Ultrasound Image of Peroneal Nerve

10.1 High Frequency Probe; Short-Axis

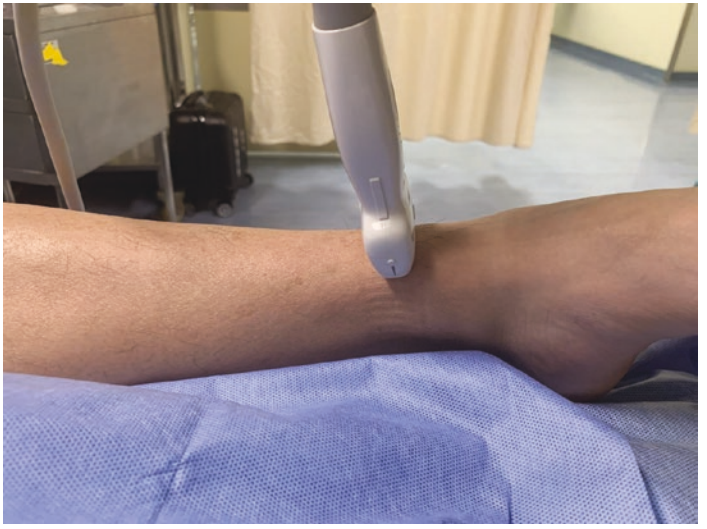


Probe position: transverse on the leg, approximately 5 cm proximal to the lateral malleolus

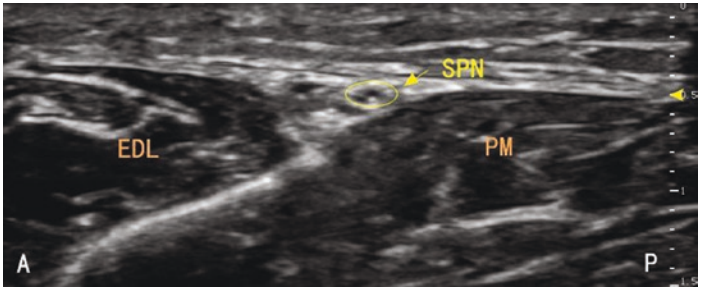


ATM anterior tibial muscle, *DPN* deep peroneal nerve, *ATA* anterior tibial artery, *L* lateral, *M* medial

10.2 High Frequency Probe; Short-Axis

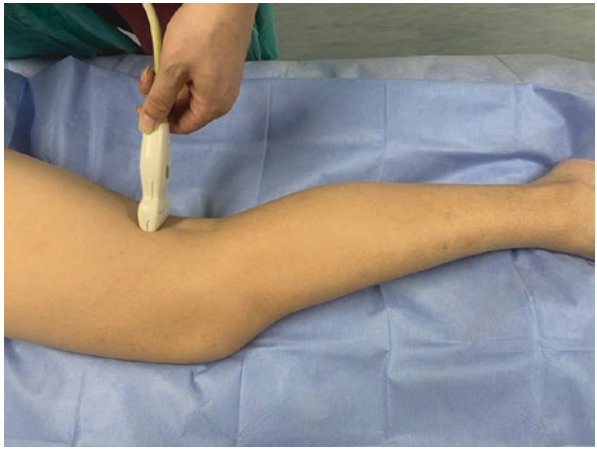


Probe position: transverse orientation at the level of the extensor retinaculum

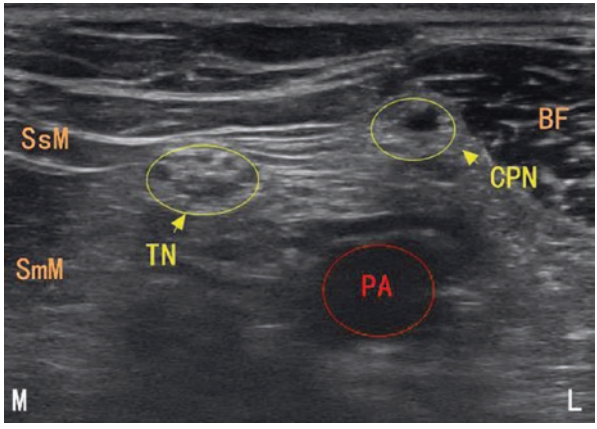


PM peroneal muscle, *EDL* extensor digitorum longus, *SPN* superficial peroneal nerve, *A* anterior, *P* posterior

10.3 High Frequency Probe; Short-Axis



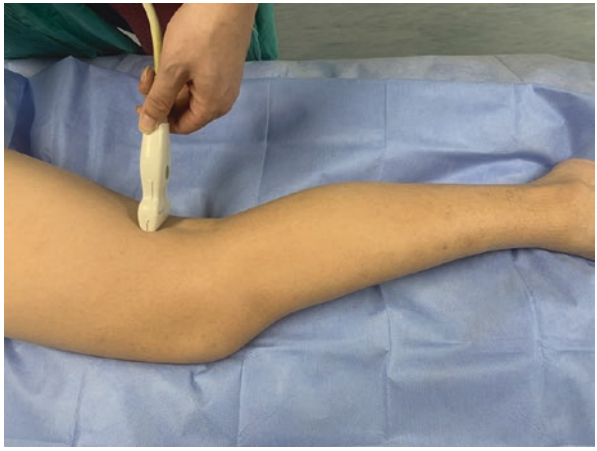
Probe position: horizontal plane, transverse on the thigh, 1–2 cm over popliteal fossa



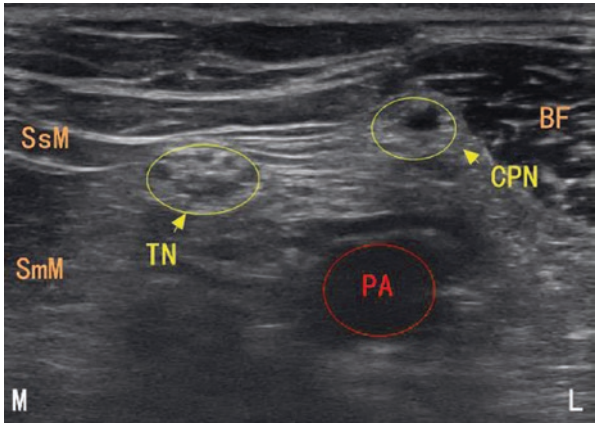
BFM biceps femoris muscle, *StM* semitendinosus muscle, *SmM* semimembranosus muscle, *TN* tibial nerve, *CPN* common peroneal nerve, *PA* popliteal artery, *M* medial, *L* lateral

11 Ultrasound Image of Tibial Nerve

11.1 High Frequency Probe; Short-Axis

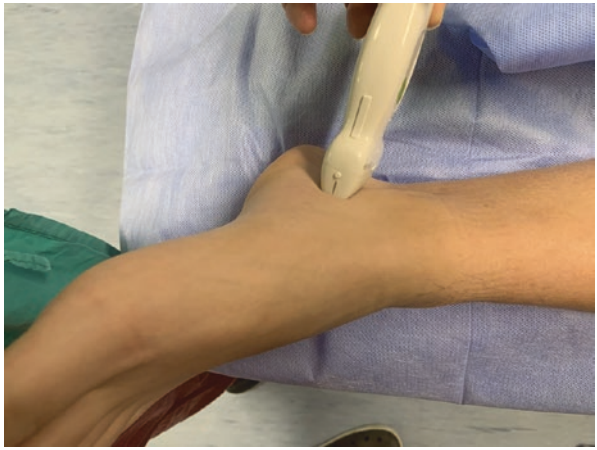


Probe position: probe position: horizontal plane, transverse on the thigh, 1–2 cm over popliteal fossa

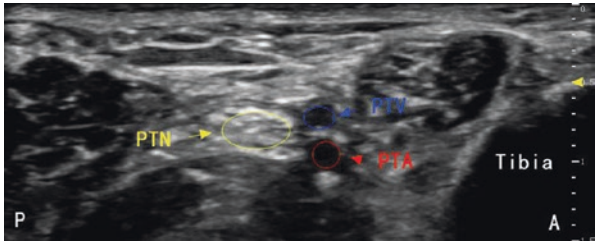


BFM biceps femoris muscle, *StM* semitendinosus muscle, *SmM* semimembranosus muscle, *TN* tibial nerve, *CPN* common peroneal nerve, *PA* popliteal artery, *M* medial, *L* lateral

11.2 High Frequency Probe; Short-Axis



Probe position: transverse posto-inferior to the medial malleolus



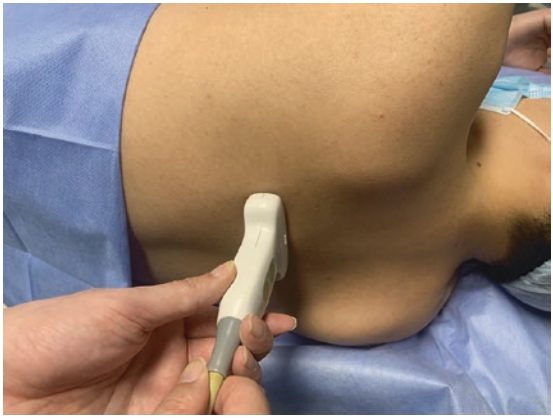
PTN posterior tibial nerve, *PTA* posterior tibial artery, *PTV* posterior tibial vein, *P* posterior, *A* anterior

Sonographic Image of Thoracic Spine and Chest Regional Anesthesia

Shenyuan Zhou and Wei Jiang

1 Ultrasound Image of Thoracic Paravertebral Space

1.1 Low Frequency Probe; Short-Axis



Probe position: horizontal plane, transverse just lateral to the spinous process at the back

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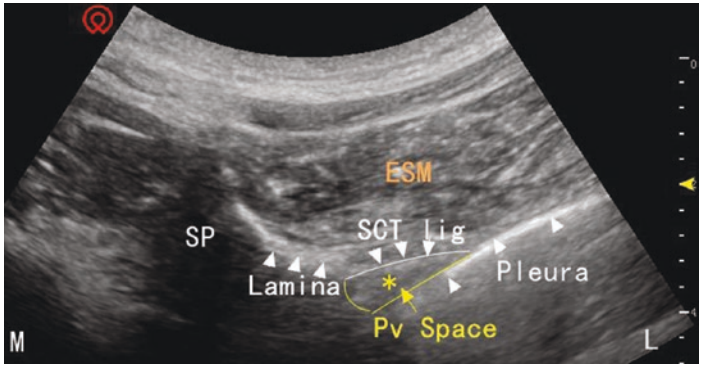
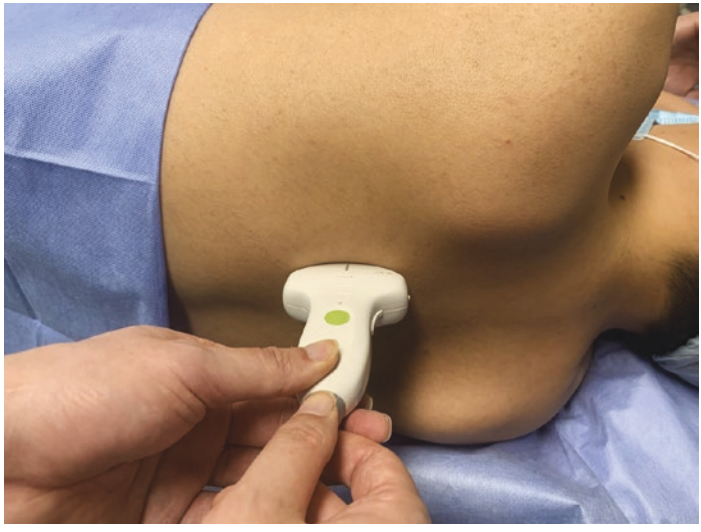
J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_5

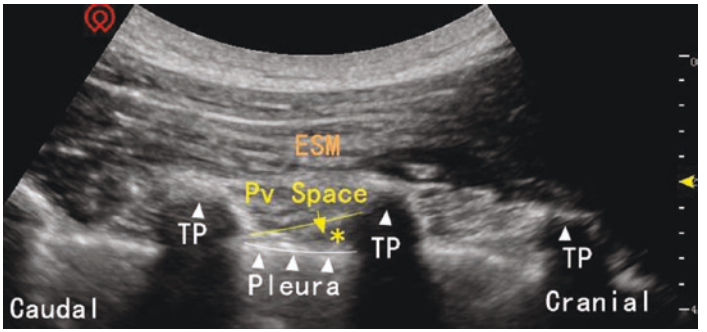


ESM erector spinae muscle, *Pv space* paravertebral space, *SCT lig* superior costotransverse ligament, *M* medial, *L* lateral

1.2 Low Frequency Probe; Long-Axis



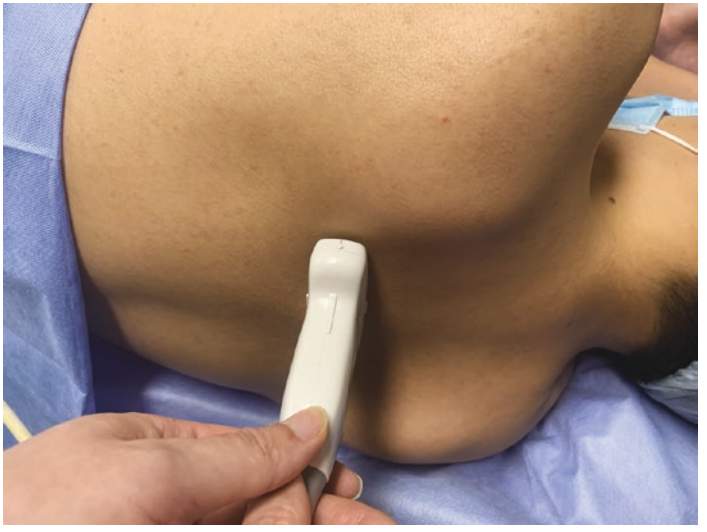
Probe position: parasagittal plane, approximately 1–2 cm lateral to the spinous process at the back



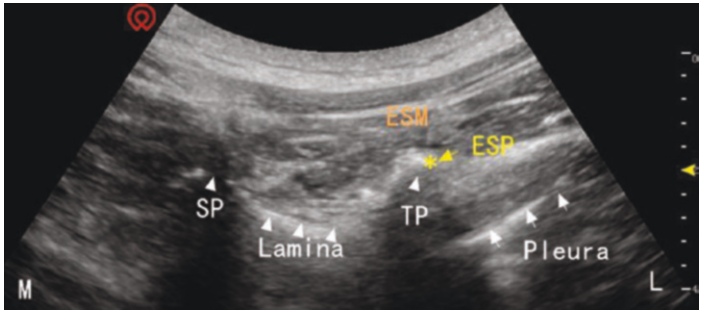
ESM erector spinae muscle, *Pv space* paravertebral space, *TP* transverse process

2 Ultrasound Image of Erector Spinae Plane

2.1 Low Frequency Probe; Short-Axis

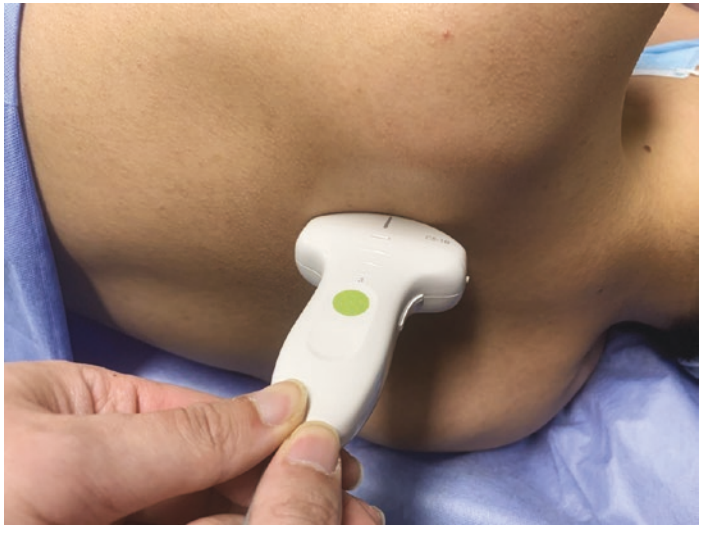


Probe position: horizontal plane, transverse just lateral to the spinous process at the back

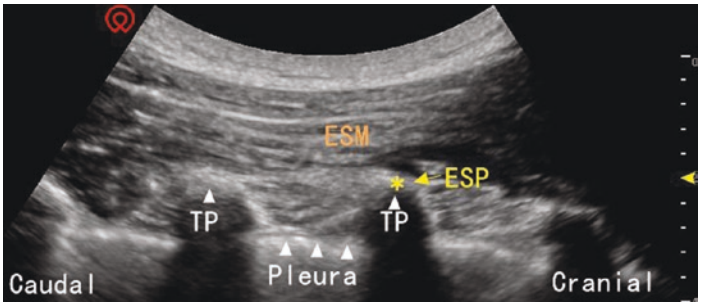


ESM erector spinae muscle, *ESP* erector spinae plane block, *SP* spinous process, *TP* transverse process, *M* medial, *L* lateral

2.2 Low Frequency Probe; Long-Axis



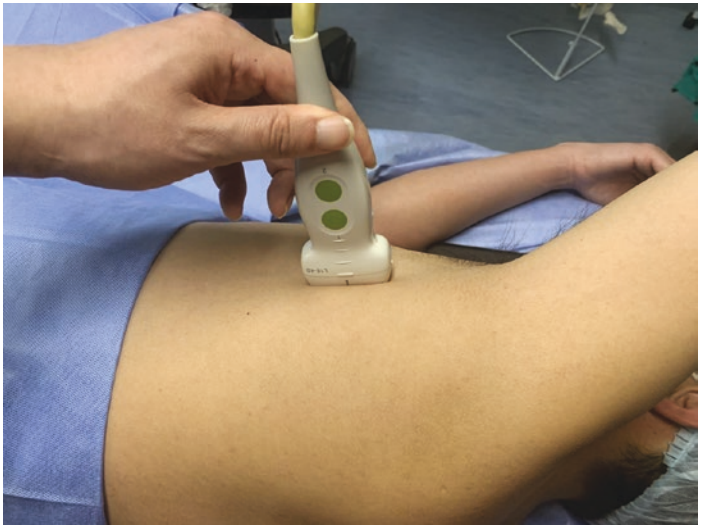
Probe position: parasagittal plane, approximately 3–4 cm lateral to the spinous process at the back



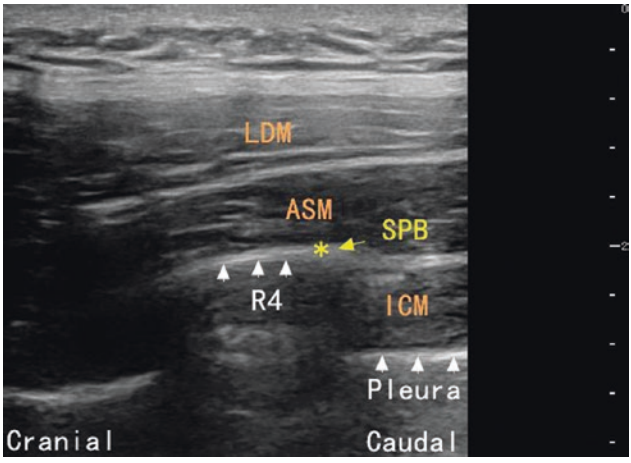
ESM erector spinae muscle, *ESP* erector spinae plane block, *TP* transverse process

3 Ultrasound Image of Serratus Plane

3.1 High Frequency Probe; Short-Axis



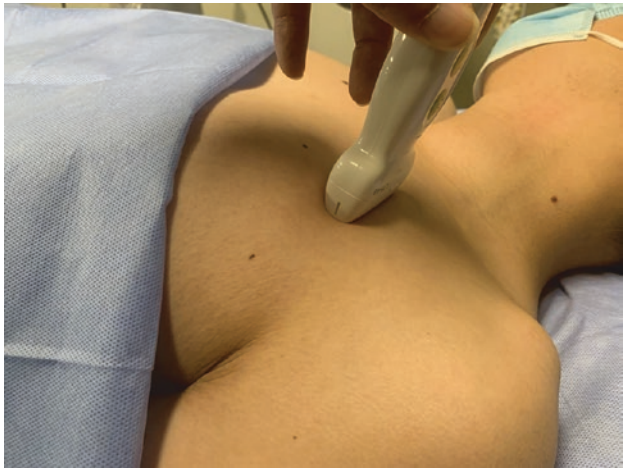
Probe position: coronal plane, longitudinal on the middle axillary line, just inferior to the axillary fossa



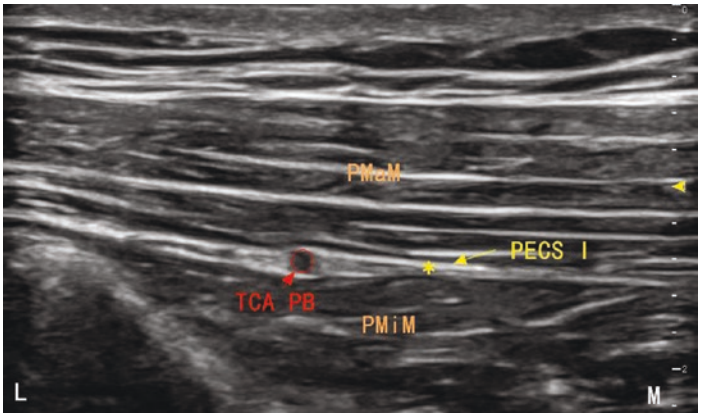
LDM latissimus dorsi, *ASM* anterior serratus muscle, *ICM* intercostal muscle, *SPB* serratus plane block, *R4* 4th rib

4 Ultrasound Image of Pectoralis Plane Blocks

4.1 High Frequency Probe

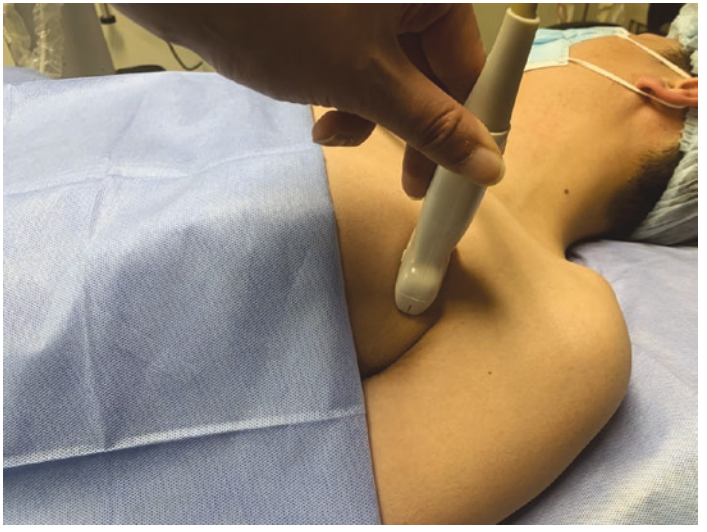


Probe position: horizontal plane, transverse on anterior chest wall

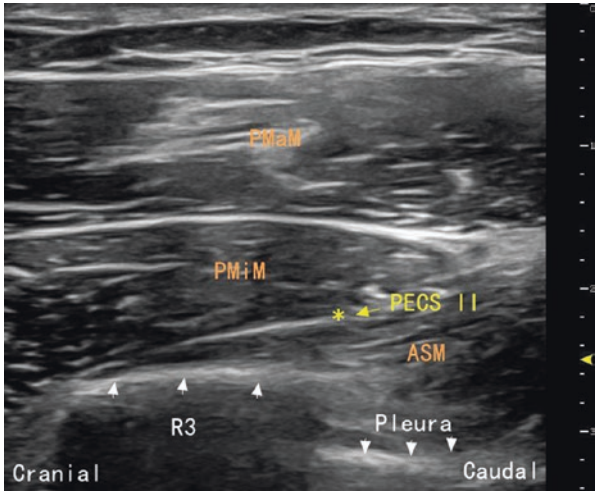


PMaM pectoralis major muscle, *PMiM* pectoralis minor muscle, *TCA PB* pectoracromial branch of thoracoacromial artery, *PECS I* pectoralis block I, *L* lateral, *M* medial

4.2 High Frequency Probe



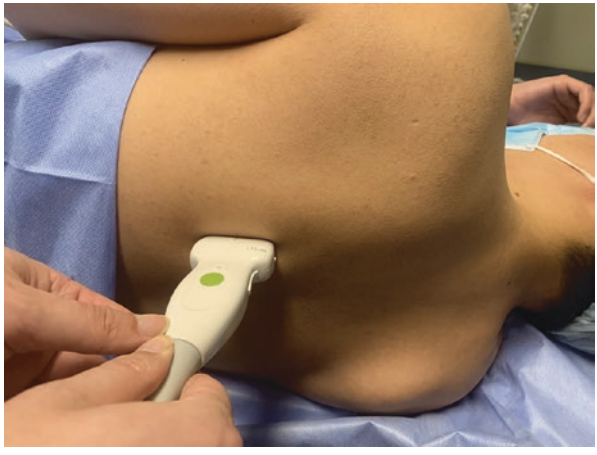
Probe position: horizontal plane, transverse on anterior chest wall, just medial to the anterior axillary line



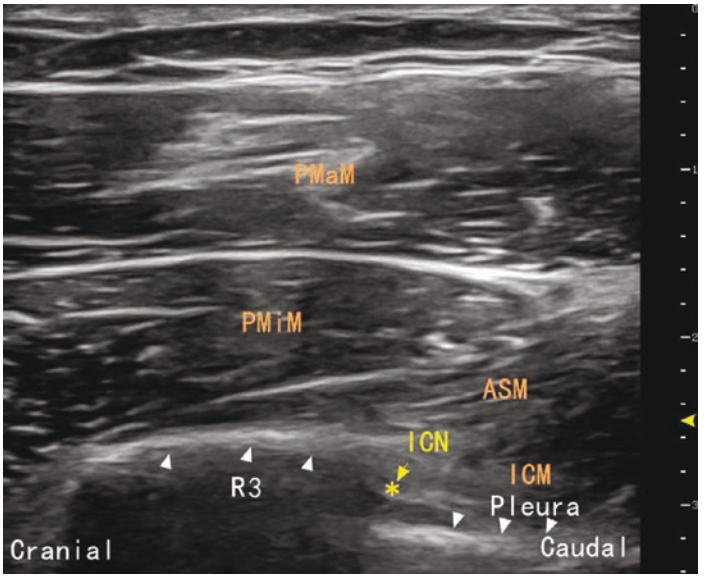
PMaM pectoralis major muscle, *PMiM* pectoralis minor muscle, *ASM* anterior serratus muscle, *PECS II* pectoralis block II, *R3* 3rd rib

5 Ultrasound Image of Intercostal Nerve

5.1 High Frequency Probe; Short-Axis



Probe position: parasagittal or coronal plane, vertical to the rib



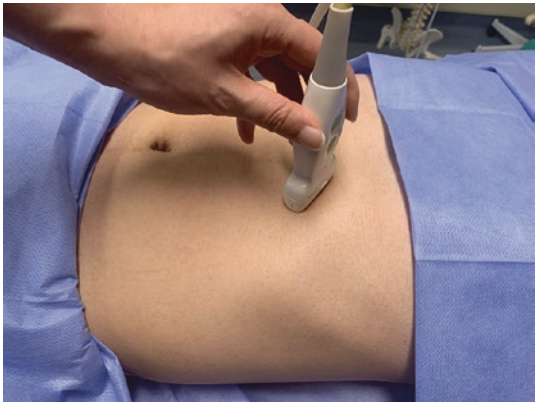
PMaM pectoralis major muscle, *PMiM* pectoralis minor muscle, *ASM* anterior serratus muscle, *ICM* intercostal muscle, *ICN* intercostal nerve

Sonographic Image of Lumbar-Sacral Spine and Abdomen Regional Anesthesia

Shenyuan Zhou and Wei Jiang

1 Ultrasound Image of Transversus Abdominis Plane

1.1 High Frequency Probe; Short-Axis



Probe position: horizontal plane, transverse on the anterior abdominal wall, just inferior to the costal margin

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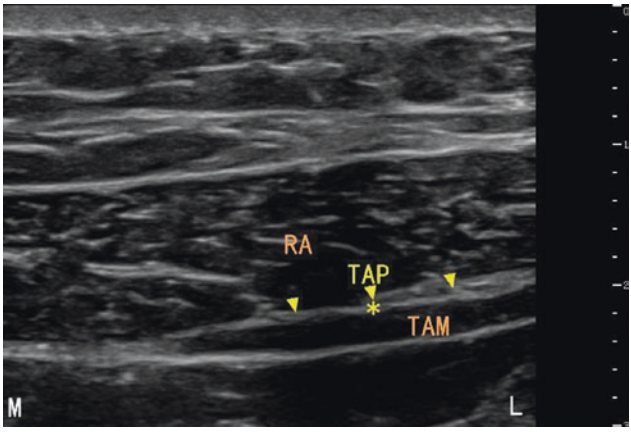
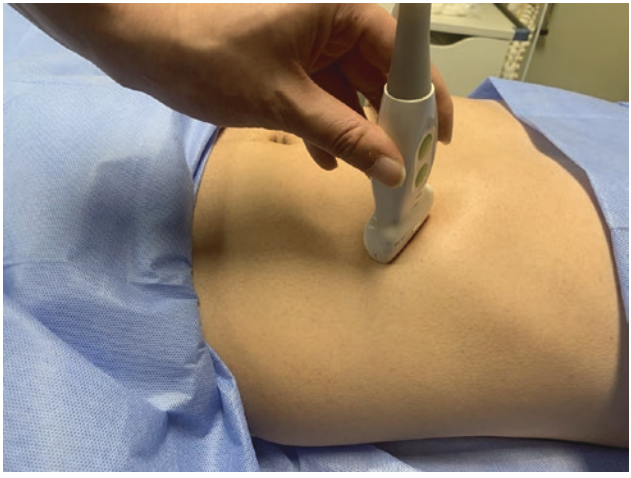
J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_6

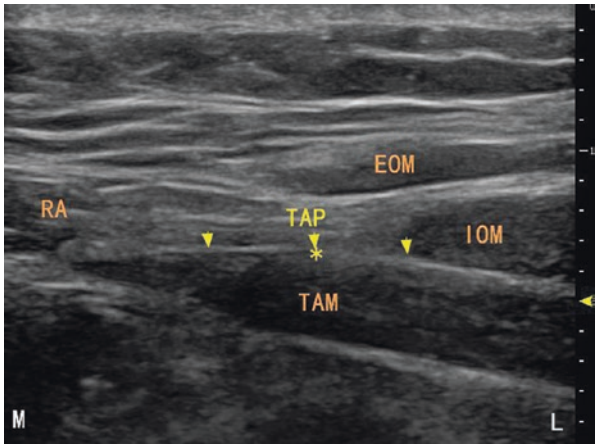


RA rectus abdominis, *TAM* transversus abdominis, *TAP* transversus abdominis plane block, *L* lateral, *M* medial

1.2 High Frequency Probe; Short-Axis

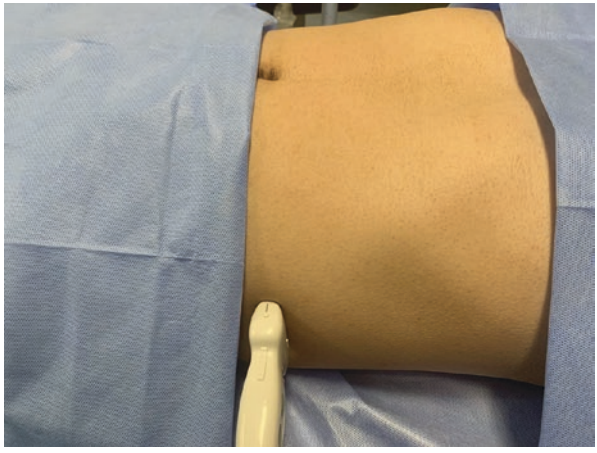


Probe position: horizontal plane, transverse on the anto-lateral abdominal wall, just inferior to the costal margin

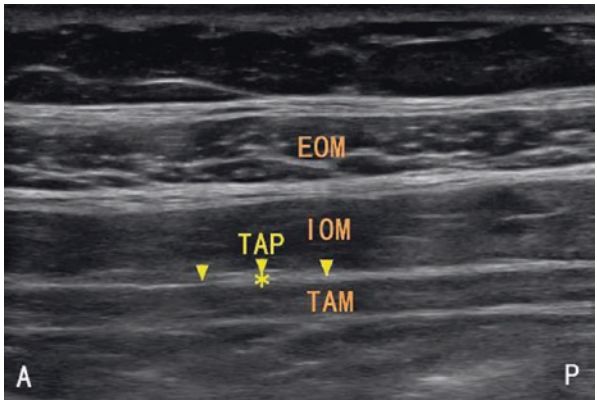


RA rectus abdominis, *EOM* external oblique muscle, *IOM* internal oblique muscle, *TAM* transversus abdominis, *TAP* transversus abdominis plane block, *L* lateral, *M* medial

1.3 High Frequency Probe; Short-Axis



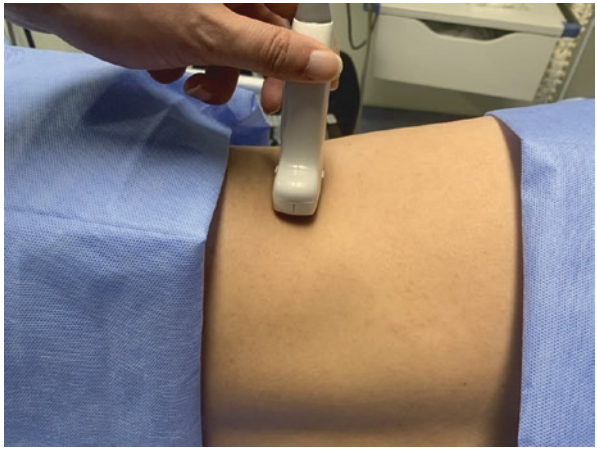
Probe position: horizontal plane, transverse on the abdomen, at the anterior axillary line, between the costal margin and the iliac crest



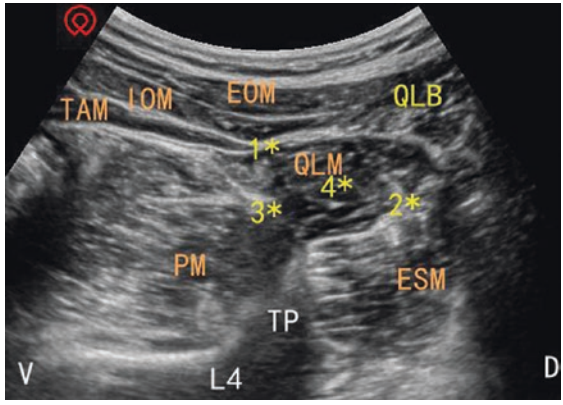
EOM external oblique muscle, *IOM* internal oblique muscle, *TAM* transversus abdominis, *TAP* transversus abdominis plane block, *L* lateral, *M* medial

2 Ultrasound Image of Quadratus Lumborum Plane

2.1 Low Frequency Probe; Short-Axis



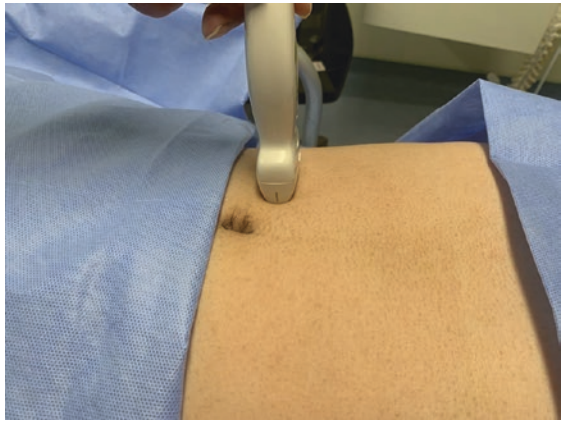
Probe position: horizontal plane, transverse on the abdomen, at the anterior axillary line, between the costal margin and the iliac crest



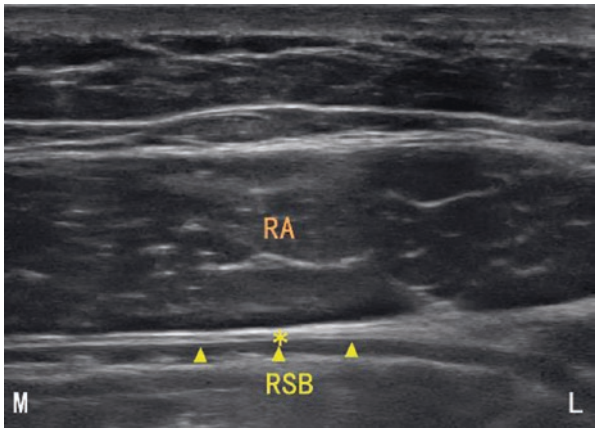
EOM external oblique muscle, *IOM* internal oblique muscle, *TAM* transversus abdominis, *QLM* quadratus lumborum muscle, *PM* psoas, *ESM* erector spinae muscle, *TP* transverse process, *QLB* quadratus lumborum block, *V* ventral, *D* dorsal

3 Ultrasound Image of Rectus Sheath Plane

3.1 High Frequency Probe; Short-Axis



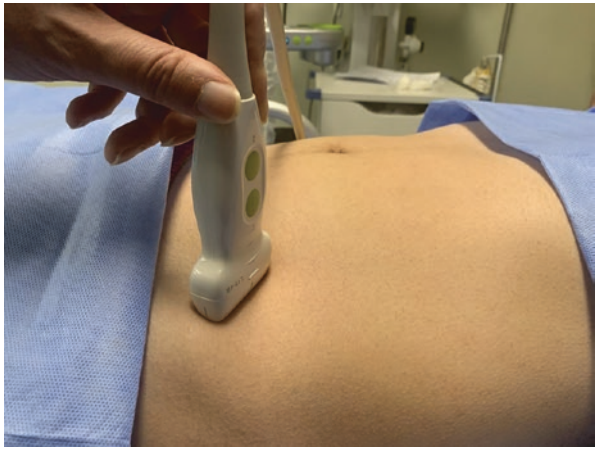
Probe position: horizontal plane, transverse on abdomen, just lateral to umbilicus



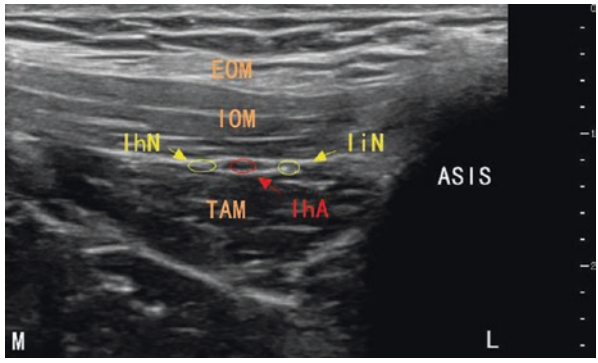
RA rectus abdominis, *RSB* rectus sheath block, *M* medial, *L* lateral

4 Ultrasound Image of Ilioinguinal and Iliohypogastric Nerve

4.1 High Frequency Probe; Short-Axis



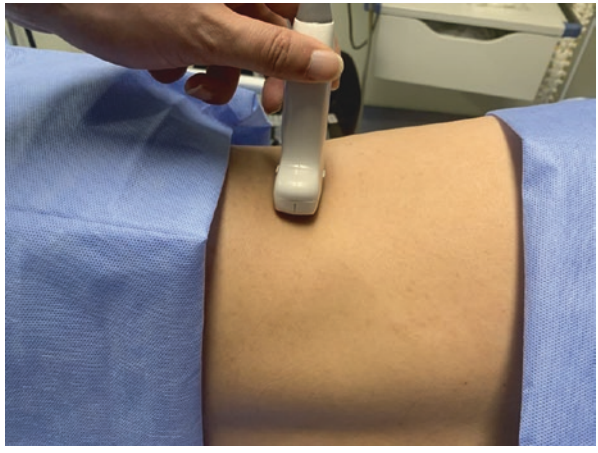
Probe position: horizontal plane, oblique on abdomen, between the anterior superior iliac spine and umbilicus



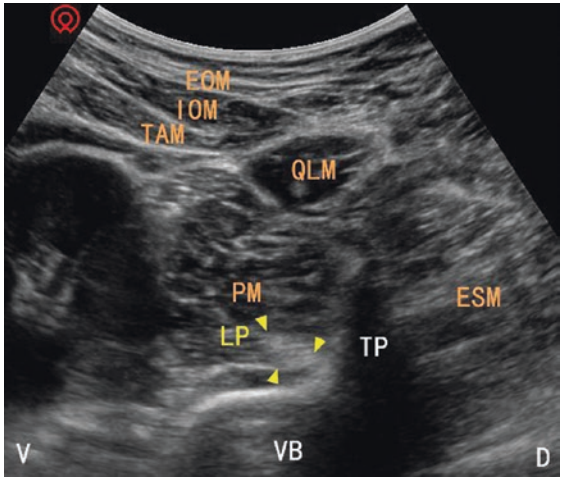
EOM external oblique muscle, *IOM* internal oblique muscle, *TAM* transversus abdominis, *IhN* iliohypogastric nerve, *IiN* ilioinguinal nerve, *IhA* iliohypogastric artery, *ASIS* anterior superior iliac spine, *M* medial, *L* lateral

5 Ultrasound Image of Lumbar Plexus

5.1 Low Frequency Probe; Short-Axis

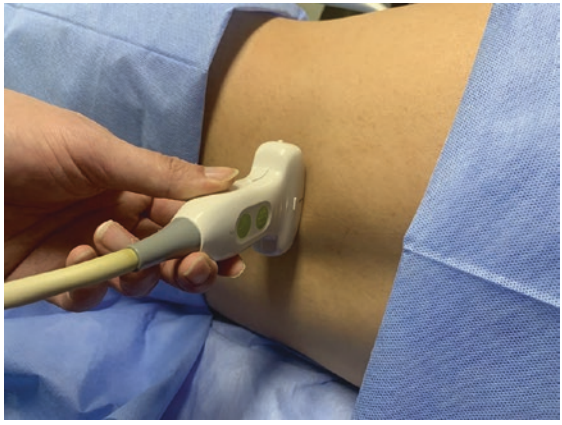


Probe position: horizontal plane, transverse on the abdomen, at the anterior axillary line, between the costal margin and the iliac crest

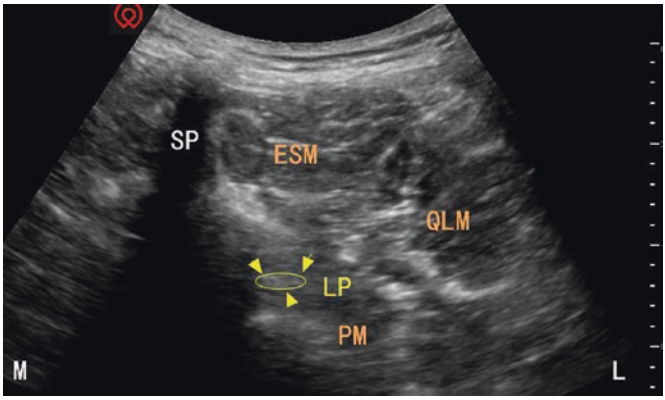


EOM external oblique muscle, *IOM* internal oblique muscle, *TAM* transversus abdominis, *QLM* quadratus lumborum muscle, *PM* psoas, *ESM* erector spinae muscle, *TP* transverse process, *LP* lumbar plexus, *V* ventral, *D* dorsal

5.2 Low Frequency Probe; Short-Axis

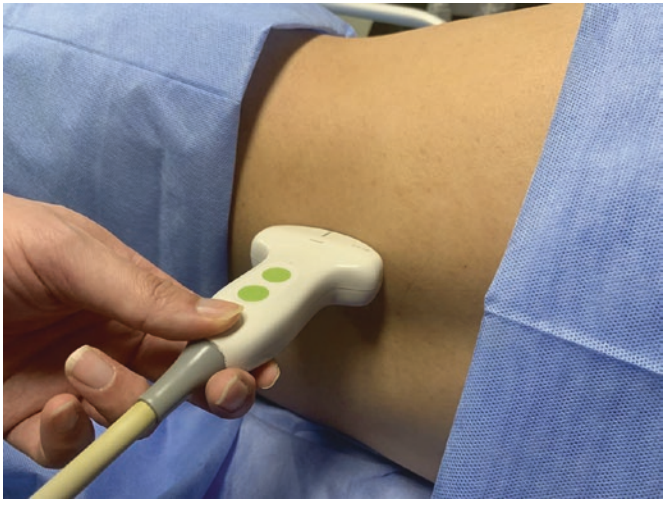


Probe position: horizontal plane, transverse at the lower back

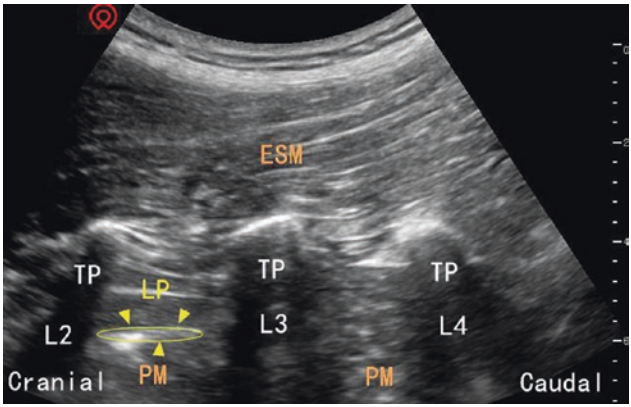


QLM quadratus lumborum muscle, *PM* psoas, *ESM* erector spinae muscle, *SP* spinous process, *LP* lumbar plexus, *M* medial, *L* lateral

5.3 Low Frequency Probe; Long-Axis



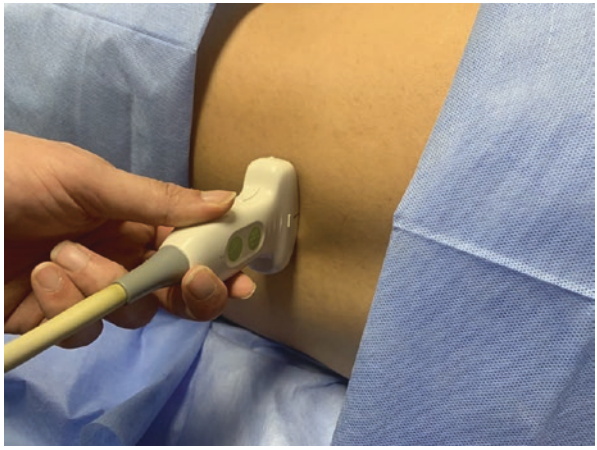
Probe position: parasagittal plane, approximately 4–5 cm lateral to the spinous process at the lower back



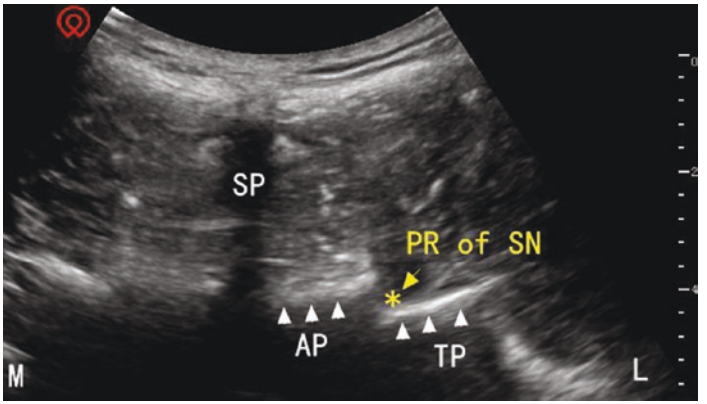
PM psoas, *ESM* erector spinae muscle, *TP* transverse process, *LP* lumbar plexus

6 Ultrasound Image of Posterior Ramus of Spinal Nerve

6.1 Low Frequency Probe; Short-Axis

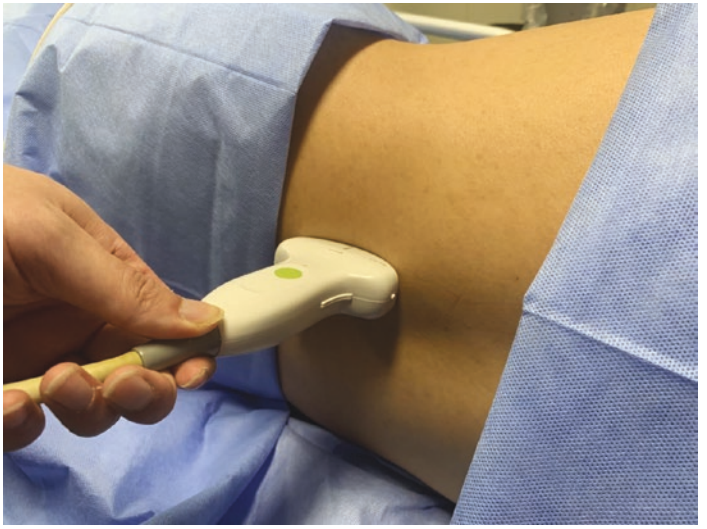


Probe position: horizontal plane, transverse at the lower back

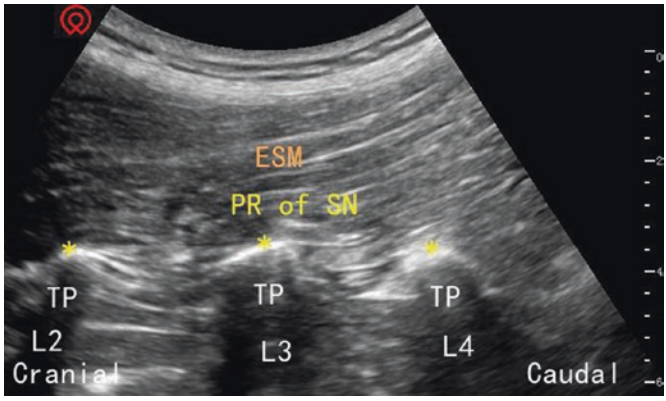


SP spinous process, *AP* articular process, *TP* transverse process, *PR of SN* posterior ramus of spinal nerve, *M* medial, *L* lateral

6.2 Low Frequency Probe; Long-Axis



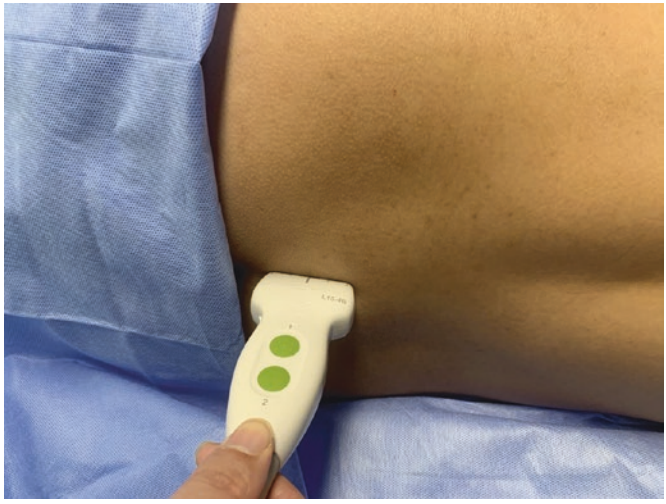
Probe position: parasagittal plane, approximately 3–4 cm lateral to the spinous process at the lower back



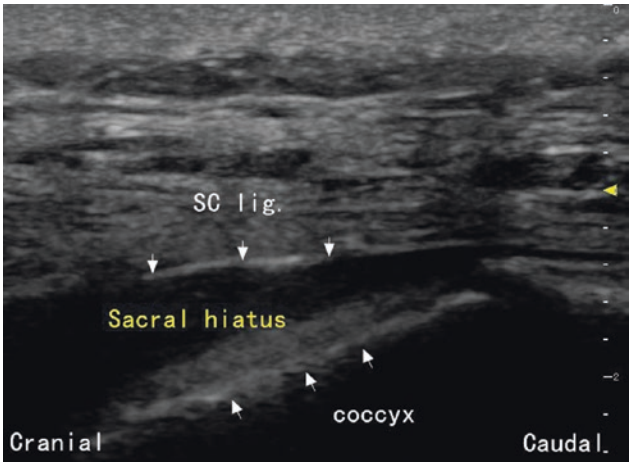
ESM erector spinae muscle, *TP* transverse process, *PR of SN* posterior ramus of spinal nerve

7 Ultrasound Image of Sacral Canal

7.1 High Frequency Probe; Long-Axis

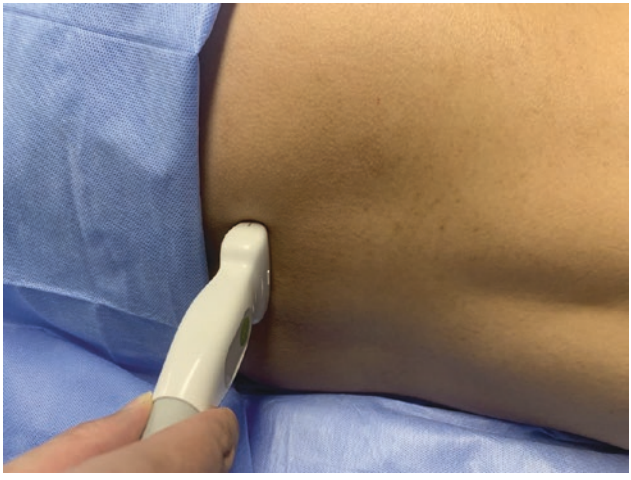


Probe position: sagittal plane, just proximal to the gluteal cleft

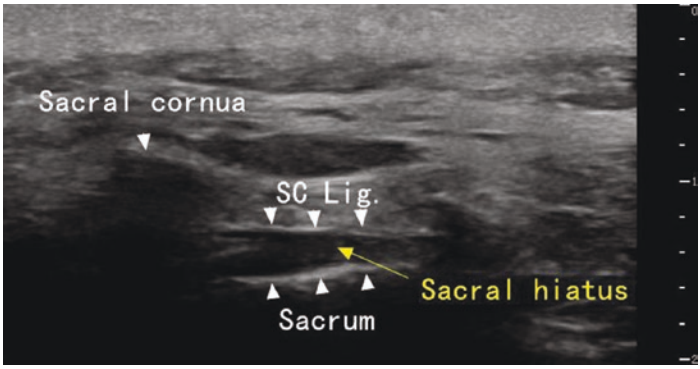


SC lig sacrococcygeal posterior longitudinal ligament

7.2 High Frequency Probe; Short-Axis



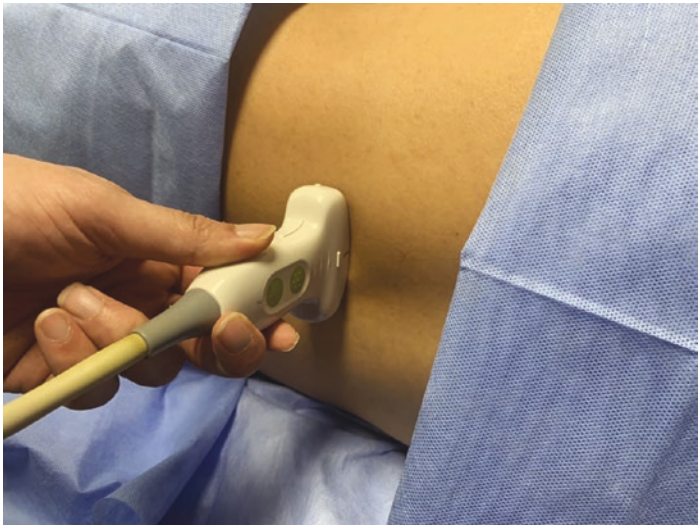
Probe position: horizontal plane, transverse just proximal to the gluteal cleft



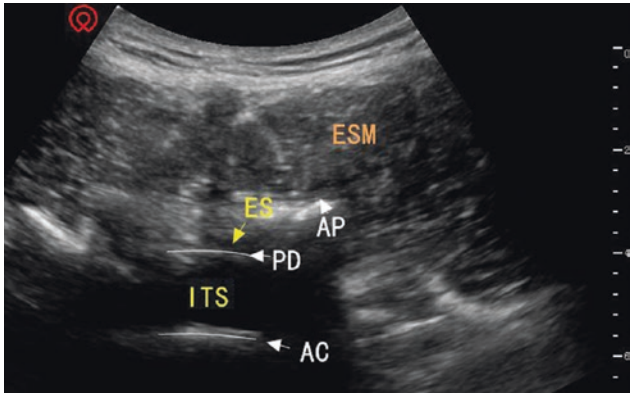
SC lig sacrococcygeal posterior longitudinal ligament

8 Ultrasound Image of Spinal Canal

8.1 Low Frequency Probe; Short-Axis

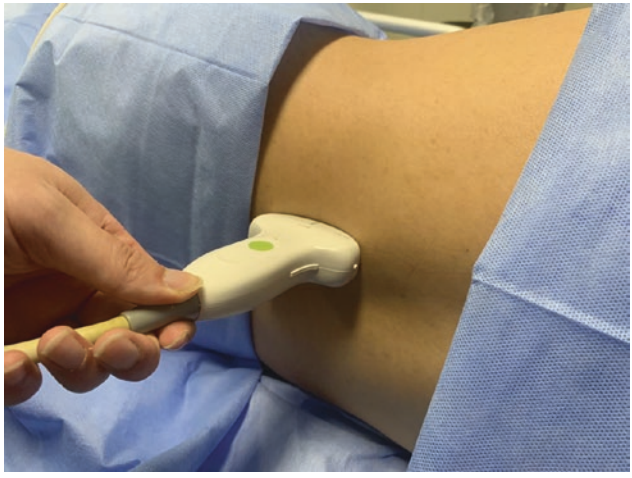


Probe position: horizontal plane, transverse at the lower back

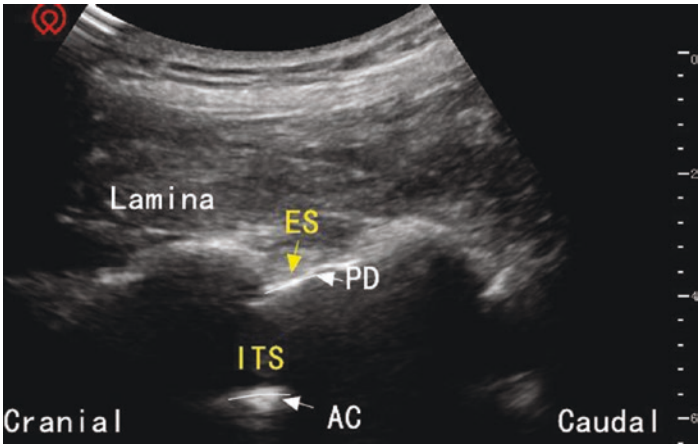


ESM erector spinae muscle, *AP* articular process, *PD* posterior dura, *AC* anterior complex, *ES* epidural space, *ITS* intrathecal space

8.2 Low Frequency Probe; Long-Axis



Probe position: parasagittal plane, 1–2 cm lateral to the spinous process at the lower back



PD posterior dura, *AC* anterior complex, *ES* epidural space, *ITS* intrathecal space

Part II

Evidence-Based Utilization of Opioid and Non-opioid Analgesics

Acetaminophen

Kristin Brennan and Henry Liu

1 Introduction

Acetaminophen or paracetamol as it is called internationally, its chemical name is *N*-acetyl-*p*-aminophenol, was originally synthesized in 1878 and first used clinically in 1887 [1, 2]. Marketed as the safer analgesic alternative to nephrotoxic phenacetin when it became available to the United States in 1955 and to the United Kingdom in 1956, acetaminophen gained wide acceptance for the treatment of headache and various mild pain by the 1970s [1–3]. The intravenous (IV) formulation of acetaminophen was not approved for clinical use in patients in the USA by the Food and Drug Administration (FDA) until 2011 [4], though the same intravenous formulation was approved in Europe in 2002 and became the top analgesic in less than 10 years. Today, acetaminophen is regularly consumed by almost 80% of the general population and is the most commonly prescribed medication in children [5–7].

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_7

2 Mechanism of Action

Acetaminophen's mechanism of action is not completely understood [8]. Its analgesic effects are believed to be predominantly via activation of descending serotonergic pathways in the central nervous system (CNS) [4]. Interactions with opioid, eicosanoid and/or nitric oxide-containing pathways have been speculated as well [2, 9].

Acetaminophen easily crosses the blood brain barrier and distributes homogenously throughout the CNS, as demonstrated by the presence of acetaminophen in cerebrospinal fluid (CSF) [1]. The close correlation between acetaminophen's analgesic effect and its concentration in the CSF—not the plasma concentration of the drug—supports its likely central mediation [10]. Acetaminophen is suggested to inhibit the activity of the COX enzymes (likely COX-3) by reducing the amount of its oxidized form. Studies have concluded that this mechanism of action actually results in a dual effect on the brain. At low doses, acetaminophen demonstrates a protective effect by preventing the accumulation of reactive oxygen species. In contrast, total microsomal lipid peroxidation and calcium levels are increased at higher doses of acetaminophen, resulting in higher activity of peroxidase and calcium-dependent ATPase [11]. Acetaminophen inhibition of the COX-pathway occurs only in areas where peroxide levels are low (i.e., in the brain) but not in the peripheral tissues [12, 13].

In addition to centrally-mediated COX inhibition, the involvement of endogenous vanilloid and cannabinoid signaling pathways have also been proposed as mechanisms of action for the analgesic properties of acetaminophen [1]. This interaction has been suggested to account for the "relaxation" or "calming" effect described by some patients after the administration of acetaminophen [14, 15]. Acetaminophen is thought to undergo de-acetylation to *p*-aminophenol and then conjugate with arachidonoyl-phentolamine in the brain, spinal cord, and dorsal root ganglia [16]. Arachidonoyl-phentolamine is structurally similar to the endogenous cannabinoid *N*-arachidonoylethanolamine (AEA) and acts as a weak agonist of cannabinoid receptors as well as an inhibitor of anandamide membrane transport, thereby increasing levels of endogenous cannabinoids in thermoregulatory and pain centers of the

brain. Interestingly, the pharmacological mechanism of acetaminophen as a cannabinoid system modulator may be related to its reported neuroprotective effects at low doses as well as its paradoxical brain tissue toxicity at higher doses; however further study to elucidate this potential mechanism is indicated [1]. Acetaminophen is also believed to function as weak COX-1 and COX-2 inhibitors, which might contribute to its analgesic effects.

Acetaminophen's antipyretic effects on heat-regulating centers in the hypothalamus have been suggested to occur through a distinct oxidative stress-reducing mechanism to inhibit prostaglandin release and fever [1].

3 Clinically-Relevant Pharmacodynamics and Pharmacokinetics

Acetaminophen is a non-opioid analgesic agent and a non-salicylate antipyretic. Its pharmacokinetic features are illustrated in Table 1.

Table 1 Pharmacokinetics of acetaminophen

Pharmacokinetics of acetaminophen	(at therapeutic levels)
Distribution	• 10–25% binding to plasma proteins
	• Distributed to most body tissues (except fat) [8]
	• Absorbed from the small intestine; dependent on gastric emptying, especially in the perioperative period [10]
Metabolism	• Oral formulation: 25% first-pass, primarily by the liver [17]
	• Intravenous formulation bypasses first-pass
Excretion	• By the kidney
	• 5% unconjugated (free), 1% unchanged [18]
	• More than 90% of the administered dose is excreted within 24 h [8]
	• Metabolites are non-toxic, water-soluble (cysteine and mercapturic conjugates) [18]
	• Mainly eliminated in the urine, also in bile [1]

3.1 Metabolic Pathways for Acetaminophen

The liver's first order metabolism of acetaminophen involves three separate pathways

1. Conjugation with glucuronide (40–67%)
2. Conjugation with sulfate (20–46%)
3. Oxidation via the cytochrome p450 (CYP450) enzyme pathway (5–15%) [1]

Microsomal CYP540 oxidizes acetaminophen into *N*-acetyl-*p*-benzoquinone imine (NAPQI), a highly reactive, hepatotoxic intermediate. At therapeutic levels of acetaminophen, NAPQI is rapidly reduced by glutathione and subsequently converted to relatively-benign cysteine or mercapturic conjugates [18].

3.1.1 Pharmacokinetics of Oral Versus Intravenous Acetaminophen

Compared to the oral route, peak plasma concentrations and mean CSF concentrations are greater and achieved faster with IV acetaminophen administration [10]. The IV formulation of acetaminophen bypasses first-pass metabolism by the liver, resulting in a bioavailability of 100% compared to the oral formulation's bioavailability of 85–95% [9], which is often affected by the administration of opioid medications and altered peristalsis perioperatively. Recent studies have hypothesized that the IV acetaminophen's increased bioavailability may be beneficial in the setting of postoperative ileus [19]. With the exception of bioavailability, both oral and IV formulations share identical pharmacokinetic properties with respect to metabolism, elimination, half-life and protein-binding [9].

4 Practical Perioperative Use

Guidelines for non-opioid analgesic selection frequently cite the 1991 randomized, double-blind trial for treatment of chronic pain due to osteoarthritis of the knee. This study concluded that

for short-term symptoms of osteoarthritic knee pain, the efficacy of acetaminophen is similar to that of ibuprofen whether the latter is administered in an analgesic or an anti-inflammatory dose [20]. Acetaminophen does not possess significant anti-inflammatory activity, most likely due to its site of pharmacological action predominantly within the central nervous system [1]. Its centrally-mediated COX-inhibition also accounts for why short- and long-term therapeutic use of acetaminophen does not produce the same adverse effects (e.g., gastric ulceration, inhibition of clot-formation promoting factors) as produced by classical non-steroidal anti-inflammatory drugs (NSAIDs) in peripheral tissues [1, 2]. Because acetaminophen and NSAIDS have different mechanisms of action, evidence supports the combination of acetaminophen with NSAIDS to be more effective than either drug alone when used in conjunction with opioids to minimize postoperative pain and reduce total opioid consumption [21].

5 Indications

The World Health Organization [22] (WHO) recommends acetaminophen as the first step in any pharmacological treatment of all pain conditions. A robust evidence base supports the use of acetaminophen for acute pain treatment, as shown in Table 2.

Concurrent administration of primarily non-opioids with different mechanisms of analgesia (e.g., acetaminophen and NSAIDs) or delivered via different techniques (e.g., oral acetaminophen and regional anesthesia) is a popular multimodal pain management strategy to produce superior analgesia while minimizing the use and side effects of opioids [4, 29, 30]. Acetaminophen is recommended by the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia as a component of multimodal analgesia for several surgical procedures [21], including: Cesarean section, coronary artery bypass-graft, open laparotomy, spinal fusion, thoracotomy, and total hip and total knee placement.

Table 2 Indications for acetaminophen recommended by World Health Organization

• Mild to moderate pain (single agent therapy)
• Moderate to severe pain (with adjunctive opioid analgesia) [8]
• Postoperative pain [23]
• Postpartum pain [24]
• Dental pain [25]
• Migraine [26]
• Pain and fever in children [2] (recommended first choice due to aspirin's association with Reye's syndrome) [27]
• Pain in geriatric patients [28]

6 Contraindications

Compared to other pharmacological treatment options for pain, acetaminophen possesses a limited number of side effects [31], specifically nausea, vomiting, skin irritation, insomnia in adults, and agitation in pediatric patients. Acetaminophen is sometimes avoided because of concern for masking presentation of fever; however, studies support treatment of fever in patients with suspected infection [32].

Although considered a safe analgesic and antipyretic, acetaminophen is also associated with significant morbidity and mortality. Administration of acetaminophen is contraindicated in patients with severe hepatic impairment or severe active liver disease due to the occurrence of hepatotoxicity and acute liver failure with inappropriate acetaminophen use and in patients with known hypersensitivity to acetaminophen.

7 Dosage Choice

For perioperative use in adult and adolescent patients greater than 50 kg, a preoperative dose of acetaminophen (1000 mg) is commonly administered orally and repeated in the post-operative period every 6 h, but not exceeding 4000 mg in 24 h [4]. Hospital formulations of 650 mg may be dosed every 4 h (not to exceed 3900 mg in 24 h), however the 1000 mg dosing regimen has been suggested to be more effective [9]. For patients less than 50 kg

(including children), the recommended dose is reduced to a 15 mg/kg every 6 h (or 12.5 mg/kg/dose every 4 h) to a maximum of 75 mg/kg (or 3750 mg total) in 24 h [4]. Studies suggest that scheduled (rather than "as-needed") dosing of acetaminophen is more effective for postoperative pain [29].

Dosing of intravenous acetaminophen has not been studied for children younger than 2 years old. The reduction of IV acetaminophen dose by 50% in neonates up to 28 days old and by 33% in infants (1 month to 2 years of age) with a minimum dosing interval of 6 h has been simulated from pharmacokinetic data to produce an exposure proposed to be similar to children older than 2 years old. Intravenous acetaminophen should be stored at 20–25 °C (68–77 °F) and administered within 6 h after opening. It should be administered only as a 15-min infusion [8].

Importantly, greater than recommended dosing of acetaminophen may result in hepatic injury, including the risk of severe hepatotoxicity and hepatic failure-related death [33].

8 Duration of Usage

Repeated exposure to therapeutic levels of acetaminophen (using either dosing regimen, 1000 mg every 6 h or 650 mg every 4 h) has been well-tolerated for up to 5 days postoperatively with no clinically relevant adverse effects [23]. The FDA specifies that administration of acetaminophen should not exceed 10 days [34]. Chronic acetaminophen usage of 4000 mg daily has been found to increase the international normalized ratio (INR) in patients receiving sodium warfarin for anticoagulation [8].

9 How to Titrate Up and Down If Relevant

Combined acetaminophen-opioid analgesic formulations do not permit the titration of individual medications, thereby increasing the risk of inadequate pain control, opioid misuse, and acetaminophen-related liver injury [35]. Independent administration of acetaminophen and opioids grants the flexibility to titrate each to optimal pharmacological effects while reducing adverse

events. Recommended interventions to improve pain medication titration practices include the following:

- Removing combined acetaminophen-opioid preparations from hospital formularies
- Separating acetaminophen and opioid selections for inpatient and outpatient electronic order sets
- Educating prescribers of perioperative analgesia [35]

10 How to Continue/Stop Medication Preoperatively

A single 1000 mg dose of acetaminophen administered 10–30 min prior to surgical incision is associated with significantly lower pain at rest and with movement during the early postoperative period, and with less opioid consumption and lower incidence of postoperative nausea and vomiting, compared to the same dose given at the end of surgery [36]. Because acetaminophen is commonly included as one component of a multimodal perioperative analgesic protocol, it is important to determine whether the patient's existing analgesic regimen includes acetaminophen prior to administration [29, 33]. It is also noteworthy that any substance (e.g., alcohol, anti-epileptics) that interferes with the activity of hepatic cytochrome enzyme CYP2E1 (one of the many CYP450 pathway enzymes catalyzing the conversion of acetaminophen into NAPQI) or condition that alters the metabolism of acetaminophen (e.g., chronic malnutrition depletes glutathione stores in the liver, reducing the rate of NAPQI elimination) can increase the risk of hepatotoxicity [18].

11 How to Restart Postoperatively

Continuation of regularly scheduled acetaminophen as a single agent or as part of a multimodal perioperative analgesic regimen is recommended [29]. For patients unable to tolerate oral formulations, rectal and IV acetaminophen have demonstrated no differ-

ence in the time before the first dose of rescue analgesia, in early postoperative pain scores, or in the time to discharge from the post-anesthesia care unit (PACU) [37]. While both have shown similar speeds to achieve analgesic effects, the effect of IV acetaminophen appears to be shorter lived than of the rectal formulation [38].

12 Toxicity

The onset of the signs and symptoms of acetaminophen toxicity are listed in Table 3. Unfortunately, the incidence of acetaminophen-related liver toxicity has increased so significantly in the last several decades that it is currently the leading cause of acute liver failure in the entire northern hemisphere [1]. Acetaminophen toxicity accounts for almost 50% of all acute liver failure cases in the United States [39] and between 40 and 70% in the United Kingdom and Europe [40]. Patients must be educated about the hepatotoxic potential of excessive acetaminophen dosing and the risks of concurrent over-the-counter acetaminophen use with acetaminophen-opioid combination formulations. Even therapeutic doses of acetaminophen can potentially result in severe acute liver injury under certain conditions [1].

12.1 Mechanism of Acetaminophen Toxicity

Ingestion and breakdown of large acetaminophen doses deplete protective stores of sulfate and glutathione. When the function of these two metabolic pathways is compromised, acetaminophen is shunted toward oxidation via the CYP450 enzymatic pathway, resulting in the accumulation of the hepatotoxic intermediate, NAPQI. This process further disrupts homeostasis with subsequent mitochondrial activation of caspases and lysosomal enzymes that initiate and amplify apoptosis in the liver and kidney, leading to tissue necrosis and ultimately multisystem organ dysfunction [18]. Limited retrospective case analyses suggest that renal insufficiency associated with acetaminophen toxicity may

Table 3 Timeline for signs and symptoms of acetaminophen toxicity [41]

Time after ingestion:	Hour 12–24	Hour 25–48	Hour 49–96
Clinical signs and symptoms	• Nausea	Symptoms may actually appear to improve	• Hepatic necrosis
	• Vomiting		• Renal tubular necrosis
	• Abdominal pain		• Somnolence
	• Diaphoresis		• Stupor
	• General malaise		• Coma
	• NO immediate symptoms		• Cerebral edema
			• Brain stem herniation
			• Thrombocytopenia
			• Vascular collapse
			• Skeletal muscle cytolysis
Laboratory Findings		Abrupt increases in	• Hyperammonemia
		• ALT to >10,000 U/L (normal <40 U/L)	• Serum creatinine peaks 3–16 days post-ingestion (average 7 days) [18]
		• AST to >10,000 U/L (normal <40 U/L)	• Lactic acidosis
		• INR to ≥4.0	
		Laboratory changes may not be evident up to 72 h after ingestion	

ALT alanine aminotransferase, *AST* aspartate aminotransferase, *INR* international normalized ratio

occur more often in children and adolescents than older adults, but the explanation for this finding is unknown [18]. The distribution of acetaminophen across the blood brain barrier and the presence of CYP2E1 in the hippocampus, olfactory bulbs, olfactory cortex, cerebellum and brainstem indicate that the reactive intermediate NAPQI can also affect the central nervous system [42]. Although hepatic necrosis is the most common serious adverse

event in acute acetaminophen overdose, encephalopathy, renal tubular necrosis, and coagulopathy all signal worsening acetaminophen-induced fulminant hepatic failure [1, 8, 43]. If acetaminophen toxicity does not progress to multi-organ failure, hepatic recovery can occur quickly, as demonstrated by rapid resolution of aminotransferases and international normalized ratio (INR). Recovery to baseline renal function can occur over 1–4 weeks, especially for patients with isolated renal dysfunction [41]. Approximately 1% of recovering patients require dialysis as a temporizing measure; these patients more commonly have other comorbidities, including multisystem organ failure [18]. Management steps of acetaminophen toxicity are listed in Table 4.

Table 4 Acetaminophen toxicity management [8]

If acetaminophen toxicity is suspected:	
Obtain serum acetaminophen assay	Plot level against time since oral ingestion, to assess hepatic injury. For example, after 4 h:
	• >300 μg/mL is associated with hepatic damage
	• <150 μg/mL (or <37.5 μg/mL after 12 h) suggests minimal hepatic damage
Obtain liver function studies	• Perform at presentation
	• Repeat every 24 h
Administer antidote *N*-acetylcysteine	• Oral or intravenous
• A precursor in the synthesis of glutathione, *N*-acetylcysteine	• If serum acetaminophen is above the lower threshold, administer the entire *N*-acetylcysteine course
• Restores intracellular glutathione	• If serum acetaminophen is below the lower threshold, withhold *N*-acetylcysteine therapy
• Neutralizes residual NAPQI	• Administration within 12–18 h effectively precludes most severe liver injury
	• *N*-acetylcysteine has been shown to reduce incidence of hepatic necrosis, but has not demonstrated benefit (or harm) in other organ (e.g., kidney) injury [18]

NAPQI *N*-acetyl-*p*-benzoquinone imine

13 How to Use in Opioid Naïve Patients

Because systemic opioids may not be required in all patients and should be avoided in conditions when they are not indicated, acetaminophen is recommended as a first-line option for analgesia, especially in opioid-naïve patients [24]. The concurrent administration of acetaminophen and opioid has been found to reduce the total dose of opioid required and to decrease opioid-related adverse events including postoperative nausea and vomiting and sedation [29].

14 How to Use in Chronic Pain Patients

Although acetaminophen has been recommended as the first-line analgesia for many chronic pain conditions [44], little evidence supports acetaminophen as an effective therapy for chronic pain [3].

15 How to Use in Hepatic or Renal Insufficient Patients (Including Dialysis Patients)

Extreme caution is advised when administering acetaminophen to patients with hepatic impairment, active hepatic disease, chronic malnutrition or chronic alcohol consumption, severe hypovolemia, or renal impairment. For patients with severe renal impairment (diagnosed by a creatinine clearance $\leq$30 mL/min) consideration of prolonged dosing intervals and a reduction of the total dose of acetaminophen over 24 h is recommended [8].

16 Evidence of Efficacy and Safety of Perioperative Use and Use in ERAS Protocols

The American Society of Enhanced Recovery recommends that any multimodal pain management strategy include a minimum of two non-opioid analgesics to minimize perioperative opioid usage and

reduce opioid-related adverse effects [36]. Acetaminophen is the most commonly used non-opioid analgesic in ERAS pathways, however compelling evidence for its use is not as often encountered.

- For lumbar spine fusion [45], acetaminophen 975 mg is administered orally with gabapentin 900 mg PO on the day of surgery in the preoperative holding area and postoperatively every 6 h with celecoxib 200 mg every 12 h and gabapentin 300 mg every 8 h. After 1 week of this regimen, no significant difference is observed in the number of patients requiring short-acting opioids immediately postoperatively and at the first postoperative follow-up visit, but a reduction in the use of extended-release and long-acting opioids has been reported.
- For cesarean section [46], acetaminophen's benefit in the obstetric population is not entirely clear, although a systemic review of patients undergoing cesarean section suggested that the effect of combining scheduled NSAIDs and acetaminophen was synergistic for postoperative pain (compared to alternating the dose of each non-opioid analgesic).

Several ERAS-related studies have focused on the comparison of oral, rectal and/or IV formulations of acetaminophen:

- For colorectal surgery, Marcotte et al. [19] compared the efficacy of two dosing regimens of acetaminophen: one group received only IV acetaminophen during the entire postoperative hospital admission, the second received the first perioperative dose of acetaminophen intravenously, and subsequent doses of oral acetaminophen. This study found no differences in the maximum or average pain scores in the first 3 postoperative days or at the time of discharge. Compared to the IV acetaminophen only group, the oral acetaminophen group received significantly more post-operative opioids in the first 72 h. This group was also more likely to experience postoperative nausea and vomiting. In contrast, the IV-only group required greater amounts of total acetaminophen, especially in the first 24 h of surgery. Previous investigation of ERAS pathways in the

colorectal surgical population had found no significant decrease in opioid usage or in opioid-related adverse effects with intravenous acetaminophen compared to oral acetaminophen. The patients from this earlier data claims analysis only received a single dose of IV acetaminophen during their admission. Marcotte et al. suspect that the colorectal patient population may be at increased risk of not easily tolerating oral acetaminophen in the postoperative setting and recommend further study to establish whether unrestricted administration of IV acetaminophen during the early postoperative period would optimize non-opioid analgesia.

- For gynecological oncology surgery [47], no difference in postoperative opioid consumption was detected between patients within the ERAS program receiving preoperative acetaminophen intravenously or orally.

Common Pitfalls

- The cost of intravenous acetaminophen is up to 600 times more than that of the oral formulation. As multimodal analgesia therapy gains popularity, newer opioid-sparing agents in intravenous formulations cost considerably more than their oral alternatives [4]. A cost-responsible provider in today's healthcare environment must weigh this expense against its lack of evidence for extra benefit. Judicious administration of perioperative IV acetaminophen has been reported to save over $400,000 per year in a single institution [48]. On the basis of current evidence, if a patient has a functional gastrointestinal tract and is able to tolerate oral acetaminophen, the IV formulation is not indicated. No robust evidence exists supporting IV acetaminophen as the standard of care. At most, the IV formulation could function as an alternative for patients unable to tolerate oral acetaminophen [49].
- Acetaminophen is one of the most popular analgesics in the world and has relatively few side effects, but acetaminophen toxicity can be lethal. Many prescriptions and non-prescription formulations contain acetaminophen alone or in combination with other medications. Safe administration and prescription

require diligent monitoring of all acetaminophen use, especially patients' self-medication practices and in patients at risk of opioid-tolerance and dependence [1].

Clinical Pearls

- Acetaminophen is very safe when used in limited doses, but this margin of safety is relatively narrow [41].
- Acetaminophen—both after single doses and prolonged use—has not been found to have any immediate or delayed effects on platelet aggregation or small-vessel hemostasis. These findings occurred in healthy subjects and in patients with hemophilia [8].
- Patients eliciting any suspicion for acetaminophen toxicity should provide a thorough history, including all over-the-counter and prescription products, doses and quantities ingested, illicit substances used and the time course for their ingestion. Medical comorbidities (including malnutrition and/or chronic alcohol consumption) and risk factors for nephrotoxicity should be elucidated. Laboratory workup should include a serum acetaminophen level, liver function studies, creatinine and blood urea nitrogen. The antidote *N*-acetylcysteine should be administered (orally or intravenously) as soon as possible.
- Sufficient and convincing evidence exists for neuroprotective effects of low-dose acetaminophen. Further investigation of the mechanism for this effect may lead to new modalities of treatment and management for neurological pathophysiology [1].

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Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

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1 Mechanism of Action

NSAIDs inhibit the enzyme cyclooxygenase (COX). In response to pain and inflammation, COX induces the production of prostaglandins and thromboxane (Fig. 1) [1]. Prostaglandins are proinflammatory. They increase vascular permeability and the release of bradykinins. The primary anti-inflammatory and analgesic properties of NSAIDs are accomplished by decreasing the production of prostaglandins, especially prostaglandin E and thromboxane, thereby reducing pain and swelling.

Three forms of COX have been identified: COX-1, COX-2, and COX-3. They share nearly 70% of the same amino acid sequences; however, they are regulated differently. COX-1 is expressed throughout the body and responds to hormones and growth factors, whereas COX-2 is expressed during injury in certain cells [2, 3]. Currently, the role COX-3 in humans remains

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_8

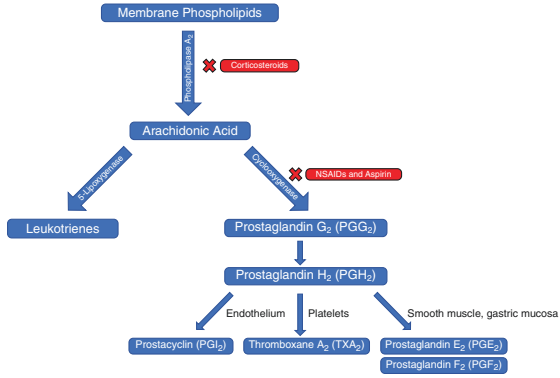

Fig. 1 Arachidonic acid pathway

unclear. In the brain, COX-2 is upregulated during periods of increased pain signals and is thought to play an important role in modulating perceived pain. The analgesic and anti-inflammatory effects of NSAIDs are mainly through COX-2 inhibition. Nevertheless, most NSAIDs are non-selective COX-1 and COX-2 inhibitors to varying degrees. COX-1 inhibition has some analgesic effects, but it is also responsible for some of the adverse side effects of NSAIDs. For example, COX-1 is integral in maintaining the gastric and duodenal mucosa. When COX-1 is inhibited, it can lead to gastrointestinal (GI) bleeding.

NSAIDs also work through non-prostaglandin mechanisms, which are not as well understood. NSAIDs are lipophilic and may become incorporated in the lipid bilayer of cell membranes that are responsible for signal transmission [4, 5]. Some evidence suggests NSAIDs may also play a role in scavenging superoxide radicals [6].

2 Pharmacology

The majority of NSAIDs are weak acids. They are easily absorbed in the GI tract then bind to serum albumin. Thus, low serum albumin levels may result in an increased concentration of unbound NSAIDs. Absorption rates depend on GI mobility and blood flow. Enteric coating on tablets and food may decrease absorption rates. NSAIDs display a ceiling effect; therefore, increasing the dose increases adverse effects without improving efficacy (Table 1).

Table 1 Drugs and dosing summary

Medication	Trade names	Onset (hours)	Starting dose	Max dose	Half life (hours)	Specific uses
Aspirin	Bayer	0.5–1	325 mg q6h	975 mg q6h	4–15	Irreversibly induce platelet dysfunction
Celecoxib	Celebrex	3	100 mg q12h	200 mg q12h	11	–
Diclofenac	Cataflam, Voltaren	0.5	50 mg q12h	50 mg q8h	2	–
Ibuprofen[a]	Motrin, Advil, Caldolor[a]	0.5	200 mg q6h *(10 mg/kg pediatrics)*	800 mg q6h	2	IV, perioperatively, pediatrics
Indomethacin	Indocin	0.5	25 mg q12h	50 mg q8h	3–11	PDA closure
Ketoprofen	Orudis, Oruvai	2–3	25 mg q8h	75 mg q6h	2	–
Ketorolac[a]	Toradol[a]	0.5–1	15 mg q6h (*0.5 mg/kg pediatrics*)	30 mg q6h (5 days max)	2	IV and IM, perioperatively, pediatrics
Meloxicam[a]	Mobic	0.5–1	7.5 mg qd	15 mg qd	20	–
Nabumetone	Relafen	Variable	1000 mg qd	2000 mg qd	20–30	Once daily for RA, OA
Naproxen	Naprosyn, Naprelan	1	250 mg q8h	500 mg q8h	13	–
Naproxen Sodium	Aleve, Anaprox	0.5–1	275 mg q8h	550 mg q8h	15	–
Oxaprozin	Daypro	Variable	600 mg qd	1200 mg qd	40–50	Once daily for RA, OA
Piroxicam	Feldene	Variable	10 mg qd	20 mg qd	30–80	Once daily for RA, OA
Sulindac	Clinoril	Variable	150 mg q12h	200 mg q12h	16	–

[a]Available in IV form

NSAIDs are metabolized primarily by the cytochrome (CYP) 450 and CYP 2C9 system in the liver and excretion occurs in the kidneys [7]. Care should be taken when administering NSAIDs to patients with renal or hepatic insufficiency.

Plasma half-lives of NSAIDs vary significantly. Piroxicam, for example, has a half-life of roughly 60 hours, whereas ibuprofen has a half-life of roughly 2 hours. NSAIDs with shorter half-lives generally have a quicker onset of action. This becomes important in patients who seek immediate relief of symptoms. NSAIDs with longer half-lives have the benefit of improving patient adherence, although clinically significant relief may take weeks [8].

Certain prodrugs, such as sulindac and nabumetone, were developed to bypass the GI mucosa and become activated after first-pass metabolism in the liver with the goal to prevent GI bleeding. It has now been shown that COX-1 inhibition still occurs regardless of the route of administration and site of activation, and therefore these prodrugs still pose a risk for GI bleeding.

3 Adverse Effects

3.1 Anaphylaxis/Asthma

The exact mechanism of NSAID induced asthma is unknown. Patients with allergic rhinitis, nasal polyposis or asthma are particularly susceptible (Table 2) [9]. Two possible explanations exist. First, prostaglandin E plays an important role as a bronchodilator. Inhibiting COX, and reducing prostaglandin prevents this bronchodilation. Second, when arachidonic acid is shunted from the prostaglandin pathway to the leukotriene pathway, there is an increase in end products that have been associated with anaphylaxis such as leukotriene B4 (Fig. 1) [10]. In either case, it is important to consider this when administering NSAIDs to susceptible patients.

Table 2 Summary of adverse effects

System	Adverse effects
Cardiovascular	May exacerbate or induce heart failure
	Increase thrombotic events (more likely with selective COX2 inhibitors)
	Premature closure of PDA in neonates
Respiratory	May exacerbate asthma/induce bronchospasm (especially in atopic patients—nasal polyps, rhinitis, asthma)
Hepatic	Hepatitis
Gastrointestinal	Increase risk of GI bleeding
	Possibly increase anastomotic complications in bowel surgery
Hematological	May increase risk of intraoperative bleeding due to platelet inhibition or dysfunction
	Potentiate anticoagulation effect of warfarin
Dermatological	Urticaria, erythema multiforme, rash
Renal	May exacerbate renal insufficiency (use cautiously in patients with renal disease)
	May cause fluid retention, papillary necrosis, or interstitial nephritis
Central nervous system	Headache, aseptic meningitis, tinnitus
Skeletal	Potential to inhibit bone growth/healing/formation
Pharmacologic interactions	Displace drugs bound to albumin potentiating their effects (e.g., warfarin)

3.2 Hematologic

Perhaps the most common concern in the perioperative period related to NSAIDs is platelet dysfunction. NSAIDs cause platelet dysfunction by inhibiting COX 1. COX 1 is found on platelets and stimulates the production of thromboxane, which plays an important role in platelet aggregation and vasoconstriction. NSAID induced platelet dysfunction can be irreversible, as in the case of aspirin, or reversible and dependent on the half-life

of the NSAID. For this reason, patients who present for elective surgery, should discontinue NSAIDs 4–5 half-lives prior to the procedure date. Aspirin, on the other hand, irreversibly inhibits platelet function by blocking formation of thromboxane A2. Thus, new platelets must be synthesized to reverse the effects of aspirin. Approximately 10–14% of platelets are replenished each day; therefore 7–19 days are required to restore the entire platelet pool. Low dose aspirin is often continued through the perioperative period in patients at high risk of thrombosis. Whether or not NSAIDs increase the risk of postoperative bleeding is inconclusive, therefore, it is best to discuss perioperative NSAID administration with the surgeon. Similarly, physicians will have varying opinions as to when it is safe to restart NSAIDs postoperatively.

Although COX-2 is not found on platelets and has no role in platelet aggregation, selective COX-2 inhibitors increase the risk of thrombotic events [11, 12]. For this reason, COX-2 inhibitors have been removed from the USA market except for celecoxib. The risk of thrombotic events may be related to an imbalance of prostaglandins and thromboxane. Prostaglandin I_2, which vasodilates and inhibits platelets aggregation, is reduced with COX-2 inhibition, whereas thromboxane production is increased due to shunting toward the COX-1 pathway, potentially leading to a prothrombotic state [13].

3.3 Gastrointestinal

One of the most common adverse effects of NSAIDs is indirect damage to the GI tract. NSAIDs may lead to a range of problems throughout the GI tract including nausea, vomiting, dyspepsia, esophagitis, gastritis, peptic ulceration, and hemorrhage. Prostaglandins produced by COX-1 help protect the GI tract and NSAID mediated prostaglandin inhibition leaves the body susceptible to these adverse effects. Patients at increased risk of GI events include those with previous GI bleeds, age greater than

60-years-old, high dose/prolonged NSAID use, and concurrent glucocorticoid use [14].

Controversy exists as to whether perioperative NSAID use increases anastomotic complications in GI surgery [15]. Nevertheless, NSAIDs are often not used as part of multi-modal analgesia in these patients.

3.4 Renal

NSAIDs can have several negative effects on the kidneys. Prostaglandins play a key role in maintaining renal blood flow and tubular transport by vasodilating the afferent renal arteriole (Fig. 2) [16]. Altering prostaglandin synthesis can reduce GFR and cause renal failure in susceptible patients. Patients at the highest risk are those with congestive heart failure, previous renal disease, atherosclerosis, diabetes, and hypovolemia. NSAIDs have also been implicated in cases of interstitial nephritis.

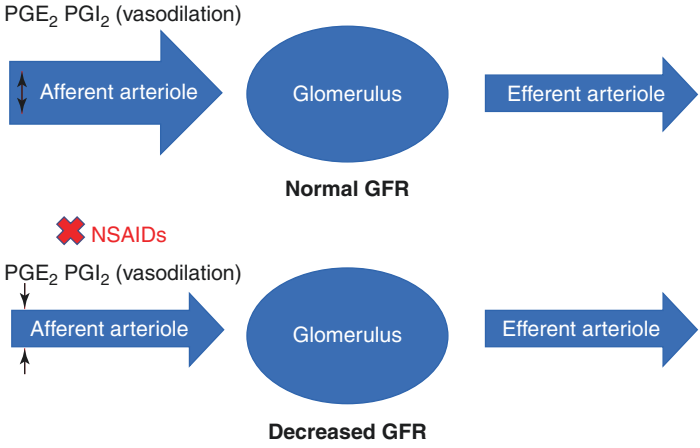

Fig. 2 Effect of NSAIDs on GFR

3.5 Hepatic

NSAID induced liver failure is rare. However, it has been reported following the use of certain NSAIDs, including sulindac and diclofenac [17]. Patients with juvenile rheumatoid arthritis and systemic lupus erythematosus can experience elevations in hepatic transaminases in the setting of NSAID use, however, this is generally not clinically significant [18].

3.6 Cardiovascular

All NSAIDs may increase the risk of thrombotic events such as myocardial infarction and strokes [19]. NSAIDs may also increase blood pressure and should be used cautiously in patients with poorly controlled hypertension. They are absolutely contraindicated in patients with severe heart failure. NSAID induced prostaglandin inhibition may result in premature closure of the fetal ductus arteriosus. Aspirin is generally stopped 8 weeks prior to delivery to minimize this risk.

3.7 Central Nervous System

Central nervous system (CNS) side effects of NSAIDs are rare but are seen more commonly in elderly patients. Higher doses are associated with tinnitus, which often resolves with decreasing the dose. Other less common side effects include aseptic meningitis, psychosis, and cognitive dysfunction [20].

3.8 Pharmacologic

- NSAIDs inhibit renal excretion of lithium and should be used cautiously in these patients
- Most NSAIDs (except the non-acetylated salicylates) when used concomitantly with warfarin increase the risk of bleeding.

NSAIDs displace warfarin from albumin leading to a prolonged prothrombin time [21].
- NSAIDs are excreted in breast milk, however, this is not considered dangerous.

4 Perioperative Use

- NSAIDs are commonly used as part of enhanced recovery after surgery (ERAS) protocols with the goal of minimizing opioid use and side effects.
- Ibuprofen and ketorolac are the most frequently used NSAIDs in children. Ibuprofen is available in both syrup and IV formulations, making it a good choice for the pediatric population. Perioperative use of ketorolac may decrease pain scores and opioid requirements in the pediatric population and serve as a good adjuvant to opioids.
- Aspirin and NSAIDs do not need to be stopped prior to neuraxial anesthesia or peripheral nerve blocks.
- NSAIDs are less commonly used in orthopedic trauma patients due to the theoretical concern of nonunion or malunion of long bone fractures [22].
- Avoid NSAIDs in patients who are continuing aspirin perioperatively.
- NSAIDs should be stopped 4–5 half-lives prior to procedures that are high risk for bleeding.
- The use of NSAIDs in patients with chronic kidney disease (CKD) should be based on the patients CKD staging (generally avoided in CKD stages 3–5).

Clinical Pearls
- Many patients can continue taking low dose aspirin in the perioperative period (risk/benefit should be weighed).
- NSAIDs can decrease opioid use in the perioperative period and reduce opioid side effects (commonly used as part of ERAS protocols).

- NSAIDs should be used with caution in patients with cardiovascular disease, renal/hepatic dysfunction, previous GI bleeds, and asthma.
- NSAIDs increase the risk of bleeding in patient's taking warfarin.
- Pregnant patients should not receive NSAIDs due to increased risk of miscarriage, premature closure of the fetal ductus arteriosus, and oligohydramnios.
- Low-dose aspirin prophylaxis is recommended in women at high risk of preeclampsia (usually initiated between weeks 12 and 28 of gestation).
- NSAIDs may be used for analgesia after cesarian section/vaginal delivery (minimal transmission of short acting NSAIDs into breast milk).
- When administering NSAIDs perioperatively, discuss use with the surgical team (often avoided in neurosurgeries, head and neck, and bowel anastomosis surgeries).
- Ketorolac and ibuprofen are widely available in IV forms and are useful in the perioperative period and in patients who are NPO.

Common Pitfalls

- Discontinuing aspirin in the perioperative period may lead to increased morbidity and mortality in patients with significant cardiac, vascular, or neurological disease.
- Aspirin should be avoided in children due to the concern for Reye's syndrome.
- Prolonged or overuse of NSAIDs can lead to GI bleed and kidney injury.

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Anticonvulsants

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1 Essential Basics

Despite their names, neither gabapentin or pregabalin demonstrate activity at the GABA receptor. Gabapentin and pregabalin share a similar chemical structure and mechanism of action in that both agents are believed to block the alpha-2 delta subunit of voltage gated calcium channels. This blockage of calcium influx in afferent nociceptive nerves results in reduced production of substance P and glutamate [1]. The pharmacokinetics comparing gabapentin and pregabalin are outlined in Table 1. Unlike pregabalin, the absorption of gabapentin observes non-linear pharmacokinetics in that a higher dose of gabapentin results in reduced bioavailability. This is due to the active transport of gabapentin by rate limiting

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_9

Table 1 Pharmacokinetics of gabapentin and pregabalin

	Gabapentin	Pregabalin
Absorption	Nonlinear bioavailability:	Linear bioavailability
	900 mg: 60%	
	1200 mg: 47%	
	2400 mg: 34%	
	3600 mg: 33%	
Metabolism	None	None
Distribution	Unbound to plasma protein	Unbound to plasma protein
Elimination	Renal (excreted unchanged)	Renal (excreted unchanged)
	Elimination half-life: 5–7 h	Elimination half-life: 6 h

absorption [2]. As a result, pregabalin displays a more predictable pharmacokinetic profile. Once absorbed in the small intestine, both agents are distributed primarily unbound to plasma proteins. Both drugs have low volumes of distribution, owed to their hydrophilicity and low degree of tissue binding. Pregabalin demonstrates significantly higher affinity for the alpha-2 delta subunit of voltage gated calcium channels than gabapentin. Moreover, gabapentin and pregabalin are largely excreted unchanged in the urine and necessitate dose adjustments in renal failure [3].

2 Practical Perioperative Use

The use of gabapentin and pregabalin in pain management extends beyond their current on-label status. Gabapentin is approved for use in post herpetic neuralgia (PHN) while pregabalin is approved for PHN, diabetic peripheral neuropathy (DPN), fibromyalgia and pain following spinal cord injury (SCI). However, gabapentinoids have increasingly been prescribed off-label in the perioperative, acute and chronic pain setting.

2.1 Dosage

Table 2 [4] and Table 3 [5] seen below, detail the recommended titration of gabapentin and pregabalin respectively. In PHN for example, titration up to 1800 mg/day (600 mg TID) is considered

Table 2 Gabapentin dosing regimen in PHN

	Dosage (max dose of 1800 mg/day of 600 mg TID)
Day 1	300 mg/day
Day 2	600 mg/day (300 mg BID)
Day 3	900 mg/day (300 mg TID)

Table 3 Pregabalin dosing regimen

Use	Dosage	Max dose
DPN	150 mg/day (divide over 3 doses)	300 mg/day within 1 week
PHN	150 mg/day (divide over 2 or 3 doses)	300 mg/day within 1 week
		Up to 600 mg/day (if insufficient pain relief following 2–4 weeks)
Fibromyalgia	150 mg/day (divide over 2 doses)	300 mg/day within 1 week. Up to 450 mg/day (if insufficient pain relief)
SCI	150 mg/day (divide over 2 doses)	300 mg/day within 1 week. Up to 600 mg/day (if insufficient pain relief following 2–3 weeks)

safe and efficacious. Nevertheless, dosages up to 3600 mg/day can be used in various clinical scenarios based on the patient's ability to tolerate such a dose.

Although these recommended regimens provide guidance on titration in specific conditions, one must adjust dosage of either agent based on the overall clinical context including a patient's response and side effects. It is not uncommon to switch between gabapentin and pregabalin based on clinical response. Some described strategies for switching between agents include: taking a final dose of pregabalin or gabapentin the night before and starting a target dose of the other agent the following day; a 4-day taper consisting of prescribing 50% of a gabapentin or pregabalin dose and 50% of a target pregabalin or gabapentin dose for 4 days, followed by discontinuing one agent and maintaining a target dose of the remaining agent. Both these strategies have been studied to achieve a steady state level of the target medication in a safe manner [6].

Few data exist to support the decision to favor one agent over the other or in combination, in the context of neuropathic pain or multimodal perioperative analgesia. One of the few existing head-to-head studies demonstrated no significant difference in efficacy and safety between pregabalin and gabapentin for neuropathic pain following SCI [7]. However, as described previously, the pharmacokinetics and pharmacodynamic profile of pregabalin appears more advantageous when compared to gabapentin in terms of predictable pharmacokinetics and higher potency.

2.2 Toxicity and Adverse Reactions

The most commonly seen adverse effects of gabapentinoids are related to CNS depression and include dizziness, somnolence and sedation. Both medications may result in angioedema with pregabalin also increasing the risk of peripheral edema. Pregabalin carries a warning of respiratory depression in the setting of use with other CNS depressants [5]. Similarly, lower doses of gabapentin should be considered with concomitant morphine, given propensity for morphine plasma concentration to increase with gabapentin administration. Moreover, gabapentin carries the warning of increased risk of suicidal ideation and behavior [4]. Just as caution should be observed with increasing doses of gabapentinoids, providers should be aware of the potential adverse reactions seen with rapid discontinuation of either medication.

Abrupt withdrawal of pregabalin has been associated with nausea, diarrhea, headache and insomnia [5]. Cases of status epilepticus and catatonia have been reported with abrupt gabapentin discontinuation [8, 9]. Although there is no established guideline regarding weaning of either medication, gradually down-titrating over the duration of 1 week has been recommended [5].

2.3 Use in Renal and Hepatic Impairment

The pharmacokinetic profile of both gabapentin and pregabalin does not require significant special consideration in patients with

compromised hepatic function. Since both medications are primarily renally excreted, specific dosing guidelines have been established based on creatinine clearance.

Tables 4 and 5 contain recommended dosage ranges based on creatinine clearance for gabapentin and pregabalin respectively. Each column contains renally adjusted doses for each regimen.

In hemodialysis patients, a supplemental dose of either medication is given following a 4 h HD session.

Despite recommendations in place for adjusting dosage regiments in patients with renal impairment, there is no clear evidence that indicates whether these adjusted doses confer efficacy at these safer doses [10].

Table 4 Gabapentin adjusted renal dosing

Creatinine clearance (mL/min)	Dosing regimen (mg)				
>59	300 TID	400 TID	600 TID	800 TID	1200 TID
30–59	200 BID	300 BID	400 BID	500 BID	700 BID
15–29	200 QD	300 QD	400 QD	500 QD	700 QD
<15	100 QD	125 QD	150 QD	200 QD	300 QD
Post hemodialysis supplemental dose	125	150	200	250	350

Table 5 Pregabalin adjusted renal dosing

Creatinine clearance (mL/min)	Total daily dose (mg/day)				Dosing regimen
>59	150	300	450	600	BID or TID
30–59	75	150	225	300	BID or TID
15–29	25–50	75	100–150	150	QD or BID
<15	25	25–50	50–75	75	QD
Post hemodialysis supplemental dose	25–50	50–75	75–100	100–150	

2.4 Use in Perioperative Care

In recent years, the use of gabapentin and pregabalin as agents in the perioperative period has grown in the context of promoting multimodal analgesia and reducing the use of opioids to treat postoperative pain.

Recent data has brought these presumed benefits into question. A meta-analysis by Verret et al., assessed the analgesic and opioid sparing effects as well as adverse effects of gabapentinoids, when administered between 1 week before and 12 h after surgery. The study was broad in its inclusion of various surgeries and anesthetics, as well as a balanced representation of gabapentin and pregabalin use. The findings demonstrated a clinically insignificant difference in pain scores between gabapentinoids and placebo during acute (72 h post-op), subacute (4–12 weeks post-op) and chronic (3–12 months post-op) time points. Moreover, no clinically significant difference was observed in opioid consumption [11].

A study pairing gabapentinoids with a sedative "placebo" such as a benzodiazepine also demonstrated this clinical insignificance [12]. The study design and findings raise the question as to whether previous literature supporting the analgesic role of gabapentinoids are biased in their design, by mistaking sedative qualities for analgesia [13]. In regards to adverse events, the meta-analysis demonstrated an association with longer hospital stays and a greater incidence of dizziness and visual disturbance, despite a reduced incidence of PONV [11]. These latter findings challenge the notion that gabapentinoids play a beneficial role in enhanced recovery after surgery.

In applying the evidence to practical perioperative use, one should consider the findings described in the context of the specific surgery and patient. If one chooses to prescribe gabapentin and pregabalin in the perioperative period, there is limited evidence, however to guide optimal dosing in the perioperative period for gabapentinoids. In an article by Schmidt et al., the authors came to the following conclusion based on their review of the literature: A preoperative dose of 1200 mg of gabapentin or

300 mg of pregabalin given 2 h prior to surgery; postoperatively 600 mg TID of gabapentin or 150 mg BID of pregabalin can be given for up to 2 weeks following the date of surgery. The available literature appears to suggest that higher doses of gabapentin (900–1200 mg) and pregabalin (300 mg) provide greater analgesia and reduction in postoperative opioid consumption when compared to respective smaller doses. The rationale of a 2-h preoperative dose has been based on time for each agent to reach peak-plasma levels. Nevertheless, evidence regarding efficacy of preoperative versus postoperative doses (or both) remains nebulous, as studies offer conflicting conclusions [14].

Clinical Pearls

- Gabapentin and Pregabalin are thought to act on the alpha-2-delta subunit of calcium channels and **do not** have any known GABA receptor activity
- Despite similar pharmacologic profiles, pregabalin demonstrates more predictable pharmacokinetics and higher potency
- Common adverse effects include somnolence, dizziness, and edema. Adjust dosing in renally compromised patients and avoid rapid discontinuation
- Gabapentinoids are believed to play a role in multimodal analgesia including ERAS protocols both for improving pain and reducing opioid requirements. Recent evidence has challenged these presumed benefits

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Muscle Relaxants

Clara Pau

Introduction

The term "skeletal muscle relaxants" (SMRs) encompasses a heterogeneous group of medications with varied mechanisms of actions. SMRs can be divided into two categories: antispasmodics and antispastics (Table 1). Antispasmodics can alleviate muscle spasms that can contribute to pain postoperatively or can be associated with musculoskeletal problems such as back pain. These medications can be further divided into benzodiazepine and non-benzodiazepine categories. In contrast, antispastics are used to treat increased muscle tone associated with conditions like multiple sclerosis or post-stroke syndrome. Overlap between these categories exist, as tizanidine and diazepam have been used in both contexts.

The prescription of SMRs has risen significantly as of late, perhaps in the face of the opioid crisis [1]. Therefore, some understanding of this diverse group of medications is necessary. A decision may need to be made whether a patient on SMRs should continue or hold them prior to surgery. In addition, SMRs may be useful as part of a multimodal analgesia regimen.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_10

Table 1 Skeletal muscle relaxants

Category	Sub-category	Medications	Clinical use
Antispasmodics	Benzodiazepines	Diazepam, Tetrazepam	• Decrease muscle spasms as commonly associated with muscle injury • Intended for short-term use (2–3 weeks)
	Non-benzodiazepines	Cyclobenzaprine, Carisoprodol, Chlorozoxazone, Metaxalone, Methocarbamol, Orphenadrine	
Antispastics	n/a	Baclofen, Tizanidine	• Decrease muscle tone (spasticity) associated with chronic conditions such as multiple sclerosis, post-stroke syndrome, traumatic brain injury

Though SMRs are an opiate-sparing option, they are not without risk. Some carry abuse potential (diazepam and carisoprodol) and some are associated with significant or potentially life-threatening withdrawal symptoms (tizanidine and baclofen). Of note, all SMRs with the exception of baclofen, are on the Beers List, also known as the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults [2]. Common side effects of SMRs are sedation and drowsiness, which may make older adults vulnerable to falls and injury.

Some controversy remains as to whether SMRs are beneficial in the treatment of pain associated with musculoskeletal conditions. There is evidence that they are, but more high-quality research is needed [3–5]. This chapter provides an overview of this diverse group of medications and discusses the role they play in the perioperative setting.

Chapter Overview
- Antispasmodics
- Antispastics
- Do antispasmodics help with pain?
- Perioperative management of SMRs
- Clinical pearls
- Common pitfalls

1 Antispasmodics

The category of antispasmodic SMRs can be further divided into benzodiazepines and non-benzodiazepines (Table 1). In the benzodiazepine group is diazepam. Tetrazepam is not available in the US. Of note, the FDA updated the black box warning on benzodiazepines in 2020 to include the risks of abuse, misuse, addiction, dependence and withdrawal.

The longer list of agents included in the non-benzodiazepine category have different mechanisms of action, emphasizing the heterogeneity of this group (Table 1). While some agents have inhibitory effects on inter-neuronal activity, some are believed to work via their sedative effects and some mechanisms remain unclear. Cyclobenzaprine is the most studied antispasmodic, but there is no good evidence that suggests one agent is superior over another. Therefore, the choice of agent should be individualized to the patient, taking into account their comorbidities and clinical status [6].

Table 2 lists the antispasmodics, their mechanism of action, dosage forms, and some distinguishing characteristics.

Table 2 Antispasmodics

Sub-category	Medication	Mechanism of action	Dosage forms	Pearls
Benzodiazepines	Diazepam (Valium)	Binds GABA-A, resulting in neuroinhibitory effect	Tablet, injection, oral and intranasal solutions, rectal gel	• Abuse potential
Non-benzodiazepines	Cyclobenzaprine (Flexeril)	5HT2 receptor antagonist, structurally related to TCAs	Tablet, ER capsule (24 h)	• Risk of serotonin syndrome • Most studied SMR
	Carisoprodol (Soma)	Barbiturate-like action (CNS depressant with anxiolytic action)	Tablet	• Abuse potential • Abrupt discontinuation can result in withdrawal • Rare idiosyncratic reaction (AMS, transient quadriplegia, vision loss)
	Metaxalone (Skelaxin)	Unclear, but causes general CNS depression (no direct effect on muscle)	Tablet	• Less sedation reported compared to other SMRs • Can cause paradoxical muscle cramps
	Methocarbamol (Robaxin)	Unclear, but causes general CNS depression	Tablet, injection	• Use with caution in renal and liver patients
	Orphenadrine (Norflex)	Unclear but structurally similar to diphenhydramine and has atropine-like effects	ER tablet (12 h), injection	• Abuse potential (euphorigenic) • Brand name Norgesic is combined with aspirin and caffeine
	Chlorzoxazone (Parafon Forte)	Unclear, but depresses spinal reflexes	Tablet	• Risk of hepatotoxicity

2 Antispastics

Included in the category of antispastics are tizanidine and baclofen. To be clear, baclofen is useful in the treatment of spasticity, but there is no evidence that supports its use as an antispasmodic. Its falling under the label of "skeletal muscle relaxants" again illustrates the heterogeneity of the term. Of note, intrathecal baclofen carries the black box warning that abrupt discontinuation can result in serious sequelae such as high fever, muscle rigidity as well as rhabdomyolysis and death.

Tizanidine stands out in many respects. While it is approved for the treatment of spasticity, it is used off-label to treat muscle spasms. There is evidence that it leads to an earlier resolution of acute lower back pain in combination therapy with ibuprofen when compared to placebo [7]. This study also found that tizanidine had gastroprotective effects. But tizanidine can cause significant side effects such as hypotension, bradycardia, and sedation. If chronic use is discontinued abruptly, rebound hypertension and tachycardia can result. It is also associated with hepatotoxicity and should be avoided in patients with impaired liver function.

Table 3 lists the antispastics, their mechanism of action, dosage forms, and some distinguishing characteristics.

Table 3 Antispastics

Medication	Mechanism of action	Dosage forms	Pearls
Baclofen	Binds GABA-B receptor, resulting in neuroinhibitory effect	Tablet, intrathecal and oral solutions	• Abrupt discontinuation of oral form can result in withdrawal • Abrupt discontinuation of intrathecal form can be life-threatening
Tizanidine (Zanaflex)	Alpha2 agonist, which increases presynaptic inhibition leading to decreased spasticity	Tablet, capsule	• Abrupt discontinuation can result in rebound HTN • Can cause hepatotoxicity • Drug interactions with CYP1A2 inhibitors

3 Do Antispasmodics Help with Pain?

While evidence does suggest some benefit, antispasmodics have the potential for significant side effects. Thus, controversy remains as to whether the benefits outweigh the risks, especially when compared to other proven medications. A study evaluated patients presenting to the emergency room with acute lower back pain. It found that combining cyclobenzaprine to naproxen did not improve pain outcomes compared to naproxen alone [8]. A Cochrane systemic review in 2003 found that muscle relaxants were effective in the treatment of non-specific low back pain, but warns that they carry adverse effects and their efficacy compared to other analgesics or NSAIDs is unknown [3]. A follow-up systemic review in 2021 casts uncertainty on the conclusions of the 2003 Cochrane review, saying that while non-benzodiazepine antispasmodics reduce acute lower back pain, the reduction may be clinically insignificant [4]. The study also found that while adverse events were reported with SMR use, treatment was not discontinued, suggesting that the side effects were tolerable. The researchers from both reviews resoundingly agree that more high-quality evidence is needed to determine the efficacy and safety of muscle relaxants in the treatment of lower back pain and other musculoskeletal conditions [3–5].

As to their role in perioperative pain management, studies suggest that antispasmodics are beneficial in lowering pain scores, decreasing opioid consumption, and improving patient outcomes. One randomized controlled trial found that pre-medicating patients undergoing laparoscopic cholecystectomy with oral tizanidine reduced their postoperative pain, opioid consumption, and PACU length of stay [9]. Another retrospective review evaluated changes when a pain protocol for patients undergoing primary total hip and knee replacement was revised to include IV methocarbamol and IV acetaminophen instead of oral oxycodone, acetaminophen, and pregabalin. They found that the protocol revision resulted in decreased opioid consumption, improved participation in physical therapy, and decreased hospital stay [10]. Another randomized controlled study found that the addition of

preoperative oral methocarbamol to the pain regimen of patients undergoing breast augmentation decreased pain scores up to 6 h after surgery [11].

4 Perioperative Management of SMRs

As the third most-prescribed medication for treating lower back pain, which in itself is responsible for the highest healthcare expenditure in the US [12], encountering patients on SMRs is likely. Preoperatively, patients may be taking SMRs chronically and postoperatively, these medications, specifically antispasmodics, may be helpful as part of a multimodal analgesia regimen.

SMRs can cause central nervous system depression and therefore, when combined with anesthesia may increase the risk of over-sedation and respiratory depression. Interactions with other medications can led to other complications. For example, the risk of serotonin syndrome increases when cyclobenzaprine is administered with other serotonergic medications like ondansetron, fentanyl, and tramadol. The most conservative approach would be to hold these medications on the day of surgery or taper them prior, if time allows. The exceptions are baclofen and tizanidine, which should not be discontinued as this could cause significant and perhaps life-threatening withdrawal. If it is necessary for intrathecal baclofen to be discontinued prior to surgery, discussion with a specialist is necessary. See Table 4 for a summary on how to manage these medications preoperatively or on the day of surgery [13].

If muscle spasms or musculoskeletal pain is present or anticipated, antispasmodics may be helpful as part of multimodal analgesia. Since high-quality evidence regarding their comparable efficacy is lacking, the choice of agent should be individualized to the patient, taking into account their comorbidities and clinical status such as hemodynamics and alertness. Over-sedation can be detrimental to a patient's participation in physical therapy, but may treat a patient who has difficulty sleeping due to pain. A bedtime dose of antispasmodic may help. Table 5 lists the oral dosing of the antispasmodics along with their adverse effects and contraindications.

Table 4 Perioperative management of skeletal muscle relaxants

Category	Medication	Periop management
Antispasmodics	Diazepam (Valium)	Hold (if time permits, taper prior to surgery. Monitor for withdrawal symptoms)
	Cyclobenzaprine (Flexeril)	Hold
	Carisoprodol (Soma)	Hold (if time permits, taper prior to surgery. Monitor for withdrawal symptoms)
	Metaxalone (Skelaxin)	Hold
	Methocarbamol (Robaxin)	Hold
	Orphenadrine (Norflex)	Hold
	Chlorzoxazone (Parafon Forte)	Hold
Antispastics	Baclofen	Continue
	Tizanidine (Zanaflex)	Continue

Clinical Pearls

- Skeletal Muscle Relaxants (SMRs) is a broad term that encompasses both antispasmodic and antispastic medications (Table 1)
- Antispasmodics are intended for short-term treatment (2–3 weeks) of muscle spasms that can result from muscle injury or can occur following surgery
- Antispastics decrease spasticity associated with chronic conditions such as multiple sclerosis or post-stroke syndrome
- Baclofen and tizanidine should be continued perioperatively, while other SMRs should be held on the day of surgery (Table 4)
- Antispasmodics can be useful in postop pain management if muscle spasms are contributing. The choice of agent should be individualized to the patient as each medication has adverse effects and contraindications (Table 5)

Table 5 Skeletal muscle relaxants: dosing, side effects, contraindications

Category	Medication	Oral dosing	Side effects	Contraindications
Antispasmodics	Diazepam (Valium)	2–10 mg three to four times a day	• Abuse potential • Confusion, drowsiness • Possible interaction with CYP450 inhibitors	• Avoid in liver patients
	Cyclobenzaprine (Flexeril)	5–10 mg three times a day	• Anticholinergic effects (drowsiness, dry mouth, urinary retention) • Risk of serotonin syndrome • Possible interaction with CYP450 inhibitors • Rare but potential for arrhythmias, AMI, seizures	• Avoid in liver and glaucoma patients • Contraindicated in patients with arrhythmias, congestive heart failure, recent MI
	Carisoprodol (Soma)	250–350 mg four times a day	• Abuse potential • Drowsiness, dizziness • Rare idiosyncratic reaction (AMS, transient quadriplegia, vision loss)	• Contraindicated in acute intermittent porphyria (AIP)
	Metaxalone (Skelaxin)	800 mg three to four times a day	• Drowsiness, dizziness • Paradoxical muscle cramps	• Caution in renal and liver patients (consider lower dose) • Contraindicated in acute intermittent porphyria (AIP)
	Methocarbamol (Robaxin)	1500 mg four times daily for 2–3 days, then 750 mg four times a day	• Drowsiness, dizziness • Black, brown, green urine possible • May worsen myasthenia gravis symptoms	• Caution in renal and liver patients (consider lower dose)
	Orphenadrine (Norflex)	100 mg twice a day	• Anticholinergic effects (drowsiness, dry mouth, urinary retention) • GI irritation	• Abuse potential • Avoid in patients with GI obstruction, myasthenia gravis, bladder neck obstruction, glaucoma, cardiospasm
	Chlorzoxazone (Parafon Forte)	250–750 mg three to four times a day	• Drowsiness, dizziness • Red or orange urine • GI irritation	• Avoid in liver patients (risk of hepatotoxicity)
Antispastics	Tizanidine (Zanaflex)	2–4 mg every 6–8 h (increase by 2–4 mg until relief achieved (Max daily dose: 36 mg)	• Sedation, bradycardia, hypotension • Rebound HTN with abrupt discontinuation	• Avoid in liver patients • Caution in renal patients (consider lower dose) • Avoid with CYP1A2 inhibitors

Common Pitfalls

- "Opiate-sparing" does not mean "benign"
- All SMRs can cause CNS depression such as sedation and drowsiness
- Some antispasmodics have abuse potential and are not intended for chronic use
- Some SMRs are potentially hepatotoxic and therefore should be used with caution with other medications like acetaminophen
- SMRs can interact with other medications, so vigilance must be maintained

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Antidepressants

Tolga Suvar

1 Introduction

Pain clinics in the United States have shown that 60–80% of patients have comorbid psychiatric illness [1]. These patients diagnosed by the Diagnostic and Statistical Manual of Mental Disorder (DSM) and by statistics, patients with psychiatric illness demonstrate greater pain intensity scores. According to the DSM 5 criteria, major depressive mood disorder (MDD) requires the presence of depressed mood and loss of interest or pleasure in most activities for at least 2 weeks. Concomitantly, patients who suffer from pain are twice as likely to be diagnosed with depression. Depression is a spectrum of feelings, ranging from diminished self-attitude to suicidal ideation in its most severe form. With major depression, inadequate treatment of the psychiatric illness will reduce the effectiveness of all pain treatments [2].

Treatment for depression with the medications noted in Table 1 will take approximately 2–4 weeks to note an initial response and approximately 4–8 weeks for noticeable improvement.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_11

Table 1 Categories of antidepressants

	Half life (h)	Doses (mg/day)	Perioperative medication interaction
SSRI			
Citalopram Fluoxetine Fluvoxamine Paroxetine Sertraline	33 96–144 15–26 15–20 26	20–40 5–40 100–300 20–40 50–200	Bleeding risk when combined with NSAIDs, antiplatelet; Serotonin syndrome with other antidepressants or antipsychotics; Inhibition of CYP 450 enzymes
SNRI			
Venlafaxine Desvenlafaxine Duloxetine Milnacipran	5–11 11 8–17 8	37.5–300 50–400 60–120 100–200	Similar to SSRIs; NSAIDs and blood thinners may induce a bleeding risk, although better side effect profile than TCAs
TCAs			
Amitriptyline Amoxapine Clomipramine Desipramine Doxepin Nortriptyline Protriptyline	31–46 8.8–14 22–84 14–62 8–24 18–93 54–198	10–300 25–500 25–300 10–300 25–300 10–150 15–60	Drug interactions may be prominent with inhaled anesthetics, sympathomimetics, anticholinergics, antihypertensives, and opioids

2 Mechanism of Action

Antidepressants are theorized to work by alterations of the noradrenergic and serotonergic neurotransmission while the precise mechanism of action (MOA) is unknown. Increases of norepinephrine and serotonin within the synapses are the proposed theorem.

3 Pharmacology

Over the course of decades, TCAs have been replaced by SSRIs primarily for the reduced side effect profile, along with the tolerability and safety of the newer generation of antidepressants. Mood elevating effects of antidepressants take place approximately 1–2 weeks after initiating treatment. A proper trial of anti-

Table 2 Starting doses and maximum doses

Drug	Starting dose	Maximum dose
Amitriptyline	10–25 mg QD	300 mg/daily
Nortriptyline	10–25 mg QD	200 mg/daily
Duloxetine	30 mg QD	120 mg/daily
Milnacipran	12.5 mg QD	200 mg/daily
Venlafaxine	37.5 mg QD	375 mg/daily

depressants should be approximately 6 weeks until other medications should be considered. Antidepressants with dual action, such as SNRIs, may have a quicker onset, but does not appear to have increased efficacy [3]. The dosing schedule of antidepressants are based on the drug's elimination half-life and the ideal dosing schedule of an antidepressant should be once a day dosing, or half-life of 24 h. Table 2 includes a dosing summary with starting doses and maximum doses of the most commonly used antidepressants. Of all the antidepressants, fluoxetine has the longest half-life, with metabolite norfluoxetine lasting 7–15 days.

Therapeutic blood levels of antidepressants can have wide interindividual variability, which can be explained by individual differences in drug-metabolizing enzymes.

Tricyclic antidepressants are absorbed from the gastrointestinal tract after oral administration. This class of medications have high lipid solubility, resulting in peak plasma concentration within 2–8 h. With its lipophilicity, and strong bind to plasma and tissue proteins, TCAs have a large volume of distribution.

4 Dosing Summary

5 Adverse Effects

Side effects of antidepressants are explained by their synaptic activity, meaning that while the majority of the effects are located on the brain, some receptors are prevalent elsewhere in the body

resulting in adverse effects and drug interactions. Synaptic effects of antidepressants include the blockade of transport of certain neurotransmitters from the synaptic cleft and blockade of receptors from neurotransmitters. Table 3 includes a summary consisting of the effects of serotonin syndrome, neuroleptic malignant syndrome, as well as the central nervous system and cardiovascular effects of antidepressants.

5.1 SSRIs

The most common side effects of fluoxetine (first introduced to the United States in 1988) are nausea, anorexia, insomnia, sexual dysfunction, agitation, and involuntary neuromuscular contractions. Appetite suppression and weight loss may also be seen with SSRI medications. Due to its long half-life, fluoxetine should be

Table 3 Adverse effects

Adverse effects summary	
Serotonin syndrome	Symptoms can range from mild tremors to altered mental status, clonus, and hyperthermia. Additional signs are mydriasis, drooling, sweating, and hyperactive gag reflex
Neuroleptic malignant syndrome	Syndrome develops over 24–72 h consisting of hyperthermia, generalized hypertonic skeletal muscle, instability of the autonomic nervous system (alterations in blood pressure, tachycardia, dysrhythmia), and fluctuating levels of consciousness
Central nervous system	Sedation, lowering of the seizure threshold, weakness and fatigue, rare side effects of extrapyramidal symptoms with elderly patients, hyperthermia, and coma
Cardiovascular system	Orthostatic hypotension, tachycardia, prolonged PR, widened QRS, flattened T waves, cardiac depression secondary to slowing of sodium ion flux into cells with alteration in repolarization
Anticholinergic	Dry mouth, blurred vision, tachycardia, urinary retention, slowed gastric emptying, including ileus

discontinued for 5 weeks before initiating treatment with a Monoamine Oxidase (MAO) inhibitor.

Fluoxetine can have profound interaction with other drugs since it is the most potent inhibitor of hepatic cytochrome P-450 enzymes. The presence of another antidepressant may result in toxic levels to build in the plasm. Careful consideration must be accounted for with other medications such as cardiac antidysrhythmic drugs that are metabolized by the same system. Combination of MAO inhibitors and SSRIs may precipitate serotonin syndrome.

5.2 SNRIs

Similar to TCAs, SNRIs drugs inhibit the reuptake of norepinephrine and serotonin. SNRIs have been used to treat major depression, fibromyalgia, and diabetic peripheral neuropathy. Like SSRIs, side effects include dry mouth, nausea, insomnia, and sexual dysfunction. Of the SNRIs, venlaflaxine, duloxetine, desvenlaflaxine, and milnacipran are the most common. Venlaflaxine is a weak inhibitor of the cytochrome P-450 enzymes, while duloxetine is a moderate inhibitor of cytochrome P-450 2D6. This class of medication should not be combined with MAO inhibitors as there is potential risk for serotonin syndrome.

5.3 TCAs

The most common side effects of TCAs are anticholinergic, cardiovascular, and central nervous system effects. Anticholinergic effects of TCAs are predominant at high doses and are more common with amitriptyline. These side effects include dry mouth, blurred vision, tachycardia, urinary retention, and slowed gastric emptying. Anticholinergic delirium is a common side effect in the elderly population, in which these medications should be used with caution. Cardiovascular effects of TCAs include orthostatic hypotension and tachycardia, attributed to the inhibition of norepinephrine reuptake. TCAs have increased risk for predisposing

patients to cardiac dysrhythmia and sudden death. The mechanism by which this occurs is depression of cardiac impulse conduction through atria and ventricle by prolongation of the P-R interval as well as widening of the QRS complex. CNS side effects of TCAs include hyperthermia, sedation, seizures, and coma.

5.4 MAO Inhibitors

The most common side effect of MAO inhibitors is orthostatic hypotension, which can be prominent and severe for the elderly patient. Impotence and anorgasmy are also side effects of MAO inhibitors. The anticholinergic properties of these medications can have mild stimulant properties, resulting in insomnia. Paresthesias and weight gain are other side effects of MAO inhibitor therapy. A rare complication of this therapy is hepatitis. Notable drug interactions with MAO inhibitor therapy are opioids, sympathomimetic drugs, TCAs, and SSRIs. Interaction with these medications can result in hypertension, CNS excitability, delirium, seizures, and death. Overdose with MAO inhibitor may be reflected by signs of excessive sympathetic activity, such as tachycardia, hyperthermia, mydriasis.

6 Perioperative Use

Antidepressants, especially SSRIs may have antiplatelet activity and the risk of bleeding is potentiated in patients taking antiplatelet medications. It would take 2–4 weeks for the antiplatelet activity to diminish upon cessation of the antidepressant, which may predispose the patient to a major depressive episode. It is advisable to continue antidepressants and SSRIs, and consider holding antiplatelets during the perioperative period if medically permissible.

Chronic antidepressant use, especially in the class of TCAs can predispose the patient to increased minimum alveolar concentration (MAC) requirements. The mechanism of action from this phenomenon is increased availability of norepinephrine at post-

synaptic receptors in the peripheral nervous system, which can result in exaggerated blood pressure response.

Clinical Pearls

Amitriptyline

- This medication is used for poster herpetic neuralgia, depression, and other neuropathic pain conditions.
- Tricyclic antidepressants lower seizure thresholds. Specifically, amitriptyline can produce the greatest degree of sedation and anticholinergic side effects.
- Anticholinergic side effects may produce anticholinergic delirium in the elderly.
- Other side effects include dry mouth, blurry vision, tachycardia, urinary retention, slowed gastric emptying, and ileus.

Nortriptyline

- Tricyclic antidepressants are metabolized by enzymes in the liver through conjugation with glucuronic acid. Metabolism is slowed in the elderly patient population.
- Nortriptyline is the pharmacologic active demethylated metabolite of amitriptyline. An excessive level of Nortriptyline can result in toxicity.
- Of note, desipramine is the principal metabolite of imipramine.
- TCA's are tertiary amines that inhibit the reuptake of both serotonin and norepinephrine at presynaptic terminals, increasing the availability of these neurotransmitters.

Venlaflaxine (*Effexor*)

- Structurally similar to tramadol, with analgesic properties independent of its antidepressant effects.
- This medication serves as an alternative for tricyclic antidepressants for those unable to tolerate the side effects.
- Effective drug for treating painful polyneuropathy.

Duloxetine (*Cymbalta*)

- This SNRI is approved in the United States for diabetic peripheral neuropathy (DPN), fibromyalgia, major depression, and generalized anxiety disorder.
- Only medication in the United States approved for both pain and psychiatric conditions.
- Side effects include dry mouth, dizziness, constipation, and sexual dysfunction.
- Moderate inhibitor of CYP2D6 liver enzyme and may increase TCA and antipsychotic levels.
- Avoid in patients with renal or liver insufficiency.

Drizalma

- Drizalma is a delayed release formulation of duloxetine which can be taken as a tablet, sprinkled over food, or placed through an orogastric or nasogastric tube.

Milnacipran (*Savella*)

- FDA approved for the treatment of fibromyalgia but not depression.
- This SNRI class of medication has efficacy in treating chronic pain and fibromyalgia.
- Nausea and constipation are the most common events reported with this treatment regimen.
- MOA is not clear; endogenous analgesic mechanisms consist of modulating descending inhibitory pathways by increases in serotonin and norepinephrine.

Desvenlafaxine (*Pristiq*)

- This drug is an active metabolite of venlaflaxine, and it has combined serotonin and norepinephrine reuptake inhibition (SNRI) and dopamine reuptake inhibition.
- Approved by the FDA for major depression disorder (MDD).

- Treats neuropathic pain at higher doses.
- Unlike venlaflaxine, the affinity for the 5HT and NE receptor does not increase with escalating doses of this medication.

Common Pitfalls

Patients who are taking antidepressants and subsequently develop sedation, coma, seizures, and cardiovascular depression, including tachycardia and hypotension are more commonly attributed to the tricyclic antidepressant class. This is an acute overdose of tricyclic antidepressants caused by blockade of the fast-acting sodium channels. ECG findings include prolonged QRS (>100 ms); treatment include fluids and vasopressors. Sodium bicarbonate can be given with goals to keep QRS <100, to keep blood pressure stable, and to keep the sodium around 150 mEq. If patient develops pulseless ventricular tachycardia or ventricular fibrillation, follow ACLS protocols. Treat seizures with midazolam. Consider intralipid for cardiac arrest refractory to treatment [4].

7 Summary

Antidepressants are a class of medications that have use for a wide range of disorders and a diverse role for modulating the monoamine neurotransmitters in the human nervous system. While the precision of the mechanism is not fully understood, the increase in noradrenergic and serotonergic neurotransmission is the proposed mechanism of action in the neurobiological cascade. It is hypothesized that these medications potentiate endogenous CNS opioids and have anti-inflammatory effects. The clinical improvement typically is seen 2–4 weeks after the initiation of these medications.

Selective serotonin reuptake inhibitors (SSRIs) block the presynaptic serotonin reuptake pump in the synaptic cleft. SSRIs have a low side effect profile but also little analgesic activity.

SSRIs are associated with bruising, bleeding, and osteoporosis. In combination with other medications, SSRIs can cause sero-

tonin syndrome when administered with serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), monomamine oxidase inhibitors (MAOIs), triptans, and antiemetics such as ondansetron and metoclopramide. Serotonin syndrome can also be precipitated by phenylpiperidine opioids such as fentanyl, tramadol, methadone, meperidine, and pentazocine. Symptoms include shivering, diarrhea, muscle rigidity, fever, and seizures.

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Alpha-2 Adrenergic Agonists

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1 Introduction

The α-2 adrenoreceptors are located on pre- and postsynaptic neurons. The α-2 receptors exert an inhibitory function in both central and peripheral nervous systems [1]. The α-2 adrenoreceptors are a heterogeneous family of G-protein coupled receptors which have four subtypes α-2a, α-2b, α-2c, and α-2d, found in a variety of species and tissues (α-2D subtype is now believed to be a variation of α-2A) [1–3]. Commonly utilized α-2 adrenoreceptor ago-

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_12

nists in perioperative medicine include clonidine and dexmedetomidine [1, 2], other less used α-2 adrenoreceptor agonists include tizanidine, guanfacine, guanabenz, guanoxabenz, guanethidine, methylnorepinephrine, (R)-3-nitrobiphenyline, lofexidine, xylazine, medetomidine, and many others [3]. Here we will focus on clonidine and dexmedetomidine, and review their clinical pharmacology, indications and contraindications, and clinical pearls for anesthesia providers.

2 Pharmacology of α-2 Receptor Agonists

2.1 Mechanism of Action

Alpha-2a and alpha-2c receptors are mainly located in the central nervous system while alpha-2b receptors are mostly concentrated on vascular smooth muscle [2, 4]. Thus, α-2a and α-2c receptors mediate their sedative and analgesic effects, while α-2b receptors responsible for hemodynamic effects [4]. All α-2 adrenoreceptor activations inhibit adenylyl cyclase, thus reducing cyclic guanosine monophosphate (cGMP) and hyperpolarizing noradrenergic neurons in the medial dorsal pons [4]. And inhibition of cGMP will cause potassium efflux via calcium-activated channels. Since calcium ions are inhibited from entering the nerve terminal, neural firing is therefore suppressed, and norepinephrine release and subsequent activation of these ascending pathways are also inhibited [4]. The negative loop feedback further reduces presynaptic norepinephrine release. α-2 adrenoreceptor exist postjunctionally and prejunctionally. Postjunctional α-2 adrenoreceptors mediate their effects on target tissues, whereas prejunctional α-2 adrenoreceptors facilitate negative loop feedback. Activations of α-2a receptor stimulation result in sedation and analgesia suitable as anesthetic adjuncts. Sedative effects are mediated in the locus coeruleus, where G-protein-coupled receptors induce hyperpolarization of the membrane and decrease the release of norepinephrine. Suppression of noradrenergic release leads to activation of a natural sleep pathway resulting in loss of wakefulness [5]. This

sedation mechanism does not carry risks of respiratory depression as opioid does. The analgesic effect is mediated by receptors in the substantia gelatinosa of the spinal cord, where similar G-protein-coupled receptors suppress conductance through N-type calcium channels, this leads to inhibition of nociceptive neurons in the dorsal horn and reduction of glutamate and substance P, further preventing signal transmission of pain to the brain α-2a agonists also produce analgesic effects by acting on I-2 imidazoline receptors in the spinal cord [2–4]. α-2a receptor stimulation also causes sympatholysis via stimulation of inhibitory neurons in the medullary vasomotor center, decreasing sympathetic outflow to peripheral tissues. Importantly in the perioperative settings, these decreased sympathetic effects increase vagal tone, leading to decreased peripheral vascular resistance, heart rate, and blood pressure [5]. Furthermore, α-2 agonists act at I-1 imidazoline receptors in the medulla to produce hypotension [6]. α-2b and α-2c receptor effects are less relevant in the perioperative setting. Activation of α-2b receptor usually results in vasoconstriction and triggers mechanisms to stop shivering, while α-3b receptor activation leads to the startle response, which encompasses withdrawal to stimulation, contraction of limb muscles, blinking, and increased blood pressure [7]. Other clinically relevant effects mediated through α-2 adrenoreceptors in the periphery include smooth muscle vasoconstriction, hyperglycemia secondary to inhibition of insulin release from the pancreas, and inhibition of lipolysis and platelet aggregation. Other less clinically relevant effects in the periphery are xerostomia, decreased gut motility, and inhibition of renin release with resulting diuresis and increased glomerular filtration [6].

Dexmedetomidine and clonidine are both α-2 adrenoreceptor agonists commonly utilized in anesthesia and perioperative medicine that have several important similarities and differences. Clonidine and dexmedetomidine are both mixed α-1 and α-2 agonists with predominant α-2 action. However, dexmedetomidine is eight times as selective for the α-2 receptor compared to clonidine [6]. Furthermore, dexmedetomidine has a reported affinity approximately 1600 times greater than that of the alpha-1 adrenergic receptor [8].

2.2 Pharmacodynamics and Pharmacokinetics

Clonidine is available in oral, intravenous, transdermal, and spinal formulations. Its distribution volume is approximately 12 L/kg. The drug is principally metabolized by the liver and excreted by the kidney. Thus, dosage should be reduced in patients with kidney disease. The half-life of clonidine varies based on its administration and kidney function: 12–16 h orally, 6–23 h intravenously, 20 h transdermal, and approximately 1.3 h spinally [9]. Additionally, clonidine is fat soluble and can cross the blood brain barrier.

Dexmedetomidine is only used intravenously in clinical environments. Following administration, majority of the drug becomes albumin-bound and alpha1-glycoprotein-bound. Like clonidine, it is also lipophilic and readily crosses the blood-brain barrier and placenta barriers. Dexmedetomidine is mainly eliminated through biotransformation in the liver via direct glucuronidation and excreted 95% renally. Dexmedetomidine has a rapid onset with a distribution half-life of 6 min, a terminal half-life of approximately 2 h. Dexmedetomidine's half-life is approximately 6–12 times shorter than clonidine, a key differentiating trait when comparing the two drugs. Major factors impacting dose variability in intensive care unit populations include hypoalbuminemia, concurrent end-organ damage, hemodynamic instability and decreased cardiac output [10].

3 Practical Perioperative Uses

3.1 Dexmedetomidine

Dexmedetomidine produces a variety of physiologic effects important in the perioperative settings, namely sedation, anxiolysis, and analgesia. As previously discussed, dexmedetomidine promotes natural sleep pathways in the cortex and thalamus, which results in a fast transition between asleep states and wakefulness states. This transition avoids paradoxical agitation that may occur with benzodiazepines and other GABA agonists.

Several studies involving ICU patients have shown dexmedetomidine to be associated with decreased rates of delirium, cognitive disturbance, and time to extubation, length of stay, and mortality when compared with midazolam [11]. Dexmedetomidine also has a faster offset effect compared to clonidine that is advantageous in the critical care setting. Another clinical application of dexmedetomidine is as a primary or adjunct sedative agent in minor surgical and interventional procedures when hypoventilation would be poorly tolerated. This includes obese patients with obstructive sleep apnea or those undergoing bariatric surgery. At clinical doses, dexmedetomidine has unique effects on the respiratory system where it increases arterial $PaCO_2$ chemoreceptor sensitivity, leading to hypercapnic arousal and stimulation hyperventilation during deeper levels of sedation. In more stimulating procedures, other adjunctive analgesic and sedative agents should be considered due to dexmedetomidine's relatively slow onset and offset times. Dexmedetomidine has been shown to be as effective as higher doses of midazolam for sedation, with minimal hemodynamic and respiratory effects [12]. However, two studies have found dexmedetomidine to be inferior to propofol for sedation for upper endoscopy procedures [13].

Comparative studies between dexmedetomidine and midazolam in pediatric patients have shown superior sedation when using dexmedetomidine with relatively prolonged onset of action. However, midazolam results in more effective anxiolysis with less sedation compared to dexmedetomidine. Furthermore, recent studies have concluded that pediatric patients premedicated with combination dexmedetomidine and midazolam have significantly improved induction compliance and faster onset to achieve a satisfactory level of sedation compared to premedication with each agent separately [14]. Dexmedetomidine has a readily available intranasal formulation, which can be advantageous in uncooperative adult and pediatric patients without intravenous access. Intravenous dexmedetomidine reduces postoperative emergence delirium in children, at the cost of prolonged time in the recovery room. However, studies comparing dexmedetomidine to midazolam have not provided sufficient evidence that either is superior in prevention of emergence delirium in the pediatric

population [15]. Dexmedetomidine is often used in the perioperative setting for its analgesic qualities. As an adjuvant medication during general anesthesia, dexmedetomidine has been shown to reduce intraoperative and postoperative opioid requirements, Minimal Alveoli Concentration of volatile anesthetics and pain intensity scores [16]. Some studies have shown that the drug allows for greater than 50% reduction in opioid requirements. The agent decreases Minimal Alveoli Concentration of inhalational anesthetics by approximately 30%. Furthermore, by reducing volatile anesthetic and opioid requirements, there is a reported decrease in incidence of postoperative nausea & vomiting (PONV) without prolonged anesthesia recovery time [17]. Studies comparing dexmedetomidine's anesthetic properties with remifentanil have shown that dexmedetomidine has better recovery quality with faster wakeup times with no significant differences in wakeup success rate. With regards to recovery, dexmedetomidine has also been shown to attenuate perioperative stress and inflammation and protect immune function, which may contribute to decreased postoperative complications and improved clinical outcomes [18]. Dexmedetomidine can also be used as an adjuvant to regional anesthesia, where it is administered as part of peripheral nerve blocks and neuraxial anesthesia. In these settings, dexmedetomidine has been shown to hasten block onset, prolong duration, and reduce pain scores [19]. These beneficial effects in regional anesthesia can further reduce early postoperative opioid consumption. Of greatest concern when administering dexmedetomidine in these procedures is bradycardia, which occurred in all neuraxial routes and peripheral nerve blocks [19].

Several studies have shown useful applications for dexmedetomidine for specific clinical scenarios. For example, dexmedetomidine is specifically indicated as a sole anesthetic agent in awake fiberoptic intubations. In comparisons between dexmedetomidine-midazolam combination sedation compared to midazolam alone, combination therapy patients were significantly calmer and more cooperative, with fewer adverse reactions, with no significant hemodynamic differences [20]. Similar benefits were seen when compared with fentanyl and propofol administration. When compared to propofol induction, dexmedetomidine was shown to have

lower rates of airway obstruction and reduced hemodynamic response to intubation. Dexmedetomidine also lead to better endoscopy scores, lower recall of intubation, and greater patient satisfaction when compared to remifentanil [21]. Dexmedetomidine has also been studied for direct laryngoscopy and endotracheal intubation. The drug was shown to attenuate the hemodynamic stress responses in these procedures without significant differences in mean arterial pressure when administered intravenously, intranasally, or intramuscularly [22]. Dexmedetomidine has also been compared to labetalol and shown to attenuate hypertension more effectively with fewer deleterious effects. Additionally, comparison with clonidine has shown that clonidine has similar hemodynamic attenuation but with lower rates of adverse effects, namely bradycardia and hypotension [23]. There is evidence of hemodynamic protection in the pediatric population as well. With a well-known side effect of hypotension, dexmedetomidine is a suitable choice for deliberate hypotension techniques in neuroanesthesia. In these procedures, use of dexmedetomidine may lead to decreased free radical formation, reduced neuronal sensitization of excitatory neurotransmitters, improved cerebral perfusion, and more favorable matching of cerebral metabolic supply and demand [24]. The result is neuroprotective effects during these procedures. Dexmedetomidine also has application in orthopedic operations, specifically with regards to tourniquet-induced hypertension. Prolonged inflation is often associated with severe pain leading to progressive increase in systemic arterial pressure. Patients given preoperative dexmedetomidine infusions have been shown to have no significant changes in arterial pressure during inflation and after deflation. This is a useful application as tourniquet induced hypertension is often poorly responsive to antihypertensives and anesthetics [25].

Lastly, dexmedetomidine has been studied for treatment for alcohol withdrawal syndrome treatment with mixed results. No relevant advantages have been demonstrated in comparison studies with benzodiazepine treatment. Whereas some studies have shown dexmedetomidine to increase length of stay in patients, others have shown decreased length of stay when combined with propofol [26].

3.2 Clonidine

Clonidine is commonly used for its antihypertensive and negative chronotropic effects in outpatient clinical medicine. However, its unique mechanism of action allows it to have beneficial applications in the anesthetic and perioperative setting as well, namely sedation, analgesia, anesthesia, and post-operative prophylaxis. Clonidine produces a unique type of sedation when compared drugs that act on gamma-aminobutyric acid (GABA receptors) such as midazolam. As previously described, clonidine mainly causes sedation via decreasing sympathetic nervous system activation and decreases consciousness via promotion of endogenous sleep pathways. This is important since clonidine causes sedation without risk of respiratory depression allowing patients to return to full consciousness quickly with minimal arousal. Furthermore, there is minimal danger of paradoxical agitation, tolerance, or dependence that is characteristic of other sedatives that act on GABA receptors [27]. Clonidine has been proposed as a promising alternative to midazolam for premedication especially in the pediatric population. Specifically, clonidine has been shown to have less effect on respiration and lower rates of adverse side effects including amnesia, confusion, and long-term behavioral disturbances. The drug has also been shown to have lower rates of emergence delirium, shivering, nausea, and vomiting in children [28].

Clonidine also has a wide range of applications as an analgesic adjuvant. Clonidine has been recommended as an adjuvant with regional anesthetic techniques, especially in the pediatric population. However, clonidine was found to have a narrow therapeutic windows and increased incidence of toxicity with regional techniques [29]. Evidence has supported the use of clonidine in spinal-epidural anesthesia, where epidural clonidine has been shown to have earlier onset and prolonged duration of motor blockade and analgesia without significant postoperative complications, including postoperative nausea and vomiting and urinary retention [30]. In addition, clonidine has also been used with hydromorphone in implantable intrathecal pumps for long-term pain control. Other applications include use of transdermal and topical forms for diabetic neuropathy. Surgical site injection with bupivacaine mixed

with clonidine has also been shown to be effective in prevention of chronic pain following mastectomy [27]. Outside of regional anesthesia, clonidine improves analgesic effects of anti-inflammatory agents, opioids, and ketamine. Numerous studies have shown clonidine to be effective in conjunction with other types of nonopioid analgesic agents to reduce overall opioid use, thus contributing to improved postoperative outcomes [27, 30, 31]. Furthermore, clonidine is effective in reducing opioid-induced muscle rigidity and attenuation of opioid withdrawal symptoms. However, one recent large-scale study demonstrated that clonidine does not significantly reduce opioid consumption or pain scores in patients recovering from noncardiac surgery. As a result, further studies may be needed to better assess the effectiveness of clonidine's analgesic properties. There is evidence that clonidine decreases the requirements of inhalational volatile agents intraoperatively. Studies comparing use of sevoflurane with clonidine has shown MAC to be lower with clonidine. This application is important to decrease exposure in patients that would have difficulty tolerating the adverse effects of volatile inhaled anesthetics [32].

Perioperative clonidine has been shown to have multiple uses as a prophylactic agent. Although not first-line, clonidine can also be used for postoperative nausea and vomiting prophylaxis and can be administered orally or as an adjunct with caudal nerve blocks for this purpose [31]. Early studies showed clonidine to reduce the risk of perioperative myocardial ischemia in patients undergoing both cardiac and non-cardiac surgery [31]. However, more recent large-scale trials have shown that clonidine does not improve outcomes with regards to cardiovascular metrics, despite increased risk of bradycardia and hypotension. Current guidelines recommend against use for prevention of perioperative cardiac events [31]. Clonidine's hemodynamic profile has numerous applications in the perioperative setting. As previously mentioned, clonidine has been shown to attenuate hemodynamic effects of laryngoscopy and endotracheal intubation and is shown to have lower rates of bradycardia and hypotension compared to dexmedetomidine (Table 1). Furthermore, these cardiovascular effects make the drug acceptable for use in cases requiring con-

Table 1 Comparison of α-2 agonists clonidine and dexmedetomidine

Drug name	Clonidine	Dexmedetomidine
Trade name	Catapres	Precedex
Mechanism of action	Alpha-2-adrenergic receptor agonist	Alpha-2-adrenergic receptor agonist
Metabolism	50% liver	Liver
Excretion	40–60% in urine, 20% bile/feces	95% urine, 4% feces
Half-life	12–16 h	2 h
Clinical indications	Hypertension Anxiety ADD/ADHD Chronic pain Withdrawal symptoms Postoperative shiver	ICU sedation Procedural sedation Adjunct to anesthesia Delirium Therapy of PONV ERAS
Precautions	Transient increases in blood pressure after initial dosing	Hypotension Bradycardia Tachyphylaxis

ICU intensive care unit, *PONV* postoperative nausea and vomiting, *ERAS* enhanced recovery after surgery, *ADD/ADHD* attention deficit disorder/attention-deficit/hyperactivity disorder

trolled hypotension [6]. Furthermore, clonidine is an important alternative in patient populations in which beta blockers are contraindicated, including asthmatics and patients with high-grade atrioventricular (AV) block [33]. Lastly, clonidine has been investigated for control of autonomic alcohol withdrawal syndrome (AWS) symptoms as a symptom-oriented adjunct to benzodiazepine-based therapy [33].

3.3 Tizanidine

Tizanidine is also an α-2 adrenoreceptor agonist, though similar to clonidine, Tizanidine has some important differences. Tizanidine has anxiolytic, sedative, and analgesic properties like clonidine, but Tizanidine has a shorter duration and less side effect on heart rate and blood pressure [2]. Tabori et al. studied the hemodynamic effect of tizanidine on the response to direct laryn-

goscopy. Subjects received either a placebo or 4 mg of tizanidine 90 min before the induction of general anesthesia with propofol. The tizanidine group showed less fluctuation in heart rate and blood pressure than the placebo group following direct laryngoscopy and intubation. Tizanidine group also had reduced propofol requirement by 25% and significantly less postoperative shivering (11.4 vs 28.6%). Tabori et al. believed that tizanidine may provide better cardiovascular stability during induction of general anesthesia. Tizanidine may also have some utilities in attenuating the stress due to direct laryngoscopy and intubation [2].

Tizanidine was also tested for the treatment of myofascial pain disorders. Tizanidine could reduce spasticity by increasing the presynaptic suppression of motor neurons in the brain and spinal cord, and by decreasing painful muscle spasms in the neck and shoulder. Tizanidine was also shown to reduce pain and tissue tenderness significantly and to improve the quality of sleep. Tizanidine was rated to be from good to excellent in alleviating pain by 89% of the patients. Tizanidine was also evaluated in patients with cerebral palsy. Tizanidine was also shown to significantly decrease spasticity by 78.8% in patients with infantile cerebral palsy when compared to 7.6% for placebo [34]. Therefore, tizanidine may be useful as a preoperative sedative prior to general anesthesia and as a management adjunct for cerebral palsy or other spastic disorders [2].

4 Indications and Contraindications

4.1 Clonidine

Clonidine is indicated in the perioperative setting for analgesia, sedation, and anxiolysis. The drug can be administered orally, intramuscularly, intravenously, transdermal, intrathecally, and in the epidural space. The doses are typically intramuscularly 2 μg/kg, intravenously 1–3 μg/kg, and intrathecal 15–30 μg respectively. Epidural clonidine is typically started at 30 μg/h in a mixture with an opioid or local anesthetic agent. When given orally, with weight-based doses typically at 3–5 μg/kg, clonidine

has a 30–60 min onset and lasts approximately 6–12 h. It is usually administered orally for chronic pain at doses between 0.1 and 0.3 mg twice daily [35]. When treating hypertension in the perioperative setting, clonidine is usually dosed at 0.1 mg twice a day, with titration to targeted blood pressure. Transdermal clonidine is available as 0.1, 0.2, or 0.3 mg/day patches, with replacement every 7 days. In all formulations, clonidine dosages should be reduced in patients with kidney disease [14].

Clonidine is relatively contraindicated in patients who took β-adrenergic blockers and in those with significant cardiac conduction abnormalities. This is due to increased risk of complications, including sedation, hypotension, and bradycardia [36]. These adverse effects are potentiated when co-administered with other hypnotic agents, general anesthetics, or sedatives. Clonidine use is also cautioned in diabetic patients, as it can mask symptoms of hypoglycemia [36]. This is because the α-2 adrenoreceptor activation inhibits insulin release.

4.2 Dexmedetomidine

Indications for dexmedetomidine include ICU sedation in mechanically ventilated patients, premedication prior to intubation and extubation, procedural sedation, awake intubations, adjuvant regional anesthesia, awake craniotomies, treatment of delirium, and as a component of multimodal anesthesia [37]. Dexmedetomidine can be administered orally, nasally, intravenously, intramuscularly, and rectally [38]. Oral dosing is typically 2–4 μg/kg, with an onset approximately 30–60 min to provide adequate sedation [37]. Recommended intravenous dosing of dexmedetomidine consists of a loading dose at 1 μg/kg over 10 min followed by an infusion at 0.2–0.7 μg/kg/h. At these rates, dexmedetomidine can provide sedation alone or in combination with other medications. However, there is significant variability of infusion rates based on clinical preference. Intranasal administration is usually at doses of 1–2 μg/kg, with an onset of 25 min and duration of 85 min [37].

Adverse effects of dexmedetomidine in the perioperative setting include bradycardia, hypotension, and hypothermia [36]. Bradycardia is exacerbated when given with other vasodilators, cardiac depressants and drugs that decrease heart rate. Omitting loading doses of dexmedetomidine has also been shown to decrease incidence of bradycardia [36]. Hypotension is potentially worsened when given with other hypnotics and anesthetic agents, which should have decreased requirements [36]. Hypotension and bradycardia can be adequately treated with atropine, glycopyrrolate, and ephedrine. However, it is important to avoid glycopyrrolate in the pediatric population as profound hypotension may occur [39]. Hypothermia is a side effect of dexmedetomidine that is thought to occur from lowering the threshold body temperature at which compensatory thermoregulation mechanisms are activated. This effect can be countered by active warming of the patient [40].

As aforementioned, the key differences between clonidine and dexmedetomidine are time of onset and offset, and selectivity of drug targets. Dexmedetomidine has a faster offset when compared to clonidine, which is advantageous in the perioperative settings [41]. Dexmedetomidine is also super-selective for the alpha 2 adrenoreceptor compared to clonidine, with eight times higher selectivity. This accounts for the drug's superior analgesic properties compared to clonidine [37].

5 Alpha-2 Adrenoreceptor Withdrawal

Long-term usage of both clonidine and dexmedetomidine may lead to super-sensitization and up-regulation of adrenoreceptors. If abrupt withdrawal of either agent, an acute withdrawal syndrome including hypertensive crisis can occur. Comparing the two agents, dexmedetomidine withdrawal manifests much faster, after only 48 h of use when the drug is discontinued. This is thought to be due to dexmedetomidine's greater affinity for the α-2 adrenoreceptor [19]. In both pediatric and adult patient populations, the incidence of withdrawal syndrome from prolonged infusions of dexmedetomidine, defined as greater than or equal to

72 h, is approximately 30%. Notably, administration of clonidine as protection from withdrawal did not appear to reduce incidence [42]. Some studies have also demonstrated that peak and cumulative daily dexmedetomidine dose, rather than duration of therapy, may be associated with higher incidence of withdrawal signs [42]. However, other studies have shown there to be no correlation between dose, exposure and weaning in occurrence of withdrawal.

Withdrawal symptoms typically include severe hypertension, potential hypertensive emergency, associated with tachycardia, headache, anxiety, tremor, and diaphoresis. In these situations, treatment may require intravenous medications with invasive monitoring of arterial pressure in an ICU setting. It is vital to avoid monotherapy with beta blockers, as this leads to unopposed α-1 adrenoceptor stimulation leading to severe vasoconstriction and worsening hypertension. Transdermal clonidine can be used in this setting to mitigate drug withdrawal in patients unable to consume the medication. However, transdermal clonidine requires approximately 48 h to achieve therapeutic concentrations in serum. Despite no change in incidence of withdrawal syndrome when given clonidine tapering, there is sufficient evidence that patients receiving clonidine can wean off dexmedetomidine more rapidly, with considerable cost savings [43]. Thus, clonidine is a safe and effective option to transition patients off prolonged dexmedetomidine infusions [44].

6 Perioperative Management of α-2 Agonists

With regards to α-2 agonists, patients may regularly take clonidine in the outpatient setting for hypertension. Current guidelines state that prophylactic clonidine should not be initiated perioperatively [45]. The major POISE trial in 2014, with an enrollment of more than 10,000 noncardiac surgical patients, showed that preoperative initiation of clonidine increased the risks of clinically significant hypotension and nonfatal cardiac arrest and did not reduce rates of mortality when compared to placebo [46]. However, patients on long-term regimens can continue them in

the perioperative period if stable, and guidelines caution that patients already on α-2 agonists should not stop them abruptly, causing rebound hypertension and tachycardia from discontinuation [45]. In patients with hepatic or renal insufficient including dialysis patients, dexmedetomidine undergoes metabolism via direct glucuronidation and cytochrome P450 mediated metabolism (particularly CYP2A6 and to a lesser extent, CYP1A2, CYP2E1, CYP2D6, and CYP2C1). Dexmedetomidine is 95% renally eliminated from the body. Accordingly, pre-existing liver and/or renal disease may have theoretical consequences for use of this medication. Regarding renal disease, some in vivo studies of the pharmacokinetics of dexmedetomidine in patients with end stage renal disease seems to be similar to those with preserved renal function. In addition, these renal patients were also found to have similar hemodynamic response to the medication indicating a comparable safety profile to those with preserved renal function. Other studies have found patients with renal impairment might experience longer-lasting sedative effects, likely due to decreased protein binding. Therefore, it is inconclusive with regards to renal dosing. Currently there is a paucity of investigations regarding in vivo effects of dexmedetomidine on liver function and more specifically on the diseased liver. As dexmedetomidine principally relies on the CYP450 and CYP2A6 enzymes for metabolism, anesthesiologists can reasonably assume medications that increase or decrease the function of this enzyme will affect availability of dexmedetomidine. The same can be expected of concurrent liver disease affecting this enzyme family. The specific metabolism of clonidine remains poorly understood, although pathways through CYP 450 CYP2D6 are an area of active investigation. Liver metabolism accounts for 40–60% of total metabolism with subsequent elimination through fecal and renal routes. There is no evidence of hepatotoxicity from clonidine use and there is limited information available on use in patients with liver disease. Clonidine has been utilized in the presence of renal disease and does not require specific dose adjustments. Additionally, clonidine has no detrimental effects of renal function when utilized as a chronic antihypertensive medication. Clonidine is not dialyzable but may be used in patients undergo-

ing regular hemodialysis. In these instances, doses may have to be reduced due to significant renal elimination irrespective of dialysis schedule [47].

7 Potential Toxicity of α-2 Adrenoreceptor

The overall safety profile of dexmedetomidine and clonidine is robust and well established. However, toxicity is still possible when these medications are prescribed or utilized outside of established dosing protocols. Maximum daily dosing of clonidine in adults is 2.4 mg/day and only 0.9 mg/day in children. Mild toxicity is possible just outside of the therapeutic range. Pharmacologically, clonidine toxicity initially manifests as transient hypertension from stimulation of postsynaptic peripheral α-2receptors followed by activation of central presynaptic α-2receptors resulting in hypotension and bradycardia. This is often accompanied by central nervous system depression, respiratory depression, hypotonia and coma [48]. Treatment for clonidine overdose is principally supportive with no specific antidote at this time. Severe toxicity with bradycardia with associated hypotension is treated with atropine or cardiac pacing as indicated [48]. Advanced airway management including endotracheal intubation may be needed in severe circumstances. Naloxone has been utilized to treat the central nervous system symptoms of clonidine toxicity with some success although this remains controversial [49].

Dexmedetomidine was approved by the Food and Drug Administration in 1999 and therefore has more limited data available on the toxicity profile and incomplete data in pediatric patients. Maximum therapeutic dosing in adults is 1 μg/kg loading dose over 10 min followed by an infusion of 0.7 μg/kg/h for a maximum of 24 h. As dexmedetomidine is almost exclusively utilized in hospital settings, the majority of reports of toxicity are iatrogenic in nature. Toxicity can manifest as initial hypertension followed by bradycardia and hypotension (similar to clonidine) [50]. Additional signs of toxicity include oversedation and respiratory depression [50].

Both clonidine and dexmedetomidine should be utilized with consideration for interaction with other drugs including opioids. Dexmedetomidine specifically may enhance the central nervous system depressant effects of opioids and concurrent use of these agents in opioid naive patients should be monitored closely. Clonidine is not known to specifically interact with opioids. Additionally, both agents have been investigated for use in the treatment of iatrogenic opioid withdrawal from ICU sedation. Dexmedetomidine was not successful in preventing opioid/benzodiazepine withdraw symptoms in pediatric patients [51]. Although other studies have shown greater success with this method, particularly in pediatric cardiac patients [51]. Clonidine has also been investigated as an agent to treat neonatal opioid withdraw syndrome with some success [51]. Although other studies were inconclusive, both clonidine and dexmedetomidine remain under active investigation in this space [51].

8 Chronic Pain

Clonidine has been investigated as both an adjunct or as a solo agent for the management of chronic pain [52]. Intrathecal, epidural, and topical applications have all been investigated. A recent review of 30 studies suggested that clonidine has the most potential benefits in treatment of chronic pain of neuropathic origin [53]. However, a recent Cochrane review refuted these results and found that the majority of evidence regarding the use of topical clonidine in chronic pain management is of low quality and suggests limited utility as a therapeutic [54]. Additional applications of clonidine include management of insomnia in chronic pain patients [55]. Although clonidine continues to show promise as an adjunct for the management of chronic pain, the drug still hasn't found its footing as a solo agent for daily use.

As previously discussed, dexmedetomidine is a newer and more highly selective agent that has rightfully garnered interest as a potential treatment for chronic pain. Accordingly, it has been used to treat myofascial pain, complex pain syndrome, spastic pain, and neuropathic pain amongst others [56]. Applications in

treatment of neuropathic pain have garnered the most attention to this point [57]. The majority of research regarding this topic is centered on the role of dexmedetomidine in attenuation of inflammatory pathways in animal models [55]. More specific applications in vivo are still under investigation. Dexmedetomidine is typically administered intravenously but can also be given in the epidural and perineural spaces. It has been utilized as an adjunct and prolongs the duration of peripheral nerve blocks, intravenous regional anesthesia, and spinal analgesia [57]. Despite ongoing research, dexmedetomidine has not found use as a single use agent for the management of chronic pain in the outpatient setting. Anesthesiologists are unlikely to encounter patients presenting on the day of surgery with dexmedetomidine as a daily medication at this point.

9 Use in Enhanced Recovery After Surgery Protocols

Enhanced recovery after surgery was first introduced in the late 1990s by a group of surgeons looking to improve outcomes following procedures [54]. Following the group's initial work, enhanced recovery after surgery protocols have been expanded to encompass nearly every surgical specialty. A critical component of any enhanced recovery after surgery protocol is effective postoperative pain management. This has led to interest in applications for clonidine and dexmedetomidine in this space [58]. Dexmedetomidine has been extensively evaluated for use in Enhanced recovery after surgery protocols [59, 60]. It is aimed to incorporate multimodal analgesia into the postoperative recovery strategy, dexmedetomidine is considered a crucial component [61]. Clonidine has smaller evidence and is less thoroughly evaluated as a component of enhanced recovery after surgery protocols. And standardized use and dosing regimens as part of a multimodal postoperative pain strategy have not yet been established. A general rule of thumb, opioid sparing strategies have gained widespread use, particularly in the context of the opioid epidemic although impacts on prescribing practices have been mixed [62].

Effective postoperative, multimodal analgesia will continue to be a critical component of enhanced recovery after surgery protocols moving forward. α-2 agonists, especially dexmedetomidine, will continue to have an expanding role.

10 Conclusion

Clonidine and dexmedetomidine are two commonly used α-2 agonists with an established safety profile and ever-expanding applications as part of a balanced anesthetic techniques. Accordingly, there are extensive uses for these agents in the preoperative, intraoperative, and postoperative settings. α-2 agonists clonidine and dexmedetomidine can be utilized in sedative, anxiolytic, analgesic, and delirum management. Risks of withdrawal syndrome due to prolonged use must be carefully balanced against clinical indications. Learning to effectively use α-2 agonists is critical for all anesthesiologists and critical care providers to appropriately use this category of drugs.

Common Pitfalls

Dexmedetomidine's adverse effects include hypotension, nausea, bradycardia, atrial fibrillation, and hypoxia [63]. Hypotension, hypertension, and bradycardia are the most reported at incidence rates of 25, 15, and 13% respectively [64]. The drugs overdose has also been known to cause first-degree or second-degree atrioventricular block. However, most adverse effects of dexmedetomidine have been observed during or briefly after loading the dose. It has been reported that omitting or reducing the loading dose can reduce incidence of these adverse effects [63]. There are rare cases of administration related cardiac arrest. Cardiac conduction disorders and co-administration with amiodarone and dexmedetomidine are potential factors contributing to development of asystole [65]. Given this side effect profile, patient selection is imperative and attention to individual patients' hemodynamic properties, such as hypovolemia or vasoconstriction, should be considered for risk vs benefit analysis [64].

Clonidine has a similar adverse effect profile compared to dexmedetomidine. The two most reported adverse effects are sedation and dryness of mouth [66]. However, these are both beneficial in the setting of anesthesia. Acute adverse effects include bradycardia and hypotension, similarly to dexmedetomidine [62]. Clonidine has been shown to be more likely to cause hypotension and lower doses (steady-state concentration < 1 ng/ml) and hypertension at higher doses (steady-state concentration > 2 ng/ml) [67]. However, observed bradycardia and hypotension in the perioperative setting rarely require intervention unless associated with hypovolemia and bleeding [68]. More serious effects of clonidine come with rebound hypertension that occurs within 24–36 h after acute cessation of therapy, which has been previously discussed [69].

Clinical Pearls

1. Clonidine and dexmedetomidine are α-2 agonists that are used extensively for sedation and anxiolysis, via activation of receptors in the brain stem and for analgesia via activation of receptors in the spinal cord.
2. α-2 agonists are unique sedatives in that they have limited respiratory depressant effects.
3. Clonidine provides sedation and anxiolysis while decreasing anesthetic and analgesic requirements.
4. Clonidine is used as an adjunct for epidural, caudal, and peripheral nerve block anesthesia and analgesia.
5. Dexmedetomidine is a parenteral super-selective agent with higher affinity for α-2 receptors than clonidine, and also provides sedative, analgesic, and sympathetic effects that blunt cardiovascular responses in the perioperative period.
6. Long-term use of α-2 agonists leads to upregulation of receptors, leading to acute withdrawal syndrome and possible hypertensive crisis upon abrupt discontinuation.
7. Caution should be taken when administering α-2 agonists to patients already on beta blockers or with cardiac conduction abnormalities.

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Ketamine

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1 Essential Basics

1.1 Pharmacokinetics

Ketamine is a phencyclidine (PCP) analog with a chiral structure that has two optical isomers, S-ketamine and R-ketamine, which are both available for human use [1]. S-ketamine has greater potency at inhibiting the receptors as compared to its R-Ketamine S-enantiomer by fourfold [2]. It has low protein binding (10–30%) but high lipid solubility that leads to extensive volume of distribution and rapid distribution to brain and all well perfused tissues of the body. Ketamine has a high clearance dependent on blood flow through liver. It is metabolized through N—demethylation and ring hydroxylation to a potent main metabolite called nor-ketamine

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_13

(80%) which is then principally hydroxylized and excreted in bile and urine. Elimination half-life of ketamine is 2–4 h [3–5]. A short half-life (2–4 min) and a short context sensitive half-life of ketamine provide the advantage of quick recovery from intravenous administration. Ketamine can be administered through multiple routes including intra-venous (IV), intra-muscular (IM), intrarectal, oral or through intra-nasal routes. Typically used through IV route, it rapidly attains maximum plasma concentration [3]. It has 93% bioavailability through intra-muscular route with peak plasma concentration achieved between 5–30 min [3–5]. Bio-availability after oral administration is 20% due to hepatic metabolism and around 50% after intra-nasal administration.

1.2 Mechanism of Action

Ketamine is a use dependent non competitive N-Methyl-D-aspartate (NMDA), hyperpolarization activated cyclic nucleotide (HCN1) and glutamate receptor antagonist. It leads to dissociative anesthesia which is a cataleptic state with open eyes, nystagmus but absence of motor response to nociceptive stimulus [3]. The laryngeal, corneal and papillary reflexes are preserved with ketamine administration. The antagonism of transmembrane NMDA receptors by ketamine in brain and spinal cord leads to its anesthetic and analgesic effects. NMDA receptors are known to be involved in pain transmission and pain modulation with contribution to phenomenas like wind-up and central sensitization which leads to development of chronic pain [6, 7]. Ketamine can block these pathways through NMDA antagonism and potentially prevent the development of chronic pain. It also exerts its analgesic effect through partial agonism of opiate mu—receptors. Further through its NMDA antagonism, ketamine has also been seen to attenuate the development of morphine tolerance and more importantly reverse established morphine tolerance which is of great benefit in chronic pain patients [8]. This effects is more pronounced with morphine as compared to other opioids like oxycodone [9]. Ketamine is also useful in controlling symptoms of depression and acute suicidal ideation in treatment resistant

patients through NMDA antagonism and involvement in other downstream pathways [10]. Among the two S-enantiomers, R-ketamine has been found to have a more potent and longer lasting anti-depressant effect compared to S-ketamine [11]. In terms of the downstream pathways, ketamine increases the expression of brain derived neurotrophic factor and leads to glutamate burst that activates another class of receptors called the AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) which leads to increased synaptic connection which contributes to its anti-depressant effects [12, 13]. Ketamine also binds to sigma receptors leading to neuronal modelling contributing to its anti-depressant effects [14]. Ketamine also prevents re-uptake of norepinephrine and its metabolites activating the sympathetic nervous system with increased heart rate, blood pressure and cardiac output [15]. It has minimal effects on the central respiratory drive, produces airway relaxation and maintains spontaneous respiratory function.

2 Practical Perioperative Use

2.1 Indications

Ketamine is used for general anesthesia and as adjunct for local anesthesia and analgesia in humans and animals [15, 16]. Ketamine can be specifically useful in the following situations—as an IV induction agent in emergency situations for hypotensive patients specifically in patients with cardiac tamponade and restrictive pericarditis due to its sympathetic stimulation. It is useful in patients with reactive airway disease and refractory status asthmaticus in intensive care unit due to its bronchodilating properties. It is useful for induction in pediatric patients with congenital heart disease with right to left shunt where by increasing the systemic vascular resistance, the shunt fraction is reduced. It is useful in burn patients for dressing change and grafting in both adult and pediatrics populations, especially where IV access is difficult and ketamine can be used IM or inter-nasal in that situation. It can also be used intra-muscularly in pediatric patients as

pre-medication specially for mentally-challenged population. Ketamine has been approved to be used as a preanesthetic before giving other general anesthetics. Ketamine is a great peri-operative analgesic adjunct in both adult and pediatric patients specially in chronic pain patients to overcome opioid tolerance and reduction in opioid induced hyperalgesia [17]. It is a great adjunct in chronic refractory cancer as well as non-cancer pain. It has a greater opioid sparing effect in chronic pain patients who are opioid dependent as compared to the opioid naïve patients. There is no added increase in adverse effects in this patient population that is opioid dependent [18]. It is also useful in short duration procedures not requiring muscle relaxation. Low dose prophylactic IV ketamine has been seen to be helpful for preventing post anesthesia shivering [15].

2.2 Safety and Use in ERAS Protocols

There are multiple studies in literature evaluating the safety and efficacy of ketamine in perioperative areas. A systematic review including 53 randomized controlled trials has shown benefit of low dose ketamine in all surgical patients as it has opioid sparing effects [19]. Low dose bolus (0.1–0.5 mg/kg with an infusion of 1–10 μg/kg/min, stopped after 48 h) showed improvement in post-operative pain scores in patients undergoing painful orthopedic surgery mostly total joint operations [20]. Use of IV ketamine intra-operatively and post operatively for 48–72 h as a part of ERAS protocol in patients undergoing living liver donation minimized post operative pain and opioid use [21]. Use of ketamine as intra-operative infusions for colo-rectal surgery has also been seen to be beneficial for patients especially if there is opioid tolerance or history of chronic pain in the patients [22]. Similarly for thoracic surgeries, a bolus of ketamine with infusion at 0.15 mg to 0.3 mg/kg/h stopped 45 min before end of the surgery has been successfully used as a part of ERAS protocol [23]. Ketamine is successfully used as a part of the ERAS protocol for peri-operative pain control, given the patients co-morbidities are taken into account for dosing.

2.3 Contraindications

Given ketamine's sympathetic stimulation it is contraindicated in conditions that can worsen due to increased blood pressure like aortic dissection, myocardial infarction, aneurysms, uncontrolled hypertension, raised intra-ocular pressure [24]. It should not be given to patients with known hypersensitivity to this drug [25]. Due to increased risk of laryngospasm and airway complications it is avoided in children aged less than 3 months. It also has the potential for exacerbating schizophrenia and should be avoided in schizophrenic patients. It was initially believed that ketamine administration can increase intra-cranial pressure (ICP) but current research shows that ketamine is safe to use in trauma patients with head injury as it has minimal effects on ICP and may in fact improve cerebral perfusion pressure and have neuroprotective properties [26, 27].

2.4 Dosing

Dosing for ketamine in the perioperative period depends on the age of the patient, underlying co-morbidities and the effect that is desired from the medication. Intravenous route is most commonly used for drug administration. For anesthetic purposes it can be given in the range of 0.5–2 mg/kg IV, 4–10 mg/kg IM, 8–10.6 mg/kg for rectal route and 3–9 mg/kg for intra-nasal route [4, 16, 28, 29]. Sedation requires lower doses as compared to the anesthetic doses. Doses in the range of 0.15–0.3 mg/kg through IV route and 0.5–1 mg/kg IM are usually used for sedation [16, 30, 31]. Sub-anesthetic doses ranging from 0.03 to 0.24 mg/kg/h can be used for sedation in critically ill patients [31]. When using as an infusion, following a bolus dose the infusion can be continued at dose 0.12–0.36 mg/kg/h for upto 48 h to improve pain control after surgical procedure [32, 33]. It has been seen that clinical benefits from a single IV bolus dose of ketamine can last upto 2 h. Continuous infusion of ketamine can be continued for 48–72 h post-operatively for better pain control and reduced opioid

requirement post operatively [31]. For titration of ketamine infusion, it should be started at a low dose with increase of 0.03 mg/kg/h every 15 min to goal sedation or maximum dose of 1.2 mg/kg/h [34]. Higher doses can be used in special population after assessment of risk and benefit but would require frequent cardiovascular monitoring. It should be noted that given its highly lipophilic nature and presence of an active metabolite, prolonged exposure to ketamine could potentially lead to toxicity. It is recommended to administer ketamine slowly to avoid adverse effects like apnea or enhanced cardiovascular response [35]. Ketamine is safe to use in patients with renal insufficiency and requires no dosage adjustment when used in patients with CKD given its pharmacokinetics [36].

2.5 Monitoring

As is with performance of sedation or monitored anesthetic care, the monitoring during ketamine administration should depend on the likelihood of deleterious signs and symptoms with potential for adverse consequences [25, 37]. The monitoring practices for ketamine are variable in literature and hence basic guidelines used for moderate and deep sedation should be followed. Fasting guidelines with nil-per-os status should be ensured, and patient's level of ventilation, oxygenation and hemodynamic status using EKG, BP and pulse monitoring should be monitored prior to sedation and periodically throughout the sedation period and prior to discharge. Supplemental oxygen can be used during deep sedation, and back up airway equipment should be available. End tidal CO_2 monitoring should be used wile ketamine is given, if its available. Further clinical judgement should be used to determine the frequency and extent of monitoring for patients based on the presence and severity of patient's co-morbidities.

2.6 Adverse Effects

It is important to review the adverse effects of ketamine as they can add to the distress for patients during the perioperative period.

Ketamine, even in sub-anesthetic doses can lead to psychomimetic and psychiatric adverse effects [38]. Patients can experience dissociative symptoms with decreased inhibition, increased confusion, perceptual disturbances, feeling of intoxication, positive and negative symptoms of schizophrenia and maniac symptoms. These effects are temporally related to administration of medication and usually subside within 60 min of administration. Patients can experience some physical adverse effects like dizziness, light headedness, drowsiness, nausea which are usually dose dependent and limited to the period of infusion or shortly after. Ketamine can cause hypersalivation which can lead to laryngospasm [25]. Higher doses and fast administration can also cause transient apnea. Higher doses and quick administration can also affect the cardiovascular system and cause increases in heart rate and blood pressure [38]. Repeat use of ketamine in higher doses (>6 mg/kg/day) can cause ketamine associated uropathy. Although it has been mostly described in chronic abuse context, it should be kept in mind for patients getting ketamine as repeat administration. Anesthetic doses of ketamine (>1 mg/kg) and continuous infusions (10–20 mg/h) can cause temporary elevation of liver enzymes.

Ketamine can cause emergence delirium which can be distressing for the patient. It can be reduced by using benzodiazepines as pre-medication and/or reducing stimulation during drug administration. Midazolam (0.02 mg/kg IV) premedication can help attenuate the emergence phenomenon [39]. In a randomized controlled study of adult emergency department patients, Sener et al. found a significant reduction in the incidence of agitation when midazolam was co-administered with ketamine for procedural sedation [40]. Preoperative haloperidol use has also been seen to reduce the incidence of post operative delirium in children undergoing ketamine anesthesia [41].

2.7 Dependence

Repetitive long term use of ketamine poses concern for dependence in patients. Studies have shown that recreational ketamine users develop cravings, physiological tolerance and a withdrawal symptoms on cessation of ketamine [42, 43]. While it has been

used in the medical and veterinary setting with good effect and good safety record, there is increase in unregulated use of ketamine outside of these controlled settings [44]. The psychomimetic effect and the potential for dependence put the recreational user at the risk of personal harm. Hence its important for the medical specialists like psychiatrists, pain medicine physicians, dentists, emergency room physicians and veterinarians to work together to ensure continued safe use of this drug as a novel clinical tool and to prevent its diversion for abuse outside the medical settings.

Common Pitfalls

- Ketamine causes increased tracheal secretions, causing increased risk of laryngospasm
- Can cause hallucinations and emergence delirium which can be distressing to patients
- Repetitive use can lead to physiological tolerance and dependence.

Clinical Pearls

- Ketamine maintains spontaneous respirations and normal pharyngeal and laryngeal reflexes.
- It is a fast acting anesthetic that can be administered through multiple routes.
- It reduced post operative opioid consumption in patients.

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Methadone

Jackson Condrey, Andrew Klein,
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1 Mechanism of Action

Methadone is a long acting opioid that has several mechanisms of action. It is a potent μ-opioid receptor agonist, an NMDA receptor antagonist, and a serotonin and norepinephrine reuptake inhibitor. Methadone also has affinity for the δ and κ opioid receptors. NMDA receptor antagonism helps avoid the development of increasing opioid tolerance and hyperalgesia, and serotonin and norepinephrine reuptake inhibition is also thought to aid in post-operative pain control. Taken together, these attributes make methadone unique among opioids, and there has been increasing interest in using methadone in the surgical population for perioperative analgesia [1, 2]. See Table 1 for a summary of the mechanisms of action of methadone.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_14

Table 1 Mechanisms of action of methadone [1, 2]

Mechanism of action	μ-Opioid receptor activation	NMDA receptor antagonism	Serotonin/ norepinephrine re-uptake inhibition
Effects	• Analgesia • Euphoria • Nausea • Miosis • Decreased GI motility • Respiratory depression	• Prevention of opioid tolerance • Protects against hyperalgesia	• Modulation of pain pathways in the central nervous system • Possible improvement in mood

2 Pharmacokinetics and Pharmacodynamics

Methadone used for the purpose of chronic pain or opioid use disorder is mostly given via the oral route, however when used for the purpose of perioperative analgesia IV administration is preferred. With IV administration, methadone has a rapid onset time. CNS concentrations equilibrate with plasma concentrations within 4 min, with onset of effect closely paralleling plasma concentrations [2, 3]. Methadone also has the longest elimination half-life (ranging from 24 to 36 h) of the opioids used in the practice of anesthesia, and in large doses (20 mg or more) the analgesic effect can approximate the elimination half-life [2]. The long half-life of methadone makes it ideal for prolonged analgesia after surgical procedures with moderate to severe postoperative pain. Purported advantages that stem from methadone's prolonged elimination half-life include stable blood concentrations of opioid levels compared to more rapidly cleared opioids such as fentanyl or morphine; this results in less fluctuations in pain control, which in turn may increase patient satisfaction with their postoperative pain control regimen [2].

Methadone is metabolized by the liver and excreted by the kidneys. Methadone does not accumulate in patients with renal failure, and is also not removed by hemodialysis or peritoneal dialysis, making it a viable analgesic option in this patient population [1]. Liver

metabolism occurs via the CYP450 enzyme system where methadone undergoes N-demethylation to inactive metabolites. The most important enzymes within this system involved in the metabolism of methadone include CYP2B6 and CYP2C19 [4]. Initially, it was thought that CYP3A4 was the main driver of methadone metabolism. CYP3A4 is able to metabolize methadone in vitro, but further studies showed that this enzyme was actually not the primary driver of methadone metabolism in vivo. It is now thought that the main driver of methadone metabolism is CYP2B6 [3, 4].

There are no specific guidelines on how to dose methadone in patients with liver disease. A recent study that sought to elucidate the main determinants of methadone disposition did not find a relationship between methadone plasma levels and concomitant liver disease, but other studies have found that patients with hepatitis C have decreased clearance of methadone [5–7]. Until further clarity is obtained with more research, it seems prudent to give a patient with concomitant liver disease a smaller initial dose of methadone and allow for more gradual titration later.

Methadone metabolism may be affected by both individual phenotype of the CYP2B6 enzyme and drug interactions that induce or inhibit CYP2B6. Drugs that induce the CYP2B6 enzyme may speed the metabolism of methadone and potentially precipitate opiate withdrawal in patients with opioid use disorder. Examples of drugs that induce CYP2B6 include the antibiotic rifampin and antiretroviral drugs efavirenz and nevirapine. Conversely, drugs that inhibit CYP2B6 may result in increased methadone concentrations and can lead to opioid overdose, or even fatal arrhythmias due to excessive QT prolongation. Examples include ticlopidine, an antiplatelet agent, and voriconazole, an antifungal agent [1]. See Table 2 for a list of some more common drugs that may affect the metabolism of methadone. The list is not exhaustive and we recommend using an online drug interaction tool to verify that a patient's home medications will not interfere with methadone metabolism. Certain alleles of CYP2B6 have been associated with faster or slower metabolism of methadone, affecting plasma concentrations, but this effect is thought to be more pronounced with oral administration of methadone [2].

Table 2 Common methadone drug interactions (not exhaustive)

Drugs that may result in decreased plasma methadone levels	Drugs that may result in increased plasma methadone levels
Antiretrovirals—nevirapine, efavirenz Anticonvulsants/barbiturates—carbamazepine, phenobarbital, phenytoin, fosphenytoin	Antifungals—fluconazole, voriconazole, ketoconazole Antidepressants—fluoxetine, fluvoxamine, paroxetine, sertraline
St John's Wort Spironolactone Dexamethasone Rifampin	Antibiotics—ciprofloxacin, azithromycin, erythromycin Diazepam Cimetidine/omeprazole Verapamil Ticlopidine

3 Indications/Contraindications

Methadone should primarily be considered in surgeries several hours in length which are expected to result in a moderate to high amount of postoperative pain. The logic is that the patient will receive methadone shortly after induction of anesthesia and pass through the period of peak respiratory depression (within 10–45 min) while an endotracheal tube is in place. By the end of the procedure, respiratory drive should be recovered but the prolonged analgesic effect of methadone will remain [2]. Methadone has been used in cardiac, open abdominal, spine, and orthopedic procedures with good results, though it should be said that many of the studies that used methadone had a relatively small number of patients.

Less common uses of methadone include use of methadone for ambulatory or laparoscopic procedures. Finally, there have been some studies where methadone has been used as part of patient controlled analgesia systems, sometimes in combination with ketamine, with positive results. However, methadone as part of a PCA analgesic strategy is uncommon and the studies using this technique had fewer than 50 patients in each study [8, 9].

Absolute contraindications to methadone are relatively few and include anaphylaxis, concurrent respiratory depression, or

ileus. Methadone taken chronically has been known to prolong the QT interval, but it is not clear how much a single methadone dose in the perioperative period would prolong the QT interval. The American Pain Society recommends avoiding methadone use in adults with a QTc interval of 500 ms or greater. If a patient has risk factors for a prolonged QT interval, or has symptoms suspicious for arrhythmia such as syncope, it may be prudent to order an ECG before the procedure to rule out a prolonged QTc prior to administering methadone [10].

4 Dosing and Titration

When methadone is given for analgesia in the perioperative period, the goal is to dose methadone to provide the patient with a stable, long lasting analgesic without inducing prolonged respiratory depression. This is typically accomplished by giving the patient a large dose of methadone immediately after induction of anesthesia, and letting the patient recover their respiratory drive over the course of the operation. Further evidence for giving methadone immediately after induction comes from a study from the 1980s in which 24 patients receiving hip replacements were dosed with methadone after induction or toward the end of the procedure. The results showed that patients that received methadone early in the procedure had lower postoperative opioid requirements than patients that received methadone at the end of the procedure [11]. For an opioid naïve patient undergoing a procedure with moderate to severe pain expected in the postoperative period (e.g. open abdominal surgery, spine, thoracic surgery), 0.2–0.3 mg/kg or a fixed dose of 20 mg may be given on induction. See Table 3 for methadone dosing strategy.

Due to the long elimination half-life, more opioids are not recommended during the case. If the patient complains of pain in the PACU, methadone may be titrated by giving 2–3 mg boluses, or 3–5 mg boluses if it was a painful procedure, and the patient should be given at least 10 min between doses to allow for assessment of the patient's respiratory status. Patients should have an unstimulated respiratory rate of at least 10 before further dosing

Table 3 Perioperative methadone dosing strategy [2, 3]

–	Minimal postoperative pain anticipated (i.e. knee arthroscopy, laparoscopic surgery, ambulatory surgery)	Moderate to severe pain anticipated (i.e. spine or open abdominal surgery)
IV methadone dose at induction	0.1 mg/kg *or* fixed dose of 10 mg	0.2–0.3 mg/kg *or* fixed dose of 20 mg If above 60 years of age or reduced physiologic reserve, consider reduced dose of 15 mg
PACU	2–3 mg IV q10 min	3–5 mg IV q10 min
Patients on oral methadone at home	Maintain home oral methadone dose perioperatively. Add additional non-opioid analgesics, regional techniques, and supplement with other opioids as needed	

of methadone to avoid respiratory depression and oversedation [12–14]. If a patient has respiratory depression postoperatively, continuous monitoring for an extended period of time and an infusion of naloxone is indicated for 24 h due to the long half-life of methadone.

Lower doses of methadone can be given for procedures with less expected pain postoperatively; a dose of 10 mg on induction is recommended for laparoscopic procedures [2]. In one of the original papers on intraoperative methadone use, Gourlay noted that increasing age was correlated with an increase in terminal half life [12]. Therefore, reduced methadone dosing should be considered in the elderly; Kharasch recommends a reduced dose of 15 mg for patients above 60 years of age [2, 3].

4.1 How to Recognize and How to Treat Withdrawal

Methadone withdrawal may be seen in patients on methadone maintenance therapy for opioid use disorder or chronic pain who have missed doses of methadone during a hospitalization. It is important to note that withdrawal can also occur secondary to

accelerated opioid metabolism as a reaction to other medications, particularly cytochrome P-450 inducers such as HIV medications and anticonvulsants. Withdrawal may start 1–2 days after the last dose with symptoms peaking 24–48 h after onset and potentially lasting up to 2 weeks. The symptoms of methadone withdrawal are similar to that of other opioids and proportional in severity to the individual's degree of opioid tolerance. The clinical opioid withdrawal scale (COWS) can be used to assess the severity of withdrawal taking into account the following factors: pulse rate (tachycardia), GI upset (nausea, vomiting, abdominal cramping, diarrhea), lacrimation, tremulousness, restlessness, yawning, pupil size (mydriasis), anxiety/irritability, bone/joint aches, piloerection, and rhinorrhea/lacrimation [15].

Treatment of opioid withdrawal is typically managed by restarting methadone, or giving the patient other opioid medications. The patient's home dose of methadone should be confirmed prior to restarting methadone. Non-opioid adjuncts such as clonidine and benzodiazepines have demonstrated benefit in treating symptoms associated with methadone withdrawal such as hypertension, tachycardia, anxiety, and irritability.

4.2 How to Continue Methadone Preoperatively

If a patient is already taking methadone chronically when they present for an operation, it is recommended to continue the patient's baseline methadone dose during the perioperative period. Continuing the methadone orally is preferred to intravenous conversion. If oral methadone to IV methadone conversion is necessary, one accepted strategy is to give 1/4th of the patient's oral dose intravenously twice daily; this could be up-titrated to four times a day if indicated [16]. With chronic oral methadone use, there can be significant interpatient pharmacokinetic and pharmacodynamic variability. As a result, converting these patients to other opioids perioperatively can be inconsistent. Therefore, it is recommended to simply supplement the daily methadone dose with additional opioids and adjunctive therapies.

Patients with chronic methadone use may have more challenges with pain control after the surgery due to opioid tolerance. Common strategies for further pain control are to supplement with additional opioids, regional anesthetic techniques, and multimodal nonopioid analgesics with the understanding that patients on methadone maintenance therapy (MMT) typically require higher doses of opioids than opioid naïve patients. Multimodal strategies for patients on maintenance methadone, including non-opioid analgesics and regional anesthesia, should be maximized to the extent possible in the perioperative period before adding additional opioids. Recommended non-opioid analgesics include acetaminophen, NSAIDS, ketamine, local anesthetics, steroids, and gabapentinoids. Gabapentin in particular has been shown to attenuate hyperalgesia in patients on methadone, with the caveat that concurrent gabapentinoid and opioid use may carry a higher risk of respiratory depression [17]. Partial opioid agonist therapy (such as butorphanol and buprenorphine) should be avoided as it may precipitate withdrawal. It is important to develop a perioperative pain management plan tailored to the specific patient based on the degree of pre-existing and expected pain.

4.3 Evidence of Efficacy and Safety of Perioperative Use

As mentioned above, methadone has been used in various surgical procedures including orthopedic, general surgery, spine, OB/GYN, and cardiac cases, with a majority of the studies reporting a positive effect on postoperative pain control. Several early studies done by Gourlay et al. showed successful use of methadone in general surgery and spinal surgery with results of patients in the methadone group achieving a longer duration of analgesia after adequate pain control was accomplished and longer interval before supplemental opioids were needed [12, 14]. The efficacy of methadone use in major spine surgery was shown by two different investigators in which methadone was compared to continuous sufentanil infusion in one study and hydromorphone in the other, and opioid requirements were reduced by 50% in the

methadone group in both studies [18, 19]. One of the largest studies that demonstrated effective perioperative analgesia with methadone was done by Murphy et al., in which methadone was compared to fentanyl when given prior to cardiopulmonary bypass in 156 patients undergoing cardiac surgery. The methadone group demonstrated decreased postoperative pain scores and opioid requirements over the first 3 days after surgery [20]. While many of the studies done to date looking at the efficacy of methadone have shown that intraoperative single dose use can produce superior pain control and decreased additional opioid requirements during the first 1–3 days post-op, most studies have had less than 100 patients enrolled. Larger studies are necessary to further clarify the efficacy of methadone in the perioperative setting [2].

One of the major concerns with the perioperative use of methadone is the risk for prolonged respiratory depression postoperatively. Thus far, no clinical trials have conclusively demonstrated that methadone carries more risk of postoperative respiratory depression despite its long elimination half-life. The risk of respiratory depression can be mitigated by dosing methadone shortly after induction of anesthesia to allow the peak respiratory depressant effect to wear off during the course of the surgery. Studies by Gourlay et al. determined the threshold for respiratory depression for plasma levels of methadone to be 100 ng/mL, with this threshold usually being surpassed for only 45 min or less after doses of methadone of 20–30 mg [12, 13]. The rapid redistribution of methadone after a bolus dose allows the blood concentration to rapidly fall. Care must be taken, however, when methadone is combined with other medications or sedatives that may also affect consciousness or respiratory drive.

QT prolongation and ventricular arrhythmias are also a risk with methadone use, though this is associated more with long term use of the drug. The potential for QT prolongation and arrhythmias is related to dose amount and administration duration [21]. There does not appear to be evidence of higher incidence of cardiac complications in clinical trials in patients receiving methadone in a single dose administration in the perioperative setting [2]. Caution should be used for patients with preexisting cardiac conditions or for those who are taking medications that affect the

cardiac conduction system. There is a strong recommendation from the American Pain Society and College of Problems of Drug Dependence to not use methadone in patients with a QTc interval of 500 ms or above, as this can be associated with an increased risk for torsades de pointes [10].

There is also a theoretical concern for increased risk of serotonin syndrome with methadone use due to methadone's serotonin reuptake inhibition. This may result in increased levels of serotonin which may become an issue in patients taking other medications that affect serotonin release or uptake such as antidepressants [22]. While serotonin syndrome in the perioperative period caused by methadone administration is extremely rare, it may be suspected in patients on pre-op antidepressants that develop signs of excess serotonin after methadone administration such as altered mental status, autonomic instability including unexplained fever and tachycardia, or neuromuscular abnormalities such as rigidity and tremors [2].

Common Pitfalls

- In opioid naïve patients, our recommendation is to dose methadone once after induction of anesthesia, and avoid further redosing of methadone until the patient's pain level can be assessed in PACU. This is the simplest way to use methadone perioperatively. If necessary, methadone may be further titrated in PACU as previously described for appropriate analgesia while assessing the patient's respiratory status. Repeated dosing of methadone intraoperatively in opioid naïve patients may lead to unwanted respiratory depression postoperatively.
- In patients that take methadone at home for chronic pain or opioid use disorder, ensure that the patient has taken their home dose of methadone prior to the surgery, as missed doses may lead to withdrawal or inadequate pain control postoperatively. Use additional non-opioid analgesics such as regional anesthesia techniques, acetaminophen, and NSAIDS when appropriate to provide sufficient analgesia. In these patients, it is acceptable to use additional opioids such as fentanyl or hydromorphone during the procedure to supplement analgesia

as these patients are opioid tolerant and will likely need additional opioids to help control their pain postoperatively.
- Be cognizant of any medications the patient takes at home in order to avoid any unwanted interactions with methadone metabolism.

Clinical Pearls
- Methadone is the longest acting opioid in use in clinical anesthesia practice, with analgesic effects lasting up to 36 h.
- Methadone may provide an overall opioid sparing effect due to its long elimination half-life.
- Methadone undergoes metabolism in the liver by the CYP450 system. CYP2B6 is currently thought to be the main enzyme involved in metabolism.
- Methadone does not accumulate in patients with renal failure, and is not removed by hemodialysis or peritoneal dialysis. It is an option in patients with end stage renal disease.
- Dose methadone once immediately after induction, and titrate further in PACU if necessary, waiting at least 10 min between doses.
- Methadone plasma levels can be affected by a number of drug interactions; be familiar with the patient's home medications to avoid any unwanted interactions and use an online drug interaction tool to check for interactions between methadone and the patient's home medications.
- If a patient has respiratory depression after the perioperative use of methadone, a naloxone infusion for at least 24 h is recommended due to the long half-life of methadone.

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Buprenorphine, Buprenorphine/Naloxone (Suboxone)

William F. Barrett and Carey Brewbaker

Abbreviations

CNS	Central nervous system
CYP	Cytochrome P450
FDA	US Food and Drug Administration
HPA	Hypothalamic-pituitary-adrenal
NMDA	N-Methyl-D-aspartate
NSAIDs	Non-steroidal anti-inflammatory drugs
ORL	Opioid receptor-like
OUD	Opioid use disorder

1 Essential Basics

1.1 Introduction

Buprenorphine is a semi-synthetic opioid derived from thebaine, an alkaloid of the opium poppy, *Papaver somniferum*, that has been on the market in various forms since the 1970s. Given the current state of the opioid crisis, alternatives to Schedule II full

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_15

mu-agonists are increasingly needed. Characterized as a Schedule III opioid, buprenorphine is approved by the United States Food and Drug Administration (FDA) for the treatment of opioid use disorder and chronic pain. Its structure allows buprenorphine to interact with several opioid receptors—mu, kappa, and delta, as well as opioid receptor-like 1. As an agonist-antagonist at those opioid receptors, buprenorphine exhibits a unique pharmacological profile making it potentially an ideal choice for the treatment of chronic pain states as well as providing an option for those with opioid use disorder.

1.2 Pharmacodynamics of Buprenorphine

At first, the concept of buprenorphine can seem confusing. It is described as a partial opioid agonist at the traditional mu receptors, but it exhibits analgesic efficacy that rivals the traditional full-agonist opioids such as morphine and fentanyl [1]. When buprenorphine binds to the mu-opioid receptor, it causes receptor phosphorylation, promoting the release of G-protein subunits, inhibition of adenylyl cyclase, reduction of intracellular cyclic adenosine monophosphate levels, and regulation of ion channels. This cascade of events limits release of neurotransmitters, resulting in hyperpolarization of the cell membrane and preventing activation of nociceptors, leading to the desired analgesic effect. Traditional opioids such as morphine, fentanyl, and methadone also recruit beta-arrestin to the opioid receptor in addition to G-protein subunits. Beta-arrestin signaling has been associated with opioid-related adverse effects, such as respiratory depression, constipation, nausea, and abuse potential [1, 2]. Since buprenorphine does not recruit beta-arrestin to the receptor, these undesired side effects of traditional opioids are largely avoided. This unique mu-receptor activation profile for buprenorphine confers the concept of "partial agonism" due to its unique structural binding and the subsequent receptor activity level it conveys. Its analgesic efficacy is maintained while the chance of respiratory depression is decreased, and abuse potential is lessened by preventing the excessive signaling of the mu-opioid receptor.

In addition to being an agonist at the mu-receptor, buprenorphine also exhibits antagonism at the delta opioid receptor and inverse agonist activity at the kappa receptor [1, 2]. Antagonist effects at these receptors confers additional protection by limiting unwanted effects typically observed with mu-opioid receptor activation. Respiratory depression, constipation, anxiety, and addiction potential are all decreased, in contrast to pure mu-opioid receptor agonists. Furthermore, there is less sedation and euphoria associated with buprenorphine due to these receptor interactions compared to drugs such as morphine and fentanyl. It is thought that the inverse-agonist activity, meaning that binding induces the opposite effect of an agonist at the same receptor, is responsible for buprenorphine-associated antihyperalgesic activity [2]. This interaction also contributes to less sedation and euphoria, in conjunction with the antagonistic interactions at the delta receptor. Some studies have investigated tissue specificity of buprenorphine as well, suggesting that buprenorphine primarily exerts it analgesic effects on the lower central nervous system (CNS) (spinal cord) rather than the higher CNS (brain) [1]. Such findings support the notion that buprenorphine's lack of supraspinal effects may help limit the risk of respiratory depression and euphoria and maximize the analgesic effects at spinal opioid receptors. Table 1 provides a succinct overview of the basic effects of buprenorphine at each receptor at which it interacts.

An important characteristic of buprenorphine to note is its high binding affinity at various opioid receptors. Binding affinity is the ability of a drug to bind to a receptor and is measured by determining the equilibrium dissociation constant (K_i) [1]. While it does exhibit high affinity for kappa and delta receptors, its high binding affinity (having a low K_i value) for the mu-opioid receptor due to its unique structure and binding position is what most contributes to its place among other opioids. While this affinity might contribute to increased receptor occupation by buprenorphine, it does not necessarily correspond to superior activity at those receptors. As such, buprenorphine exhibits slower dissociation from the mu-opioid receptor compared with other opioids. This characteristic may contribute to prolonged analgesia while limiting the potential for withdrawal when used to manage patients

Table 1 The pharmacodynamics of buprenorphine [1]

Receptor	Mu	Delta	Kappa	ORL1
Activity	Partial agonist	Antagonist	Antagonist	Agonist
Effects	• Potent analgesia • Limited CNS effects—dysphoria, respiratory depression, euphoria • Limited physical dependence and abuse potential • Limited impact on GI system—less nausea, dysmotility • Reduced impact on HPA axis and immunosuppression • Reduced risk of anxiety, depression, and suicidal ideation	• Anti-opioid effects • Limited CNS effects	• Reduced risk of anxiety, depression, and suicidal ideation • Reduced immunosuppression	• Enhanced spinal analgesia • Reduced supraspinal effects • Limited tolerance potential

Table 2 Representative binding affinity at the μ-opioid receptor [1]

Medication	Binding affinity (K_i)
Buprenorphine	0.22
Hydromorphone	0.37
Morphine	1.17
Fentanyl	1.35
Oxycodone	25.87
Hydrocodone	41.58
Codeine	734.20

with chronic pain. Table 2 demonstrates a comparison between binding affinity of buprenorphine and several other commonly prescribed opioids.

1.3 Pharmacodynamics of Buprenorphine Metabolites

The major metabolite of buprenorphine is norbuprenorphine. It is formed from the catabolism of buprenorphine through the cytochrome P450 (CYP) 3A4. Norbuprenorphine acts as a mu receptor agonist and has high affinity for both kappa and delta receptors. Similar to its precursor, norbuprenorphine triggers mu receptor G-protein binding but to a greater degree than buprenorphine, and paradoxically, exhibits only 1/50th the analgesic potency of buprenorphine [2]. Norbuprenorphine also interacts with the beta-arrestin receptor with high affinity and subsequently activates it, which is associated with opioid-related adverse effects, such as constipation and respiratory depression seen with traditional opioids. In part, this metabolite is responsible for the minor side effects seen with buprenorphine administration [2].

Table 3 Bioavailability of buprenorphine [1]

Administration route	Bioavailability
Intravenous	100%
Buccal	46–65%
Sublingual	28–51%
Transdermal	15%

1.4 Pharmacokinetics

The bioavailability of buprenorphine is largely determined by properties such as low molecular weight, high lipophilicity, and high potency. However, its oral bioavailability is very poor, only about 10–15%, largely due to high first-pass hepatic metabolism [2]. Other routes of absorption, such as sublingual, buccal, transdermal, and illicit conversion to intranasal or intravenous routes, have greater bioavailability since they bypass first-pass metabolism. Table 3 provides relative bioavailability based on route of administration. After absorption, buprenorphine remains approximately 96% protein bound, primarily to α- and β-globulin. Due to its high lipophilicity, tissue penetration, and protein binding, it has a large volume of distribution—approximately 430 L [2]. Half-life varies depending on the route of administration, but averages about 37 h due to slow receptor dissociation. Onset of action remains relatively fast—5–15 min intravenously and 30–60 min via the sublingual route. The transdermal delivery system confers the slowest onset, valued at approximately 72 h [3].

1.5 Metabolism

Buprenorphine is metabolized through CYP3A4 and CYP2C8 to the active metabolite norbuprenorphine. The major rate-limiting step involves glucuronidation of both buprenorphine and norbuprenorphine to buprenorphine-3-glucuronide and norbuprenorphine-3-glucuronide. Interestingly, the metabolites are not known to cause major interactions with other drugs metab-

olized by the cytochrome P450 system, thereby minimizing drug-drug interactions with buprenorphine [1]. Buprenorphine and its metabolites are subsequently excreted mainly via the biliary system through enterohepatic recirculation. A small amount may be eliminated via feces or urine. Because of this, buprenorphine is suitable for patients with both renal and hepatic impairment. These characteristics make buprenorphine a good choice for treatment of chronic pain in elderly patients who often have liver and kidney impairment. Additionally, since buccal and transdermal formulations bypass first-pass metabolism, those routes of administration may be helpful in patients with gastrointestinal comorbidities who are unable to tolerate oral pain medicines well.

1.6 Indications, Formulation and General Dosing

To date, there are only two approved US FDA indications for the use of buprenorphine—the management of chronic pain and for treatment of opioid use disorder. Patients may be receiving treatment for either indication separately, but it is not uncommon for a patient to have overlapping indications. It is important for the anesthesiologist to be familiar with the indications and dosing in order to help formulate a perioperative pain management strategy.

Presently there are close to a dozen branded formulations approved by the FDA. Given the poor oral bioavailability, multiple alternative routes of administration have been developed. For chronic pain, buprenorphine is approved in transdermal and buccal formulations. For OUD and opioid dependence, approved formulations include buccal, sublingual, intramuscular depot, and subdermal implants. Some patients may be receiving off-label sublingual buprenorphine for chronic pain as well. *Naloxone* is included in some buccal and sublingual formulations. Naloxone is poorly absorbed when taken buccally or sublingually; however, if it is injected intravenously, it is highly bioavailable and subsequently blocks buprenorphine's ability to bind to target receptors. This helps to decrease the potential for illicit abuse. It is important to note that, compared to the half-life of buprenorphine, the half-

life of naloxone in the buccal and sublingual combinations is only approximately 2–12 h compared to upwards of 42 h for buprenorphine itself [3]. This underlies the fact that if someone were to require naloxone for management of a buprenorphine overdose, close monitoring for an extended period of time is essential.

The dosing of buprenorphine varies among formulations due in large part to their routes of administration and associated bioavailabilities. It is also characterized as either high-dose or low-dose. High-dose formulations are approved by the FDA for the treatment of OUD. These doses are defined as any dose that equals or exceeds an equivalent dose of 24 mg of daily sublingual buprenorphine. Low-dose formulations are defined by any equivalent daily dose less than or equal to 8 mg sublingually [4]. The FDA has approved two formulations, a transdermal patch and a buccal product, for the treatment of chronic pain. Therefore, patients being treated with buprenorphine for chronic pain are receiving formulations that fall into the low-dose category.

2 Perioperative Use

2.1 How to Choose Among Similar Medications Within the Same Class

Considering that there are a multitude of options within the opioid class of medications to use perioperatively, it is important to discuss unique properties of buprenorphine that could confer benefits to the patient. The applications of buprenorphine are far from confined to intravenous administration for acute pain management. An extremely versatile opioid, buprenorphine can be administered by a variety of routes including intravenous, intramuscular, neuraxial, subcutaneous, sublingual, and transdermal. Additionally, buprenorphine could be an acceptable alternative in those patients that cannot tolerate morphine or other opioids due to allergy or sensitivity. Given its liver metabolism, buprenorphine would be an excellent choice for those patients with renal insufficiency with the major metabolites primarily excreted via the fecal route.

Buprenorphine has demonstrated a ceiling effect with respect to respiratory depression but not analgesia [5, 6]. This property could be particularly beneficial in those patients susceptible to respiratory depressant effects of opioids, such as those with obstructive sleep apnea or the elderly, as additional doses administered for analgesia would be less likely to blunt respiratory drive. In fact, one study examining the effects of buprenorphine on postoperative pain in over 7500 patients demonstrated good or adequate pain relief for at least 4 h with an incidence of drug-associated respiratory depression of less than 1% [7].

Patients with inflammatory pain may benefit from buprenorphine in comparison to traditional opioids, as buprenorphine has been reported to have anti-inflammatory activity. In fact, it has been reported to be efficacious when administered intra-articularly; one such study of patients undergoing knee arthroscopy demonstrated a significant reduction of analgesic requirement with intra-articular buprenorphine [8]. Lastly, there exists a role for buprenorphine in regional anesthesia as perineural buprenorphine has been demonstrated to prolong the effect of local anesthetics in peripheral nerve blockade [9, 10].

2.2 Indications and Contraindications

Buprenorphine is indicated for the treatment of moderate to severe pain. As mentioned previously, there are some nonconventional applications that have been described successfully such as intra-articular and perineural administration. Official FDA-approved indications for buprenorphine remain solely for the treatment of chronic pain and opioid use disorder at this time.

With regards to contraindications, the only absolute contraindication is hypersensitivity or anaphylaxis to the drug buprenorphine itself. However, there exists a variety of relative contraindications. Caution should be used in administering buprenorphine to patients with pre-existing central nervous system depression (including concomitant use with benzodiazepines and other CNS depressants) and/or altered mental status. Other relative contraindications include severe respiratory insufficiency

(albeit potentially safer than conventional opioids due to the ceiling effect described above), known or suspected gastrointestinal obstruction, hypotension, morbid obesity, pregnancy, and seizure disorders. Buprenorphine has been reported to prolong the QT interval and thus should be used with caution in patients with congenital long QT syndrome (or with concomitant use of other QT prolonging medications) due to the risk of life-threatening arrhythmias such as Torsades de pointes [2]. Caution should be used and/or dose adjustment should be considered in those with severe liver dysfunction (due to hepatic metabolism), the elderly, and opioid-naïve patients.

2.3 Dosing/How to Titrate Up or Down

Buprenorphine has been described as about 30 times as potent as morphine [11]. A starting intravenous dose of 0.3 mg every 6 h is often used, with an additional dose of 0.3 mg given as indicated. Doses up to 7 mg have been given intravenously for postoperative analgesia without associated respiratory depression [12].

Perineural buprenorphine is dosed at 0.2–0.3 mg with the local anesthetic. For neuraxial use, epidural buprenorphine is also typically given at doses of 0.3 mg with pain relief for up to 12–24 h [13]. Intrathecal dosing is typically reduced to 1/10th the parenteral dose with dosages of 0.03 or 0.045 mg producing long-lasting analgesia with nausea and vomiting as the predominant side effects.

The buccal film form of buprenorphine is usually initiated at 75 μg once daily and titrated up to twice daily if tolerated. The dose can be increased incrementally to 150 μg every 12 h with a maximum dose of 900 μg every 12 h. Sublingual buprenorphine is typically dosed in 2–12 mg tablets, dosed up to a typical maximum of 32 mg daily in divided doses. When naloxone is added, it is generally dosed at 1/4th the dose of buprenorphine (for example, 8 mg/2 mg buprenorphine/naloxone) [2].

Transdermal buprenorphine is typically initiated at 5 μg/h applied once weekly. Opioid tolerant individuals may require 10 μg/h, and the dose is titrated in 5 μg/h increments up to the max

dose of 20 μg/h. For transdermal patch discontinuation, a gradual stepwise approach is recommended, such as decreasing the dose by 10–25% every 2–4 weeks.

In patients with severe hepatic insufficiency, it is recommended to reduce the starting dose and titration doses of buprenorphine by 50% with no adjustment needed in patients with only mild or moderate liver dysfunction. No dosage adjustment is required for patients with renal insufficiency given the pharmacokinetics of buprenorphine.

2.4 Withdrawal

Opioid withdrawal is considered to be less severe with buprenorphine than with other opioids, which may be attributed to its inherent nature as a partial agonist; buprenorphine can, however, displace other opioids and precipitate acute withdrawal in individuals with opioid use disorder.

When discontinuing or tapering down buprenorphine, it is important to do so in a gradual manner and/or bridge with other opioids in order to prevent withdrawal. Withdrawal symptoms can include myalgias, restlessness, anxiety, lacrimation, rhinorrhea, hyperhidrosis, insomnia, diarrhea/GI upset, nausea/vomiting, mydriasis, tachycardia, and hypertension. If these symptoms occur during a taper, it is important to increase the buprenorphine dose back to the previous level and interrupt the taper. Further attempts to taper should utilize a strategy with more gradual reduction in dose and/or frequency of such reductions.

2.5 Toxicity

Adverse effects of buprenorphine include nausea and vomiting, drowsiness, dizziness, headache, memory loss, cognitive and neural inhibition, perspiration, itching, dry mouth, miosis, orthostatic hypotension, and urinary retention. Constipation and CNS effects are seen less frequently than with morphine.

2.6 How to Continue or Stop Preoperatively and How to Restart Postoperatively

The perioperative management of patients taking buprenorphine and buprenorphine/naloxone is a complex process, and pain control in these patients can be challenging. In short, a widely accepted strategy for continuing, stopping, and restarting buprenorphine during the perioperative period does not exist. Due to high receptor binding affinity, long half-life, and the partial agonism nature of buprenorphine, traditional opioid analgesic effects may be inhibited resulting in uncontrolled postoperative pain [14].

Generally speaking, pain relief can be more readily achievable in patients when buprenorphine is discontinued, and thus traditional opioids can exert their therapeutic actions on their receptors in a more predictable way. Historically, some experts advocated discontinuation of chronic buprenorphine at least 72 h before surgery and using a bridging strategy with opioid agonists. However, pain control may still be achievable in patients continuing buprenorphine that are undergoing surgery. One study of surgical patients taking buprenorphine revealed that patients continued on buprenorphine had similar pain control within the first 24 h compared to those that discontinued buprenorphine, despite a lower dosage of morphine-equivalents in the buprenorphine continuation group [15]. Consequently, the approach to managing pain and the perioperative use of buprenorphine should be tailored to the individual patient, accounting for several major considerations: the *urgency* of the procedure, the *dose of buprenorphine* the patient takes, the *anticipated pain* from the procedure, and the *psychological implications of pain control* (or lack thereof) in this specific patient population [4]. A multidisciplinary approach involving the patient, surgeon, anesthesiologist, and the patient's buprenorphine prescriber is critical to establish a plan for tapering and restarting buprenorphine perioperatively, should tapering be necessary.

A recent editorial in 2018 recommended continuing buprenorphine through the perioperative period, especially in patients with OUD, because of the increased risk of relapse and the complexi-

ties of re-induction onto buprenorphine postoperatively should it be discontinued [16]. The most recent consensus opinion on perioperative management advocates for continuation of the patient's home dose of buprenorphine, particularly if they are being treated for OUD. Consideration for tapering can be made if patients are on particularly high doses, such as greater than 24 mg daily, and high anticipated post-surgical opioid requirements [17]. There exists the possibility that patients who present for surgery while still taking buprenorphine may require high dosages of opioids and/or monitored care settings resulting in increased length of stay, increased cost, and decreased patient satisfaction. Finally, a multimodal analgesic regimen is critical in these patients, particularly in the setting of continued buprenorphine use, including regional and epidural anesthesia and other non-opioid analgesics such as acetaminophen, NSAIDs, gabapentenoids, alpha-2-agonists such as dexmedetomidine, and NMDA antagonists such as ketamine [18].

Management strategies can be approached by identifying the urgency of the pain state. Essentially, two main avenues exist—elective procedures/non-emergent acute pain and emergency procedures/emergent acute pain. Identifying the anticipated pain and opioid requirements will further help guide perioperative management. For elective cases, it may be feasible to develop a pain management plan that involves tapering the dose closer to 8 mg daily prior to surgery in an effort to free more opioid receptors and manage breakthrough pain with traditional opioids more effectively. That may not always be the case for urgent or emergency surgeries. Along these lines, evidence suggests buprenorphine should be continued in the peripartum setting for pregnant patients [4]. Neuraxial techniques, including spinal anesthesia and/or epidurals should be employed whenever possible, and multimodal non-opioid analgesic therapy should be optimized. Table 4 provides a basic framework for practical considerations to buprenorphine management in the perioperative setting. Tapering guidelines can vary widely, but generally speaking patients on high doses can be considered candidates for tapering in collaboration with their pain management or addiction management specialist.

Table 4 Basic algorithm for buprenorphine management [4]

Elective surgery		Emergent surgery	
Low opioid requirements	Mod/high opioid requirements	Low opioid requirements	Mod/high opioid requirements
Continue @ current dose	Low-dose (≤8 mg daily) • Continue @ current dose	Continue @ current dose	Low-dose (≤8 mg daily) • Continue @ current dose
	High-dose (>16 mg daily) • Chronic pain—consider tapering to 8–16 mg daily prior to surgery • OUD—develop plan with primary prescriber—may involve continuing at current dose vs taper plan • Optimize non-opioid analgesics		High-dose (>16 mg daily) • Chronic pain—continue buprenorphine, optimize non-opioid analgesics; consider supplemental full mu agonists; consider temporary dose reduction to no lower than 8 mg daily • OUD—continue buprenorphine, optimize non-opioid analgesics; consider supplemental full mu agonists; consider involving pain/addiction specialist for temporary dose reduction to no lower than 8 mg daily

Common Pitfalls

Many practitioners may be intimidated when encountering a patient who is taking buprenorphine. Whether the indication is for opioid use disorder or chronic pain or another off-label use, there can be an underlying assumption that pain management will be quite difficult. Patients may inappropriately have their buprenorphine discontinued or inappropriately titrated, leading to undesired effects such as withdrawal or increased risk of relapse. Alternatively, providers may be hesitant to adequately treat peri-

operative pain with full mu-agonists for fear of the effects of over narcotizing. Having a baseline understanding of the pharmacodynamics and indications for buprenorphine treatment will help anesthesiologists be prepared to implement appropriate management plans when these patients present to the perioperative arena.

Clinical Pearls

- Buprenorphine binds to all three major opioid receptors—mu, kappa, and delta; binds with much less affinity to the opioid receptor-like (ORL-1)
- High first-pass clearance with oral administration, hence sublingual, buccal, and transdermal routes are preferred.
- Metabolized to norbuprenorphine through the cytochrome P450 followed by multiple rate-limited congugases.
- Buprenorphine is a preferred analgesic option in patients with renal failure, as clearance is independent of renal function and is not cleared by dialysis.
- Mild to moderate liver failure does not influence clearance of buprenorphine.
- Similar analgesic equivalence to other opioids but exhibits a dose-dependent ceiling effect on respiratory depression, less constipation, and less hypogonadism.
- A multidisciplinary approach should be employed, with involvement of the patient, surgeon, anesthesiologist, and the patient's buprenorphine prescriber to develop a tapering plan preoperatively and postoperative resumption of an appropriate buprenorphine dose.
- In general, patients undergoing procedures with low anticipated opioid requirements or low-dose therapy ($\leq$8 mg daily sublingual equivalents) may continue their buprenorphine therapy without modification.
- Patients on higher doses of buprenorphine and/or those undergoing more severe acute pain insults could be considered for a tapering of their dose.
- Caution should be taken in those at high risk of opioid use disorder relapse; therefore, complete discontinuation is not recommended in these patients.

- A multimodal pain management approach is critical in these patients, including nerve blocks with continuous peripheral catheters, epidural analgesia, and other non-opioid analgesics such as acetaminophen, NSAIDs, gabapentinoids, dexmedetomidine, ketamine and muscle relaxants.
- Ensure appropriate setting and level of monitoring perioperatively, especially when patients are receiving concomitant full mu-agonists, respiratory depressants and other sedatives.

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Complimentary Non-pharmacological and Non-opioid Options

Christopher D. Wolla and Tara Kelly

1 Introduction

The multimodal approach to analgesia and anxiolysis has been at the forefront of research for anesthesia providers. As you have read in previous chapters, there are a variety of non-opioid pharmacologic options. This chapter will explore the non-pharmacologic/non-opioid techniques that have been employed for a variety of situations. Relaxation and distraction techniques, cognitive behavioral therapy, relaxation acupuncture, touch therapy TENS, massage, cryotherapy, and biofeedback have all been used as alternative approaches. The techniques ideally complement and/or reduce the amount of pharmacologic and opioid needs of a patient to alleviate pain and facilitate their care.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_16

2 Relaxation and Distraction Techniques

2.1 Essential Basics

Relaxation and distraction techniques have been used throughout history to assist in the perioperative experience. In recent years, research has shown that relaxation techniques can lead to statistically significant reductions in pain (typically using visual descriptor scale), vital signs suggestive of pain (including systolic blood pressure, respiratory rate, and heart rate), and analgesic-like effects. These techniques were used for patients for a variety of procedures including: elective surgery, coronary artery bypass grafting, burn wound care, abdominal surgeries, and gynecologic surgeries [1–6]. The results vary by study and there are a variety of techniques used. Overall, these techniques tend to be easy to use and can be supplements to other anesthetic approaches in order to provide the best experience for the patient.

2.2 Practical Perioperative Use

Jacobson's progressive muscle relaxation technique was introduced in the 1920s by Dr. Jacobson as a way to help alleviate his patient's anxiety. It involves tension of specific muscle groups for 5–7 s followed by relaxation of that group all while the participant focuses on deep breathing. This is often done starting at the feet, calves and legs, and progressively moving up the body finishing with the jaw and facial muscles. The patient should allow 15–20 min to complete the process. Providers can use this in conjunction with rhythmic/guided breathing [7, 8].

Deep diaphragmatic breathing involves the participant exhaling completely while placing one hand on the chest and one hand on the abdomen then a full breath in is gradually taken. Once the lungs feel full, a gradual exhalation is started. The goal is to avoid any sudden inhalation or exhalation. Exhalations should be longer and deeper than inhalations [8].

Guided imagery allows the participant to move through a daydream-like state in which they either follow a script or come

up with their own planned image. Relaxation, vivid imagery, and positive suggestions are the stages of this technique. The goal is to allow the patient to essentially "go on vacation" or "go to a safe space" where they feel ultimate relaxation [8].

Ost's applied relaxation technique involves having the person recognize early signs of anxiety and coping with the anxiety. This prevents the person from becoming overwhelmed by the anxiety. Applied relaxation uses Jacobson's progressive muscle relaxation approach to allow the participant to recognize the physical signs of their tension [8, 9].

Many other commonly known and used means can be translated to formal relaxation techniques. All of these can be used alone or together to help alleviate a patient's stress. Music, guided videos/cassettes, and handouts can help the patient understand the technique, possibly practice prior to the intervention, and therefore enhance the relaxation.

Common Pitfalls

- Relaxation and distraction techniques require the participant to believe in the possible benefits.

Clinical Pearls

- A formal rehearsed relaxation/distraction technique can improve patient experience and reduce perioperative pain and anxiety.

3 Cognitive Behavioral Therapy

3.1 Essential Basics

Cognitive behavioral therapy (CBT) is a treatment plan within psychology that focuses on the interconnection between thoughts and behaviors. The general goal of CBT is to first have the participant recognize thought distortions and/or unhelpful behavioral patterns then use strategies practiced to change that particular thought or behavior. CBT can be used to help with coping with significant pain associated with surgeries. CBT is an approach

that can be used preoperatively and postoperatively to assist in improving outcomes and controlling postsurgical pain. This technique requires a therapist or individual trained specifically in CBT. With the appropriate coordination and planning CBT can be used within a perioperative home model [10–13].

3.2 Practical Perioperative Use

Participants would be instructed on coping strategies for dealing with pain and fear-avoidance, behavioral management, and increasing self-efficacy. This often takes place over several sessions either pre or postoperatively. The participants would be able to meet and discuss their progress with their instructor. Often the patients are given additional "homework" after each session so that they have further subjects to work on and goals to achieve.

Common Pitfalls

- CBT requires longer term participation by patients.
- This type of program often demands multiple sessions with a CBT-trained therapist.

Clinical Pearls

- When enacting a perioperative home approach to procedures, CBT can be a supplement that can improve outcomes and reduce perceived postoperative pain.

4 Relaxation Acupuncture

4.1 Essential Basics

Acupuncture is an Eastern medicine technique to balance the unity between the body, universe, and flows of energy. It has traditionally been used to treat pain and diseases in Japan, China, and other eastern countries. Traditional Chinese acupuncture is based on specific points along the meridians of the body that correspond with acupuncture organs (which are not the same as the

anatomic organs of Western medicine). Each acupuncture point has a specific function and can be used to elicit a specific response. These points can be stimulated by either noninvasive (acupressure) or invasive (needling). Overall, this approach has been shown to relieve perioperative anxiety, limit opioid use, and reduce postoperative pain, nausea, and vomiting. It is theorized that acupuncture needling will stimulate type I and type II afferent nerve fibers in muscles sending impulses to the anterolateral tract of the spinal cord blocking pain signals from traveling further. It is also thought that the needling may activate midbrain structures which lead to the release of the neurotransmitters norepinephrine and serotonin in the spinal cord which block pain signals. Acupuncture can lead to the release of endogenous opioids and may modulate the hypothalamic-limbic system [14].

4.2 Practical Perioperative Uses

The practitioner should be trained in acupuncture for invasive techniques. For the acupressure techniques there are a variety of points which can help in the perioperative setting to reduce anxiety and prevent nausea which can be seen in Table 1 [15, 16].

Table 1 Perioperative use of acupressure

Phase of care	Preoperative	Postoperative for nausea/vomiting
Technique	• Pressure on yintang point ('third eye' between eyebrows) for 10 min with 20–25 cycles using thumb • Pressure on Shen men point (septum of cavity on ear on nondominant side) with plastic bead for 10 min	Elastic wrist band holding pressure on Nei-Guan point (on wrist)
Results	Reduced preoperative anxiety before abdominal surgeries	When applied 30 min prior to spinal anesthesia significantly reduced nausea in obstetric patients

Common Pitfalls

- Invasive acupuncture should be performed by a trained practitioner and therefore requires a higher level of expertise.
- There is conflicting data of the actual statistical significance in many studies of the efficacy of acupuncture

Clinical Pearls

- Acupuncture can be a relatively low risk complement to preoperative sedation and postoperative patient care.
- Acupressure or noninvasive acupuncture can be a good additive to a holistic approach to the perioperative home and requires less training.

5 TENS Therapy

5.1 Essential Basics

Touch therapy transcutaneous electrical nerve stimulation (TENS) is the therapeutic application of various types of electrical stimulation through the skin used to treat acute procedural and non-procedural pain and chronic pains states such as osteoarthritis, rheumatoid arthritis, fibromyalgia, phantom pain, chronic back/neck pain, headache, and cancer pain. The proposed mechanism of analgesia from TENS is multifactorial with components at the peripheral, spinal and supraspinal levels. At the peripheral level, TENS is thought to reduce the sensitivity caused by release of serotonin which is endogenously produced in response to injury and inflammation. The reduction in sensitivity seen with TENS was abolished when naloxone, an opioid antagonist, was peripherally administered suggesting that the effect of TENS is mediated by these peripheral substances and receptors. Different modes of TENS delivery act on different peripheral and central receptors. High frequency TENS is mediated via δ-opioid receptors while low frequency TENS is mediated via μ-opioid receptors. The most well studied mechanism is Melzack and Wall's gate control theory at the spinal level first proposed in 1967. The gate control theory proposes that stimulation of large

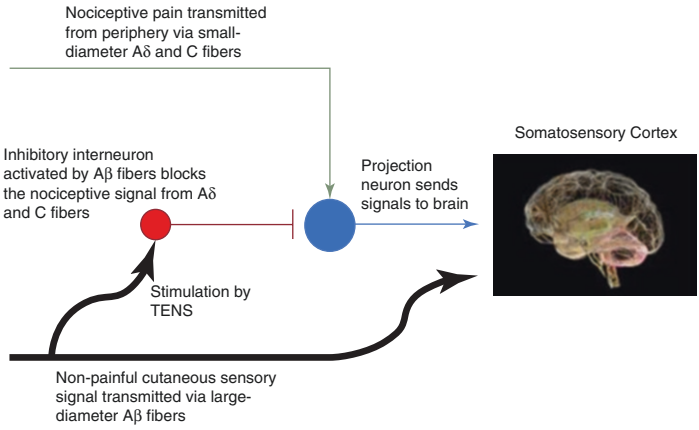

Fig. 1 Gate control theory

diameter cutaneous Aβ fibers activates the inhibitory neurons of the dorsal horn in the spinal cord therefore reducing the transmission of small diameter Aδ and C pain fibers [17]. This is shown in Fig. 1. Other proposed mechanisms at the spinal level include decreased inflammation-induced dorsal horn neuron sensitization, altered levels of GABA and glycine, and modulation of glial cell activities. At the supraspinal level, TENS is thought to increase the descending inhibitory pathways which are relayed in the midbrain periaqueductal gray matter and the rostral ventral medulla in the brainstem which are both mediated via opioidergic mechanisms [18].

5.2 Practical Perioperative Use

There are several modalities of TENS that can be used clinically which are seen below [19].

- Conventional: high frequency current of 40–150 Hz with 50–100 μs bursts (pulse width) at a low intensity (stimulates just sensory fibers)

- Acupuncture-like TENS (AL TENS): low frequency 0.5–10 Hz with pulse width > 150 μs at a high intensity (stimulates motor and sensory fibers)
- Burst TENS: high frequency 80–100 Hz at a low intensity with pulse width of 200,000 μs (5 Hz) to stimulate motor and sensory fibers (developed to minimize patient discomfort seen in AL TENS)
- Brief TENS: high frequency > 100 Hz with 150–200 μs bursts at maximal intensity to stimulate motor, sensory and nociceptor fibers
- Modulation TENS = combo of above modalities with alternating low and high frequency currents

Regardless of the modality, the cutaneous electrodes should be placed at the area of pain experienced by the patient. For post-surgical patients, electrodes should be placed around the area of the surgical incision.

The peak analgesic effect of TENS is seen during and immediately after use which may explain the inconclusive data when investigating chronic pain states. Several Cochrane Database reviews have been conducted investigating TENS applications in both acute and chronic pain. These meta-analyses showed some benefit in acute pain (procedural and non-procedural), neuropathic pain, musculoskeletal pain, chronic recurrent headache, rheumatoid arthritis joint pain and tenderness, cancer bone pain, and fibromyalgia. Data was inconclusive in chronic low back pain, osteoarthritis of the knee and phantom pain. This was likely due to study design as the quality of evidence was low due to methodological limitations, large between-trial heterogeneity and imprecision [18–26]. It seems that post-surgical patients benefit more from TENS therapy. In cardiothoracic surgeries, TENS therapy has shown to improve pain scores (mainly with movement, not at rest), improve pulmonary function (FEV1 and FVC), and reduce cytokine inflammatory response [27–29]. TENS has also been extensively studied in orthopedic surgeries and has shown to reduce pain scores and total post-operative morphine dose and improve active range of motion of the knee after total knee arthroplasty [30].

There are several factors that influence the efficacy of TENS [31].

- Dosing
  - TENS therapy delivered at a strong but comfortable intensity results in a significant analgesic effect but below this intensity threshold, it is ineffective
  - Habituation likely causes a need for higher intensities the more you use TENS
- Repeated Use
- Repeated use of TENS has shown to reduces the central excitability and restores the descending inhibitory pain pathways in essence "re-booting" inhibitory pathways
- Stimulation Frequency
  - Repeated TENS can cause analgesic tolerance
  - Mixed frequency TENS can be helpful and can significantly delay opioid tolerance
- Long-term usage
- People that use TENS >6 months have significant decreases in pain with activities, increased activity levels, and decreased use of pain medications
- Interactions with pharmacological agents
  - Low-frequency (0.5–10 Hz) activates μ-opioid receptors which is much less effective in patients on μ-opioid agonists
  - High frequency (50–100 Hz) activates δ-opioid receptors so can be used in opioid tolerant patients

Common Pitfalls

Although TENS therapy is safe, inexpensive, portable, easy to use, and generally available without a prescription, it can cause discomfort during use as well as skin irritation and in rare cases, dermatitis. Absolute contraindications include presence of cardiac pacemaker or AICD, stimulation of neck over carotid artery bifurcation (can stimulate baroreceptors), pregnancy (except for use with low back pain), difficulty understanding the method, electrophobia, and uncontrolled epilepsy [17].

Clinical Pearls

- TENS therapy is a safe, inexpensive, portable, easy to use, and generally available without a prescription
- The mechanism of action is multifactorial with actions at the peripheral, spinal and supraspinal levels. Gate Control Theory proposes that non-nociceptive sensory signals can stimulate the inhibitory neurons of the dorsal horn of the spinal cord
- TENS has shown benefit in both acute and chronic states of pain but the level of evidence is very low

6 Massage

6.1 Essential Basics

Massage therapy is a safe non-pharmacological treatment that has been shown to be beneficial in a multitude of conditions including acute and chronic pain, sports-related injuries, physical therapy, prenatal depression, autism, skin conditions, hypertension, autoimmune disease, dementia, and Parkinson's disease among numerous other condition [32]. Swedish massage is the most common form of massage therapy and the analgesic mechanisms are multifactorial in nature. It is postulated that the mechanisms of massage can be divided into biomechanical, physiological, neurological, and psychological [33]. The biomechanical mechanism behind massage therapies analgesic effect consists of the application of mechanical pressure to muscles with the aim of decreasing muscle tension resulting in increased muscular compliance. This stimulates the mechanoreceptors within the muscular and connective tissues resulting in a reduction in the firing rate of the muscle unit. Physiological mechanisms include increased skin and muscle temperature to a depth of 2.5 cm which leads to an increase in local blood microcirculation but not necessarily total muscle blood flow as studies have failed to effectively prove this assumption. Hormonal changes are also seen including a reduced level of cortisol in saliva which is seen after 5 consecutive weeks of massage therapy. An increase in activation of the parasympathetic nervous system has been shown in some studies. Gate con-

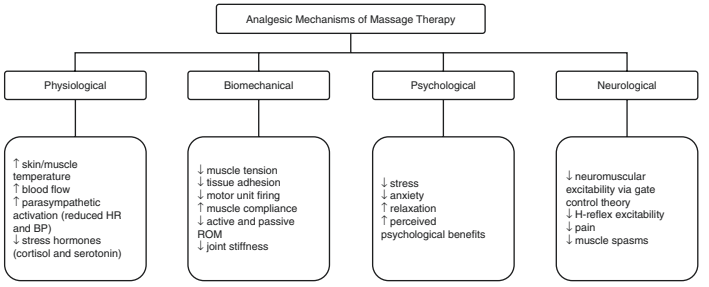

Fig. 2 Summary of analgesic mechanisms of massage therapy

trol theory is involved in the neurological mechanism as is it speculated that massage therapy increases the inhibitory pathways in the dorsal horn of the spinal cord resulting in decreased neuromuscular excitability and reduction in muscle pain and spasm. Finally, massage therapy had shown to reduce anxiety in several studies by an unknown mechanism illustrating a psychological component of massage therapy. The analgesic mechanisms of massage therapy are summarized in Fig. 2 [32, 33].

6.2 Practical Perioperative Use

The majority of the clinical data associated with massage therapy is centered around non-procedural acute and chronic pain states as well as sports performance and rehabilitation. In terms of sports-related massage therapy, the data does not show significant differences in preventing muscular injury, sport performance or recovery. Although, it did show that massage therapy increases blood lactate removal but light exercise was actually more beneficial than massage therapy in this circumstance. There was also an increased concentration of neutrophils in muscle tissue after massages which is postulated to enhance inflammation reduction but these studies did not show a decrease in limb size as a correlate for reduced edema. Overall, there was an increase in perceived recovery but little evidence of physiological data that massage improved performance, prevention of injury or recovery [33].

Massage therapy has reduced pain scores in various non-procedural acute and chronic pain states as follows: [32]

- Musculoskeletal pain (foot, knee, osteoarthritis, rheumatoid arthritis, pelvic, back/neck pain, carpal tunnel syndrome)
- Fibromyalgia
- Labor pain (also shortened labor by 5 h in one study when massage occurred at the beginning of each stage of labor for 15–30 min)
- Cancer pain [34]

Postoperatively, massage therapy has shown to reduce anxiety and pain scores after coronary artery bypass grafting as well as cancer surgeries but the effects only last in the short-term and do not improve long term pain. Overall, anxiety and cognitive stress are known correlates of pain and massage therapy is effective in reducing stress and anxiety, therefore this may be the reason there is less perceived pain [34–38].

Common Pitfalls

Contraindications include massage over an area with severe acute inflammation, skin infection, DVT, fracture, burn, and active malignancy. Side effects include minor pain or discomfort during or immediately after therapy which can be seen in up to 13% of patients [37].

Clinical Pearls

- Massage therapy is a safe non-pharmacological treatment for pain and anxiety that is proposed to work through biomechanical, physiological, neurological, and psychological mechanisms.
- A reduction in pain scores was seen in both acute and chronic as well as procedural and non-procedural pain.
- Anxiety and cognitive stress are known correlates of pain and massage therapy is effective in reducing stress and anxiety, therefore this may be the reason there is less perceived pain.

7 Cryotherapy

7.1 Essential Basics

Cryotherapy is the application of any substance that removes heat from the body in order to decrease the temperature of the tissue. Local hypothermia induces vasoconstriction, decreased tissue blood flow and rate of oxygen consumption, and reduced inflammation and muscle spasms. Along with compression, cryotherapy can reduce edema as extravasated fluid is mechanically pushed proximally into non-compressed and non-inflamed tissues where the lymphatic system can more effectively reuptake. The analgesic action is proposed to be mediated via multiple mechanisms as follows:

- Cold-induced neuropraxia → local anesthetic effect from decreased temperature of the skin and underlying tissue up to a depth of 2–4 cm. This decreases activation threshold of tissue nociceptors as well as nerve conduction velocity through activation of transient receptor potential ion channels (found in skin and spinal cord) in cold-sensitive peripheral sensory neurons
- Gate control theory → increased inhibition of neurons in dorsal horn of spinal cord
- Reduced muscle spasms → Hypothermia-induced inhibition of spinal cord reflex loop

Other beneficial effects of cryotherapy include prevention of secondary hypoxic injury via reduced oxygen demand of cooled tissues and decreased delivery of inflammatory markers to the site of injury [39–41].

7.2 Practical Perioperative Use

Cryotherapy is a staple of musculoskeletal injury treatment as seen in the mnemonic RICE (rest, ice, compression, elevation).

Cryotherapy can be achieved through multiple modes of administration and delivery including:

- Ice (crushed ice, ice in water)
- Cold gel packs
- Cryo-pneumatic devices (cold and compression)
- Continuous cold compression
- Ice massage
- Cold whirlpool
- Vapocoolant sprays

Ice water has been shown to be more effective at reducing muscle temperature when compared to ice alone. Continuous cryotherapy is preferable to intermittent therapy for reduction of post-traumatic edema but comes with a greater risk of cold-induced side effects so should be used with caution. Vapocoolant sprays, which contain the counterirritant menthol, create the sensation of cooling and analgesia through activation of transient receptor potential ion channels in cold-sensitive peripheral sensory neurons but they do not actually decrease the temperature of the skin of underlying tissue [39–43].

Clinically, cryotherapy has been shown to reduce pain and decrease opioid requirements after anterior cruciate ligament (ACL) reconstruction and total knee arthroplasty (TKA). Reduction in post-operative blood loss in TKA has also been shown. The benefits of cold compression therapy decrease over time, therefore cryotherapy is best in the acute period (first 48 h) after injury or procedure. Overall, the use of cold compression after MSK injury or orthopedic procedures results in improved clinical outcomes [40, 42, 44].

Common Pitfalls

While there are no known absolute contraindications to cryotherapy, it should be used in caution in patients with cold urticaria, cryoglobulinemia, paroxysmal cold hemoglobinuria, Raynaud's phenomenon, advanced diabetes and circulatory insufficiency. Side effects include bradycardia, transient neuropathy of superficial nerves (peroneal, ulnar, axillary, lateral femoral cutaneous, etc.), and frostbite [39, 42, 43].

Clinical Pearls

- The goal of cryotherapy is to create local hypothermia at the site of pain or injury in order to decrease pain, inflammation and edema via vasoconstriction and reduction of both tissue blood blow and metabolic consumption of oxygen.
- Analgesic relief from cryotherapy is proposed to act through cold-induced neuropraxia, gate control theory and reduction of muscle spasms.
- Cryotherapy has shown to improve clinical outcomes after musculoskeletal injury and orthopedic procedures.

8 Biofeedback

8.1 Essential Basics

Biofeedback is technique that provides the patient with biological information, known as augmented or extrinsic feedback, that is not naturally available to the patient in real-time. The type of feedback can be either direct or transformed where direct feedback is a measured variable that is directly displayed to the patient (ie. heart rate or heart rate variability) and transformed feedback is a measured variable that is processed and presented to the patient through auditory, visual or tactile forms. Categories of biofeedback are outlined below: [45] (Fig. 3)

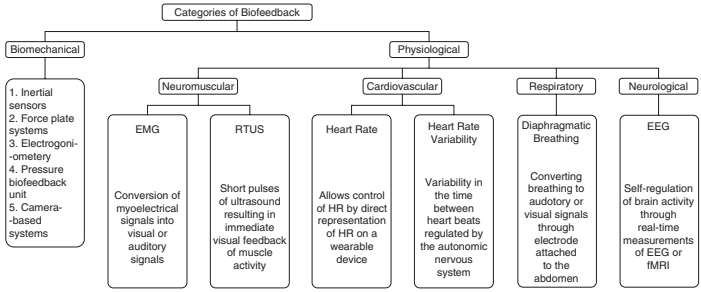

Fig. 3 Categories of biofeedback mechanisms

- Biomechanical (measurements of movement, postural control, or force)
  - Inertial sensors
  - Force plate systems
  - Electrogoniometery
  - Pressure biofeedback units
  - Camera-based systems
- Physiological
  - Neuromuscular (electromyography and real-time ultrasound)
  - Cardiovascular (heart rate, heart rate variability)
  - Respiratory (diaphragmatic breathing control)
  - Neurological (electroencephalography)

The most common form of biofeedback is electromyography (EMG) which uses surface or subcutaneous electrodes to measure and detect changes in skeletal muscle activity, specifically muscle tension. This is a form of operant conditioning of physiological activity. Muscle tension is measured in microvolts (5–40 μV) and is then processed into transformed feedback. Patients are then able to perceive and modify muscle tension in order to "retrain" muscles by creating a new feedback loop that can both increase activity in a weak or paretic muscle and decrease activity in a spastic muscle. Muscle fibers nearest the electrode will have the greatest influence on the combined signal from surface electrodes. Wide electrode spacing increases the volume of tissue measured while narrow spacing will be more specific to the intended muscle being measured. Electrodes should be placed in parallel with the muscle fibers being measured [45–47].

8.2 Practical Perioperative Use

EMG biofeedback has been studied in both acute and chronic pain states. In chronic neck and back pain, EMG biofeedback leads to a reduction in muscle tension resulting in a generalized muscle relaxation effect which reduces perceived pain and disability while improving quality of life. EMG biofeedback has also been

shown to facilitate recovery and quadriceps muscle strength after anterior cruciate ligament reconstruction. It also improves patellofemoral pain syndrome by equalizing vastus medialis and vastus lateralis muscle activity during quadriceps exercises. Overall, EMG biofeedback can reduce muscle tension leading to decreased pain but it also has a psychological effect leading to increased patient motivation in recovery due to the requirement of active participation in rehabilitation [45–48].

Common Pitfalls

Biofeedback is a safe and non-invasive form of rehabilitation however skin electrodes can cause skin irritation and in severe cases, dermatitis. If subcutaneous electrodes are used, infection and pain are side effects. Overuse of muscles during EMG biofeedback can lead to musculoskeletal injury [48].

Clinical Pearls

- Biofeedback is a safe technique that allows users to perceive measured biomechanical or physiological variables in order to gain more control over bodily functions.
- EMG biofeedback is the most common form of biofeedback and has been shown to reduce muscle tension and improve pain in many acute and chronic pain states.

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Part III

Acute Pain Management Protocols for Surgical Procedures

Acute Pain Management Protocol for Cranial Procedures

Shane M. Barre and Sanjib Das Adhikary

Case Stem

A 30 year-old, 90 kg male presents to his primary care physician with recurrent migraines. He has a past medical history significant for anxiety/depression and chronic back pain on chronic opioids. He states that he has been having increasing frequency of migraine symptoms, now about 3 days a week. He endorses photophobia, phonophobia, nausea, and severe occipital head pain. When the pain is severe, he also states that he feels "dizzy" and "unsteady" on his feet. He has failed treatment with over-the-counter analgesics and triptan medications. His primary care doctor decides to trial greater occipital nerve blocks to see if this provides any relief. The patient follows up in 2 weeks and his symptoms have not improved but have gotten more severe. The patient's doctor decides to obtain imaging and orders an MRI of the brain. A 1 × 3 cm lesion in the patient's cerebellum is discovered and is concerning for malignancy. He is evaluated by neurosurgery who recommends for posterior craniotomy for tumor resection. The surgeon states he would like to use a Mayfield head holder for the surgery. Neuromonitoring

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_17

will include somatosensory evoked potentials (SSEP's), motor evoked potentials (MEP's), and electroencephalography (EEG). The surgeon states that he typically likes to inject his own local anesthetic at the end of the procedure, but you convince the surgeon to allow you to perform preoperative scalp blocks.

Questions and Answers

1. **Have nerve blocks been shown to be beneficial for migraines?**
   Greater occipital nerve blocks have been shown to be effective in the short-term for treatment of chronic migraine by reducing the frequency and severity of headaches [1, 2]. Lesser occipital nerve block has also been shown to be helpful in treating occipital neuralgia in the short-term but had no significant benefit at 6 months post-injection [3].
2. **What is the anatomy and innervation of the scalp, skull, and dura?**
   (a) *Scalp*
   The scalp consists of five layers: skin, subcutaneous tissue, epicranium, subaponeurotic areolar tissue and the pericranium [4]. It is densely innervated with C-fibers (unmyelinated) and A-delta fibers (thinly myelinated) [5]. The primary sensory innervation of the scalp includes the supraorbital, supratrochlear, zygomaticotemporal, auriculotemporal, greater occipital, and lesser occipital nerves. The ophthalmic division of the trigeminal nerve gives off, via the frontal nerve, the supraorbital and supratrochlear nerves, which innervate the skin from the forehead to the lamboidal suture. The zygomaticotemporal nerve is one of the two branches of the zygomatic nerve that arise from the maxillary division of the trigeminal nerve. It innervates a small area of the forehead and temporal area. The auriculotemporal nerve arises from the mandibular division of the trigeminal nerve. It innervates the posterior portion of the skin of the temple. The greater occipital and lesser occipital originate from the ventral and the dorsal rami of C2 and

C3 spinal nerves. The lesser occipital nerve passes superiorly along the posterior border of the sternocleidomastoid muscle (SCM), dividing into the cutaneous branches that innervate the lateral portion of the posterior scalp and the cranial surface of the pinna of the ear. The greater occipital nerve travels up to the vertex, and the lesser occipital nerve innervates skin behind the ear [6].

(b) *Skull*

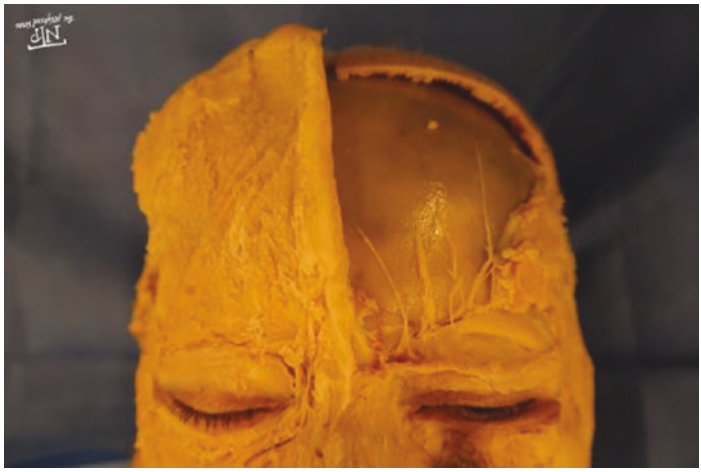
The upper part of the cranium forms a covering to enclose and protect the brain; it is often termed the calvaria. The remainder of the skull forms the facial skeleton, of which the lower part is the freely moveable mandible. The region of the forehead is formed by the frontal bone, which passes backwards in the vault of the skull up to the coronal suture, where it meets the right and left parietal bones. These two bones make up most of the cranial vault and articulate with each other at the sagittal suture. They extend posteriorly to the occipital bone, all three bones meeting at the lambdoid suture. When the skullcap or calva is removed, the base of the skull is exposed. It shows a natural division into three regions: anterior, middle and posterior cranial fossae. The inferior surface of the base of the skull is very irregular and exhibits a number of important foramina through which exit the brain stem, cranial nerves and blood vessels [4].

(c) *Dura*

The brain is enveloped by three membranes or meninges: the dura mater, the arachnoid mater, and the pia mater. The cerebral dura mater lines the interior of the skull and forms both an internal periosteal layer and a supporting membrane for the brain. The supporting role of the dura is evident in that it forms the falx cerebri and cerebelli, tentorium cerebelli and diaphragm sellae [4]. The dura is innervated by branches of the trigeminal nerve, ventral and dorsal rami of the cervical nerves, branches of the vagus, and hypoglossal nerves. Sources of post-craniotomy pain include tissue injury (scalp, cranial muscles soft tissue, and

dura mater) and nerve disruption, traction, entrapment, and compression [7]. The dura mater is innervated mainly by the major three branches of the trigeminal nerve, and hence blockade of these branches in the right location will provide analgesia to the dura as well [8]. Brain tissue itself does not contain any nociceptors, and therefore theoretically does not contribute to the pain response after surgery.

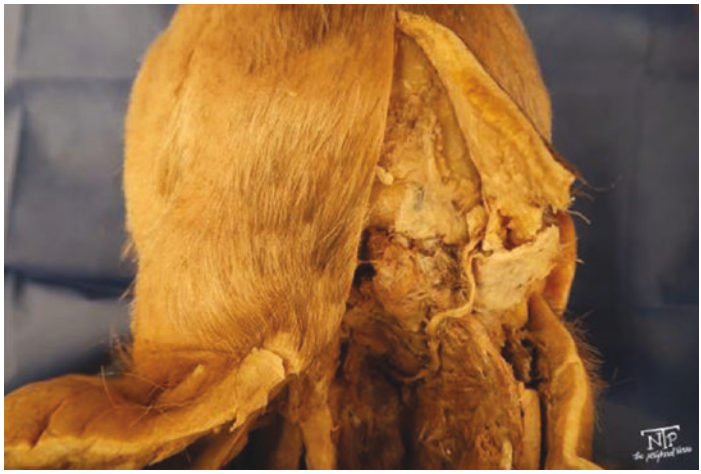
3. **How are scalp blocks performed?**
   In adults scalp blocks are typically performed with use of a 25–30 g needle and a syringe to inject local anesthetic. These smaller gauge needles tend to be better tolerated when these blocks are performed on awake patients. Due to the superficial location of the scalp nerves, typically a 1 or 1.5 in. needle provides enough length in adults. The scalp is highly vascular, and since the arteries and veins of the scalp tend to run along the nerves, aspiration of the syringe should be performed before any injection. In addition, careful consideration should be taken to calculate the maximum doses of local anesthetics that can be used based on the patient's ideal body weight. There are three main approaches to anesthetizing the nerves of the scalp: local infiltration, performance of a "ring block", or the targeted approach listed in more detail below. Local anesthetic tends to be minimized with the more targeted approach although some clinicians choose to perform a "ring block", where the injection sites listed below are connected to form a ring of local anesthetic around the head in an imaginary line from the occipital protuberance to the eyebrows to ensure no nerves or branches are missed. This technique often requires increased volumes of local anesthetic solution and can limit the concentration of local anesthetic that can safely be used. Typically, with a targeted approach, injection of 1–3 ml of local anesthetic per injection site is enough to provide adequately blockade of each of the nerves listed below. A thorough understanding of the anatomy of the scalp and discussion with the surgeon about location of the surgical incision is crucial, as not all of the nerves of the scalp need to be blocked for every surgical procedure.
   (a) *Supraorbital and Supratrochlear Nerves*



Anterior view of the head/scalp. Left side of scalp dissected showing the supratrochlear nerve (medial) and supraorbital (lateral) nerve. Cadaver dissection and photography performed by Neel Tushar Patel M.D., Penn State Health Milton S. Hershey Medical Center

The supraorbital nerve can be blocked by palpating the supraorbital notch (located at the middle portion of the superior orbit, 2–3 cm from the midline of forehead) and directing the needle to the medial brow. The supratrochlear nerve can be blocked by palpating the notch and depositing local anesthetic in a medial and lateral direction to capture lateral supraorbital fibers. Ultrasound guidance can also be used to block both nerves as well. A linear probe is placed in a transverse position above the orbital rim to identify the supraorbital notch and local anesthetic is deposited next to, but not directly into the foramen [9]. The full area of sensory loss for both nerves include the frontal scalp, forehead, bridge of nose, and the upper eyelid. Even if a unilateral surgery is planned, often bilateral nerve blocks need to be performed because there tends to be significant overlap in nerve coverage. Care should be taken to avoid injection directly into the supraorbital or supratrochlear arteries or veins.

(b) *Greater Occipital Nerve*



Posterior view of the head/scalp. Right posterior scalp reflected to show course of greater occipital nerve. Cadaver dissection and photography performed by Neel Tushar Patel M.D., Penn State Health Milton S. Hershey Medical Center

The greater occipital nerve can be blocked using anatomic landmarks, or by ultrasound guidance as well. Anatomically, the occipital artery can be palpated approximately one-third the distance from the external occipital protuberance to the mastoid process on the superior nuchal line closer to the occiput [10]. The nerve is medial to the artery, which should be carefully avoided. The injection site is 2 cm inferior and 2 cm lateral to the external occipital protuberance. Under ultrasound guidance, there are two areas where the greater occipital nerve can be blocked. The first location is by placing a linear probe at the level of the superior nuchal line in a transverse plane with the probe slightly lateral to the external occipital protuberance. Another approach is placing the same probe on the spinous process of C2 then moving the probe laterally to identify the

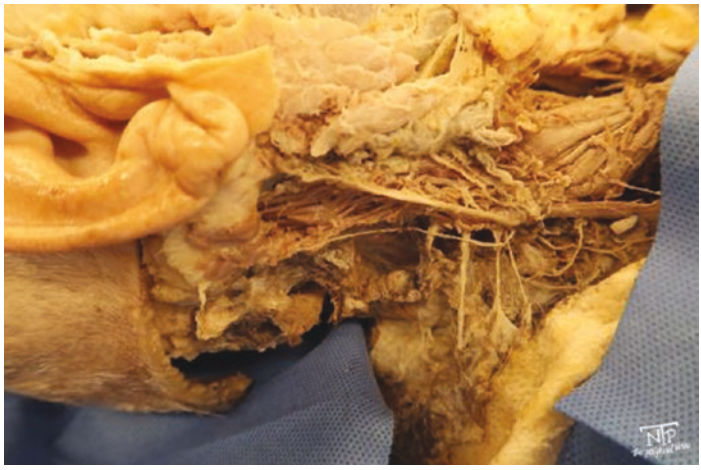
obliquus capitis inferior muscle of the neck. The greater occipital nerve is a hypoechoic structure visualized just below the caudate border of the semispinalis muscle and crossing the obliquus capitis inferior muscle from lateral to medial [9].

(c) *Lesser Occipital Nerve*

The lesser occipital nerve lies two-third along the superior nuchal line closer to the mastoid process. Anatomically, the lesser occipital nerve can be blocked 5 cm lateral and 1 cm inferior to the external occipital protuberance [10]. For ultrasound guided block, place a linear probe on the spinous process of C2 then moving the probe about 5 cm laterally to identify the attachment point of the sternocleidomastoid on the mastoid, the lesser occipital nerve lies along the posterior border of the muscle. The block can be performed using an out-of-plane technique and injecting 1–2 ml of local anesthetic after aspiration. Ultrasound-guided occipital nerve blocks appear to be relatively safe, effective, and an easy procedure for both the diagnosis and treatment of occipital neuralgia secondary to direct visualization of the greater occipital nerve and lesser occipital nerve [11].

(d) *Auriculotemporal Nerve*

The auriculotemporal nerves are blocked 1.5 cm anterior to the ear at the level of the tragus [9]. Blockade of the auriculotemporal nerve is possible at several levels. For low temporal intracranial surgery, it should be blocked 1.5 cm anterior to the tragus with infiltration of local anesthetic superficially (as deep injection may unnecessarily anesthetize the facial nerve). Otherwise, the auriculotemporal nerve may be effectively blocked 1–1.5 cm anterior to the superior border of the pinna, obviating any risk of facial nerve blockade [12]. Caution is necessary due to the vicinity of the temporal artery.



Lateral view of the right head/neck showing the course of the great auricular and lesser occipital nerves. Cadaver dissection and photos taken by Neel Tushar Patel M.D., Penn State Health Milton S. Hershey Medical Center

(e) *Zygomaticotemporal Nerve*
The zygomaticotemporal nerve arises between the supraorbital and auriculotemporal nerves with its foramen located on the anterior wall of the temporal fossa behind the lateral orbital rim at the level of the lateral canthus [13, 14]. Deep and superficial planes should be injected as the nerve may branch extensively. The nerve may be anesthetized by palpating the lateral orbital rim at the level of the frontozygomatic suture. The index finger is left in the depression of the posterior lateral aspect of the lateral orbital rim and the needle introduced approximately 1 cm posterior to the suture. The needle should be "walked down" the concave wall of the lateral orbital rim until it reaches the level of the lateral canthus. Two milliliters of local anesthetic is generally recommended for an effective block [14].

(f) *Postauricular Nerve*
The postauricular branches of the greater auricular nerves are blocked 1.5 cm posterior to the ear at the level of the tragus [9]. The posterior branch of the great auricular nerve is blocked 1.5 cm posterior to the pinna at the level of the tragus. Targeting this nerve is not absolutely neces-

sary for routine scalp blockade, as the sensory contribution is minimal. However, blockade may be beneficial for surgery centered near the mastoid process (i.e., acoustic neuroma resection, particularly for the translabyrinthine approach). One milliliter of local anesthetic should be sufficient for blockade [12]. Table 1 below provides a non-

Table 1 Regional Anesthesia for Surgical Procedures of the Head and Face

Nerve Blocks	Surgical and Medical Procedures
Greater occipital nerve	Posterior craniotomies
	Insertion of ventriculoperitoneal shunt
Lesser occipital nerve	Headaches caused by posterior fossa tumors
	Arnold-Chiari malformation, cervicogenic tension and occipital headaches
Supraorbital and supratrochlear nerve	Frontal sinus surgery
	Frontal craniotomies
	Cosmetic nasal surgery
	Ophthalmic surgery
Infraorbital nerve block	Computed tomography endoscopic sinus surgery
	Rhinoplasty
	Cleft palate surgery
	Upper lip cosmetic surgery
Sphenopalatine	Cleft palate surgery
	Septoplasty
	Nasal laceration
Anterior ethmoid nerve	Septoplasty, rhinoplasty
Mandibular nerve block	Mandbular bone
	Mandbular first molar (anterior)
	Lower teeth to the midline
	Buccal muccoperiosteum, mucous membrane
	Anterior two thirds of the tongue
	Surgeries involving floor of the oral cavity (ingual nerve) and lingual soft tissues
Mental nerve (inferior-alveolar) block	Mandibular surgery
	Lower lip laceration repair
	Chin laceration repair
	Lower molars surgeries

Open Access Table taken from: Muse, Iyabo O. Straker, Tracy. A comprehensive review of regional anesthesia for head and neck surgery. Journal of Head and Neck Anesthesia. (2021) 5:e33. https://doi.org/10.1097/HN9.0000000000000033

comprehensive list of nerve blocks that have been shown to be useful for a variety of surgical procedures of the head and face. Some of the nerve blocks listed will not be discussed in this chapter.

4. **What specific scalp nerves will be most important to block for this procedure? What about for the use of the Mayfield head holder?**
   To cover the incision for a posterior craniotomy it will be crucial to ensure blockade of the greater and lesser occipital nerves bilaterally. The location of the Mayfield pins should be discussed with the surgeon as well so that the appropriate nerve blockade can be performed, as pin insertion can lead to a significant sympathetic surge and pain response leading to detrimental increases in heart rate and blood pressure. Some practitioners prefer to inject local anesthetic subcutaneously at the anticipated pin sites instead of targeting the specific nerves covering the area.
5. **What are the benefits of scalp blocks?**
   Prior clinical trials of scalp blocks for craniotomy patients have found them to be superior to placebo and provide similar postoperative pain relief to intravenous morphine [15, 16], with a lesser response to surgical stimulation as measured by ACTH, serum cortisol, and hemodynamic changes [17]. Scalp blocks have shown to decrease the frequency of request for rescue analgesics, increase the time between completion of surgery and first request of analgesics, and decrease pain scores in the initial postoperative phase [18]. Scalp blocks have the advantage of blunting the hemodynamic responses during perioperative period and also facilitate more rapid and smooth emergence with lesser cognitive dysfunction in craniotomies [19]. Blunting of the hemodynamic response can be especially beneficial in surgeries where avoiding increases in intracranial pressure are imperative. A randomized controlled study demonstrated that scalp nerve block with 0.75% ropivacaine had a modest preventive effect on postoperative inflammation demonstrated by lower IL-6, IL-10, and C-reactive protein concentrations at different time points after craniotomy for cerebral aneurysms [20]. Scalp blocks have also been found to be useful

for awake craniotomies and are often combined with dexmedetomidine-based anesthesia. This approach can enable physiologic testing before and during tumor resection facilitating real-time surgical decision-making based on intraoperative brain mapping with patients awake thereby minimizing the risk of neurologic deficit and increasing the opportunity for optimal surgical resection. One study showed no requirement for urgent airway intervention or unplanned conversion to a full general anesthetic with awake craniotomy [21].

In addition, the treatment of acute post-craniotomy pain has implications for long-term recovery as the severity of acute postsurgical pain predicts the incidence of chronic postsurgical pain after a number of surgical procedures [22]. Likewise, regional infiltration with ropivacaine reduced the incidence of persistent and neuropathic pain 2 months after craniotomy, suggesting that mitigating acute post-craniotomy pain may help diminish the possibility of chronic post-craniotomy pain [23].

6. **Are there any differences in outcomes between ultrasound guided vs. landmark techniques?**

   High-resolution ultrasound has the potential to visualize small peripheral nerves and to facilitate real-time local anesthetic blocks with high precision**.** Even if a nerve cannot be identified by itself on ultrasound imaging, ultrasound can be useful in helping to find bony landmarks such as the supraorbital foramen, which are traditionally found anatomically with palpation. Studies evaluating ultrasound guided techniques show that use of an ultrasound can decrease the amount of local anesthetic needed, while achieving a higher block success rate. Specifically, for greater occipital nerve block, researchers found that they could use volumes as low as 0.1 ml in cadavers and achieve an 80–100% success rate dependent on the location that the block was performed [24]. Theoretically, the use of ultrasound may prevent inadvertent puncture of vessels that are in close proximity to the nerves.

7. **Are there any differences in outcomes with local infiltration vs. targeted nerve blocks?**

   Published randomized controlled trial on scalp blocks are small and difficult to compare with one another due to the technique's heterogeneous application, including different choice

of local anesthetics and different outcome variables [19]. Nonetheless, it seems that postoperative analgesia provided by scalp block can last up to 24 h postoperatively and is superior to analgesia provided by scalp infiltration [13, 16, 25, 26]. Other studies have not been as conclusive and have not shown the same benefits [27].

When compared to local infiltration or routine anesthesia, scalp nerve blocks have been found to better blunt the hemodynamic response to skin incision. Also, when compared to a local anesthetic infiltration group and control group, a scalp nerve block group had lower postoperative pain intensity, longer duration before the first dose of oxycodone, less consumption of oxycodone, and lower incidence of post-operative nausea and vomiting (PONV) 48 h postoperatively [20].

8. **Have scalp blocks been found to be useful for anything else?**

Scalp blockade can also be used in other subspecialty surgery involving the cranium, including dermatological (photodynamic surgery for actinic keratosis, resection of infiltrating carcinoma of the scalp) and plastic (cranioplasty) surgery [28, 29]. Non-surgically, greater occipital nerve blocks has been shown to be effective in the short-term for treatment of chronic migraine by reducing the frequency and severity of headaches [1, 2]. Lesser occipital nerve block has also been shown to be helpful in treating occipital neuralgia in the short-term but had no significant benefit at 6 months post-injection [3].

9. **What complications are associated with scalp blocks?**

As with any injection there are risks of infection, bleeding, and damage to nerves or blood vessels. Fortunately, complications of head and scalp blocks are rare partially due to the superficial locations of the nerves. However, intravascular injection and spinal spread of local anesthetic are potential complications, so aspiration prior to any injection should be performed. The vertebral and greater occipital arteries are in close proximity to the greater occipital nerve. The spinal cord is medial and deep to the muscles, and in children with prior spine surgeries extreme caution should be taken to remain subcutaneously during injection to avoid a total spinal anesthetic and respiratory compromise [11]. Because of the highly vascular nature of the scalp,

attention should be paid to the total dose of local anesthetic being used to minimize the risk of local anesthetic systemic toxicity (LAST).

10. **What are some risk factors for severe postoperative pain in craniotomy patients?**
    Female [30–32] and younger patients [30, 33] have the highest incidence of pain after craniotomy. The probability of experiencing post-craniotomy pain is reduced by 3% for each additional year of life [33]. However, these patient-related factors are not uniformly accepted with regard to post-craniotomy pain as some studies show opposite results: namely that age, sex, and also the American Society of Anesthesiologists Physical Status Classification are not predictive of pain character or intensity [34]. Anxiety, depression, and preoperative pain are also possible risk factors for postcraniotomy pain [32, 34]. As seen in other types of surgery, chronic opioid use and abuse will likely make patients susceptible to severe postoperative pain.
11. **Does location of craniotomy affect postoperative pain?**
    Patients who undergo infratentorial procedures have more pain than those submitted to a supratentorial approach [35]. The subtemporal and suboccipital surgical routes have shown to have the highest incidence of postoperative pain [30]. Frontal craniotomy is associated with lower pain scores and a significantly lower consumption of opioid analgesics [36]. The relationship between craniotomy location and pain intensity may be explained, at least in part, by the anatomical location of pericranial muscles and the muscle dissection involved in posterior fossa craniotomies leads to a relatively higher postoperative pain experience [36–38]. Aside from craniotomy location itself, patients with vascular malformations and/or cerebral aneurysms tend to require more postoperative analgesia to achieve pain control compared with their tumor counterparts [39].
12. **What local anesthetic would you use for scalp blocks and how much volume?**
    Bupivacaine, ropivacaine, and levobupivacaine are long-acting local anesthetics suitable for use in scalp blockade. Ropivacaine and levobupivacaine have a better safety profile

than bupivacaine showing altered thresholds for cardiovascular and neurologic toxicity [40, 41]. In healthy human volunteers, the heart was affected at lower doses and serum concentrations of bupivacaine than with ropivacaine [42].

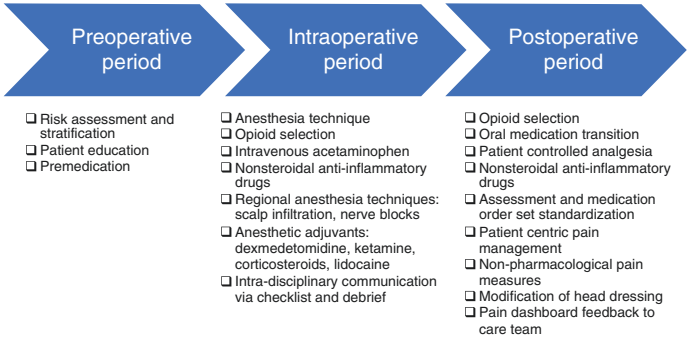
Regardless of which local anesthetic is used, injection at multiple sites and selectively blocking peripheral nerves of the scalp should help prevent absorption-related toxicity, since as little as 10 ml of local anesthetic per side of the cranium is needed. Additional economy with respect to local anesthetic volume is achieved by blocking only the nerves relevant to the anticipated surgical incision. Selective blockade with minimal volume, as opposed to ring blockade, allows for the use of maximal local anesthetic concentration. Commonly, a concentration of 0.5% ropivacaine or bupivacaine is used. Lidocaine is rarely used alone for scalp blockade due to its shorter duration of action. However, its more rapid onset may be valuable for treating dural pain or during frame placement in awake patients. Some practitioners combine bupivacaine or ropivacaine with lidocaine to capitalize on both the shorter onset of lidocaine and the longer duration of action of the other local anesthetics. Some caution must be exercised with this practice, as combining local anesthetics lowers the effective concentration of both drugs in the mixture [43]. The combination of medications also reduces the duration of the efficacy of the block. Table 2 below lists several commonly used local anesthetics and their toxic doses with and without epinephrine. Toxic doses vary slightly from different sources, so some dose ranges are included.

Table 2 Toxic Doses of Commonly Used Local Anesthetics with and without Epinephrine

Local anesthetic	Toxic dose plain (mg/kg)	Toxic dose with epinephrine (mg/kg)
Lidocaine	4–5	7
Mepivacaine	4–5	7
Bupivacaine	2–2.5	3
Ropivacaine	3	3
Chloroprocaine	10–11	14–15

13. **Is there any benefit to adding epinephrine to your local anesthetic solution?**
    Another issue to consider which has had mixed results is whether to add epinephrine to the local anesthetic. Five studies have used epinephrine in concentrations of 1:200,000 or 1:400,000. In two safety and efficacy studies of local anesthetic with epinephrine during awake craniotomy, it was unclear whether epinephrine actually slowed the absorption of local anesthetic, since epinephrine was used in all patients [44, 45]. Ropivacaine with and without epinephrine has been used for brachial plexus blockade, with little demonstrated difference in serum levels [46, 47]. Despite the use of epinephrine, a rapid rise in local anesthetic serum level was observed (peaks $\leq$ 15 min) but did not result in any cardiovascular or central nervous system toxicities in either study [44, 45]. Serum levels also peaked substantially faster than the times observed in studies of epinephrine-supplemented local anesthetic during other regional techniques (epidural, intercostal, and axillary nerve blockade) [48–50]. Interestingly, more recently epinephrine was implicated in eliciting hypotension shortly after scalp infiltration, although the mechanism was unclear [51]. Epinephrine does play a role in incisional scalp infiltration, as it provides the added benefit of hemostasis.
14. **What other interventions have been proven to be effective for patients undergoing craniotomy or other surgeries of the head?**
    Table 3 lists perioperative interventions that anesthesia providers should consider during the preoperative, intraoperative, and postoperative periods. These interventions are discussed in more detail below.
    (a) **Preoperative**
        Identifying high-risk patients (anxiety, depression, and chronic pain) may improve pain management. The benefits include improved multidisciplinary communication about potential pain outcomes, risk adjusted therapeutic interventions and optimization, or protocol variation based on risk assessment, and triggering pain consulta-

Table 3 Perioperative Interventions



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tion or behavioral cognitive intervention [52]. The procedure-specific benefit with regard to pain outcomes is not yet available. Educational material such as information about anticipated pain, treatment options, and side effects of pain medications may improve patient's pain experience [53–55]. In patients undergoing craniotomy, preoperative gabapentin administration decreases anesthetic and analgesic consumption up to 48 h after surgery, but it also delays tracheal extubation and increased sedation postoperatively [56]. The effect appears to be beneficial only when given over an extended period preoperatively and not a single premedication dosage [57]. Other potential effects include decreased incidence of delirium, possibly due to its opioid-sparing effect [58], reduced perioperative anxiety, improved sleep quality [59], lowered postoperative nausea and vomiting (PONV) [57], and attenuated hemodynamic effects from the placement of the pin holder [60]. The procedure specific analgesic benefit of preoperative administration of acetaminophen is undetermined.

(b) **Intraoperative**

Some studies showed that inhalational anesthesia with sevoflurane is associated with a higher probability of postcraniotomy pain in comparison to intravenous techniques [33, 61]. A Cochrane review of postoperative outcomes did not find differences in the probability of postcraniotomy pain [62]. Apart from evidence that intravenous techniques reduce postoperatively nausea and vomiting, the authors could not draw definitive conclusions regarding other outcomes.

(i) *Remifentanil*

Remifentanil has a dose-dependent potential to amplify postoperative pain and induce pain sensitization [63, 64]. Limiting the dose of remifentanil to less than 0.2 $\mu g.kg^{-1}.min^{-1}$ and combination with other analgesics might be useful to mitigate acute opioid tolerance and opioid-induced hyperalgesia [64].

(ii) *Acetaminophen*

The administration of acetaminophen is unlikely to cause significant additive sedation and likely to provide additive analgesia [65]. A retrospective analysis showed that while intraoperative acetaminophen is a safe intervention, no significant differences were found in postoperative pain scores [66].

(iii) *Non-Steroidal Anti-Inflammatory Drugs (NSAID's)*

The intraoperative use of non-selective COX-1/COX-2 inhibitors for the patient undergoing craniotomy is questionable. Due to antiplatelet effects, preoperative use can be linked to intracranial hemorrhage in 1.1% of patient [67]. Studies provide inconclusive evidence for the safety of drugs such as ketorolac [68] demonstrating a higher risk for intracranial hematoma associated with intraoperative use but not in the postoperative setting [69]. Further, trial studies do not show an increase in complication rates for hematomas, renal failure, or peptic ulcers following neurosurgery [70].

(iv) *Dexmedetomidine*
Several studies support a role for intraoperative dexmedetomidine in mitigating postcraniotomy pain. Dexmedetomidine has an opioid-sparing effect [71, 72] and provides better control of perioperative mean arterial pressure [73], as well as superior analgesia [74].

(v) *Ketamine*
Its use in patients undergoing craniotomy was initially questioned due to its reported effects on intracranial pressure, seizure threshold, and mentation. Studies have since shown that ketamine does not affect cerebral hemodynamics [75] and may actually improve cerebral perfusion [76]. When used in combination with a GABAergic agent, the hallucinatory side effects seem to be blunted [76]. Use of a subanesthetic dose of ketamine can further attenuate the hemodynamic response to skull-pin placement [77]. Nonetheless, the lack of available studies and the potential to induce cognitive changes, negative experiences, blurred vision as well as dizziness make it controversial in the neurosurgical population [78, 79].

(vi) *Corticosteroids*
Corticosteroids, namely dexamethasone, are frequently administered perioperatively in patients undergoing craniotomy in order to mitigate cerebral edema and PONV. The absence of dexamethasone during craniotomy appears to increase postcraniotomy pain [33]. This finding is consistent with a salutary effect in other surgeries [80, 81].

(vii) *Lidocaine infusion*
A review of RCTs revealed improvement in early postoperative pain in patient undergoing abdominal surgery [82]. Lidocaine administration was shown to improve postoperative analgesia after supratentorial craniotomy [83].

(c) **Postoperative**

Table 4 provides a summary of the advantages and disadvantages of scalp blocks, infiltration of local anesthetic, analgesics, and non-pharmacologic interventions used

Table 4 Summary of Strategies for the Treatment of Acute Postcraniotomy Pain

Treatment	PRO/CON	LOE
Codeine	Pro: Historical treatment, widely used Con: Potential respiratory depression and sedation; less effective than morphine; genotype variation	3 RCT
Morphine and long acting opioids	Pro: Widely used, effective, small incremental dosing and/or PCA Con: Respiratory depression and sedation; nausea and vomiting; potential to alter carebral hemodynamics; quality of recovery	3 RCT
Tramadol	Pro: Less potential form respiratory depression Con: High risk for nausea and vomiting; potential for inducing seizures	3 RCT
PCA	Pro: No major adverse effects; lower pain scores Con: Potential respiratory depression and sedation; prescribing errors; need for staff and patient education	4 RCT
Intraoperative Acetaminophen	Pro: Analgesia without sedation or respiratory depression; established component of multimodal analgesia; no nausea or vomiting Con: Not adequate alone; benefit not established; requires careful attention to cumulative doses and caution in,liver patients	2 RCT
NSAIDS Non-selective Cyclooxygenase inhibitors	Pro: Effective; minimal sedation; postoperative use Con: Safety to be established; potential for systemic bleeding; intraop intracranial hemorrhage; does not reduce opioid consumption	1 RCT
NSAIDs selective Cyclooxygenase inhibitors	Pro: Effective; minimal sedation; postoperative use; safer that non-selective agents Con: Benefit not established; caution in cardiac patients	2 RCT
Ketamine	Pro: Effective pain reliet; improves cerebral perfusion; attenuates hemodynamic response Con: Hallucinations; ill-defined potential to confound neurological assessment	2 RCT
Scalp Infiltration	Pro: Attenuates hemodynamic response; reduces pain in 1st hour; may decrease long term neuropathic pain Con: Does not reduce need for other medication	6 RCT
Scalp Nerve Block	Pro: Attenuates hemodynamic response; superior to scalp infiltration Con: Not attenuates alone; benefit not well established	5 RCT
Gabapentin	Pro: Attenuates hemodynamic response; decreases anesthetic and analgesic consumption; anxiolytic; improves sleep quality Con: Delayed tracheal estubation, increase sedation; administration over extended periods	4 RCT
Nonpharmacological Measures	Pro: No major side effects, tailored to patient preferences Con: Evidence not established	3 RCT

NSAIDs: Nonsteroidal anti-inflammatory drugs, RCT: Randomized controlled trial, PCA: Patient controlled analgesia

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for postoperative pain control after craniotomy. Specific analgesics used for postoperative craniotomy pain are discussed in more detail below.

(i) *Opioids*

Codeine, a weak opioid with limited analgesic effect, was traditionally the opioid of choice in several neurosurgical centers because of a perceived ceiling to respiratory depressant effects and a lower risk of masking of pupillary signs [84]. However, several studies have shown codeine to be inadequate in the management of all postcraniotomy pain [85, 86]. Morphine analgesia, while superior to other opioids [86], has been questioned in the postcraniotomy pain setting because it might influence cerebral circulation and metabolism, with the potential to jeopardize the former [87]. Hydromorphone is widely used across surgical specialties including neurosurgery for acute pain management. Studies have suggested some advantage of hydromorphone over morphine for analgesia [88], though none have specifically addressed this comparison in neurosurgical patients. Tramadol is less likely to cause respiratory depression compared to other opioids. Despite this potential advantage for neurosurgical patients, tramadol does share the negative side effects of other opioids namely nausea, vomiting, sedation, and drowsiness [89]. Even though tramadol has been used successfully after craniotomy [90], its side-effects have limited its use [86, 91] and its efficacy remains lower than that of morphine [86].

(ii) *Patient-controlled analgesia (PCA)*

Patient-controlled analgesia (PCA) is another option for postcraniotomy pain treatment. Limited studies show it to be subjectively better than nurse-administered analgesia [92, 93]. PCA with either morphine or fentanyl, reduced pain scores without significant differences in nausea, vomiting, or sedation scores [93–96].

(iii) *Non-Steroidal Anti-Inflammatory Drugs (NSAID's)*
Postoperative administration of non-selective COX-1/COX-2 inhibitors, such as ketorolac, in the early postoperative period is an area of controversy [97]. Some centers introduce them in a selective criteria-based fashion, such as in uncomplicated cases with no clotting issues or after 6, 12, or 24 h [98]. Several studies have shown no adverse effect of postoperative administration [69].

(iv) *Nonpharmacologic Therapies*
Nonpharmacologic therapies for postsurgical pain include the application of heat and cold, massage therapy, aromatherapy, guided imagery, music therapy, biofeedback, hypnosis, and acupuncture. Live music therapy using patient preferred music has shown to decrease anxiety and stress, but not pain or analgesic requirements, after elective craniotomy [99]. Periorbital cryotherapy was shown to decrease eyelid edema and ecchymosis, but not postcraniotomy pain scores [100]. Electroacupuncture decreased pain scores in the first 6 h after supratentorial craniotomy [101]. The potential value of other nonpharmacological strategies to mitigate pain mentioned above, as well as patient education and pain management planning have not been studied in patients undergoing craniotomy

1 Summary

Unfortunately, there is a very high incidence of acute and chronic pain after craniotomy for various types of intracranial procedure. Benefits of scalp blocks have included decreased opioid consumption, blunted hemodynamic response to incision, decreased inflammatory response, and the reduced incidence of the development of chronic pain. Scalp blocks have also been successfully used for various extracranial surgeries and have been beneficial for patients suffering from different migraine conditions. Scalp blocks alone, however, are not enough to manage postoperative

pain. A multimodal approach should be taken in the preoperative, intraoperative, and postoperative periods. High risk patients for difficult pain control should be identified, and a variety of medications targeting different pain receptors should be used, as well as non-pharmacologic analgesic strategies.

Common Pitfalls

- Always be sure to calculate the maximum allowable/toxic doses of local anesthetics for scalp blocks. Be aware of volume of local anesthetic given at each site. Targeted scalp blocks of each individual nerve should limit the amount needed to be injected, performance of a "ring block" may increase volumes needed. The amount and concentration of local anesthetics planned to be used by surgeons supplying additional infiltration of the scalp should be discussed.
- Always aspirate before injection of local anesthetic into the scalp. The scalp is highly vascular and blood vessels often run alongside the targeted nerves.

Clinical Pearls

- Scalp blocks have been shown to be beneficial for a wide variety of surgical procedures including superficial surgeries of the scalp but have been more widely studied for their use in craniotomy patients, both awake and under general anesthesia. Benefits have included decreased opioid consumption, blunted hemodynamic response to incision, decreased inflammatory response, and the reduced incidence of the development of chronic pain.
- A volume of 1–3 ml of local anesthetic is typically all that is needed per each individual nerve that is targeted when performing scalp blocks. Most commonly used local anesthetics include 0.25–0.5% ropivacaine or bupivacaine for longer duration with 1:200,000 or 1:400,000 epinephrine for vasoconstriction.
- Ultrasound guidance has been shown to be useful for identifying some of the scalp nerves or their landmarks, potentially decreasing the volumes of local anesthetics that are needed.

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Acute Pain Management Protocol for Ophthalmic Procedures

Rahul M. Dhodapkar, Andrew Jin, and Ji Liu

Case Stem #1

A 61-year-old man with well controlled type 2 diabetes mellitus not on insulin presented to his general ophthalmologist with gradually worsening visually acuity and glare at night. He was found to have visually significant nuclear sclerosis cataracts in both eyes and was scheduled for a routine cataract extraction with intraocular lens placement (CEIOL). The patient has never had ocular surgery in the past, and no abnormalities besides cataract are appreciated on ophthalmological examination or in routine preoperative testing.

Questions and Answers

What are the important considerations for anesthesia in this case?

For a routine cataract extraction with phacoemulsification and intraocular lens placement, total akinesia of the eye is not required, and appropriate topical and intraoperative intracameral anesthesia is usually sufficient.

What are the choices for topic anesthetic?

Commonly used topical anesthetics used in ophthalmic settings include proparacaine 0.5% and tetracaine 0.5%. Proparacaine

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_18

is often used in clinic settings, and has very similar properties as compared to tetracaine. Both have a similar duration of action and time of onset, though one head to head comparison for cataract surgery found that anesthesia from proparacaine lasted slightly longer (10.7 vs. 9.4 min) and was slightly less painful during initial application as compared to tetracaine [1]. Both agents may be considered for use in cataract surgery, though proparacaine must be refrigerated, while tetracaine is stable at room temperature and easier to store. In one study, tetracaine was found to yield reduced postoperative pain for laser in-situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) as compared to proparacaine [2]. During the procedure itself, intracameral lidocaine 1% may also be used, which has been shown by some studies to reduce pain score postoperatively and is used at some centers [3].

1 Summary

In general, uncomplicated cataract surgery can be managed with light sedation and ophthalmic topical anesthetic solutions (e.g. tetracaine 0.5% drops) with or without intracameral local anesthetic. If complications arise during a procedure, such as posterior capsular rupture, secondary akinesia or additional longer lasting anesthesia may be achieved in a step-up fashion through retrobulbar, peribulbar, or sub-Tenon's block as discussed in detail later.

Common Pitfalls

- Patients should not be given anesthetic eye drops to take home, as such use is indicated with toxic keratopathy, and insensitivity to corneal abrasion caused by vigorous eye rubbing [4].
- Topical anesthetics are toxic to the ocular surface and may delay abrasion healing.

Clinical Pearls

- It is important to warn patients prior to instilling topical anesthetics as they can cause significant irritation and pain when initially instilled.

- Topical anesthetics are effective for epithelial anesthesia, but will not alleviate intraocular pain (i.e. from elevated eye pressure in angle closure glaucoma or iritis).

Case Stem #2

A 53-year-old male with high myopia presented to the emergency department describing new onset flashes and floaters and a "curtain" going down over his vision in the right eye. A full ophthalmological examination was performed which identified a large retinal detachment associated with a tear in the inferotemporal quadrant. The patient was referred emergently for retinal detachment repair with pars plana vitrectomy.

Questions and Answers

What are the important considerations for anesthesia in this case?

The patient has a retinal detachment and will undergo pars plana vitrectomy. For retinal surgeries such as these, often **full akinesia** of the globe is required **in addition to anesthesia**, as sudden movement of the eye during the procedure can cause worsening of a retinal tear, or other damage caused by intraocular instruments.

What types of anesthesia may be considered?

For vitreoretinal surgeries, a variety of local techniques, including **retrobulbar block**, **peribulbar block**, and **sub-Tenon's block** may be used to achieve akinesia and anesthesia. Akinesia is obtained by blockade of cranial nerves III (oculomotor), IV (trochlear), and VI (abducens), which supply the extraocular muscles. Anesthesia is achieved by blockade of the ciliary nerves. These techniques may be used in conjunction with, or as an alternative to **general anesthesia**, either with endotracheal tube or laryngeal mask airway based on local practice [5].

How are the blocks performed?

The **retrobulbar block** was first described in 1884 and was long considered the gold standard for regional ophthalmic anesthesia [6]. The upper and lower lids are first cleansed with povidone-iodine solution, and the patient is instructed to look straight ahead (in primary gaze). A round tipped retrobulbar needle or a 1.5 in. 25 gauge needle is first inserted just above the

inferior orbital rim, parallel to the orbital floor, approximately 2/3 laterally (Fig. 1). The needle is advanced through the orbital septum, feeling a pop as it passes. The needle is advanced an additional 1–1.5 cm until the needle tip is past the equator. Once past the equator, the needle is redirected medially approximately 45° superiorly and 45° nasally. The needle is then advanced approximately 2.5 cm until a pop is felt passing through the muscular cone. Prior to administration of anesthetic the needle tip is aspirated to ensure no blood return. If not intravascular, 3–5 mL of local anesthetic is slowly injected, monitoring for resistance to injection, increased pain, or rotation of the globe. Finally, gentle pressure is applied to the globe to aid in infiltration, and akinesia is verified after 5 min.

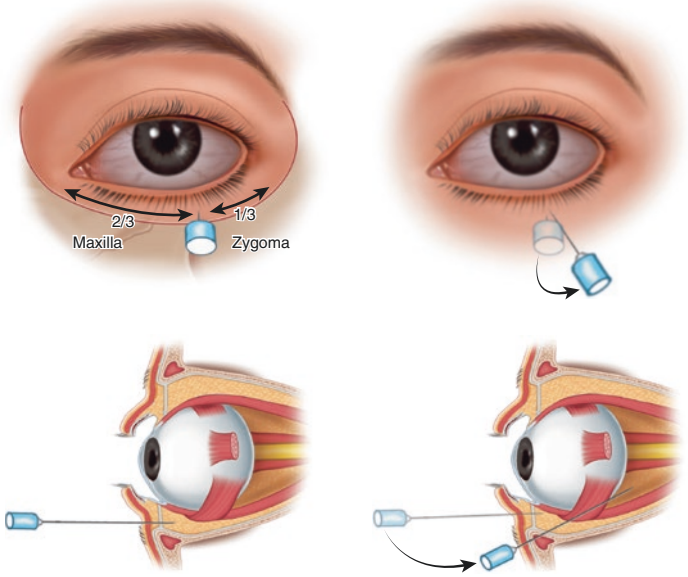

Fig. 1 Anatomy of the retrobulbar block, showing needle advancement first through the orbital septum, then to the intraconal space. Lateral rectus muscle was "cut" in the sagittal series, showing the needle tip entering the intraconal space without touching the optic nerve sheath

The **peribulbar block** was developed as a less invasive alternative to the retrobulbar technique, taking advantage of the fact that there is no contiguous fascial membrane that separates the intraconal and extraconal spaces behind the globe [7, 8]. However, some reports suggest that the duration of block is shorter and the effects may be less reproducible with peribulbar block as compared to retrobulbar block [9, 10]. Both single-injection and multiple-injection techniques have been described, but comparative studies have demonstrated non-inferiority of the single-injection technique described here [11]. After cleansing the lids, a 25 gauge, 16-mm bevel needle is advanced percutaneously into the region bounded superiorly by the inferior lacrimal canaliculus, inferiorly by the inferior margin of the orbit, laterally by the lateral margin of the nose, and medially by a line perpendicular to the line drawn from the inferior lacrimal papilla to the inferior margin of the orbit. The needle is advanced anteroposteriorly for half its length, and then obliquely to remain parallel to the medial orbital wall (the needle tip will be rotated medially approximately 10°, directed at the optic foramen). After aspiration, 5–6.5 mL of local anesthetic (e.g. 2% lidocaine) is injected slowly over 30 s.

A **sub-Tenon's (a.k.a. episcleral) block** may be used as an alternative to or in conjunction with either peribulbar or retrobulbar blocks to achieve robust akinesia and anesthesia for ophthalmic procedures [12]. After instillation of local anesthetic onto the ocular surface (e.g. 1% tetracaine) and cleaning the eye with betadine, the patient is instructed to look upwards and temporally, exposing the inferonasal quadrant. The conjunctiva and Tenon's capsule are grasped with tooth forceps and lifted together off the globe. A small incision is made through these layers and a blunt, curved, posterior sub-Tenon's cannula is inserted through the hole along the curvature of the sclera (Fig. 2). Resistance will be felt during insertion of the cannula during traversal of the intermuscular septum. After this, the cannula should pass easily to the posterior sub-Tenon's space. Once the cannula is correctly positioned, 3–5 mL of local anesthetic can be slowly injected, with smaller volumes sufficient for anesthesia and larger volumes more likely to result in akinesia [13].

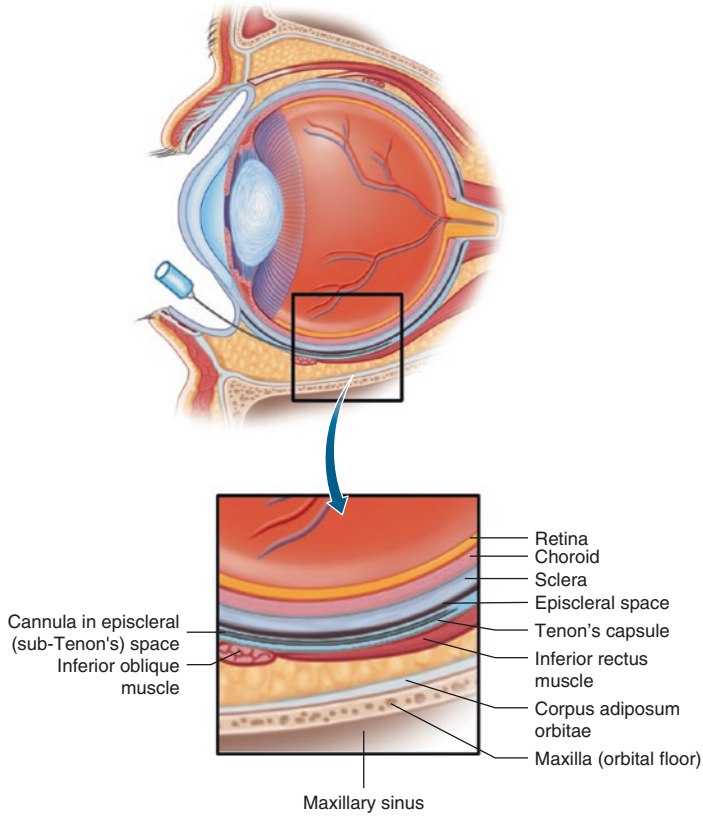

Fig. 2 Anatomy of the sub Tenon's (episcleral) block showing advancement of the cannula into the inferior episcleral space and associated structures

What are the common and/or critical risks involved with these blocks?

While it is able to achieve good akinesia and anesthesia with a relatively small volume of local anesthetic, the retrobulbar block also advances a needle into an area with a high density of neurovascular structures, and risks associated damage. Retrobulbar blocks have been associated with **retrobulbar hemorrhage**, a rare, but vision threatening complication caused by bleeding in

the retrobulbar space [14]. Damage to the globe, or the optic nerve may also be vision threatening and may be caused by inappropriate direction of the advancing retrobulbar or peribulbar needle. These risks are also present with peribulbar and sub-Tenon's blocks though they are less than with a retrobulbar block [15]. Chemosis may also occur, especially after large volume peribulbar injections and usually resolves spontaneously or with pressure reducing devices without long term effects [16]. Subconjunctival hemorrhage may also be observed after blocks, and may be more common after sub-Tenon's as compared to peribulbar block [17]. If the intraocular muscles are irritated or infiltrated with local anesthetic, stimulation of the oculocardiac reflex may occur, resulting in transient bradycardia that may lead to cardiovascular decompensation in the case of pre-existing atrioventricular nodal or structural heart disease [18].

What other types of ophthalmic procedures require similar anesthetic profiles?

Other types of ophthalmic procedures that may have similar requirements for anesthesia or regional nerve blocks are those that would be impeded or potentially harmed by movement of the eye intraoperatively. These procedures include other types of retinal surgeries outside of vitrectomy, including scleral buckle, and may also be desirable in cases of complicated cataract surgery. For example, if, during cataract extraction with phacoemulsification, the posterior capsular bag is ruptured, management of the complication may require akinesia.

2 Summary

During vitreoretinal surgery, complicated cataract surgery, or other procedures in which akinesia of the eye is desired, retrobulbar, peribulbar, or sub-Tenon's blocks may be employed. Common complications of these blocks include subconjunctival hemorrhage, chemosis, and ecchymosis. Serious complications of these blocks include retrobulbar hemorrhage, direct injury to the optic nerve, and damage to or perforation of the globe.

Common Pitfalls

- Retrobulbar nerve blocks should be performed in primary gaze with the patient looking straight ahead, as looking in any other direction will either move the muscular cone or cause exposure of the optic nerve, increasing the probability of complications.
- Make sure you withdraw your syringe initially after entering the retrobulbar space to make sure the needle is not in an artery. Only after confirming you are in the correct location should you begin injecting the anesthetic.

Clinical Pearls

- Ask the surgeon for the expected duration of the procedure and factor this into selection of the nerve block. Retrobulbar or sub-Tenon's blocks can provide longer lasting, more durable results for akinesia as compared to the peribulbar method, but the peribulbar approach is less invasive and may have a lower complication rate for shorter procedures.
- Patients may develop double vision as a result of the akinesia and should be warned beforehand that it is temporary and will resolve. If their double vision persists after the block has worn off, then there may have been injury to an extraocular muscle.

Case Stem #3

A 67-year-old female with no significant past medical history was referred to the oculoplastics clinic for dermatochalasis leading to decreased vision in her superior visual fields bilaterally. The diagnosis was confirmed and she was planned for bilateral blepharoplasty to improve both vision and cosmesis.

Questions and Answers

What are the important considerations for anesthesia in this case?

Most oculoplastics procedures such as blepharoplasty can be performed under local rather than general anesthesia, depending on the patient's level of anxiety and cooperation. Sensory innervation of the lids and periorbital tissues are mostly provided by branches of the ophthalmic (V1) and maxillary (V2) divisions of the trigeminal nerve (CN V). Motor innervation of the muscles of facial expression, including frontalis and orbicularis oculi, is sup-

plied by the temporal and zygomatic branches of the facial nerve (CN VII).

What are the key sites for sensory nerve block in the periorbital region?

There are many sensory blocks of the periorbital branches of the trigeminal nerve and many techniques that have been described to approach these blocks, both ultrasound-guided and blind. In general, these blocks may be considered as targeted subcutaneous instillation of local anesthetic at nerve trunks with known sensory distributions. Several key targets include the **supraorbital**, **supratrochlear**, **infratrochlear**, **infraorbital**, **lacrimal**, and **zygomaticofacial** nerve blocks. An overview of the relevant anatomy of these blocks is presented in Fig. 3 and a summary of injection site, as well as the field anesthetized by the block is provided in Table 1 In our case of bilateral upper lid blepharoplasty, a supraorbital block, or combined supraorbital with supratrochlear block could be considered.

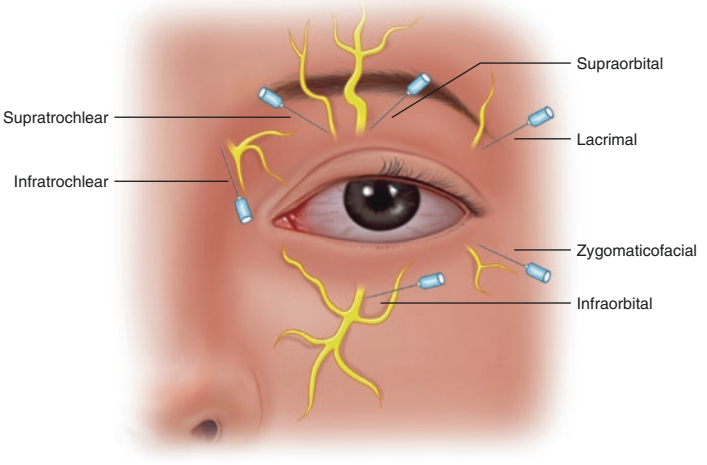

Fig. 3 Injection sites for key periorbital sensory nerve blocks. Described as clock positions from the pupil above—12-o-clock: supraorbital; 2-o-clock lacrimal; 4-o-clock zygomaticofacial; 6-o-clock infraorbital; 10-o-clock infratrochlear; 11-o-clock supratrochlear

Table 1 Summary of periorbital sensory blocks for ophthalmic procedures

Block	Location	Sensory/motor distribution	Common indications	Region-specific pitfalls
Supraorbital block	Supraorbital notch/foramen [19]	*Sensory:* innervation to the forehead to the anterior scalp margin, and upper eyelid	Facial laceration repair, oculoplastics surgery of the upper lid	Injections in this area may cause upper eyelid ptosis [20]
Supratrochlear block	3mm medial to the vertical line drawn from the lacrimal caruncle to the superior orbital margin [21]	*Sensory:* innervation to the medial aspect of the forehead to the anterior scalp	Facial laceration repair, migraine headache	Injections in this area may cause upper eyelid ptosis [20]
Infratrochlear block	1cm superior to the medial canthus, close to the ethmoidal foramen	*Sensory:* skin and conjunctiva of the lower lid, lower part of nose and upper lip	Facial laceration repair, lacrimal surgery procedures involving the nose	Use of epinephrine may increase risk of retinal artery spasm [22]
Infraorbital block	Infraorbital foramen approach either extraoral or intraoral	*Sensory*: innervation to the lower eyelid, upper lip, lateral nose, and upper teeth	Lower lid lacerations, endoscopic sinus surgery	The infraorbital nerve travels in close proximity with its vein and artery which may be damaged
Zygomaticofacial block	Inferotemporal orbital rim, inferior to the lateral canthus	*Sensory:* innervation of the lateral prominence of the cheek [23]	Orbital wall fracture repair	Advancing the needle in this area too deeply may cause damage to the lateral orbital rim
Lacrimal block	Lacrimal notch, superolateral orbital rim	*Sensory:* innervation to lateral upper conjunctiva and eyelid, as well as lateral forehead and anterior scalp	Upper eyelid and scalp procedures	The lacrimal gland is highly vascular and damage to this organ may cause significant hemorrhage

What are the options for local anesthetic to be used? What considerations drive selection of local anesthetic agent in eyelid surgery?

Commonly used local anesthetic agents include lidocaine, bupivacaine, and ropivacaine with and without epinephrine. All of these anesthetics are sodium channel blockers and have different onsets and durations of action as well as time to onset, which have been well described elsewhere. As a general rule, the maximum safe dose of tumescent lidocaine is 5 mg/kg alone and 7 mg/kg with epinephrine. The maximum safe dose of tumescent bupivacaine is 2.5 mg/kg alone and 3.5 mg/kg with epinephrine [24]. Epinephrine causes a local vasoconstrictive effect that can increase duration of action of anesthesia, with a risk of causing reduction of tissue perfusion if overly concentrated. Epinephrine at a concentration of 1:100,000 (10 μg/mL) creates sufficient vasoconstriction for eyelid surgery [25].

Supposing that the patient was found to have a strong blink reflex and was unable to prevent their eye from squeezing during the procedure, what could be done?

Closure of the eyelid is mediated primarily by the **orbicularis oculi** muscle, a sphincter muscle composed of skeletal muscle fibers innervated by terminal branches of the temporal and zygomatic branches of the facial nerve (CN VII). The facial nerve emerges from the cranium at the stylomastoid foramen, where it may be blocked by the **Nadbath technique**, now rarely used due to the risk of respiratory distress from off-target anesthesia of the vagus (CN X), glossopharyngeal (CN IX) and spinal accessory nerves (CN XI) [26]. Following this, the nerve courses anteriorly and ramifies into its five cardinal branches, the temporal, zygomatic, buccal, marginal mandibular, and cervical. The nerve trunk coursing superiorly, containing the temporal and zygomatic branches, passes anterior to the tragus, where it may be blocked with the **O'Brien technique**. Following this, the nerve traverses the inferior margin of the zygomatic arch, where it may be blocked by the **Atkinson technique**. Finally, terminal branches innervate the orbicularis muscle, which may be blocked by the **van Lint technique**. A summary of this anatomy is provided as Fig. 4, and information on the blocks is provided in Table 2.

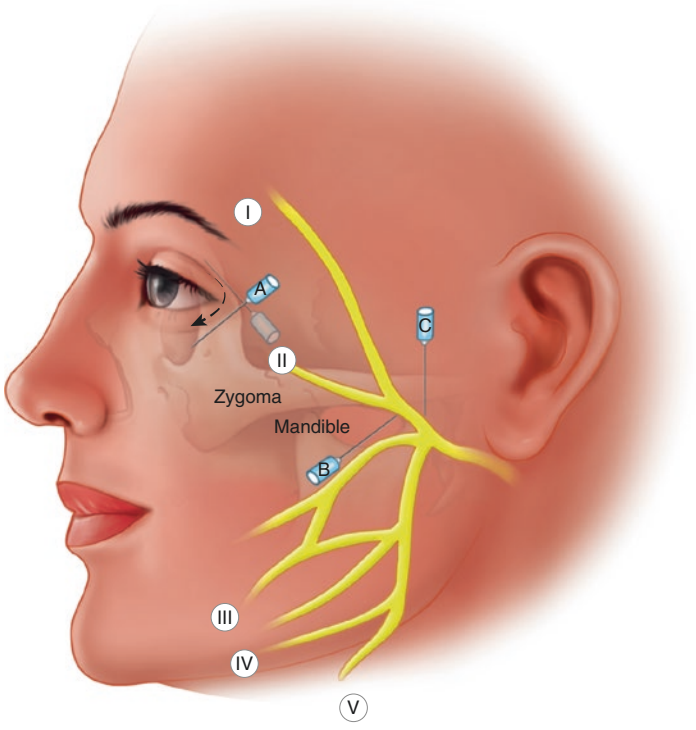

Fig. 4 Subcutaneous blocks of the facial nerve. (**A**) van Lint technique: a "v" is created by instilling local anesthetic along the lower and upper margin at the lateral canthus. (**B**) Atkinson technique: linear block at the inferior zygomatic arch blocking the superior divisions of the facial nerve. (**C**) O'Brien technique blocking the facial trunk at the level of the mandible near the condyloid process. (i) temporal (ii) zygomatic (iii) buccal (iv) marginal mandibular (v) cervical branches of the facial nerve

Table 2 Summary of motor blocks of the facial nerve

Block	Location	Sensory/ motor distribution	Common indications	Region-specific pitfalls
O'Brien block	Level the mandible near the condyloid process, anterior to the tragus	*Motor*: orbicularis oculi, frontalis	Oculoplastics, surgery requiring orbicularis paralysis	Increased risk of permanent facial nerve trunk damage [27]
Atkinson block	Inferior margin of the zygomatic arch [28]	*Motor:* orbicularis oculi, frontalis	Oculoplastics, surgery requiring orbicularis paralysis	Anatomic variability at injection site may lead to unpredictable off-target effects
van Lint block	Superior and inferior field block 2 cm posterior to the lateral canthus.	*Motor*: orbicularis oculi	Oculoplastics, surgery requiring orbicularis paralysis	Increased risk of ecchymosis, periorbital edema

3 Summary

Oculoplastics procedures can generally be performed under local rather than general anesthesia. Blockade of terminal divisions of the trigeminal nerve can provide anesthesia while preserving local anatomy. Targeting of branches of the facial nerve can provide akinesia of the muscles of the face and lid if needed by the surgeon. Akinesia of the globe is usually not required for these procedures. A knowledge of the sensory and motor nerve distributions in the periorbital region is crucial for the anesthesiologist participating in these procedures.

Common Pitfalls

- Temporally, the facial nerve runs superficial to the superficial layer of the deep temporal fascia. It is therefore important to stay in this plane to reduce risk of nerve injury.

Clinical Pearls

- Facial nerve blocks can be tailored to the specific procedure at hand in order to achieve maximum efficacy. Make sure to discuss with the surgeon which nerves should be blocked to achieve maximum therapeutic benefit.
- Ultrasound guidance is commonly used to help localize the nerve and increase the success of the block.

Case Stem #4

A 36-year-old gentleman with keratoconus, irregular steepening of the cornea, has progressively worsening vision in both eyes. He has tried to wear specialty contact and scleral lenses for the past few years, but his vision is now 20/40 in the right eye, 20/400 in the left eye due to irregular astigmatism. Medical history is significant for asthma. The plan is to perform a full thickness corneal transplant of the left eye.

Questions and Answers

What are the important considerations for anesthesia in this case?

The vast majority of ophthalmologic surgeries are performed under **monitored anesthesia care (MAC) anesthesia**. During MAC anesthesia, local anesthesia is combined with sedation and analgesia, to achieve a level of **conscious sedation** where the patient is able to maintain control of and protect their own airway [29]. It is more easily reversed than general anesthesia and patients are more readily able to go home afterwards. Further, it maintains some degree of patient cooperation with the procedure, as it can be beneficial to have patient participation. This is especially useful in certain oculoplastics procedures such as external levator muscle advancement where the degree of eyelid lift can be adjusted intraoperatively by having the patient open and close his or her eyes to assess the eyelid position. Other surgeries where it may be beneficial to have patient cooperation include cataract and

conjunctival procedures in order to gain better visualization of the desired surgical plane.

Generally, anesthesiologists provide some combination of benzodiazepine, opiate, and induction agent such as ketamine or propofol. This combination can then be titrated to allow for the desired level of patient cooperation while maintaining patient comfort and airway stability.

4 Summary

Many ophthalmic procedures can be performed under MAC anesthesia, which improves patient outcomes and reduces hospital length of stay. A further benefit of MAC anesthesia is that patient cooperation may be obtained intraoperatively to expedite the procedure.

Common Pitfalls

- Older patients or those with more medical comorbidities may require fewer sedatives and are more prone to cardiovascular instability.

Clinical Pearls

- It is very helpful to have a rapid-acting analgesic such as alfentanil on board prior to performing a regional block.

Case Stem #5

A 64-year-old farmer comes in with growths on the conjunctiva in both eyes. He is found to have large pterygia encroaching on the pupil, causing decreased vision. Medical history is significant for high blood pressure and Crohn's disease. The decision is made to perform bilateral pterygium resection with conjunctival autograft to reduce the risk of recurrence under minimal sedation with subconjunctival anesthesia.

Questions and Answers

What are the important considerations for anesthesia in this case?

Pterygium surgery requires manipulation of the conjunctiva, which can be painful and will require anesthesia. However, aki-

nesia is not necessary and a local anesthetic injection will suffice. Subconjunctival injection of local anesthetic is preferred in these cases, with dose varying by the site and size of lesion. One study used 1 mL of lidocaine 4% without epinephrine for pterygium surgery [30]. Conversely 0.1 mL of lidocaine 4% without epinephrine has been described for acute pain management of intravitreal injection [31]. A topical local anesthetic gel of lidocaine, either 2% or 5% has also been used and shown to be effective [32]. When considering topical anesthetic versus subconjunctival injection, the size of the pterygium should be considered, as well as local institutional practices. Subconjunctival injection also comes with a risk of subconjunctival hemorrhage, which usually self resolves but can cause patient discomfort and dissatisfaction.

5 Summary

Pterygium surgery, or other cases with manipulation of the conjunctiva can be managed with subconjunctival or topical anesthetic. Subconjunctival anesthesia is more durable but may lead to subconjunctival hemorrhage or damage to other surrounding structures.

Common Pitfalls

- When preparing to deliver the subconjunctival injection, be aware of the surrounding anatomy, as too close to the limbus it is possible to traverse both the conjunctiva and tenon's capsule and inadvertently deliver anesthetic to the episcleral space.

Clinical Pearls

- In many cases, topical application of local anesthetic can suffice and may be less painful than subconjunctival anesthetic injection, however it may require re-application during a procedure, and logistics should be coordinated with the surgical team.

Case Stem #6

A 3-year-old boy was referred to a pediatric ophthalmology clinic after his mother noticed his eyes were turning in. He was found to have an esotropia of 30 prism diopters in all directions of gaze. Nonsurgical management including prism glasses and exercises were tried but failed to relieve symptoms. The patient was scheduled for a bilateral medial rectus recession for surgical management of his strabismus.

Questions and Answers

What are the important considerations for anesthesia in this case?

Strabismus surgery is an invasive procedure that requires general anesthesia, and is often performed in young children to reduce the risk of amblyopia and improve long term visual outcomes. As strabismus surgery involves direct manipulation of the extraocular muscles, it commonly triggers the oculocardiac (Aschner's, or trigeminovagal) reflex [33], leading to bradycardia or other arrhythmias, which must be treated appropriately. Less commonly, an oculorespiratory reflex, slowing and/or shallowing of breathing with traction on the extraocular muscles, may present and can exacerbate the effects of the oculocardiac reflex [34].

What is the oculocardiac reflex and how can it be managed?

The oculocardiac reflex is caused by the activation of stretch receptors in the extraocular muscles transmitted by afferent fibers of the short and long ciliary nerves. These signals travel through the trigeminal nerve to the brainstem and trigger increased vagal tone, leading to decreased conduction velocity through the atrioventricular node and, most commonly, sinus bradycardia. In susceptible patients, more dangerous rhythms may occur, including ventricular fibrillation [35].

In general, the effects of the oculocardiac reflex are transient and can be managed with removal of tractional stimulus on the extraocular muscles. If this is insufficient, vagolytic agents should be administered (e.g. atropine, glycopyrrolate), with careful attention to support of underlying cardiovascular function. In addition to management of a manifest oculocardiac reflex, the anesthesiologist may take several precautions to promote the primary prevention of severe extraocular reflex.

Usage of volatile anesthetic agents for maintenance of general anesthesia has been identified with reduced incidence of oculocardiac reflex as compared to propofol [36]. The addition of regional anesthesia, either peribulbar or sub Tenon's blocks, in combination with general anesthesia can also be used to reduce the incidence of oculocardiac reflex, as can pretreatment with anticholinergic agents, such as atropine [37, 38].

6 Summary

During strabismus surgery, manipulation of the extraocular muscles can lead to sudden and severe increases in vagal tone which may elicit malignant arrhythmias and/or lead to cardiovascular compromise. The addition of regional anesthesia, pretreatment with anticholinergics, and open communication between anesthesiologist and surgeon regarding extraocular muscle manipulation can help reduce the risks of procedural anesthesia.

Common Pitfalls

- Patient status may rapidly change during strabismus surgery or similar ocular procedures involving manipulation in the orbit such as scleral buckle placement or open globe repair. Special attention should be paid to continuous vital sign monitoring.
- Propofol as a maintenance agent was associated with increased risk of oculocardiac reflex, volatile agents should be preferred for this purpose unless contraindicated.

Clinical Pearls

- When proceeding a procedure that will involve traction on the extraocular muscles, pre-surgical planning is crucial. Premedication with anticholinergics and adjuvant regional anesthesia targeting the ciliary nerves will give your patients the best chance of avoiding a severe oculocardiac response.

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Acute Pain Management Protocol for Neck Procedures

Alex Yu, Samuel DeMaria Jr., and Shane Dickerson

Case Stem

A 42-year-old female with a past medical history of hypertension, depression, and a recent diagnosis of left papillary thyroid cancer presents for a left hemithyroidectomy. Upon interviewing her, the patient states that she had significant postoperative nausea during an appendectomy 15 years ago.

1 Superficial Cervical Plexus Block

The superficial cervical plexus, originating from nerves C2, C3, and C4, innervates a large swathe of the frontolateral neck. Blocking this plexus can provide analgesia from the mandible to the clavicle for thyroidectomy, parathyroidectomy, neck dissections, lymph node biopsy, and carotid endarterectomies. Bilateral blocks

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_19

are indicated for midline procedures. They can be performed both as a primary technique or as an analgesic adjunct. In this specific case, it may decrease the amount of opioid medication required both intraoperatively and postoperatively, decreasing the chance of nausea and vomiting.

Preinduction, the supine patient is asked to contract their sternocleidomastoid muscle by turning their head towards the side contralateral to the block. The posterior border of the sternocleidomastoid is demarcated, and a marking is made at the midway point between the mastoid process and the tubercle of C6 as shown in Fig. 1.

The block can be performed post-induction or on an awake patient, depending on patient characteristics and preference. For the landmark based technique, use a 1.5-in., 25-gauge needle to inject 10cc of 0.5% bupivacaine, entering at the marked midpoint. The local anesthetic is injected superficially along the marked border above and below the entry point, making sure to remain superficial and aspirate prior to injection to avoid intravascular injection. This is repeated on the contralateral side.

For the ultrasound-based technique, the skin is disinfected and the transducer is placed transversely on the lateral neck overlying the sternocleidomastoid at the level of its midpoint. Locate the sternocleidomastoid muscle on the ultrasound and attempt to identify the anterior and middle scalene muscles. The brachial plexus should lie between these two muscles. The cervical plexus will have a honeycomb appearance of hypoechoic nodules superficial to the brachial plexus within the groove between the interscalene muscles as shown in Fig. 2. Once identified, the needle is slowly advanced following the posterior border of the sternocleidomastoid muscle. After confirming negative aspiration, inject 10 ml of 0.5% bupivacaine. Of note, visualization of the plexus is not necessary to administer an effective nerve block, as injection just deep to the sternocleidomastoid provides reliable analgesia for the cervical plexus.

The onset time of the block is approximately 10–15 min. While risks of hematoma, infection, and local anesthetic systemic toxicity remain, the superficial cervical plexus block is generally considered low risk given its superficial nature.

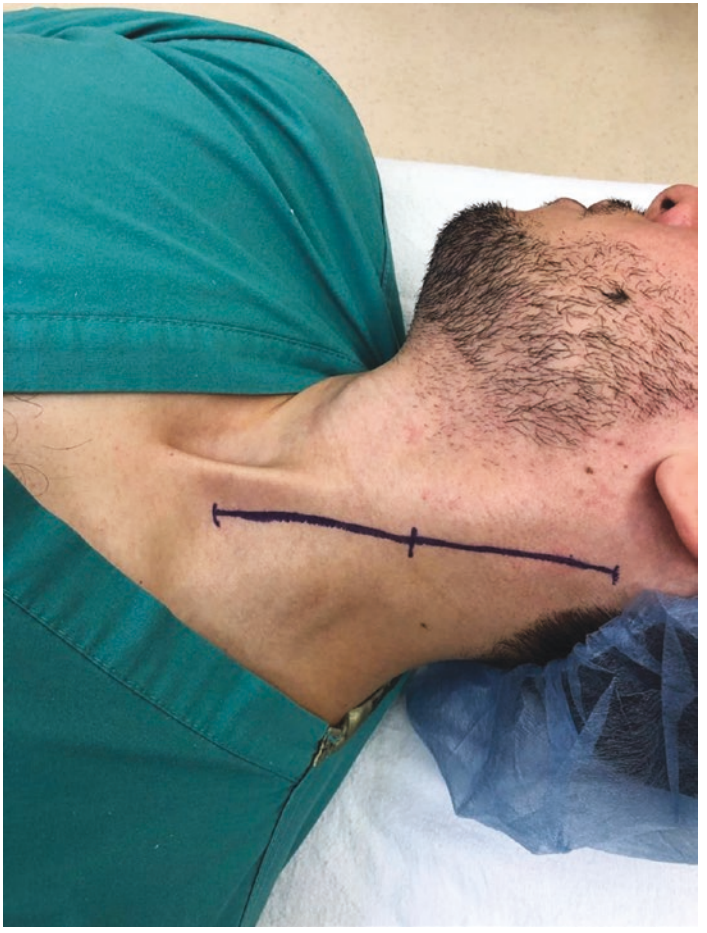

Fig. 1 Superficial cervical plexus landmarks

Common Pitfalls

After the surgery, the patient complains of blurry vision. Upon examination, the eye ipsilateral to the block appears to have ptosis, miosis, and conjunctival injection.

Horner's syndrome is a potential side effect of the superficial cervical plexus block. The mechanism occurs through inadvertent deep spread of local anesthetic, leading to sympatholysis of the

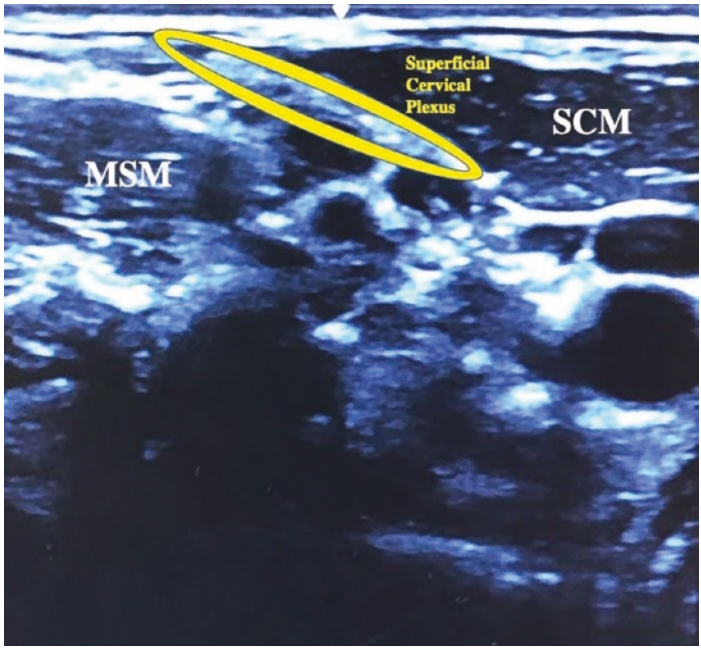

Fig. 2 Superficial cervical plexus ultrasound

ipsilateral cervical plexus chain. In order to minimize the probability of this complication, clinicians must ensure that the injection is shallow (just underneath the belly of the sternocleidomastoid muscle) and no more than 10 ml of local anesthetic is deposited. The phenomenon is typically self limiting and the physician should reassure the patient that it will resolve.

Clinical Pearl

Postoperative nausea and vomiting (PONV) can increase the rate of surgical complications, lead to metabolic derangements, decrease patient satisfaction, and delay PACU discharge. Patient risk factors for PONV include history of PONV, female sex, nonsmoker, and younger age. Surgical risk factors for PONV include intra-abdominal surgery, gynecological surgery, and strabismus surgery. There are numerous strategies designed to mitigate the likelihood of postoperative nausea and vomiting.

Minimizing triggers such as nitrous oxide, volatile anesthetics, and opioids decreases the incidence of PONV. Regional anesthesia or propofol based anesthesia are useful adjuncts in achieving this goal. Additionally, commonly employed pharmacologic strategies include dopamine receptor antagonists (i.e. haloperidol), histamine receptor antagonists (i.e. diphenhydramine), anticholinergics (i.e. scopolamine patch), corticosteroids (i.e. dexamethasone), 5HT3 receptor antagonists (i.e. ondansetron), and NK-1 receptor antagonists (i.e. aprepitant). When administering one or more of these agents, the anesthesiologist must carefully consider the potential benefit vs. financial cost in the setting of risk of PONV. Patients deemed medium risk necessitate 1–2 of the above interventions, while patients considered high risk require >2 interventions [1]. In this case, the patient had more than two risk factors for PONV, and thus would warrant at least two interventions.

Case Stem

A 69-year-old male with hypertension and base of tongue squamous cell carcinoma presents for partial glossectomy, radical neck dissection, and free flap microvascular reconstruction.

2 Glossopharyngeal Block, Superior Laryngeal Block, Transtracheal (Recurrent Laryngeal) Block

There are numerous components to a successful awake intubation. We routinely perform glossopharyngeal, superior laryngeal and transtracheal blocks to anesthetize the posterior tongue, larynx above the vocal cords, and larynx below the vocal cords, respectively. These blocks work in conjunction with topicalization, either via atomizer or nebulizer, to blunt the stimulation of an awake intubation.

The glossopharyngeal nerve innervates the posterior third of the tongue and serves as the sensory limb of the gag reflex. As such, anesthetizing the glossopharyngeal nerve allows for smoother passage of the fiberoptic scope through the oropharynx and suppresses the gag reflex when performing an awake intubation. The block is performed by spraying local anesthetic, apply-

ing pledgets soaked in local anesthetic, or direct injection of local anesthetic. After adequate mouth opening, use a tongue depressor to visualize the posterior tonsillar pillars (palatopharyngeal arch) as shown in Fig. 3. Use an atomizer spray to apply topical local anesthetic directly over the caudal aspect of the posterior tonsillar pillar. Alternatively, pledgets soaked in local anesthetic can be

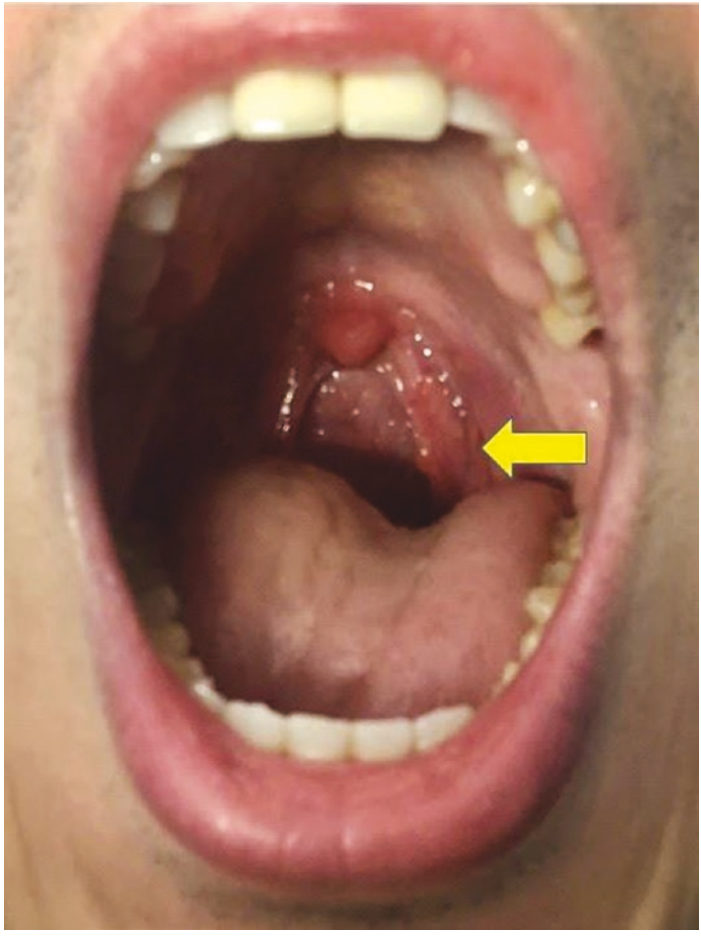

Fig. 3 Glossopharyngeal nerve block

placed against the posterior tonsillar pillars. Direct injection of local anesthetic, however, remains the most effective method. Using a 25-gauge needle, 2–5 ml of 2% lidocaine is injected just under the mucosa following negative aspiration. This is repeated on the contralateral side.

The superior laryngeal nerve innervates the base of tongue, posterior epiglottis, aryepiglottic folds, and arytenoids. The block is performed with the patient in supine position. The hyoid bone is palpated and held between the index finger and thumb. The index finger is left on the hyoid as stabilization on the opposite side of the injection site as shown in Fig. 4. A 25-gauge needle is inserted until it meets resistance at the greater cornu of the hyoid bone, withdrawn 1 mm, checked for negative aspiration, and 2 ml of 2% lidocaine is injected. This is repeated on the contralateral side.

The recurrent laryngeal nerve innervates the glottis and the trachea. For the transtracheal block, the patient is positioned supine, the neck is placed in significant extension, and the cricothyroid membrane is palpated. A 5cc syringe filled with 4% lidocaine is attached to a 20-gauge peripheral angiocatheter and inserted into the cricothyroid membrane while aspirating as shown in Fig. 5. As soon as a pop is felt and air bubbles return, the lidocaine is injected as the patient is instructed to take a deep breath and informed that they will likely cough upon injection. The patient's cough will then disperse the local anesthetic and allow it to coat the vocal cords and trachea. In the case of pathological contraindication to recurrent laryngeal block, the vocal cords can be anesthetized under fiberoptic visualization with 4 ml of 4% lidocaine introduced through the instrument port of the fiberoptic device.

Clinical Pearl

Patients with head and neck cancers frequently require multiple rounds of radiation that can lead to significant post-radiation skin changes such as chronic radiation dermatitis and radiation induced fibrosis. Chronic radiation dermatitis is characterized by fibrosis, atrophy, hypopigmentary or hyperpigmentary changes in addition to possible development of skin malignancies. Radiation induced fibrosis presents with limited range of motion, contractures, skin

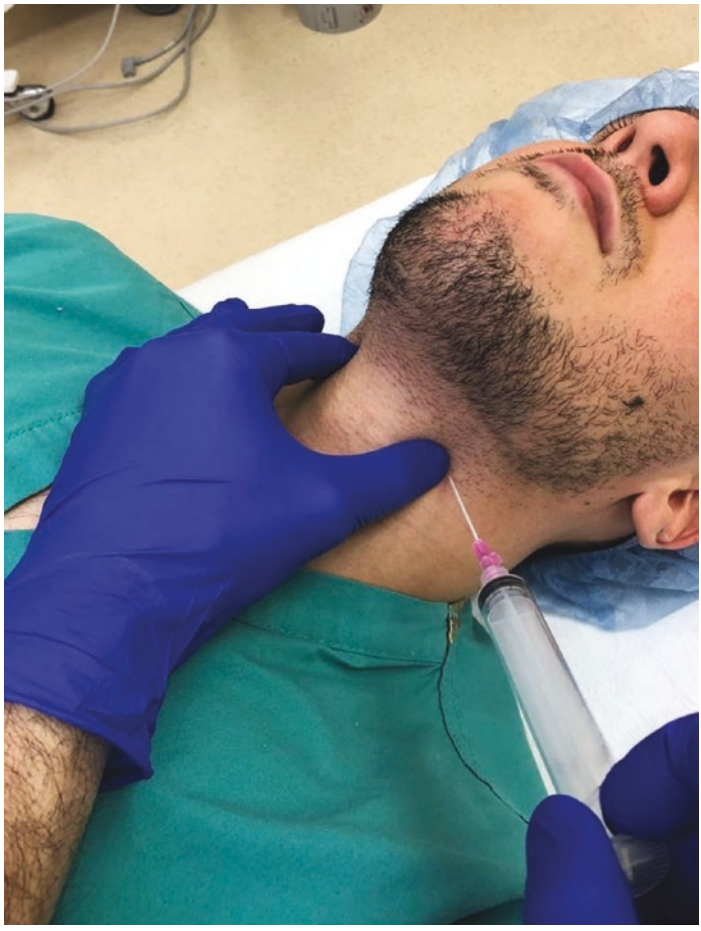

Fig. 4 Superior laryngeal nerve block

retraction, and induration. These skin changes present a unique challenge to the anesthesiologist in the setting of advanced airway maneuvers. Direct laryngoscopy can be problematic given limited range of motion resulting in inability to extend the neck into the optimal sniffing position. Additionally, the subcutaneous induration increases the difficulty of needle entry to perform blocks such

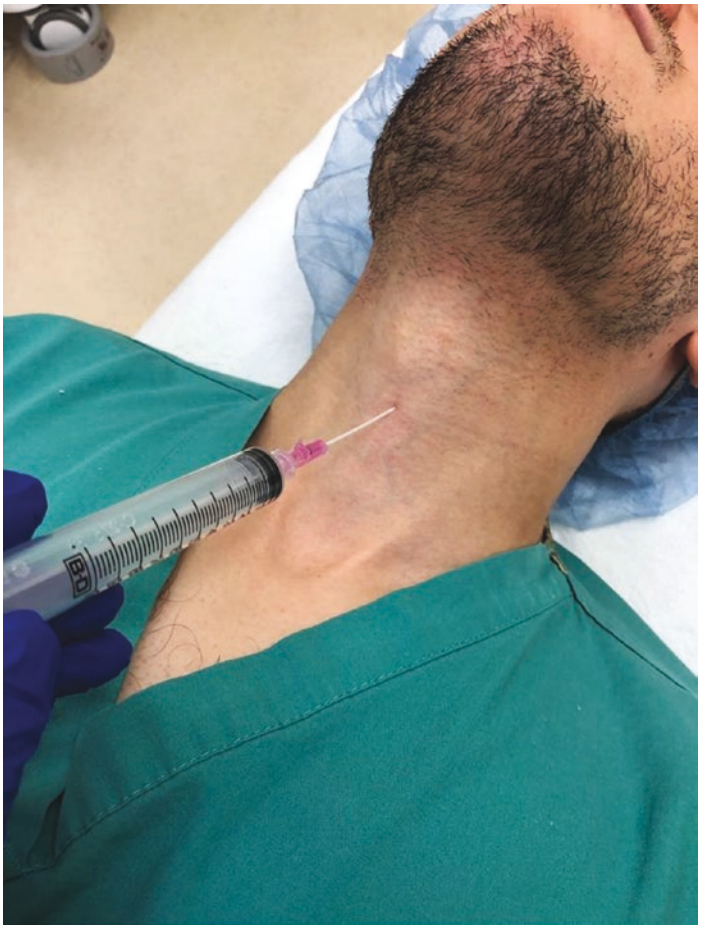

Fig. 5 Recurrent laryngeal nerve block

as the superior laryngeal nerve block and recurrent laryngeal nerve block.

In this case, the anesthesiologist can consider nebulized local anesthetic such as 4% lidocaine in conjunction with direct spraying of the vocal cords and trachea with local anesthetic through an epidural catheter passed through a fiberoptic scope's

instrument port. Once a good view of the vocal cords has been obtained, the epidural catheter is advanced so that the tip comes into view. The vocal cords and trachea are then sprayed with local anesthetic. This effectively numbs the glottis in order to facilitate passage of the fiberoptic scope and endotracheal tube through the vocal cords. A multi-orifice epidural catheter is preferred as it facilitates more widespread distribution of local anesthetic. Similar to regional blocks, it is of utmost importance to remain cognizant of the total amount of local anesthetic administered in order to avoid local anesthetic systemic toxicity.

Case Stem

A 27-year-old male with no significant past medical history arrives in the emergency department complaining of right shoulder pain after a motor vehicle accident. A clavicular fracture necessitating an open reduction internal fixation is diagnosed.

3 Interscalene Brachial Plexus Block, Superficial Cervical Plexus Block

The interscalene nerve block targets the superior trunk of the brachial plexus, specifically the ventral rami of the C5 and C6 nerve roots. There is often spread to the C7 level as well, although the C8-T1 levels are usually spared. This provides reliable coverage of the lateral two thirds of the clavicle, the shoulder, and the proximal lateral humerus while sparing the ulnar distribution of the medial arm down to the 4th and 5th digits. While clavicle ORIFs have traditionally been performed under general anesthesia, regional techniques have become more prevalent in recent years. The interscalene nerve block, when performed in conjunction with the superficial cervical plexus block, can be utilized as either the primary anesthetic technique or an analgesic adjunct to general anesthesia for clavicle ORIF. Interscalene blocks also provide excellent coverage for shoulder surgery.

The patient is typically placed in the supine, beach chair, or lateral decubitus position. The patient is asked to lower the shoul-

der on the side that is being blocked, with their head turned towards the contralateral side. The skin is disinfected and the ultrasound is placed transversely across the lateral neck, approximately 3–4 cm above the clavicle, onto the interscalene groove as shown in Fig. 6.

While in the transverse plane, the carotid artery is first identified. The transducer is then moved medially to laterally in order to identify the anterior and middle scalene muscles. The superficial cervical plexus and sternocleidomastoid muscles are seen superfi-

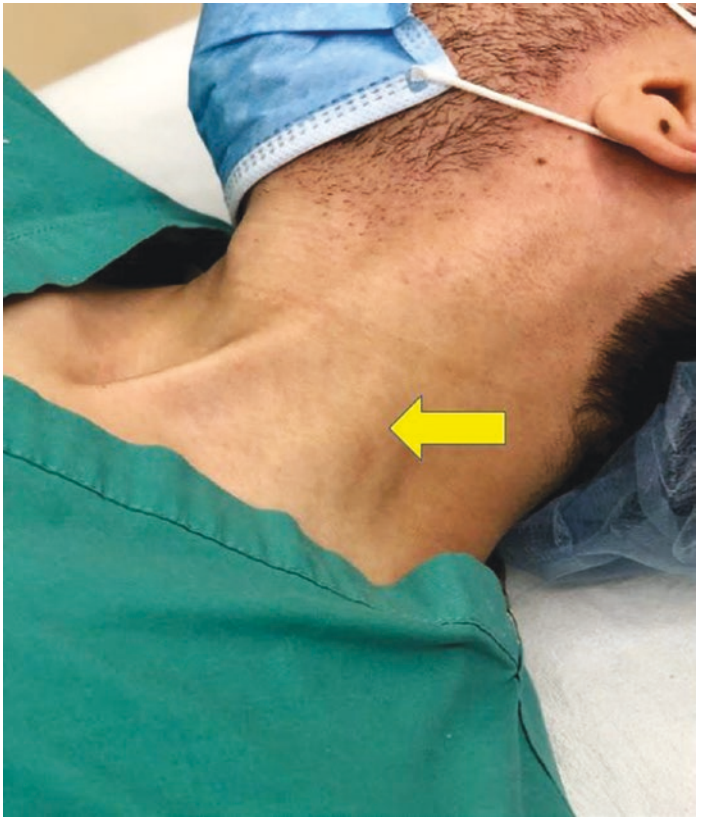

Fig. 6 Interscalene nerve block landmark

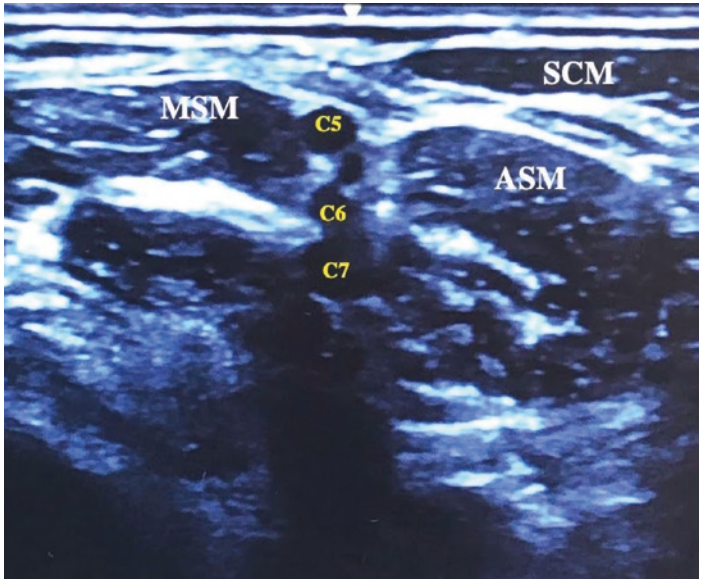

Fig. 7 Interscalene nerve block ultrasound

cial to the brachial plexus. The transducer is then scanned in a proximal to distal direction to locate at least two or more branches of the brachial plexus (typically in a "stop sign" distribution) between the scalene muscles. The plexus is usually seen at a depth of 1– 3 cm deep as shown in Fig. 7.

Once the optimal view is obtained, the needle is inserted in plane to the ultrasound, typically entering from a lateral to medial direction. The goal is to aim in between the nerve roots in order to minimize the chance of nerve injury. There is often a "pop" sensation felt as the needle traverses the fascia. After aspiration, 1–2 ml of local anesthetic (i.e. 0.5% ropivacaine, 0.5% bupivacaine) is deployed as a test dose to verify needle placement. In the setting of high resistance on injection, the needle is likely either contacting the nerve or intrafascicular and should be pulled back and redirected. In an adult patient, 10–15 ml of local anesthetic is typically sufficient to produce a rapid onset of dense nerve blockade.

Common Pitfalls

While efficacious as a primary anesthetic technique or adjunct, the interscalene block is associated with significant risks that must be discussed with the patient prior to performing the block. Apart from the risk of intravascular injection, neurological injury, and pneumothorax from needle misadventure, the block is associated with numerous known side effects from unwanted blockade of associated nerves. Horner's syndrome can result, with the presentation and treatment having been discussed earlier in this chapter. Accidental blockade of the recurrent laryngeal nerve can cause unilateral vocal cord palsy and result in hoarseness. Although this might be alarming to the patient, it is usually self limiting and not harmful unless the patient has significant respiratory comorbidities or palsy of the contralateral recurrent laryngeal nerve.

Perhaps the most recognized complication of interscalene blockade is phrenic nerve palsy. Due to blockade of the phrenic nerve (C3–5), hemi-diaphragmatic paresis occurs at an almost 100% incidence with interscalene blocks [2]. This can lead to a 25% reduction in pulmonary function, and can lead to respiratory compromise especially in patients with pre-existing pulmonary pathology [3]. The combination of residual anesthetic from general anesthesia and hemi-diaphragmatic paresis can lead to disastrous consequences. One should have a high index of suspicion if a patient with comorbid pulmonary pathology begins exhibiting respiratory compromise after interscalene blockade. Assessing the severity of hemidiaphragmatic paresis includes bedside pulmonary function tests and point-of-care ultrasound (POCUS) lung exams. On ultrasound exam, a forceful rapid sniff test can demonstrate partial diaphragmatic parsis with 25–75% reduction in caudal movement, while complete palsy is diagnosed by paradoxical cephalad movement of the diaphragm or >75% reduction of diaphragmatic movement [3]. While intubation and mechanical ventilation remain the definitive treatment for complete respiratory failure, the patient can often be treated supportively with supplemental oxygen. Strategies used to mitigate phrenic blockade include decreasing local anesthetic volume, performing the interscalene nerve block more caudally (at approximately C7 level), or choosing an alternative nerve block [4].

4 Local Anesthetic Systemic Toxicity/ Seizures

Given the robust vasculature in the neck region, it is important to carefully aspirate prior to each injection of local anesthetic. Inadvertent intravascular injection can result in both local anesthetic systemic toxicity (LAST) and central nervous system symptoms at lower doses compared to that required for LAST.

4.1 Mechanism of Action

Local anesthetic toxicity can be seen in the organ systems that depend on sodium channels to properly function, including the CNS and heart. The CNS is significantly more sensitive to local anesthetic compared to the heart, and thus CNS symptoms usually present prior to cardiovascular symptoms.

Local Anesthetic Systemic Toxicity affects the central nervous system by causing tinnitus, blurry vision, dizziness, and perioral numbness. Excitatory behavioral signs can also present in the form of anxiety, agitation, and restlessness. Effects at higher doses cause CNS depression in the form of slurred speech, fatigue, and progression to unconsciousness and respiratory arrest. Patients who have received benzodiazepines or other IV anesthetics that raise the seizure threshold can exhibit symptoms of CNS depression prior to manifesting excitatory symptoms.

Local anesthetics also directly block the sodium channels of the conducting tissue within the heart, decreasing the rate of depolarization and conduction times leading to prolonged PR intervals and widened QRS complexes on EKG. Sinus bradycardia can result, as well as ventricular arrhythmias such as ventricular fibrillation. Of note, ventricular fibrillation occurs more commonly with bupivacaine compared to other local anesthetics. It is important to recognize that while cardiac symptoms usually occur after CNS symptoms present, patients who are under general

anesthesia may present with cardiovascular symptoms as their only indication of LAST. Table 1 below presents maximum doses for each local anesthetic for reference.

It is likewise important to consider the site of injection when risk stratifying for LAST. In general, the risk of LAST is directly proportional to the vascularity of the injection site. The absorption of local anesthetics from least to most is subcutaneous, femoral/sciatic, brachial plexus, epidural/caudal, intercostal, and intravenous.

Given the proximity to the brain, CNS symptoms can present on inadvertent intravascular injection of the neck. This occurs at much lower doses than the maximum doses listed above. In this case, initial CNS symptoms of LAST can be present in the same way of tinnitus, blurred vision, dizziness, and perioral numbness. However, inadvertent bolusing of local anesthetic directly into the vasculature of the neck can commonly result in immediate seizures. In these cases the seizures usually subside rapidly compared to in the case of true LAST, and if the seizure is isolated and the patient remains hemodynamically stable should be treated with IV benzodiazepines.

Table 1 Maximum dose and duration of ester and amide local anesthetics

Ester local anesthetic	Maximum dose	Duration
Chloroprocaine	12 mg/kg	30 min–1 h
Procaine	12 mg/kg	30 min–1 h
Cocaine	3 mg/kg	30 min–1 h
Tetracaine	3 mg/kg	1.5–6 h

Amide local anesthetic	Maximum dose	Duration
Lidocaine	5 mg/kg (7 mg/kg with Epi)	1 h–1.5 h
Mepivicaine	5 mg/kg (7 mg/kg with Epi)	1–2 h
Prilocaine	8 mg/kg	30 min–1 h
Bupivicaine	3 mg/kg	1.5–8 h
Ropivicaine	3 mg/kg	1.5–8 h

4.2 Treatment Modalities

The treatment for LAST consists of four main tenets: seizure management, airway management, cardiovascular support and lipid emulsion administration.

Seizures in the setting of LAST should be recognized and treated promptly to prevent worsening hypoxia and hypercarbia, which would potentiate the effects of local anesthetics in LAST. Isolated seizures are typically treated with IV benzodiazepines such as midazolam. Small, divided doses of propofol are a viable alternative, although it is important to be wary of its hemodynamic effects given the possibility of impending cardiovascular collapse with LAST.

Patients with mild symptoms can be treated with 100% oxygen by facemask, while ones with more severe CNS derangements might benefit from a supraglottic airway or endotracheal intubation. Specifically, patients who exhibit apnea, hemodynamically unstable arrhythmias, or cardiac arrest will require immediate aggressive airway management. This is done not only to preserve pulmonary ventilation and organ perfusion, but also to mitigate the effects of worsening acidosis on LAST.

The cardiac arrhythmias and arrest that may result from LAST is treated with ACLS, with notable modifications. The goal is to maintain coronary and end organ perfusion for long enough to administer lipid emulsion, and then circulate the lipid emulsion that is administered. Amiodarone is administered as a first line antiarrhythmic instead of local anesthetics such as lidocaine, or sodium channel blockers such as Class 1 antiarrhythmics. The bolus of epinephrine is reduced to <1 mcg/kg to avoid arrhythmogenic effects, and vasopressin is avoided given its association with poor outcomes [5]. Cardiopulmonary bypass may be necessary in extreme cases.

Administration of 20% lipid emulsion remains the definitive treatment of LAST. If it is not immediately available, it is imperative to send help to obtain the emulsion in the setting of suspected LAST. While its mechanism of action remains unclear, it has been postulated that the lipid emulsion works through both

its scavenging and its cardiotonic effects. It is considered a binding substance for local anesthetic, removing it from the heart and brain so it can be effectively metabolized and detoxified. Additionally, it has been theorized to increase cardiac output through a combination of volume and cardiotonic effects. The emulsion is bolused over 2–3 min at a dose of 1.5 ml/kg IV for patients <70 kg and 100 ml IV for patients >70 kg, followed by an infusion of 0.25 ml/kg/min IV. Boluses can be repeated and the infusion rate can be increased up to double for persistent cardiovascular collapse. Infusions are typically continued for 10 min after hemodynamic instability has resolved. The maximum dose given should not exceed 12 ml/kg. Adverse effects include interference with lab testing and rare cases of transaminitis, hepatosplenomegaly, pancreatitis, and bacterial contamination typically associated with prolonged infusions [5].

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Acute Pain Management Protocol for Proximal Upper Extremity: Shoulder and Proximal Humerus Procedures

Marcelle Blessing

Case Stem

A 54-year-old man with a past medical history significant for hypertension, obstructive sleep apnea, type 2 diabetes mellitus and obesity (BMI = 36) presents for right arthroscopic rotator cuff repair. The surgery is to be performed in the beach chair position at an ambulatory surgical center. He reports no problems with prior anesthetics. His current medications include hydrochlorothiazide, lisinopril, metformin, aspirin (81 mg) and oxycodone. His blood pressure is 167/84, HR 74, SaO_2 = 96% on room air. He did not take any medications this morning. He reports pain and limited range of motion in his right shoulder.

Questions

Preoperative

1. **Describe the innervation of the shoulder and proximal humerus?**
   The sensory innervation of the shoulder is supplied mainly from the brachial plexus, but also has contributions from the

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_20

supraclavicular nerves from the third and fourth cervical nerves of the cervical plexus as well as the intercostobrachial nerve from the second intercostal nerve. The motor innervation of the shoulder is entirely from the brachial plexus. Most of the motor and sensory innervation is from two terminal branches of the brachial plexus: the suprascapular nerve (supplies 70% of the sensory innervation to the joint and the motor innervation to supraspinatus and infraspinatus) and the axillary nerve.

2. **What are the options for regional anesthesia techniques for this surgery for postoperative analgesia?**
   Options for regional anesthesia include interscalene block (ISB), supraclavicular block (SCB), superior trunk block and suprascapular nerve block (SSNB). The ISB has been the gold standard for regional anesthesia for shoulder surgery for many years, long before the introduction of ultrasound into regional anesthesia practice. It provides reliable anesthesia at the level of the nerve roots of the brachial plexus and can be used for surgical anesthesia or postoperative analgesia for shoulder surgery. Interscalene block was performed by landmark techniques, paresthesia techniques and utilizing nerve stimulation prior to the routine adoption of ultrasound use in regional anesthesia practice. Ultrasound has made the block even easier to perform since the nerve roots are easy to identify because they are superficial (1–2 cm depth) and have a reliable hypoechoic appearance in the interscalene groove. Ultrasound improves the success rate for the block for providing surgical anesthesia [1]. Ultrasound has made it possible to perform this block in a targeted fashion and reduced the volume of local anesthetics needed to perform the block, potentially decreasing the risk of local anesthetic systemic toxicity and other side effects. McNaught et al. demonstrated that the block could be performed successfully with ultrasound with as little as 1 mL of 0.5% ropivacaine producing blocks lasting at least 6 h [2].

   Traditionally performed at the level of C6, a stack of three hypoechoic nerve roots resembling a stoplight is identified between the anterior and middle scalene muscle using a high frequency linear probe. Previously assumed to be the C5, C6 and C7 nerve roots stacked, recent re-evaluation of the anat-

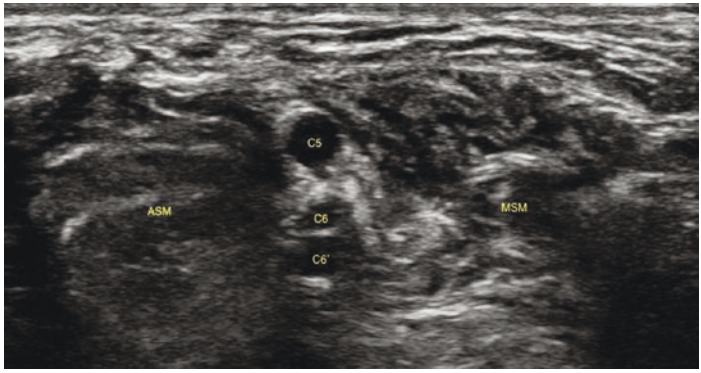

Fig. 1 Classic "stoplight" symbol in the interscalene groove for performing interscalene block. *ASM* anterior scalene muscle, *MSM* middle scalene muscle. Nerve roots stacked between the scalene muscles

omy revealed that the C6 nerve root frequently splits (Fig. 1). Care must be taken not to inject "between" the upper and lower fascicles of the C6 nerve root because this constitutes an intraneural injection that could potentially spread into the neuraxis [3].

The needle is directed using an in-plane, lateral-medial approach to deposit local anesthetic around the nerve roots. Care must be taken to avoid vascular structures. The vertebral artery frequently lies deep to the nerve roots in the interscalene groove. Considerable anatomic variations are possible and color doppler is recommended.

3. **What local anesthetic would you choose and what volume would you administer if you perform an interscalene block for this patient?**
   In clinical practice, long acting amide local anesthetics are usually used. 20–30 mL of ropivacaine 0.5% or bupivacaine 0.5% are common, although much smaller volumes of as little as 1 mL have proven effective for surgical anesthesia [2]. Blocks using only 5 mL of 0.5% ropivacaine have been shown to work as well as blocks using 20 mL and provide a better side effect profile with preserved duration of analgesia; however, these ultra-low volumes are rarely used in clinical practice [4].

4. **What potential side effects of an interscalene block will you discuss with this patient?**
Hemidiaphragmatic paralysis due to associated phrenic blockade is a common side effect of ISB. All patients receiving ISB or SCB should be warned of this side effect. It is poorly tolerated in patients with baseline compromised pulmonary function. Because the phrenic nerve is on the anterior scalene muscle in close proximity to the brachial plexus at the C6 level, there is a high incidence of associated phrenic blockade—historically reported to be 100%. The distance between the phrenic nerve and brachial plexus increases as the structures move caudally. Maneuvers used to reduce the incidence of phrenic nerve block include: performing the block lower in the neck, reducing the volume of local anesthetic used and injecting posterior to the plexus. The rate of phrenic block is likely lower than 100% when modifying a traditional ISB by using lower volumes injected lower in the neck under ultrasound guidance, but it is still unacceptably high for performing the block in patients with pulmonary compromise or in patients with contralateral hemidiaphragmatic paralysis. Even though successful phrenic-sparing ISB has been described with low volumes, even 5 mL of 0.5% ropivacaine was associated with as much as a 45% risk of phrenic block, so reducing volumes cannot guarantee a phrenic-sparing block [4]. Also, successful ultra-low volume techniques require a high level of precision and may not be applicable in real world practice.

The supraclavicular block (SCB), the block of the brachial plexus at the level of the trunks, can also provide reliable analgesia of the shoulder. To perform the block, the subclavian artery is identified in the supraclavicular fossa above the first rib, and the trunks of the brachial plexus are visualized posterolateral to it. Variations in the vascular anatomy in this area are common, including arterial branches within the brachial plexus, so the use of color doppler is recommended to avoid inadvertent vascular puncture or intravascular injection (Fig. 2).

Though many clinicians harbor concerns that the suprascapular nerve and superficial cervical plexus will be spared

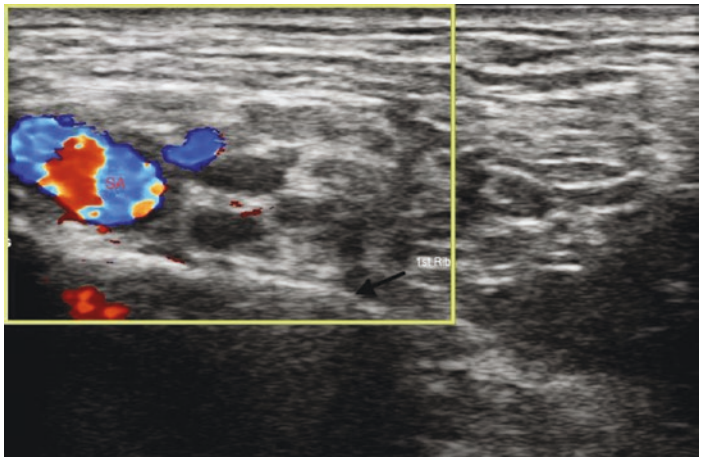

Fig. 2 Subclavian artery visualized above the first rib. Color doppler shows an arterial branch within the brachial plexus

with the supraclavicular block, studies have shown it provides equivalent analgesia to ISB; however, the rate of phrenic block is inconsistent in the literature and is still unacceptably high for patients with limited pulmonary reserve [5]. The superior trunk block (Fig. 3) is a new variation of the supraclavicular block that targets only the superior trunk of the brachial plexus; it has been reported to have a low risk of associated phrenic nerve block (4.8%) when performed with 15 mL of 0.5% bupivacaine [6].

5. **You are concerned that this patient will have some dyspnea after receiving an ISB because of his obesity and you warn him of this. Even though you explain that he should tolerate it easily, he is very anxious about this. Are there other nerve block options that you can offer him that eliminate the risk of hemidiaphragmatic paralysis?**
   Ultrasound has made more targeted approaches to the individual nerves that supply the shoulder possible. These blocks have the potential to eliminate the risk of hemidiaphragmatic paralysis while still providing shoulder analgesia. The suprascapular nerve (SSN) is a branch of the superior trunk of the brachial

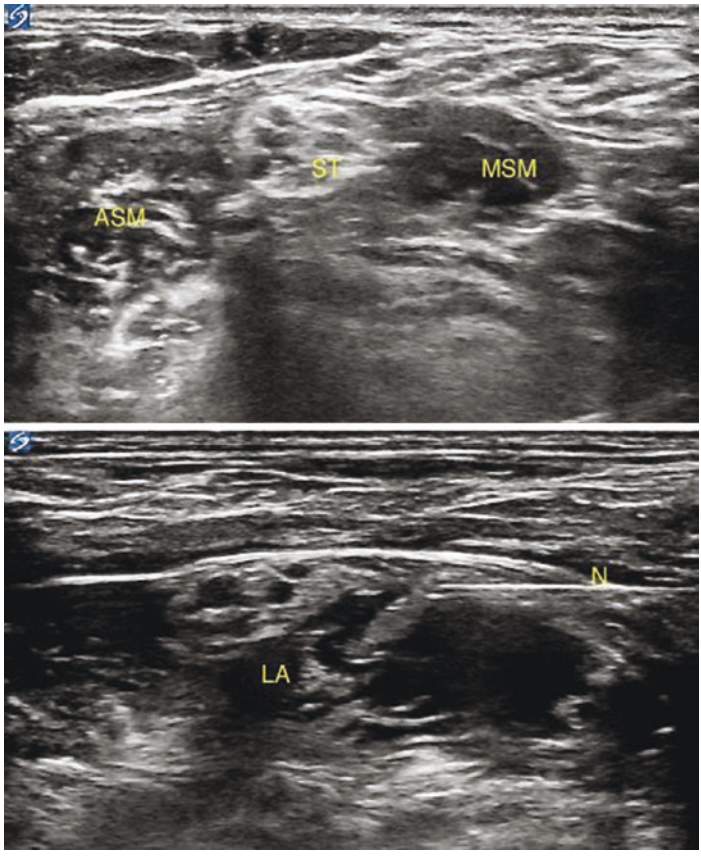

Fig. 3 Superior trunk block. *ST* superior trunk, *ASM* anterior scalene muscle, *MSM* middle scalene muscle, *N* needle approaching in a lateral to medial fashion towards the superior trunk, *LA* Local anesthetic with good perineural spread

plexus (C5 and C6). It provides innervation to 70% of the shoulder joint and can be blocked in the suprascapular fossa. Ultrasound-guided block of the suprascapular nerve (SSNB) is a more challenging block than the ISB or SCB because the target is deeper and the nerve lies directly on the bone, making scanning more challenging because of bony artifacts (Fig. 4).

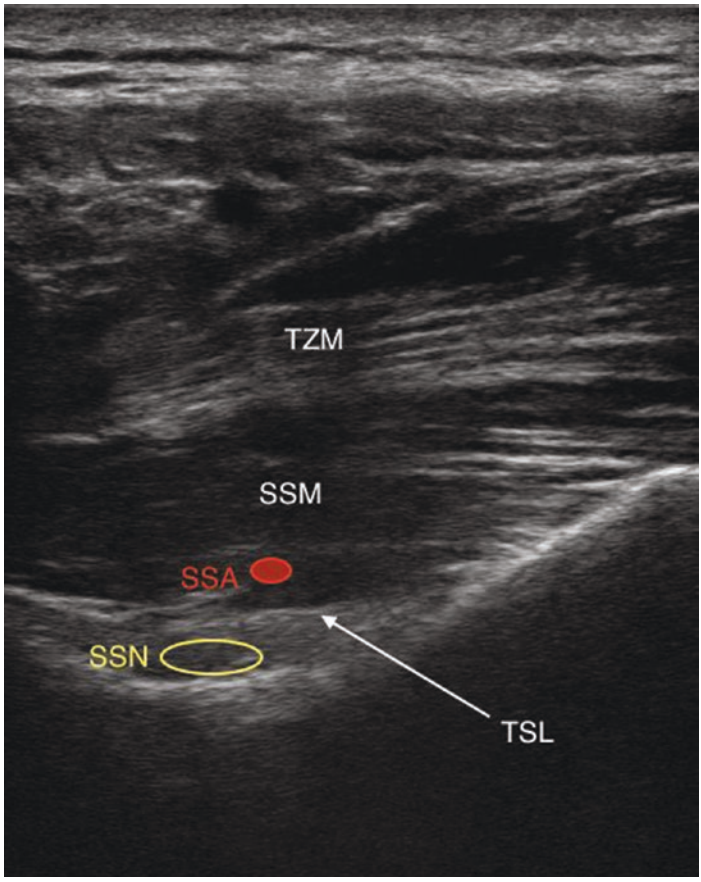

Fig. 4 Image of the Suprascapular fossa. *TZM* trapezius muscle, *SSM* supraspinatus muscle, *SSA* suprascapular artery, *SSN* suprascapular nerve, *TSL* transverse scapular ligament. The nerve may not be visible so local anesthetic is deposited in the suprascapular notch with care to avoid the suprascapular artery

Precise needle visualization is key because there is a risk of pneumothorax if the needle is guided inadvertently anteriorly towards the thorax. An anterior approach to the SSNB can also be performed where the nerve lies under the omohyoid muscle;

however, this approach carries some risk of phrenic blockade. A systematic review and meta-analysis of 16 studies comparing interscalene and suprascapular nerve blocks for shoulder surgery found that ISB patients had better pain control for the first hour postoperatively but had more side effects and both groups had similar 24-h morphine consumption [7]. A significant disadvantage of SSNB is that it cannot provide surgical anesthesia, only analgesia, and that analgesia likely will require opioid supplementation. SSNB has been combined with axillary nerve block to augment the analgesia for shoulder surgery and SSNB has also been combined with infraclavicular block to provide surgical anesthesia without respiratory dysfunction [8, 9].

6. **You decide to perform an ISB and the patient expresses anxiety about how he will cope with the pain after the nerve block wears off. What can you do to prolong his block?**
Options for prolonging nerve blocks include placing perineural catheters or using perineural adjuvant medications. Many local anesthetic adjuvants have been tried including steroids, alpha-2 agonists and opioids. Dexamethasone is widely used as an off-label additive to local anesthetics in nerve blocks to both improve the quality and duration of analgesia. Preservative free formulations are available and can address concerns about administering preservatives in standard preparations. There is some evidence that intravenous dexamethasone can prolong analgesia from peripheral nerve blocks, but a recent meta-analysis of 11 randomized control trials showed perineural dexamethasone prolonged analgesia more than intravenous [10]. The optimal dose of perineural dexamethasone is not clear, with a broad range of 1–10 mg used in clinical trials, but 4 mg may represent a therapeutic ceiling [11]. However, though it's use remains off-label, it is very common and has a well-established safety record. Administering dexamethasone intravenously is an option for providers uncomfortable with using perineural adjuvants, since dexamethasone is commonly administered intravenously for prophylaxis for postoperative nausea and vomiting and it has shown some benefit for block prolongation. Dexmedetomidine is also gaining popularity as an adjuvant; however, it may not be as effective as dexametha-

sone in brachial plexus blocks, and it can cause hypotension and bradycardia [12].

A perineural catheter is another option to prolong analgesia. It can be attached to a disposable elastomeric pump that the patient can easily remove at home, allowing analgesia to be prolonged for days at home safely. Dilute local anesthetics such as ropivacaine 0.2% can be delivered at low infusion rates with on demand boluses and are associated with higher satisfaction rates than more concentrated local anesthetics because pain can be controlled without the arm becoming completely insensate and preserving hand motor function [13].

7. **The patient does not want an ambulatory perineural catheter because he was told by his surgeon that he could get a brand new numbing medicine in his block that works for 3 days? What is the patient referring to? Is this true?**
   The patient is referring to ISB performed with liposomal bupivacaine. Liposomal bupivacaine is a relatively new depo form of bupivacaine that was FDA approved in 2011, with claims it can last for 72 h. It received FDA approval for the first time for a nerve block in 2018 for ISB; however, its ability to provide analgesia that lasts longer than plain bupivacaine has not been consistently produced in randomized controlled trials [14]. Regardless, excitement about even the possibility of an extended release local anesthetic option exists and has fueled it's use for this nerve block. Because liposomal bupivacaine has a slower onset than plain bupivacaine, it is typically mixed with 0.25% or 0.5% bupivacaine to accelerate the onset of blockade. Care must be given to follow the recommended dosing and mixing guidelines to reduce the risk of toxicity.
8. **Is it a problem that the patient has been taking his baby aspirin until the day before surgery?**
   Baby aspirin does not need to be stopped for any block, even deep peripheral nerve blocks and neuraxial blocks according to the American Society of Regional Anesthesia guidelines [15]. The brachial plexus blocks described here are superficial blocks and can safely be performed on aspirin. When aspirin is combined with other weak anticoagulants, or the patient has additional risk factors for bleeding, then more caution should be considered.

9. **The patient asks if it is necessary for him to go to sleep for the procedure? He reports that he would like to be awake and talk to the surgeon during the case.**
   Shoulder surgery can be performed under regional anesthesia with or without sedation. Shoulder surgery is most often performed in the United States in the sitting or beach chair position, but can also be performed in the lateral decubitus position. The beach chair position is more amenable to performing the surgery under regional anesthesia because it is more comfortable for an awake patient. Choice of regional versus general anesthesia as the primary technique for this surgery will largely be dictated by the local practices of the surgeon and anesthesiologist. ISB is the most frequently used regional method for providing primary anesthesia for shoulder surgery because it reliably provides motor block of the shoulder and almost complete sensory block of the surgical field. If pain is encountered, a surgeon can provide supplemental local anesthesia. Even with an excellent ISB, supplemental anesthesia may be needed for a posterior arthroscopic port site or the cephalad skin of the shoulder because this is innervated by the supraclavicular nerves from the cervical plexus. Sometimes a separate superficial cervical plexus block is performed by injecting 5 mL of local anesthetic superficial to the middle scalene muscle. Also, a separate intercostobrachial nerve block may be needed if axillary incisions are needed, often when biceps tenodesis is performed, if shoulder surgery is performed on a truly awake patient.
10. **Now the patient reports that he is very needle phobic and actually wants to be "put to sleep" for the block—how do you respond?**
    Catastrophic complications have occurred when ISB has been performed on patients under general anesthesia, including severe spinal cord injuries, likely as a result of direct injections into the cervical spine [16]. Because of these complications, general anesthesia has been considered a relative contraindication to ISB, even though these complications occurred before the routine use of ultrasound for nerve blocks.

ISB has been safely performed using ultrasound under general anesthesia for patients who cannot be still for the procedure while awake, especially children or for patients who cannot control their movements. However, needle phobia is fairly common and readily treated with anxiolytics. Virtually all adult patients can tolerate this small procedure after anxiolysis with midazolam with or without analgesia with fentanyl.

11. **You successfully perform an interscalene block under ultrasound guidance using 20 mL of 0.5% ropivacaine with 4 mg of preservative-free dexamethasone. After you perform the block the patient coughs weakly and complains that he cannot clear his throat and his voice is hoarse. What is going on?**
    The patient is experiencing another side effect of ISB, ipsilateral recurrent laryngeal nerve block, that can occur because of the proximity of the recurrent laryngeal nerve to the anterior scalene muscle. It is generally well tolerated if unilateral, but, because of this potential side effect, ISB should not be performed in patients who have contralateral recurrent laryngeal nerve dysfunction or a contralateral paralyzed vocal cord to avoid the potential for bilateral vocal cord dysfunction. Bilateral vocal cord paresis is not well tolerated and can cause airway obstruction. Though less common than phrenic block, this side effect should be mentioned when discussing ISB or SC block with patients so it is not concerning when it occurs.
12. **After you perform the ISB block, the patient's wife is brought back into the holding area to see her husband off to the operating room. She is concerned that the right side of his face is "droopy"—what is going on?**
    Horner's syndrome is common after ISB and is typically well tolerated and short-lived. It occurs because of the close proximity of the sympathetic chain to the cervical nerve roots. Patients are often unaware of this side effect and it is family members who note the ipsilateral ptosis and conjunctival redness. Reassurance is usually all that is needed that this common side effect is temporary and frequently resolves before the brachial plexus block has terminated.

Intraprocedure

1. **The case is underway and going smoothly under interscalene block with sedation, as the patient requested. However, an incision is now made in the axilla to perform an open biceps tenodesis. The patient's heart rate increases and he becomes restless but the arm does not move. What is going on? How could this be avoided?**
   As discussed, brachial plexus blockade via ISB or SCB does not provide sensory coverage of the axilla. Blockade of the intercostobrachial nerve, a branch of the second intercostal nerve, is necessary for complete coverage of the axilla. This can be achieved by performing a PECS II block or by direct intercostobrachial nerve block in the axilla. PECS II block has been shown to decrease pain scores in PACU after open biceps tenodesis, when combined with ISB [17]. It likely also helps with pain from arthroscopic biceps tenodesis. Since the PECS II block is a fascial plane block, it is typically performed with a large volume of dilute local anesthetic (20 mL of 0.2% ropivacaine or 0.25% bupivacaine) deposited in the plane between the pectoralis minor and serratus anterior muscle at the level of the fourth rib. PECS II block targets the intercostal nerves T2-6 and is typically used for analgesia for breast surgery, but it can be beneficial when shoulder surgery involves the axilla. Since the case is underway at this point, the surgeon could give supplemental local anesthetic in the axilla and a PECS II block could be offered to the patient in the recovery room if there is ongoing pain.
2. **The surgeon complains of poor working conditions because bleeding is interfering with arthroscopic visualization. Deliberate hypotension is requested. How would you respond?**
   Small amounts of surgical bleeding can make visualization in arthroscopic procedures challenging, historically leading to surgeons requesting deliberate hypotension. However, cases of cerebral and spinal cord ischemia have been reported in shoulder surgery patients with hypotension in the beach chair position [18]. Though rare, these events can be catastrophic and should be avoided at all costs, thus deliberate hypotension has been discouraged by experts [19].

Postprocedure

1. **The case is completed and the patient is brought to PACU. When he is more awake, he reports he has no pain in his shoulder, however, he is experiencing some shortness of breath. His oxygen saturation is 94% on room air. What is going on? Is a chest X-ray needed to evaluate this?**
   Hemidiaphragmatic paralysis is common after ISB and may occur after SCB as well. It is usually well-tolerated in patients without baseline pulmonary compromise; however, some patients like the patient here may be surprisingly symptomatic with it. A chest X-ray is not usually necessary to confirm this diagnosis, but if obtained will show the telltale sign of an elevated hemidiaphragm. Point-of-care ultrasound can also be used to confirm the diagnosis and rule out pneumothorax. Same day discharge is usually possible even with mild dyspnea. The patient can be reassured that this side effect almost always resolves even before the brachial plexus block is gone; however, there have been rare cases of permanent hemidiaphragmatic paralysis after ISB [20]. Since the complication is likely underreported, follow up with the patient for resolution of all symptoms of the block is crucial. The mechanism for permanent phrenic palsy is unknown; however, risk factors have been identified such as male gender, arthroscopic rotator cuff repair surgery, obesity and cervical stenosis [20, 21].
2. **If the patient reported that he is having pain in his shoulder, would you consider repeating his ISB?**
   Brachial plexus blocks have high success rates, but failure is always possible, often from anatomic variations. Repeating brachial plexus blocks after shoulder surgery can be challenging. Fluid from arthroscopy can cause local edema making nerve visualization more difficult. Surgical dressings often cover the supraclavicular fossa, eliminating the helpful landmark of identifying the trunks of the brachial plexus posterior and lateral to the subclavian artery. When pain occurs after a block that appeared straightforward, careful examination of the patient should be performed to assess the location of the pain and rule out potential non-brachial plexus causes such as the cervical plexus or intercostobrachial nerve. Exposing the patient to additional nerve blocks will increase the risk of block

complications, and since anatomical variations of the brachial plexus can contribute to block failure; attempts to repeat blocks should only be performed by experienced providers. Also, sometimes small areas of residual sensation are easily tolerated with multi modal analgesics, so this could be offered to the patient instead of repeating a regional anesthetic.

3. **The patient is discharged home the same day. On follow up phone calls, he reports that his nerve block has not completely worn off and he has some residual numbness and weakness. What should you do?**
   Residual numbness or weakness is a common issue after shoulder surgery with or without regional anesthesia. If this continues significantly past the expected length of the block, immediate evaluation is crucial to rule out reversible causes such as a hematoma from either the block or surgery, or even an overly tight sling. The patient should be examined in person. Sometimes patients when questioned over the phone will report "weakness" when they are in fact able to move but are limited by pain. It can be difficult to perform an accurate neurologic exam of the upper extremity postoperatively because of limited range of motion, pain and dressings around the shoulder. Neurologic examination of the hand and wrist can help discern what part of the brachial plexus is affected. Truthfully, in the immediate postoperative period, other than assessing for surgical or brachial plexus hematoma, there is not much that can be done to diagnose or provide prognosis for a nerve injury. Communication with the surgeon to coordinate a care plan is crucial. Some providers will pursue immediate EMG and neurologic evaluation to assess whether there is a baseline unrecognized nerve injury, while others will wait 3–4 weeks to allow for spontaneous improvement and for the EMG to be more diagnostic. EMG is not expected to change as a result of the injury for weeks. Reassurance should be provided to the patient that permanent neurologic injuries from the surgery or block are uncommon so improvement is likely.

1 Summary

Arthroscopic and open shoulder surgery are commonly and increasingly performed in both the inpatient and outpatient setting and familiarity with providing regional anesthesia for these cases and managing common side effects of these blocks is high-yield. Surgery of the proximal humerus, typically proximal humerus fracture repairs, can also be managed using the same regional anesthesia. Knowledge of the anatomy of the brachial plexus as well as other nerves in the area is needed to safely perform these blocks. Because nerve injuries can occur from either injuries to the shoulder itself or the surgeries to repair the shoulder, follow up with patients for complete resolution of the nerve block and early evaluation of residual numbness or weakness are recommended.

Common Pitfalls

- Side effects such as phrenic block, Horner's syndrome and hoarseness are common and usually well tolerated form ISB or SC block but need to be discussed with patients.
- The neck is very vascular and variations in vasculature are common. Using color doppler and injecting local anesthetics in small aliquots with frequent aspiration are key to avoiding intravascular injection.
- Postoperative neurologic complications from shoulder surgery can occur from nerve bock, or from positioning and traction, or from the surgery itself. It is often not easy to distinguish the cause.
- Axillary pain can occur when biceps tenodesis is performed as part of shoulder surgery with a brachial plexus block alone. Supplemental local anesthesia, PECS II blocks or supplemental multimodal analgesia can treat this pain.

Clinical Pearls

- Interscalene block provides excellent analgesia for shoulder surgery but with an unacceptably high rate of phrenic block
- Supraclavicular block also provides excellent analgesia for shoulder surgery but does not eliminate the risk of phrenic block
- Suprascapular block is an effective alternative for postoperative analgesia for patients who cannot tolerate any degree of phrenic block
- Perineural catheters for shoulder surgery with dilute local anesthetics infusing at low volumes are associated with high patient satisfaction.

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Acute Pain Management Protocol for Distal Upper Extremity: Elbow, Wrist and Hand Procedures

Olga Salianski, Margaret Griesemer, and Jinlei Li

Clinical Case

75-year-old man (BMI 27) with PMH of smoking, HTN, COPD, Right lung cancer s/p Right lower lobectomy, and history of known difficult airway, presents with a Left distal radius fracture for ORIF distal radius. The patient tells you he has had severe emergence delirium after his past anesthetics. The surgeon tells you this procedure will take 2–3 h and plans to use a tourniquet.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_21

1. *What upper extremity block options would you consider for this procedure?*

   Answer:

   A brachial plexus block would provide reliable coverage for this procedure.

Nerve blocks for distal upper extremity: Brachial plexus blocks

The brachial plexus is formed by the ventral rami of C5-C8, and the greater part of the ramus of T1, with possible contributions from C4 and T2. As the nerve roots exit the spinal foramina, they converge and separate at several points, forming trunks, divisions, cords, branches, and finally, terminal nerves [1]. Therefore, the brachial plexus anatomy allows for local anesthetic deposition at several sites along its length, depending on the intended effects of the block [2] (Table 1).

Distal upper extremity block ultrasound techniques

Supraclavicular block

(a) The subclavian artery is identified (Fig. 1).
(b) The pleura and first rib are visualized deep to the artery.
(c) The brachial plexus appears as a bundle of hypoechoic nodules just posterior and superficial to the artery [3].
(d) The goal is for the needle to enter the brachial plexus sheath and deposit the local anesthetic so that it surrounds the trunks and divisions of the brachial plexus [3].
(e) Due to close proximity to pleura, this block has an increased risk of pneumothorax; good needle visualization is necessary [3, 5].

Table 1 Brachial plexus blocks for distal upper extremity surgery

	Supraclavicular	Infraclavicular	Axillary
Brachial Plexus Level Blocked	Divisions [3]	Cords [3]	Large terminal branches [2, 3]
Sensory Coverage			
	Upper 2/3 of upper limb, +/− some of the shoulder [3]	Upper limb below the shoulder [2, 3]	Distal to level of mid-arm [3]

(continued)

Table 1 (continued)

	Supraclavicular	Infraclavicular	Axillary
Nerves/Areas Not Covered by Block	T2 (intercostobrachial)—skin over the upper medial arm [3]	T2 (intercostobrachial)—skin over the upper medial arm [3]	T2 (intercostobrachial)—skin over the upper medial arm [3]
			Axillary nerve—skin over the deltoid muscle [3]
			Musculocutaneous nerve [3]
Incidence of phrenic nerve blockade	50–67%	~15%	Should not occur
Patient Position	Supine; head of bed elevated to 30°; head turned to contralateral side [4]	Supine; head turned to the contralateral side; ipsilateral arm abducted to 90°; elbow flexed [2]	Supine; arm abducted to 90°; head turned to contralateral side [3]
Ultrasound transducer and position	Linear transducer, placed in the supraclavicular fossa superior to the clavicle [2]	Linear or small curvilinear transducer, placed parasagittally medial to the coracoid process and inferior to the clavicle [2, 3]	Linear transducer, placed distal to the pectoralis major insertion on the humerus
Needle	22 gauge block needle [3]	8–10 cm, 22 gauge block needle [3]	5 cm, 22 gauge needle [3]
Local anesthetic amount	20–30 mL [2, 3]	20–30 mL [3]	20 mL [3], +10 mL for musculocutaneous nerve block [2, 3]

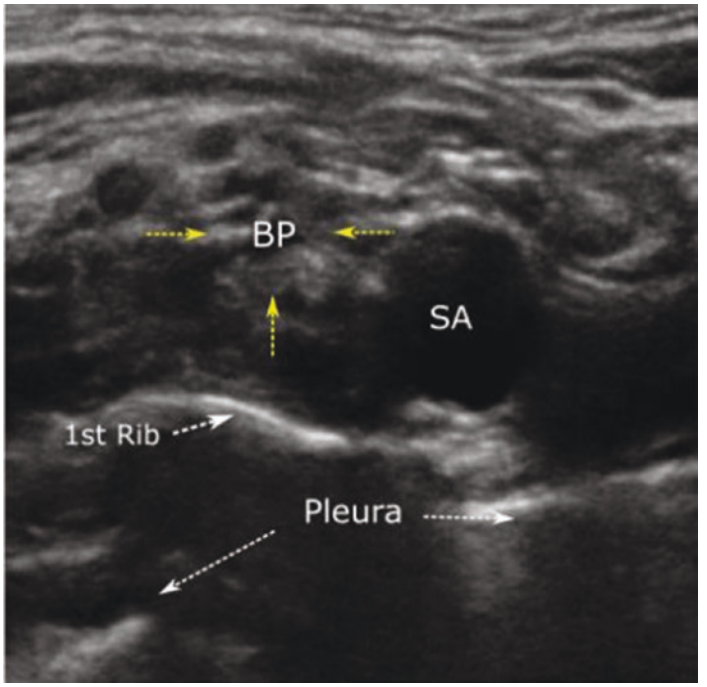

Fig. 1 Supraclavicular block sonoanatomy. *BP* brachial plexus, *SA* subclavian artery

Infraclavicular block

(a) The axillary artery and vein are identified in the ultrasound view in cross-section (Fig. 2).
(b) The cords (medial, lateral and posterior) are visualized surrounding the artery.
(c) needle is inserted in plane from the cephalad end of the probe, just inferior to the clavicle, aiming at the posterior aspect of the axillary artery between the artery and posterior cord.

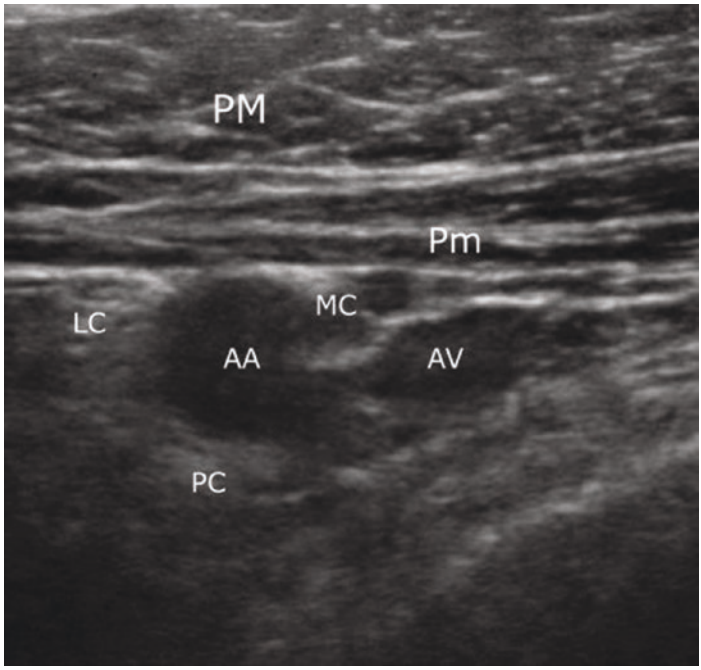

Fig. 2 Infraclavicular block sonoanatomy. *PM* pectoralis major muscle, *Pm* pectoralis minor muscle, *AA* axillary artery, *AV* axillary vein, *LC* lateral cord, *MC* medial cord, *PC* posterior cord

(d) goal is to visualize local anesthetic spread around the artery; this approach will reliably block the cords of the brachial plexus, even when they are not clearly identifiable on ultrasound [3].
(e) Of note, a single injection of local anesthetic with good spread around the axillary artery has been shown to be as effective as individual injections aimed at each cord [2, 6].

Axillary block

(a) The axillary artery can be palpated and its pulse identified in the axilla.
(b) The pectoralis major muscle is palpated where it inserts into the humerus, and a high frequency linear transducer is placed just distal to this point, which allows to visualize the axillary artery and vein in cross-section.
(c) The brachial plexus is identified as it surrounds the artery (Fig. 3).
(d) The musculocutaneous nerve is then visualized between the biceps and coracobrachialis muscle, and a separate injection of local anesthetic is deposited to target this nerve.
(e) Goal of block is good spread around axillary artery (typically requires 2–3 needle redirections).

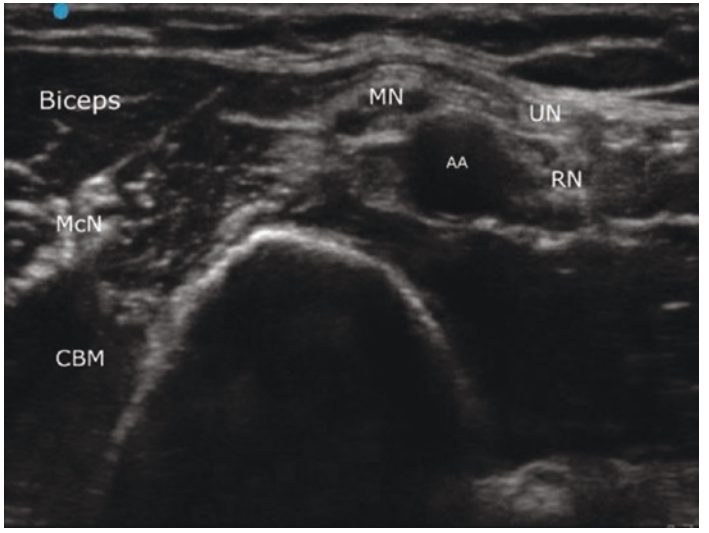

Fig. 3 Axillary block sonoanatomy. *AA* axillary artery, *McN* musculocutaneous nerve, *MN* median nerve, *UN* ulnar nerve, *RN* radial nerve, *CBM* coracobrachialis muscle

Table 2 Commonly used local anesthetics for brachial plexus blocks

Local anesthetic	Commonly used dose for brachial plexus blocks (mL)	Onset of action (min)	Typical duration of analgesia (h)	Indication for use
2% Lidocaine	20–30	10–20	3–8	Surgical anesthesia only
1.5% Mepivacaine	20–30	10–20	3–10	Surgical anesthesia only
0.25% Bupivacaine	20–30	15–30	5–26	Post-op analgesia
0.5% Bupivacaine	20–30	15–30	6–30	Post-op analgesia
0.2% Ropivacaine	20–30	15–30	5–16	Post-op analgesia
0.5% Ropivacaine	20–30	15–30	5–24	Post-op analgesia

2. *What local anesthetic would you use for this block? What patient and drug factors would influence your choice of local anesthetic?*

   Answer:

   Local anesthetic medications can be grouped into three broad categories: (1) Rapid-onset short-acting ones (e.g., chloroprocaine), (2) intermediate-onset intermediate duration (e.g., lidocaine), and (3) slower-onset long-acting ones (bupivacaine, ropivacaine). In this patient who is undergoing a necessary yet non-emergent procedure, one would opt for a local anesthetic that combines a surgical block with longer-lasting pain relief, such as ropivacaine or bupivacaine [7]. Common local anesthetic agents are summarized in Table 2 [4].

   (a) Epinephrine is frequently added to LA solutions to cause vasoconstriction and to serve as a marker for intravascular injection [8].

(b) Other popular LA additions include clonidine, $NaHCO_3$, opioids, dexamethasone, and hyaluronidase [8].

3. *What are the common risks of brachial plexus nerve blocks? What risks are important to consider in this patient?*

Answer:

In this patient who has had lung resection on the contralateral side, it is important to discuss the risks and benefits of the block, giving special attention to the risks of pneumothorax and hemidiaphragm paralysis.

Common risks of brachial plexus nerve blocks can be divided into two broad categories: those associated with needle placement, and those associated with the local anesthetic.

Needle placement-associated risks

(a) **Pneumothorax.** Although the risk of pneumothorax is decreased with the widespread use of ultrasound during needle placement, such risk is not zero, and therefore should be discussed with the patient while obtaining informed consent. The risk of pneumothorax is typically higher with proximal brachial plexus blocks (supraclavicular, interscalene) and decreased with more distal blocks (infraclavicular), and should not occur with an axillary block [4].

(b) **Phrenic nerve blockade.** The phrenic nerve travels in close proximity to the brachial plexus and can be affected by the spread of local anesthetic from the brachial plexus block on the ipsilateral side, resulting in hemidiaphragm paresis. Although well tolerated by most patients, this may cause worsening of respiratory symptoms in patients with preexisting pulmonary conditions [4, 9], such as this patient with COPD and contralateral lung lobe resection. The risk of phrenic nerve blockade is increased with proximal brachial plexus blocks and decreased with more distal ones [4].

(c) **Horner syndrome.** Temporary blockade of the stellate ganglion may occur due to spread of local anesthetic from the brachial plexus block site. This may result in Horner syndrome, which is a self-limited side effect of the block.

(d) **Hoarseness.** There may be spread of the local anesthetic to the ipsilateral recurrent laryngeal nerve, which may manifest as temporary hoarseness which resolves with the resolution of the block.

Local anesthetic-associated risks

(a) **Local anesthetic systemic toxicity (LAST).** Although the overall risk is low, systemic toxicity may occur, for example, from inadvertent intravascular injection of local anesthetic, or from systemic absorption of local anesthetic out of a tissue depot. Local anesthetics at increased blood levels can block cortical inhibitory pathways, resulting in excitatory symptoms such as perioral numbness, metallic taste, anxiety/restlessness, muscle twitching, and ultimately, seizures. Cardiovascular adverse effects typically occur at even higher local anesthetic blood levels

4. *Given the patient's history of Right-sided lung resection, you decide to minimize the risk of pneumothorax and/or hemidiaphragm paresis on the left, and opt for an axillary block. How would you supplement your block considering the surgeon will use a tourniquet?*

Answer:

To minimize tourniquet pain, the coverage of the medial upper arm can be achieved by performing an intercostobrachial (T2) block (shown below), or pectoralis nerve (PEC) II block under ultrasound guidance (will be discussed elsewhere in this book).

Supplemental blocks: Intercostobrachial block

(a) The intercostobrachial nerve does not originate from the brachial plexus; it originates from T2 thoracic level
(b) This is a sensory nerve which innervates the skin of the medial upper arm, thus surgeries which require use of a tourniquet (such as a distal radius fracture repair) necessitate a separate block for the T2 nerve

(c) Patient is positioned supine with the arm abducted and externally rotated [10].
(d) A 1.5-in. 25-gauge needle is used [10].
(e) 5 mL of local anesthetic is deposited superficially along the axillary crease [10].
(f) This block can be performed as a field block by creation of a linear skin wheal from the deltoid prominence toward the medial aspect of the upper arm.
(g) Alternatively, this block can be performed with ultrasound guidance, which has been shown to improve both speed of onset and tourniquet comfort in patients [11].

5. *This is your patient's first time getting an upper extremity block. He is asking you what he should expect in terms of sensation and use of his upper extremity.*

Answer:

(a) *Set the expectation for absence of sensation or motor function in the upper extremity both during the procedure and for a period of time afterward. Of note, a 2019 study found that despite prolonged postoperative pain control, an insensate and uncontrollable upper extremity after a regional block was named as a major reason for decreased patient satisfaction with anesthesia* [12]. *Therefore, the effects of a prolonged sensory and motor block should be discussed with the patient preoperatively.*
(b) *Discuss possible block failure or insufficient coverage, which may require a rescue block or induction of general anesthesia* [13].

6. *Fifteen minutes after the block, you come in to check on your patient. He tells you that he still has sensation over his lateral forearm and anatomic snuff box. What can you do to supplement your block? What other individual nerve blocks can be implemented in case of incomplete blockade with a brachial plexus block?*

Answer:

It appears that the patient's block is incomplete, and the radial nerve is spared. To supplement an incomplete brachial

Table 3 Individual nerve blocks of the upper extremity

Block type	Radial	Median	Ulnar
Patient position	Proximal block: supine, arm is adducted, elbow flexed 90°	Supine, arm abducted 90° at shoulder, elbow extended	Supine, arm abducted 90° at shoulder, elbow extended
	Block at the forearm: supine, arm abducted 90°		
Equipment	High-frequency (6–13 MHz) linear probe	High-frequency (6–13 MHz) linear probe	High-frequency (6–13 MHz) linear probe
	22 or 25-gauge 3.8 cm needle	22 or 25-gauge 3.8–5 cm needle	22 or 25-gauge 3.8–5 cm needle
Local anesthetic amount	~5 mL	~5 mL	~5 mL

plexus block, an individual block of a terminal nerve can be implemented. Other terminal nerve blocks are summarized in Table 3.

Radial nerve ultrasound guided block [14]

(a) The radial nerve is located in the lateral aspect of the distal arm, deep to the brachialis and brachioradialis muscles (Fig. 4).
(b) The transducer is placed anterolaterally perpendicular to the long axis of the arm, about 3 cm proximal to the elbow crease.
(c) A block at this location covers both the sensory and motor branches of the radial nerve

In the forearm, the radial nerve is located lateral to the radial artery (Fig. 5).

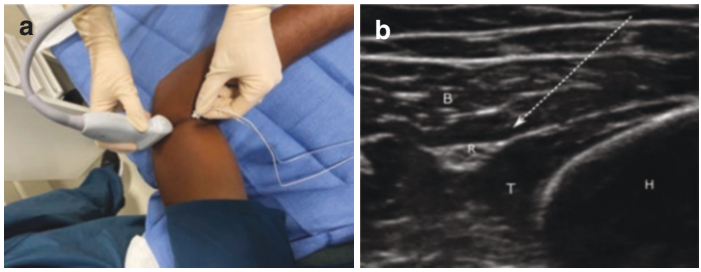

Fig. 4 Radial nerve block at the arm. (**a**) Patient position and needle entry point. (**b**) Sonoanatomy of radial nerve in distal arm. R—radial nerve, B—brachialis muscle, T—triceps muscle, H—humerus; long arrow—needle direction and target point

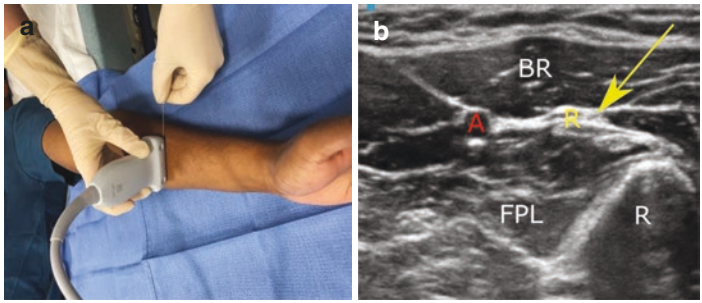

Fig. 5 Radial nerve block at the forearm. (**a**) Patient position and needle entry point. (**b**) Sonoanatomy of radial nerve at forearm. A—radial artery; R—radial nerve close to the radial artery, BR—brachioradialis muscle, FPL—flexor pollicis longus muscle, long arrow—needle direction and target point

Median nerve ultrasound guided block [14]

(a) The median nerve can be blocked individually at the level of the forearm or at the distal arm above the elbow (Fig. 6).
(b) In the distal arm, the median nerve lies superficially and is located medial to the brachial artery. The brachialis muscle can be seen deep to the median nerve, and the humerus can be visualized deeper.

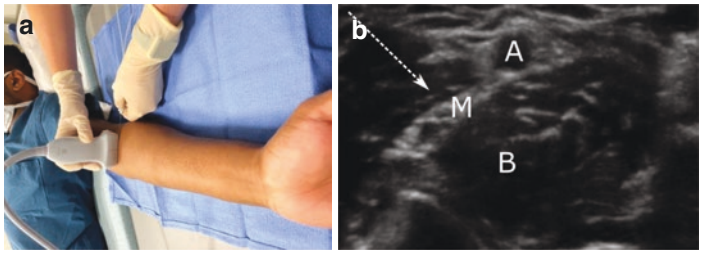

Fig. 6 Median nerve block at the arm. (**a**) Patient position and needle entry point. (**b**) Sonoanatomy of median nerve in distal arm. A—artery; M—median nerve; B—biceps muscle; long arrow—needle direction and target point

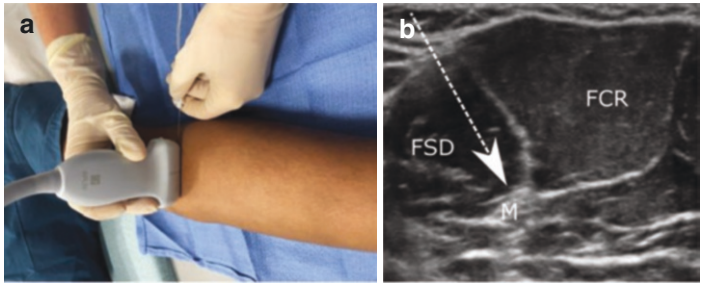

Fig. 7 Median nerve block at the forearm. (**a**) Patient position and needle entry point. (**b**) Sonoanatomy of median nerve in the forearm. M—median nerve; FCR—flexor carpi radialis muscle; FSD—flexor superficialis digitorum muscle, long arrow—needle direction and target point

(c) The ultrasound probe is placed perpendicular to the long axis of the arm, and the needle is inserted in plane.

In the forearm, the median nerve is found among the flexor tendons (Fig. 7). As in the distal arm approach, the probe is positioned perpendicular to the long axis of the arm and the needle is inserted in-plane.

Ulnar nerve ultrasound guided block [14]
The ulnar nerve can be blocked proximal to the ulnar groove or in the forearm.

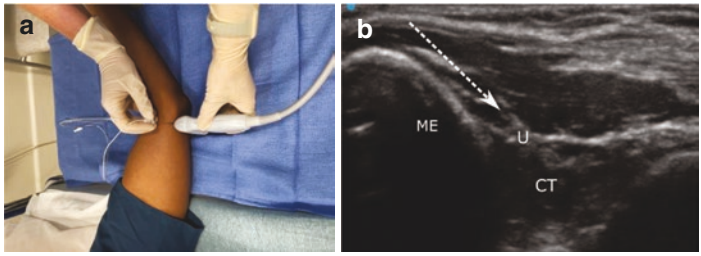

Fig. 8 Ulnar nerve block at the arm. (**a**) Patient position and needle entry point. (**b**) Sonoanatomy of ulnar nerve in cubital tunnel. U—ulnar nerve; ME—medial epicondyle, CT—cubital tunnel, long arrow—needle direction and target point

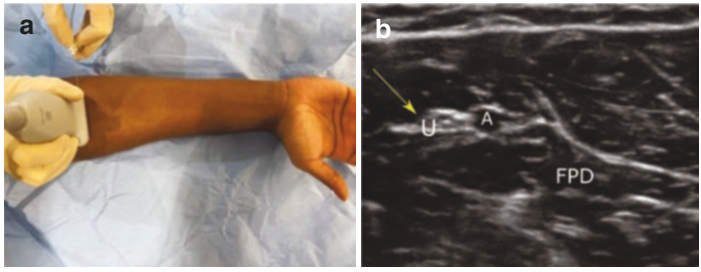

Fig. 9 Ulnar nerve block at the forearm. (**a**) Patient position and needle entry point. (**b**) Sonoanatomy of ulnar nerve in distal arm. U—ulnar nerve; FPD flexor profundus digitorum muscle; long arrow—needle direction and target point

(a) In the arm, the ulnar nerve is seen superficially above the brachialis and triceps muscles (Fig. 8).
(b) The probe is positioned perpendicular to the long axis of the arm, just proximal to the ulnar groove, and the needle is inserted in-plane.

In the forearm, the ulnar nerve lies close to the ulnar artery (Fig. 9). The probe is positioned perpendicular to the long axis of the forearm, and the needle is inserted in-plane.

1 Summary

A variety of regional anesthetic techniques can be utilized for distal upper extremity procedures. According to the demands of the surgical procedure, upper extremity nerves may be blocked at several levels along the upper extremity. Nerve blocks at the level of the brachial plexus are commonly accomplished via supraclavicular, infraclavicular or axillary approaches. Brachial plexus blocks are especially useful for cases where tourniquet pain needs to be managed in addition to incisional pain. A supplemental block for the intercostobrachial (T2) nerve or a pectoralis (PECII) is commonly required for coverage of the upper inner arm which is not innervated by the brachial plexus. For minor procedures or as a supplement to an incomplete brachial plexus block, individual nerves (radial, median, ulnar) can be blocked more distally, at the level of the arm or forearm.

Local anesthetic choices depend on the type of pain relief intended. For instance, faster-onset shorter-acting agents are preferred for surgical anesthesia, whereas slower-onset longer-acting ones are best suited for post-operative analgesia.

Common Pitfalls

- Common side effects of brachial plexus blocks include ipsilateral Horner syndrome, hemidiaphragm paralysis, and (rarely) pneumothorax.
- Failure to consider the patient's medical history when choosing the appropriate block may lead to complications in the setting of the patient's pre-existing comorbidities.
- The risk of inadvertent intravascular injection, although low with ultrasound-guided techniques, is nevertheless present with upper extremity nerve blocks and may lead to local anesthetic systemic toxicity.
- Failure to set the expectation for insensate and uncontrollable upper extremity may lead to patient dissatisfaction despite a working block with adequate pain relief.

Clinical Pearls

- Choose the appropriate brachial plexus block based on the patient's comorbidities and the surgical procedure being performed
- Patients with pre-existing pulmonary conditions may not be able to tolerate temporary hemidiaphragm paralysis often accompanying interscalene and supraclavicular blocks.

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Acute Pain Management Protocol for Pelvic, Hip and Proximal Femur Procedures

Nicole Hollis and Katelyn Glines

Case Stem 1 Femoral Shaft Fracture

A 40-year-old, 80 kg male presents to the emergency department with a mid-shaft femur fracture following an ATV accident. He has no significant past medical history and takes no medications. He is scheduled for an open reduction and internal fixation (ORIF) of his right femur.

Questions/Answers

1. What regional block could you offer this patient?

   A femoral nerve block could be offered to a patient with a mid-shaft femur fracture for analgesia. A femoral nerve block is utilized to provide cutaneous and osteotome analgesia to the hip, thigh, and knee via nociceptive blockade with local anesthetic medications. The femoral nerve originates from the posterior division of the ventral rami of L2-L4 nerve roots and is the largest terminal branch of the lumbar plexus. The femoral nerve runs lateral to the psoas muscle in the pelvis and then passes underneath the inguinal ligament to enter the anterior compartment of the thigh where it quickly branches

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_22

to provide innervation to the muscles, bones, joints, and skin in the anterior thigh [1].

2. What is the distribution of anesthesia from a femoral nerve block?

   The femoral nerve block is performed to provide analgesia to the hip, knee, and thigh. A femoral nerve block provides anesthesia and analgesia to the anterior thigh, hip, femur, knee, and most of the lower leg and foot.

   (a) **Sensory Innervation:** The sensory distribution of a femoral nerve block is the anterior and medial thigh extending down to and including the knee, and a strip of skin overlying the medial leg and foot.

   (b) **Motor Innervation:** The major muscles innervated by the femoral nerve include the muscles of the anterior compartment. The anterior compartment muscles include the quadriceps femoris, sartorius, and pectineus. The muscles of the anterior compartment primarily act to extend the leg at the knee joint [2].

3. What is the spatial relationship of the femoral nerve in relation to the femoral artery?

   The spatial relationship of the femoral nerve is lateral to the femoral artery. On the anterior thigh at the inguinal crease in the femoral triangle, the nerve is positioned lateral to the femoral artery and vein [3]. The femoral nerve lies under the fascia lata and fascia iliaca fascial planes, sits above and slightly medical to the iliacus muscle, and is typically 1–2 cm lateral to the femoral artery [2]. Immediately after the femoral nerve passes under the inguinal ligament, the nerve starts to divide. After the femoral nerve divides, it is more difficult to visualize with ultrasound.

4. How is a femoral nerve block performed?

   A femoral nerve block is performed under ultrasound guidance and with local anesthetic deposited lateral to the nerve to provide analgesia. Femoral nerve blocks are performed at the bedside with the patient in the supine position and the table flat with the patient's legs extended. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied,

and equipment is readily available near the operator. After a timeout, the high-frequency linear ultrasound transducer is placed over the femoral crease to identify the femoral artery and nerve. At the level of the femoral artery prior to splitting, identify the femoral nerve 1–2 cm lateral to the artery. The femoral nerve should be on top of the iliacus muscle and underneath fascia lata and fascia iliaca (Fig. 1). An 80–100 mm block needle is inserted under the ultrasound probe in a lateral-to-medial direction. The needle tip passes through fascia lata and fascia iliaca until the tip of the needle is lateral to the femoral nerve. Administration of 10–15 mL of local anesthetic (LA), 5 mL at a time is performed after confirming negative aspiration. Local anesthetic should be surrounding the femoral nerve under fascia iliaca [2–4].

5. What type of local anesthetic would you choose for this patient?

   The type of local anesthetic selected for this patient should be based on onset, duration, and blockade desired. Ropivacaine would be a suitable choice for this patient as it offers a duration of action similar to bupivacaine while resulting in less motor blockade. A comparison of local anesthetics used for peripheral nerve blocks can be found in Table 1.

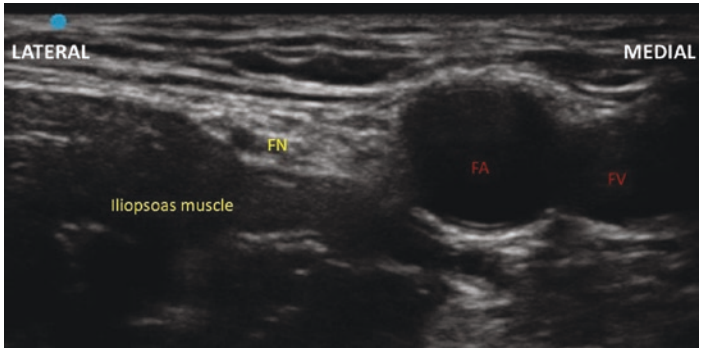

Fig. 1 Femoral nerve ultrasound. Femoral Nerve (FN) seen lateral to the Femoral Artery (FA) and Femoral Vein (FV)

Table 1 Comparison of local anesthetics

Local anesthetics used for peripheral blockade [5, 6]			
Esters	Available concentrations	Duration (min)	Maximum dose (mg/kg)
Chloroprocaine	1%, 2%, 3%	30–60	12
Amides			
Lidocaine	0.5%, 1%, 1.5%, 2%, 4%, 5%	60–120	4.5 (without epi) 7 (with epi)
Mepivacaine	1%, 1.5%, 2%, 3%	90–180	4.5 (without epi) 7 (with epi)
Bupivacaine	0.25%, 0.5%, 0.75%	240–480	3
Ropivacaine	0.2%, 0.5%, 0.75%, 1%	240–480	3

The potency, speed of onset, duration of action, and differential sensory versus motor block in isolated nerves are determined by the physiochemical characteristics of the local anesthetic.

(a) **Potency:** Potency of a local anesthetic is associated with lipid solubility. Local anesthetics with greater lipid solubility can permeate nerve membranes more readily. For example, bupivacaine is more lipid soluble than lidocaine, and is more potent.

(b) **Speed of onset:** The speed of onset of a local anesthetic depends on properties of the specific drug, the concentration of the solution, and the site of the injection. The time of onset increased with increasing lipid solubility.

(c) **Duration of action:** The duration of action for a local anesthetic depends on the chemical structure of the drug, lipid solubility, site of injection, local tissue conditions, and protein binding.

(d) **Differential blockade:** Nerve fiber characteristics lead to differing susceptibility to local anesthetics.

6. If the surgical team approached the distal femur fracture through a medial thigh incision, blockade of what nerve would provide analgesia to this area?

Innervation of the medial thigh is from the obturator nerve. The obturator nerve provides sensory and motor innervation to the medial thigh and knee. The obturator nerve also pro-

vides articular branches to the hip and knee joints. The obturator nerve forms within the lumbar plexus from the ventral rami of the L2-L4 nerve roots. The obturator nerve runs within the medial side of the psoas muscle and exits the pelvis by passing through the obturator foramen. The obturator nerve then divides into the anterior and posterior branches. The anterior branch of the obturator nerve is located between pectineus (or adductor longus distal to the inguinal crease) and adductor brevis muscles. The posterior branch of the obturator nerve is located between the fascial planes of the adductor brevis and adductor magnus muscles [2].

(a) **Sensory Innervation:** The sensory distribution of an obturator nerve block is the medial region of the upper thigh.

(b) **Motor Innervation:** The major muscles innervated by the obturator nerve include the muscles of the medial compartment. The medial compartment muscles include the adductor longus, external obturator, adductor magnus, adductor brevis, and adductor gracilis. The muscles of the medial compartment primarily act to adduct the thigh.

7. What is the motor and sensory distribution of an obturator nerve block?

The motor and sensory distribution of the obturator nerve is to the adductor muscles and the medial thigh respectively.

(a) **Sensory Innervation:** The sensory distribution of an obturator nerve block is the medial region of the upper thigh.

(b) **Motor Innervation:** The major muscles innervated by the obturator nerve include the muscles of the medial compartment. The medial compartment muscles include the adductor longus, external obturator, adductor magnus, adductor brevis, and adductor gracilis. The muscles of the medial compartment primarily act to adduct the thigh [2].

8. How is an obturator nerve block performed?

An obturator nerve block is performed at the bedside with the patient in the supine position and the table flat with the patient's leg slightly abducted and laterally rotated. The ultra-

sound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a time out, the high frequency linear or curvilinear ultrasound transducer is placed on the medial aspect of the proximal thigh at the level of the femoral crease. Ultrasound imaging is used to identify the fascial planes containing the branches of the obturator nerve. The anterior branch is located between the pectineus and adductor brevis, the posterior branch is located between the adductor brevis and adductor magnus (Fig. 2). Five to 10 mL is injected in each plane, respectively.

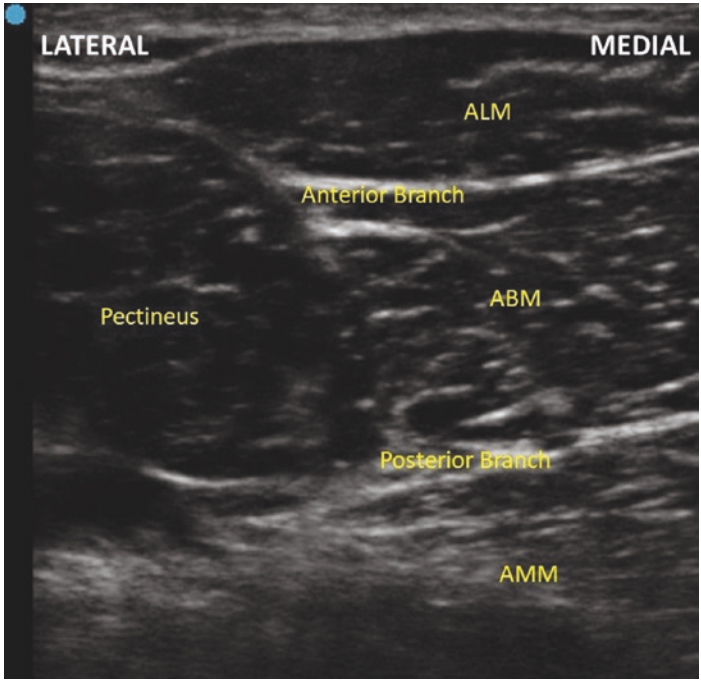

Fig. 2 Obturator nerve ultrasound. The anterior branch of the Obturator Nerve is between the adductor longus muscle (ALM) and the adductor brevis muscle (ABM). The posterior branch of the Obturator Nerve is between the adductor brevis muscle (ABM) and the adductor magnus muscle (AMM)

Alternatively, ultrasound and nerve stimulation may be used to identify the anterior and posterior branches individually and inject 5–7 mL of local around each branch [2].

9. If the patient in the above scenario underwent an intramedullary nail placement and was experiencing postoperative posterior thigh and knee pain. Which block could provide analgesia to this region?

   Analgesia to the posterior thigh and knee can be accomplished by a sciatic nerve block. A sciatic nerve block can be utilized for analgesia of the posterior thigh, knee, and most of the lower leg, ankle, and foot. The sciatic nerve also provides articular branches to the knee capsule [2].

10. What is the sensory and motor distribution of a sciatic nerve block?

    The cutaneous distribution of the sciatic nerve is to the posterior thigh, hamstring muscles, posterior aspect of the knee, and most of the lower leg, ankle, and foot. The sciatic nerve is formed by the ventral rami of the L4-S3 nerve roots. The sciatic nerve exits the pelvis through the greater sciatic foramen deep to the piriformis muscle. The sciatic nerve then progresses down the posterior compartment of the thigh deep to the long head of the biceps femoris muscle. Prior to reaching the popliteal fossa, the sciatic nerve divides into the tibial nerve and common peroneal nerve [2].

    (a) **Sensory Innervation:** The sensory distribution of a sciatic nerve block includes the posterior thigh, the posterior aspect of the knee, and most of the lower leg, ankle, and foot.

    (b) **Motor Innervation:** The major muscles innervated by the sciatic nerve are the muscles of the posterior compartment of the thigh. The muscles of the posterior compartment of the thigh include the biceps femoris, semimembranosus, semitendinosus, and ischial portion of the adductor magnus.

11. What are possible approaches to a sciatic nerve block?

    (a) Popliteal: Will not be discussed in this chapter

    (b) Anterior: Proximal medial thigh

(c) Transgluteal: Between ischial tuberosity and greater trochanter
(d) Subgluteal: Gluteal crease

12. How is a sciatic nerve block performed?
    (a) **Anterior Approach to the Sciatic Nerve (**Fig. 3**):** The anterior approach to the sciatic nerve is performed at the bedside with the patient in the supine position and the table flat with the patient's hip abducted to assist with transducer and needle placement. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a timeout, the curvilinear ultrasound transducer is placed over the inguinal crease to identify the femoral artery and the sciatic nerve. The sciatic nerve is visualized between the adductor magnus and hamstring muscles. A block needle is inserted under the ultrasound probe in-plane in a medial-to-lateral direction towards the sciatic nerve. If nerve stimulation is also being used, the contact of the needle tip with the sciatic nerve will

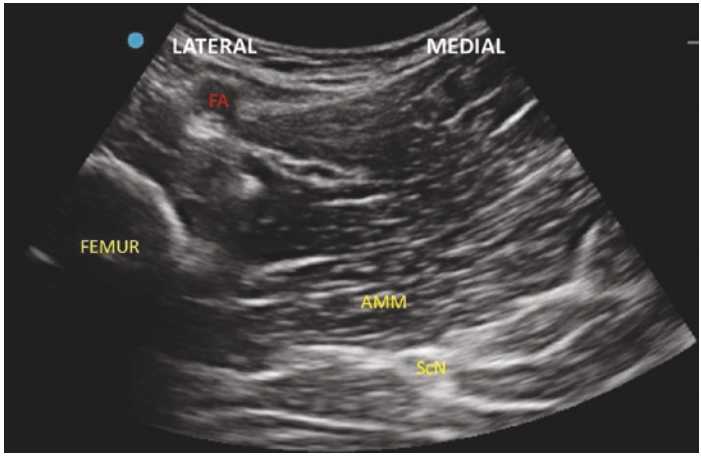

Fig. 3 Sciatic nerve (anterior approach) ultrasound. Femoral Artery (FA), Adductor magnus muscle (AMM), Sciatic Nerve (ScN)

trigger a motor response. Administration of 1–2 mL of local anesthetic is injected to confirm the adequate distribution. Administration of 10–15 mL of local anesthetic, 5 mL at a time after confirming negative aspiration [2].

(b) **Transgluteal Approach to the Sciatic Nerve (**Fig. 4**):** The transgluteal approach to the sciatic nerve is performed at the bedside with the patient in the lateral position with the hip and knee flexed and the table flat. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a timeout, the curvilinear ultrasound transducer is placed at the level of the ischial tuberosity and the greater trochanter of the femur. A block needle is inserted under the ultrasound probe in-plane in a lateral-to-medial direction towards the sciatic nerve. The sciatic nerve is located deep to the gluteus maximus muscle. If nerve stimulation is also being used, the contact of the needle tip with the sciatic nerve will trigger a motor response.

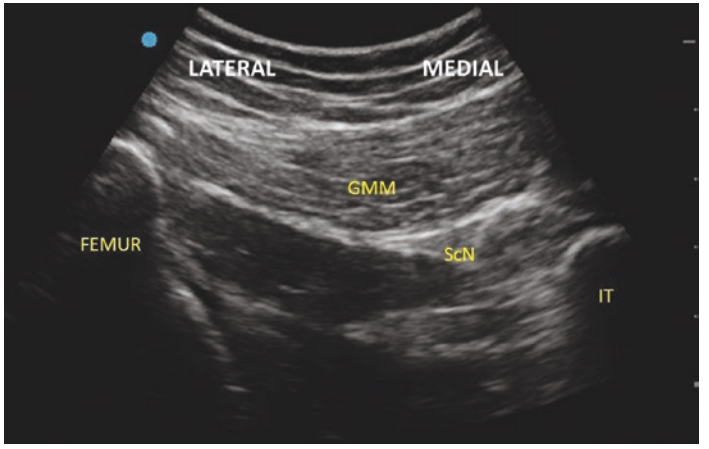

Fig. 4 Sciatic nerve (transgluteal approach) ultrasound. The Sciatic Nerve (ScN) is a triangular shape deep to the gluteus maximus muscle (GMM) between the femur and the ischial tuberosity (IT)

Administration of 1–2 mL of local anesthetic is injected to confirm the adequate distribution. Administration of 10–15 mL of local anesthetic, 5 mL at a time after confirming negative aspiration [2].

(c) **Subgluteal Approach to the Sciatic Nerve** (Fig. 5)**:** The subgluteal approach to the sciatic nerve is performed at the bedside with the patient in the lateral decubitus position. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a timeout, the curvilinear ultrasound transducer is placed transversely over the posterior thigh at the gluteal crease. The femur is located, and the probe is slide proximally to the level of the greater trochanter. The probe is then slide medially from the greater trochanter to visualize the sciatic nerve deep to the gluteus maximus. A block needle is inserted under the ultrasound probe in-plane in a lateral-to-medial direction towards the sciatic nerve. If nerve stimulation is also

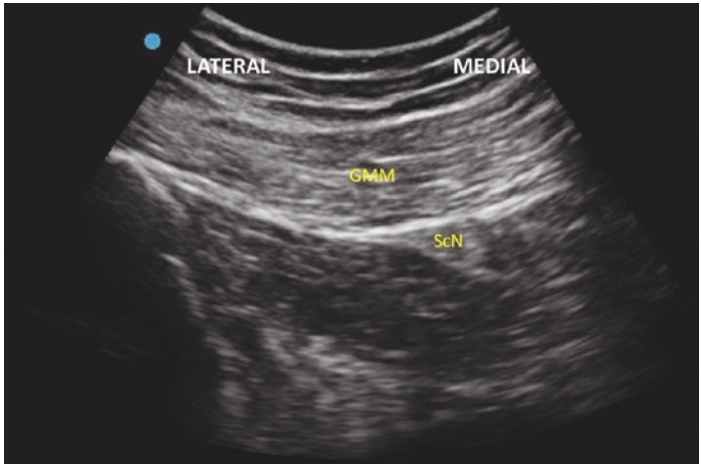

Fig. 5 Sciatic nerve (subgluteal approach) ultrasound. The Sciatic Nerve (ScN) is positioned deep to the gluteus maximus muscle (GMM)

being used, the contact of the needle tip with the sciatic nerve will trigger a motor response. Administration of 1–2 mL of local anesthetic is injected to confirm the adequate distribution. Administration of 10–15 mL of local anesthetic, 5 mL at a time after confirming negative aspiration [2].

Case Stem 2 Femoral Neck Fracture

An 80-year-old female presents to the emergency department status post fall with a femoral neck fracture. She is scheduled for ORIF of the left femoral neck. A surgical incision will be made over the lateral proximal leg and hip.

Questions/Answers

13. What nerve provides sensation to the proximal lateral thigh?

    The lateral femoral cutaneous nerve provides sensation to the anterolateral thigh. The lateral femoral cutaneous nerve emerges from the lateral border of the psoas major muscle and courses inferior and laterally towards the anterior superior iliac spine. A lateral femoral cutaneous nerve block is used for analgesia to the lateral thigh and knee [4].

14. How is a lateral femoral cutaneous nerve block performed?

    A lateral femoral cutaneous nerve block is performed at the bedside with the patient in the supine position with the bed flat and bilateral lower extremities extended. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a timeout, the high-frequency linear ultrasound transducer is placed inferior to the anterior superior iliac spine at the lateral edge of the sartorius muscle. The lateral femoral cutaneous nerve can often be visualized between the tensor fasciae latae muscle and the sartorius muscle (Fig. 6). The block needle is inserted in-plane in a lateral-to-medial direction towards the lateral femoral cutaneous nerve. Visualizing the local anesthetic in the plane between the tensor fasciae latae muscle and the sartorius muscle confirms correct placement of the nee-

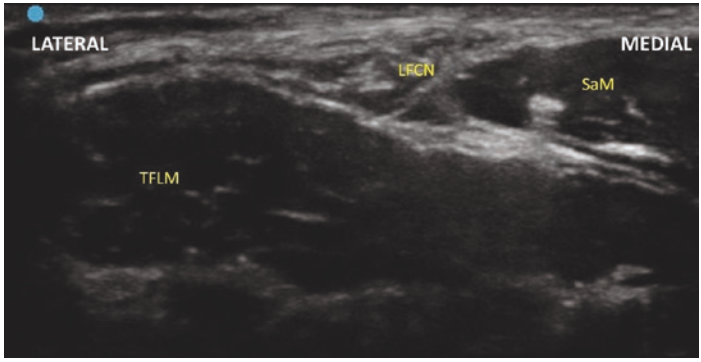

Fig. 6 Lateral femoral cutaneous nerve ultrasound. The Lateral Femoral Cutaneous Nerve (LFCN) is located between the tensor fasciae latae muscle (TFLM) and the sartorius muscle (SaM)

dle. Alternatively, the lateral femoral cutaneous nerve may be blocked with a subinguinal technique in which the nerve may not be clearly visualized. Ultrasound is placed over the anterior superior iliac spine and anterior inferior iliac spine. Approximately 5 mL of local anesthetic is injected under the inguinal ligament [4].

15. What other nerve block could be offered to this patient for improved analgesia?

    An alternative nerve block that could be offered to a patient with a femoral neck fracture is a fascia iliaca block. The fascia iliaca block is a useful block for analgesia of the lower extremity. The use of a fascia iliaca block for hip fractures can result in lower pain scores and a reduction in opioid consumption. The fascia iliaca compartment is a potential space formed by the fascia iliaca and the psoas and iliacus muscles. It is thought that a large enough local anesthetic volume under the fascia iliaca will result in blockade of branches from the lumbar plexus [7].

16. What is the distribution of a fascia iliaca block?

    The potential distribution of a fascia iliaca block include the femoral nerve and the lateral femoral cutaneous nerve since both nerves are located deep to the fascia iliaca. It is

also thought that a large enough local anesthetic volume under the fascia iliaca will result in blockade of multiple branches from the lumbar plexus [7].

(a) **Sensory Innervation:** The sensory distribution of a femoral nerve block is the anterior and medial thigh extending down to and including the knee, a strip of skin overlying the medial leg and foot. The lateral femoral cutaneous nerve provides sensation to the anterolateral thigh.
(b) **Motor Innervation:** The major muscles innervated by the femoral nerve include the muscles of the anterior compartment. The anterior compartment muscles include the quadriceps femoris, sartorius, and pectineus. The muscles of the anterior compartment primarily act to extend the leg at the knee joint [2].

17. How is a fascia iliaca block performed?

The fascia iliaca block can be performed from a suprainguinal approach or an infrainguinal approach.

(a) **Suprainguinal (**Fig. 7**):** A suprainguinal fascia iliaca block is performed under ultrasound guidance. The block is performed at the bedside with the patient in the supine position and the table flat with the patient's legs extended. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a timeout, the high-frequency linear ultrasound transducer is placed over the inguinal ligament in a parasagittal orientation. The iliacus muscle is identified superficial to the ilium. An 80–100 mm block needle is inserted under the ultrasound probe. The needle tip is placed between the fascia iliaca and the iliacus muscle. Administration of 30–40 mL of local anesthetic (LA), 5 mL at a time after confirming negative aspiration. Appropriate spread of local anesthetic occurs as the iliacus muscle is hydrodissected away from the fascia iliaca [7, 8].

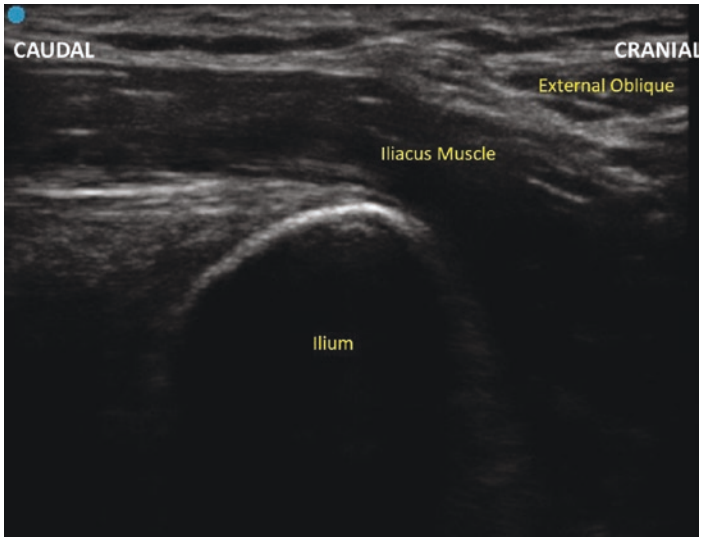

Fig. 7 Suprainguinal fascia iliaca ultrasound

(b) **Infrainguinal:** Anatomic orientation begins similarly to that of a femoral nerve block. Once the femoral nerve, artery, and fascia iliaca are identified, the probe is moved laterally until the sartorius muscle is located. After a time-out, the need tip is placed under the fascia iliaca at the lateral third of the line connecting the anterior superior iliac spine to the pubic tubercle. 20–40 mL of LA is injected and spreads laterally underneath the sartorius muscle and medially toward the femoral nerve [2].

18. If this patient received low molecular weight heparin (LMWH) for DVT prophylaxis, how long would you wait prior to performing a peripheral nerve block?

No definitive recommendation exists concerning anticoagulation management in patients receiving peripheral nerve blocks. The *American Society of Regional Anesthesia and Pain Medicine* guidelines recommend following neuraxial guidelines for deep plexus or deep peripheral blocks. The decision to perform other peripheral nerve blocks in antico-

agulated patients depends upon the compressibility of the site and potential consequences of bleeding if it were to occur [9].

Case Stem 3 Hip Arthroplasty

A 65-year-old female presents for a right total hip arthroplasty. You would like to minimize her intraoperative and postoperative opioid requirements.

Questions/Answers

19. If this patient refused neuraxial anesthesia, what regional blocks could be utilized for analgesia for a right total hip arthroplasty?

    Regional blocks that can be utilized for a right total hip arthroplasty include a lumbar plexus block, a fascia iliaca nerve block, a femoral nerve block, or a pericapsular nerve block group (PENG) which will not be discussed in this chapter.

    (a) **Lumbar Plexus Block:** The lumbar plexus block is useful in providing analgesia for a total hip arthroplasty. The use of a lumbar plexus block can result in lower pain scores and a reduction in opioid consumption [10]. The major branches of the lumbar plexus include the femoral, lateral femoral cutaneous, and the obturator nerves. The femoral nerve supplies motor fibers to the quadriceps muscles, sensory to the anteromedial thigh and medial aspect of the leg below the knee and foot. The obturator nerve supplies motor branches to the adductor muscles of the hip and sensory to the medial thigh and knee joint. The lateral femoral cutaneous nerve provides sensory to the anterolateral thigh. The lumbar plexus block is the only technique that consistently blocks the femoral, lateral femoral cutaneous, and the obturator nerves.

    (b) **Fascia Iliaca Block:** The fascia iliaca nerve block is a useful block for providing analgesia for a total hip arthroplasty. The use of a fascia iliaca block for a total hip arthroplasty can result in lower pain scores and a reduction in opioid consumption. The fascia iliaca compart-

ment is a potential spaced formed by the iliac fascia and the psoas and iliacus muscles. It is thought that a large enough local anesthetic volume under the fascia iliaca will result in blockade of branches from the lumbar plexus [7].

(c) **Femoral Nerve Block:** A femoral nerve block could be offered to a patient having a total hip arthroplasty. A femoral nerve block is utilized to provide cutaneous and osteotome analgesia to the hip, thigh, and knee via nociceptive blockade with local anesthetic medications. The femoral nerve originates from the posterior division of the ventral rami of L2-L4 nerve roots and is the largest terminal branch of the lumbar plexus. The femoral nerve runs lateral to the psoas muscle in the pelvis and then passes underneath the inguinal ligament to enter the anterior compartment of the thigh where it quickly branches to provide innervation to the muscles, bones, joints, and skin in the anterior thigh [1].

20. Where is the lumbar plexus located?

The lumbar plexus is located in the fascial plane within the posterior one third of the psoas muscle. The lumbar plexus is formed by the anterior rami of the first four lumbar roots with variable contributions from T12 and L5 anterior rami [11]. The nerve roots emerge from the vertebral foramen and run along the posterior portion of the psoas muscle.

21. The lumbar plexus is comprised of what nerves?

The lumbar plexus is formed by the anterior rami of the first four lumbar roots with variable contributions from T12 and L5 anterior rami. The major branches of the lumbar plexus include the femoral, lateral femoral cutaneous, and the obturator nerves [11].

22. What is the motor and sensory distribution of a lumbar plexus block?

The motor and sensory distribution of the lumbar plexus include primarily contributions from the femoral nerve, the obturator nerve, and the lateral femoral cutaneous nerve.

Additionally, the iliohypogastric, ilioinguinal, and genitofemoral nerves are also branches of the lumbar plexus [12].

(a) **Sensory Innervation:** The femoral nerve provides sensory to the anteromedial thigh and medial aspect of the leg below the knee and foot. The obturator nerve provides sensory to the medial thigh and knee joint. The lateral femoral cutaneous nerve provides sensory to the anterolateral thigh.

(b) **Motor Innervation:** The femoral nerve provides motor fibers to the quadriceps muscles. The obturator nerve supplies motor branches to the adductor muscles of the hip.

23. How is a lumbar plexus block performed?

Blocking the lumbar plexus can be completed by landmark based, nerve stimulation-guided, ultrasound-guided, or a combination of techniques. A lumbar plexus block is performed at the bedside with the patient in the lateral decubitus position with the operative side up. The ultrasound machine should be positioned on the opposite side of the bed facing the operator. Standard monitors are applied, and equipment is readily available near the operator. After a timeout, the curvilinear ultrasound transducer is used in a transverse position to identify the L4 transverse process, psoas muscle, and the lumbar plexus within the psoas muscle (Fig. 8). The needle trajectory is in-plane and lateral to the probe, aiming medially. Quadriceps contraction is the twitch that should be obtained. After identification of the correct anatomic location and negative aspiration, injection of a total of 20–25 mL of local anesthetic. This highly vascularized region poses increased risk of intravascular injection. In addition, injection under high pressure (>20 psi) may result in bilateral sensory and motor blockade as well as possible neuraxial blockade. Variation exists in the approach to ultrasound imaging. The transverse approach is shown in Fig. 8 [2, 13, 14].

24. If the patient in this scenario was on Eliquis, how long would you recommend she hold her anticoagulation prior to a lumbar plexus block?

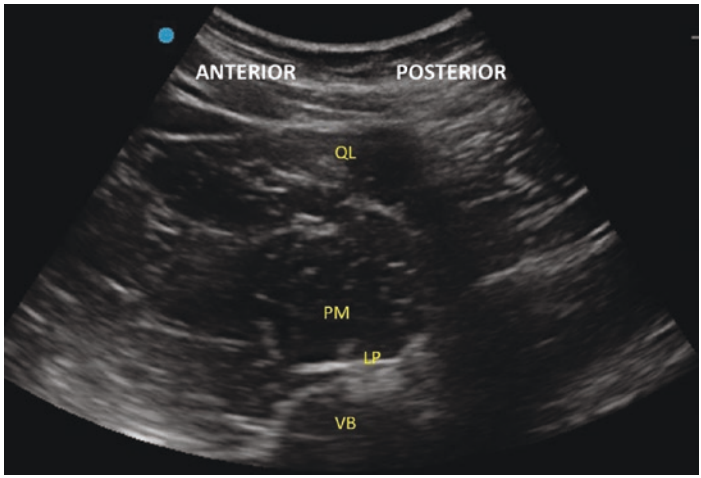

Fig. 8 Lumbar plexus ultrasound. The lumbar plexus (LP) is located within the psoas muscle (PM). VB, vertebral body; QL, quadratus lumborum muscle

Table 2 Anticoagulation/antiplatelet guidelines for neuraxial procedures

Unfractionated heparin (prophylaxis)	4–6 h
Unfractionated heparin (treatment)	4–6 h if intravenous
	8–12 h if subcutaneous
Low molecular weight heparin (prophylaxis)	12 h
Low molecular weight heparin (treatment)	24 h
Rivaroxaban (prophylaxis)	22–26 h
Apixaban (prophylaxis)	26–30 h
Coumarins	INR $\leq$ 1.4
Acetylsalicylic acid	None
Clopidogrel	7 days
NSAIDs	None

Prior to a lumbar plexus block it would be recommended that the patient's Eliquis be held 72 h. For patients undergoing a lumbar plexus block, it is recommended to follow guidelines regarding neuraxial techniques about anticoagulation status (Table 2).

1 Summary

Common surgical procedures of pelvis, hip and upper leg [15]	
Procedure	Incision location
ORIF of the pelvis or acetabulum	Anterior approach: Pfannenstiel's, ilioinguinal (anterior)
	Posterior approach: Curving along the iliac crest
Closed reduction and external fixation of the pelvis	Percutaneously or small incisions along the iliac crest
ORIF of acetabulum fractures	Anterior: Ilioinguinal
	Lateral: Extended iliofemoral
	Posterior: Kocher-Langenbeck
Osteotomy and bone graft augmentation of the pelvis	Anterior: Ilioinguinal or iliofemoral and Smith-Peterson
Arthrodesis of the sacroiliac joint	Anterior: Lateral portion of ilioinguinal
	Posterior: Straight vertical incision just lateral to the PSIS
Arthroplasty of the hip	Anterior, lateral, or posterolateral over the hip joint
Arthrodesis of the hip	Anterior or lateral thigh
ORIF of proximal femoral fractures (femoral neck, intertrochanteric, subtrochanteric)	Proximal lateral thigh
ORIF of distal femur fractures	Anterior knee, lateral or medial thigh
ORIF of the femoral shaft with plate	Lateral thigh +/− iliac crest incision
Intramedullary nailing of femoral shaft	Proximal lateral thigh or anterior knee

Common Pitfalls and Clinical Pearls

Regional anesthesia for hip and upper leg procedures [2]			
Block	Distribution	Local anesthetic	Pearls and pitfalls
Lumbar plexus	Femoral n. Obturator n. Lateral femoral cutaneous n. Iliohypogastric n. Ilioinguinal n. genitofemoral n.	20–25 mL LA, choice of medication depends on indication for block (analgesia vs. anesthesia)	Generally considered an advanced block. Use of ultrasound guidance may decrease number of needle passes. Highly vascularized region increases risk of intravascular injection or hematoma. Coagulopathy and thromboprophylaxis are relative contraindications. High-pressure injection may result in inadvertent neuraxial block.
Femoral nerve	Anterior thigh, including knee. Variable strip of skin on medial leg and foot Quadriceps muscle	10–15 mL LA	Pressure to the transducer compresses veins, making the femoral vein more difficult to identify. Excessive transducer may also compress tissues, inhibiting the adequate spread of the local anesthetic. Circumferential spread of local around the femoral n. is not required for this block, a pool of local either anterior or posterolateral is adequate.
Fascia Iliaca	Femoral n. Lateral femoral cutaneous n.	20–40 mL LA	Must have adequate spread for success in blocking the lateral femoral cutaneous n. and the femoral n. Success can be predicted by visualization of the spread of LA underneath the sartorius muscle laterally. Alternative to a lumbar plexus or femoral n. block.

Regional anesthesia for hip and upper leg procedures [2]			
Block	Distribution	Local anesthetic	Pearls and pitfalls
Obturator	Variable sensation to medial thigh Adductor muscles	5–10 mL LA between fascial planes or 5–7 mL surrounding each branch	Sensation provided by obturator nerve is highly variable. Only way to confirm obturator nerve block is through demonstration of adductor muscle weakness.
Sciatic	Posterior knee/thigh Hamstring muscles Lower limb (except medial leg/foot)	10–20 mL LA	Multiple approaches. Anterior approach is useful in patient who cannot be positioned laterally. Most commonly utilized for knee or lower leg and foot surgery.

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Acute Pain Management Protocol for Distal Femur, Proximal Tibia/ Fibula and Knee Procedures

Janet Hong and Yan H. Lai

Case Stem

A 76-year-old female with a BMI of 34, ASA 2 patient presents for a revision of right total knee arthroplasty (TKA). You are an attending anesthesiologist in an academic hospital meeting the patient in the preoperative holding area. The patient reports a past medical history of hypertension, hyperlipidemia, and osteoarthritis for which she takes losartan-hydrochlorothiazide, amlodipine, atorvastatin, and ibuprofen as needed. She had an elective right TKA 8 years ago for treatment of primary osteoarthritis (OA) and has recurrence of right knee pain due to failed knee prosthesis and presents for this procedure. On physical exam, she has a mallampati II airway, thyromental distance >6 cm, normal neck circumference and good neck range-of-motion, lungs are clear bilaterally with normal heart sounds. Preoperative electrocardiogram reveals normal sinus rhythm with a HR of 79 bpm.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_23

Key Question 1: What intraoperative anesthetic techniques can be offered to this patient?

Anesthetic options for TKA include general anesthesia (GA) or neuraxial anesthesia. A systematic review in 2016 comparing neuraxial anesthesia versus GA for total hip and knee arthroplasty revealed that neuraxial anesthesia significantly reduced length of stay but had limited quantitative evidence that perioperative outcomes were improved compared to GA [1]. However, several retrospective studies revealed that GA was associated with an increased rate of unplanned readmission, failure to discharge to home, blood transfusion, deep surgical site infection, and extended length of stay compared to neuraxial anesthesia [2].

In comparison to blocking both lower extremities with neuraxial anesthesia, regional anesthesia (RA) via plexus (lumbar and sacral) and nerve blocks can selectively block the operative limb. However, as the lower extremity nerve supply divides into the anterior and posterior compartments, adequate surgical anesthesia requires more than one block. Furthermore, full motor blockade is essential for TKA and assessment of the passive range of motion of the prosthesis and peripheral RA does not reliably provide surgical anesthesia.

Case

When you ask the patient about her anesthetic experience from her previous right TKA, she remembers terrible pain after that surgery requiring intravenous pain medications that made her nauseous. She struggled to participate in physical therapy (PT) and stayed longer in the hospital. She voices concern and asks if there's anything that can be done to improve her experience this time.

Key Question 2: What perioperative anesthetic techniques can be implemented to optimize patient outcomes (i.e., patient functional status, patient safety, and patient satisfaction)?

TKA

- Shown to improve functional status and quality of life [3].
- However, also known to cause moderate to severe pain in most patients and is considered one of the most painful orthopedic surgeries [4].

- Strongly linked to increased risk for chronic opioid use after surgery [5].

Interventions (see Table 1)

- Multimodal analgesia—pain management using pharmacologic and nonpharmacologic techniques
- Limiting parenteral opioid use to mitigate adverse effects (e.g., nausea, vomiting, ileus, pruritis, sedation, urinary retention)
- Facilitate rehabilitation and hospital discharge

Case

After thorough discussion of the anesthetic options, the patient agrees and consents to neuraxial and RA for the surgery. As you leave the holding area, the surgeon remarks that the patient has a complicated pathology and that the revision may take several hours longer than a simple TKA.

Table 1 Perioperative multimodal analgesia options [6]

Preoperative	Acetaminophen
	Oxycodone immediate or sustained release
	Celecoxib
	Gabapentin or Pregabalin (can cause over sedation in elderly)
Intraoperative	Intrathecal opioids
	Epidural catheter
	Peripheral nerve block or catheter
	Periarticular local anesthesia infiltration
Postoperative	Acetaminophen
	Oxycodone immediate release
	Ketorolac
	Tramadol
	Ketamine
	Lidocaine
	Dexamethasone
	Clonidine
	Peripheral nerve block or catheter

Key Question 3: What are the variations in surgical approach to knee surgery? What is the necessary anatomical coverage and duration of anesthesia?

Proper selection of anesthetic technique requires a broad knowledge of anatomy and the type of planned surgical procedure. In addition, discussion with the surgeon about unique considerations and special applications such as tourniquet placement, appropriate prosthesis, special instruments, bone grafting, and projected surgical duration can be valuable.

For the distal femur, knee joint, proximal tibia and fibula, there is a mixture of surgical procedures with variations in positioning, incision sites and surgical duration (Table 2) [7]. These procedures entail supine positioning, an incision anteriorly or anteromedially over the patella for arthrotomy of the knee joint, exposure of the femur, patella, and tibia, excision of cartilage and minimal bone with a saw, and cementation of metallic, plastic, and/or ceramic components to replace the knee joint surfaces [7].

- Knee arthroplasty: one or more compartments of the knee can be replaced (i.e., medial/lateral unicompartmental knee arthroplasty vs. TKA)
- Revision: one or more components of the old joint are removed and new components are placed
- Resection or excision: infection of the prosthesis (removed and not replaced)

Anesthesia from T12 to S2 (T8 if a tourniquet is used) is appropriate for knee procedures with full motor blockade when placement of joint prosthesis and assessment of range of motion or fixation of the patella is necessary [7].

- Spinal anesthesia: procedures of known duration in the lower extremities, perineum, pelvic girdle, or lower abdomen.
- Epidural anesthesia: same coverage with added benefit of intermittent or continuous catheter-based LA delivery for more prolonged anesthesia or for postoperative pain control; however, can impair early mobility or PT.

Table 2 Distal femur, knee joint, proximal tibia and fibula procedures [7]

Procedure	Position	Incision	Duration
Open Reduction and Internal Fixation (ORIF) of Distal Femur Fractures	Supine or lateral decubitus	Lateral thigh along length of femur ± iliac crest incision	3 h
Closed Reduction and External Fixation of Femur	Supine or lateral decubitus	Percutaneously or small incisions	1 h
Arthroplasty of the Knee	Supine	Anterior or anteromedial over patella	2–4 h
Arthrodesis of the knee	Supine	Anterior midline over knee	3–4 h
Arthroscopy of the Knee	Supine	3–4.5 cm portal incisions	0.5–3 h
Knee Arthrotomy	Supine	Medial or lateral parapatellar	1–2 h
Repair or Reconstruction of Knee Ligaments	Supine	Over collateral ligament, anterior and lateral ACL or medial PCL	2 h
Open Reduction and Internal Fixation (ORIF) of Patellar Fractures	Supine	Anterior over patella	1.5–2 h
Patellar Realignment	Supine	Anteromedial or anterolateral to knee	1–1.5 h
Open Reduction and Internal Fixation (ORIF) of the Tibial Plateau and/or Fibula Fracture	Supine	Lateral to knee, usually; medial, rarely	2.5–3 h
External Fixation of Tibia and/or Fibula	Supine	Stab wounds. Small-pin fixator may require metaphyseal incision for osteotomy	0.5–1 h

- Combined spinal epidural block (CSE): an initial spinal injection followed by epidural catheter placement.
- GA: deeper plane of anesthesia or opioids may be required to treat tourniquet pain that can arise after 60–75 min of tourniquet time, which is generally prevented by spinal anesthesia.

Case

The patient receives a CSE in the OR and adequate anesthesia is confirmed. Intraoperative course is prolonged due to moderate difficulty replacing the knee prosthesis but otherwise uncomplicated. The surgeon discusses the patient's difficult postoperative course previously due to urinary retention, poorly controlled pain, and delayed PT that might have led to early prosthesis failure. While wanting optimal postoperative pain control, he inquires whether there are more motor sparing regional anesthetic techniques to expedite removal of the epidural catheter.

Key Question 4: What considerations should be made when selecting single-injection peripheral nerve block (SSPNB) or continuous peripheral nerve block (CPNB) for RA?

PNB can be placed as a single injection of LA or CPNB for analgesia after TKA. Both of these modalities have proven to decrease perioperative complications, conserve hospital resources, reduce hospital length-of-stay, and enhance patient satisfaction [8, 9].

- SSPNB: less invasive, avoids the need for an infusion or elastomeric pump that may restrict mobility, and can reduce cost and utilization of resources. However, single-injection of LA limits its duration of analgesia and rebound pain can occur as the nerve block subsides.
- CPNB: placement of a percutaneous catheter adjacent to a peripheral nerve (perineural catheters) with administration of LA as repeated bolus doses, a basal infusion, or a combination of the two methods (programmed intermittent boluses).
  - Extends analgesia beyond what is achievable with a SSPNB [10].
  - Allows personalization or tailoring of LA based on a specific need (aggressive PT, complex surgery, chronic pain or opioid use, or history of polysubstance abuse) [11].
  - Complications: failed block, LA toxicity, infection, nerve injury, hematoma formation, and catheter dislodgement or retention [9].

Studies comparing the efficacy of SSPNB versus CPNB in TKA patients have been inconclusive in terms of lowering pain scores and decreasing opioid requirements, with a primary focus on femoral nerve blocks [10, 12].

Lastly, contraindications to RA and PNB should be confirmed:

- Absolute: LA allergy and patient refusal.
- Relative: infection, anticoagulation or bleeding disorders, preexisting neurological deficits, and inability to cooperate [13].

Case

After the procedure is finished, the epidural catheter was pulled out accidentally during transfer to the PACU. The PACU resident, who has been reading about different lower extremity blocks, asks which is most appropriate for this patient and why.

Key Question 5: What are the current best practices and recommendations for RA in TKA? What PNB are available for distal femur, knee joint, proximal tibia and fibula procedures?

Historically, epidural analgesia or lumbar-sacral plexus blocks were utilized to control pain after TKA. These modalities are effective analgesics but they significantly reduce postoperative mobility and can impair patient outcomes (prosthesis survival, thromboembolic, and cardiopulmonary complications, etc.). PNB has proven to provide equivalent analgesia, fewer adverse effects, and improved outcomes for TKA and has emerged as best practice [9, 14]. Femoral nerve blocks (FNB) and sciatic nerve blocks (SNB) were widely employed, however, concerns for delays in mobility, ambulation, and PT [15], increased risk of fall [16], and delays in the diagnosis of perioperative common peroneal nerve injury [17] arose over the years. Contemporary practice has shifted away from these in favor of more distal, selective, and motor sparing PNB such as adductor canal block (ACB) and infiltration between popliteal artery and capsule of the knee block (IPACK) for TKA patients.

ACB targets the superficial femoral nerve distally and has motor sparing benefits to the quadricep muscles [18]. Studies

have shown similar analgesia and earlier postoperative ambulation compared to FNB within an established multimodal analgesia clinical pathway [18].

The IPACK targets the terminal branches of the sciatic nerve behind the knee capsule and has been proposed as an alternative to the SNB for controlling posterior knee pain without significant motor block to branches of sciatic nerve [19, 20]. Studies have found supplementation of ACB with IPACK decreased posterior knee pain and improved functional recovery [19, 20].

Local infiltration analgesia (LIA) is an alternative technique performed by surgeons directly on the surgical field when the knee capsule is exposed. It entails injecting LA with adjuvants (epinephrine, morphine, steroids, NSAIDS, etc.) into the tissues surrounding the knee [21]. Studies combining LIA with PNB for TKA patients have consistently revealed better outcomes [22] while studies isolating LIA to PNB in a head-to-head comparison have been conflicting [21]. As such, LIA can be a useful technique, especially in a setting where RA skills or equipment is not readily available.

FNB technique
• Targets the anterior muscles of thigh (sartorius and quadratus group), adductor of thigh (pectineus and iliopsoas muscle), skin over anteromedial surface of thigh and the medial surface of the leg and foot.
• Supine position with linear transducer placed at the inguinal crease to visualize the femoral nerve (lateral to the femoral artery).
• In-plane (needle approach lateral to medial) or out-of-plane approaches (better for catheter placement).
• Inject 20–30 mL of LA.
SNB technique
• Targets posterior aspect of the knee, hamstring muscles, and the lower limb below the knee except for the skin on the medial leg and foot.
• Anterior approach: supine with the leg externally rotated and a low frequency curvilinear transducer applied transversely over the medial thigh at the level of the lesser trochanter. The femur and femoral vessels are identified along with the sciatic nerve in the fascial plane between the adductors and gluteus muscles, posterior to the femur. Use a long 10 cm needle to reach the sciatic nerve in-plane or out-of-plane at a depth of 6–8 cm and inject 15–20 mL of LA while observing appropriate spread around the sciatic nerve.

• Posterior: patient can be positioned lateral, oblique or prone with the leg flexed at the hip and knee. A low frequency curvilinear transducer is placed transversely on the posterior buttock between the ischial tuberosity and greater trochanter. Gluteal muscles can be identified superficially with a fascial layer along the deep border, the sciatic nerve is located deep to this fascial layer, superficial to the quadratus femoris muscle at a depth of 3–6 cm. A long 10 cm needle with 15–20 mL of LA is used.
ACB (saphenous nerve block above the knee) technique
• Supine with the thigh abducted and externally rotated and linear transducer is placed transversely over the anteromedial thigh at the mid-thigh level to visualize the femoral artery underneath the sartorius muscle.
• A 5 cm needle is inserted in-plane from a lateral-to-medial orientation toward the femoral artery at a depth of 2–4 cm. Once the needle tip is adjacent to the femoral artery in the adductor canal and underneath the sartorius muscle, 10–20 mL of LA can be injected.
• ACB also blocks the nerve to the vastus medialis muscle and can lead to partial quadriceps weakness.
IPACK (infiltration between popliteal artery and capsule of the knee) technique
• Targets small sensory articular branches of the tibial component of the sciatic nerve in the posterior knee.
• Supine with low-frequency curvilinear transducer placed at the medial knee joint to identify the femoral condyle and scanned proximally to identify the popliteal artery.
• A 5 cm needle is inserted in-plane from a medial-to-lateral direction and advanced parallel to the femoral condyle until the needle tip is visualized between the femoral condyle and popliteal artery. 20 mL of LA can be injected.

Case

The continuous ACB is placed uneventfully in the PACU. You follow up with the patient the next day and the patient reports pain has been well controlled but she is experiencing some weakness of her right leg and is hesitant to try physical therapy.

Key Question 6: What are potential complications of peripheral nerve blockade in distal femur, proximal tibia and fibula, and knee joint procedures?

Intravascular injury and subsequent hemorrhage or hematoma can be a potential complication. As such, patients should be carefully evaluated for coagulopathy peri-procedurally, proper ultrasound

guidance should be employed, and PNB in deep and noncompressible areas should be performed with caution.

Nerve injury is an extremely rare but catastrophic complication of RA. Risk factors: preexisting neurologic disease, diabetes, smoker, male gender, BMI extremes, and elderly. Any preoperative neurologic deficits should be considered and well documented.

Compartment syndrome is a rare occurrence after lower extremity surgery, but a delay in diagnosis or treatment can lead to poor outcomes. Other surgical etiologies should be ruled out. Risk factors include prolonged tourniquet time, surgical trauma, improper patient positioning, tightly applied casts or surgical dressings, and prolonged hospitalization [23].

Combined complications where a hematoma or compartment syndrome causing a neurologic disturbance is also possible. If a hematoma is suspected, urgent imaging should be pursued, any coagulopathy should be corrected, and surgical evacuation is advised if severe. A timely and open discussion with the surgical team for appropriate management is desirable.

Unexpected spread of LA can also account for significant motor weakness:

- ACB spread to femoral triangle and popliteal fossa [24, 25].
- Continuous ACB spread to the posterior compartment of the thigh to block the sciatic nerve [26].

1 Summary

- A clinical pathway consisting of a balanced and focused platform of multimodal oral and intravenous analgesia, RA, and LIA can optimize perioperative TKA outcomes.
- Understanding the anatomy and variations in surgical approach to the distal femur, knee joint, proximal tibia and fibula helps guide selection of anesthetic techniques.
- Selection of SSPNB or CPNB entails consideration of surgical complexity, patient characteristics (chronic pain or polysubstance abuse), and available expertise and resources.

- RA for TKA has evolved to more distal and selective peripheral nerve blocks such as ACB and IPACK block to allow for earlier postoperative ambulation.
- In the presence of postoperative neurologic dysfunction, evaluate for possible bleeding, compartment syndrome, nerve injury, prolonged LA effect, or blockade of other nerves.

Common Pitfalls

- Failure to provide adequate patient education and reliable multidisciplinary care of patients receiving RA after lower extremity surgery can lead to adverse outcomes such as falls, delayed ambulation, and prolonged hospital stay.
- Failure to consider patient and surgical risk factors for nerve injury, and understand peripheral nerve anatomy and path of local anesthetic distribution can lead to improper workup and management of neurologic complications.

Clinical Pearls

- Our institution uses the protocol below for knee replacement surgery:

Medications or Procedure	Total knee replacement	Partial knee/ unicondylar knee replacement	Knee revision
Acetaminophen	1300 mg extended-release PO preoperatively		
Celecoxib	400 mg PO preoperatively		
Oxycodone	10 mg extended-release PO preoperatively		
Primary anesthetic	Spinal		Spinal or CSE
Tranexamic acid	10 mg/kg IV on induction and at procedure finish		
Steroids	Dexamethasone 0.1 mg/kg		
LIA Joint infiltration	Ropivacaine 300 mg		
	Morphine 10 mg		
	Ketorolac 30 mg		
	Epinephrine 600 µg		
Peripheral nerve block	ACB: single-shot or continuous (Bupivacaine 0.1% 8–12 mL/h with demand 3–5 mL Q 20 min). Consider IPACK block		Continuous ACB (Bupivacaine 0.1% 8–12 mL/h with demand 3–5 mL Q 20 min)

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Acute Pain Management Protocol for Distal Tibia/ Fibula, Ankle and Foot Procedures

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1 Lower Extremity Nerve Blocks

1.1 Introduction

Regional blockade of the lower extremities can be used as an opioid sparing adjunct or sole analgesic anesthetic options for some of the most frequently performed operations in the United States (US). For example, over 700,000 knee replacements and 180,000 other lower extremity operations are performed each year in the US [1]. In addition, both of these operation types rank among the top 10 fastest growing procedures performed in the US each year [1]. Coupled with this increased surgical demand, and in considering a national push for opioid-sparing anesthetic approaches to lower extremity surgeries, multimodal enhanced recovery strategies and regional anesthetic techniques are increasingly important in today's

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_24

clinical practice. To illustrate this point, when regional blocks are used in conjunction with an aggressive multimodal analgesia technique, patients have significantly reduced hospital stays, mobilize earlier, and utilize decreased opioid requirements and subsequently experience fewer opioid related side effects compared to patients who did not receive regional anesthesia [2]. Furthermore, regional techniques such as the femoral nerve block can significantly reduce patient's perioperative pain scores and total opioid requirements by as much as 38 mg at 48 h following knee replacements [3]. As the population ages and healthcare costs continue to increase, lower extremity nerve blocks will become a key part of treating and optimizing these patients peri-operatively.

This chapter will focus on practical applications of regional nerve blocks by utilizing a case-based approach. Each section will consist of a case presentation followed by a brief set of clinical questions related to the case that bring into focus the important role regional anesthesia can play within the scenario. A summary is then provided of high-yield information related to the lower extremity block being presented, as well as common mistakes and challenges encountered when first performing the block. Key ultrasound images are also provided for each block.

High-yield regional neve blocks for surgeries of the lower extremity:

1. Femoral nerve block
2. Adductor canal block
3. Popliteal sciatic nerve block
4. Ankle blocks

1.1.1 Femoral Nerve Block

Scenario

R.W. is a 68-year-old female with past medical history (pmh) hypertension (htn), hyperlipidemia (hld), and bilateral (b/l) hallux valgus (HV) foot deformities. She previously had a left HV deformity repair under general anesthesia (GA) at outside hospital and suffered from post-op nausea and vomiting (PONV) and required large amounts of narcotics and antiemetics post-op to control pain and PONV, respectively, and was generally dissatisfied with her

care. She is otherwise active and has been scheduled for outpatient same-day surgery.

Questions (q) and Answers (a)

1. How would you tailor this patient's peri-operative anesthetic plan given her prior PONV and difficulty in pain control?
2. What regional block(s) could be employed to aid in peri-operative pain control?
3. What are the benefits of a combined regional and spinal anesthetic approach for surgeries of the ankle and foot?
4. What are some disadvantages to regional anesthesia?
5. What is a femoral nerve block and what terminal nerves are targeted during this regional procedure?

2 Summary

Femoral nerve block The femoral nerve block targets the femoral nerve within the inguinal crease prior to its division into anterior and posterior femoral branches. After identifying the femoral artery in the inguinal crease, identify the hyperechoic nerve bundle lateral and adjacent to the femoral artery. With the probe in long axis view and the needle in plain from lateral to medial you should be able to appreciate a pop as the needle passes through the fascia lata and fascia iliaca (Fig. 1) Deposition of 20–40 mL of

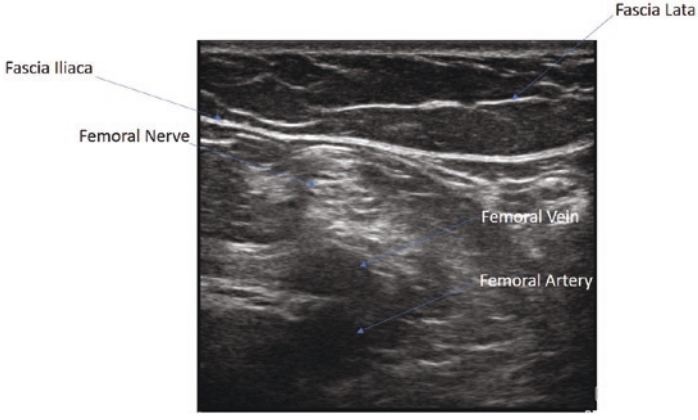

Fig. 1 Ultrasound view of the femoral nerve block

Table 1 Ultrasound-guided block positioning, anatomy, and other key information

Nerve block name	Block distribution	Associated surgeries	Patient position/materials/local anesthetic	Probe type and position
Femoral nerve block	Blockade of femoral nerve prior to anterior and posterior nerve division. Anterior and medial thigh, hip joint, knee joint, medial leg (terminal branches form the saphenous nerve), ankle joint, and foot.	Surgeries of the hip, anterior thigh or femur, knee, and surgeries involving the superficial medial lower leg. Can be combined with sciatic nerve block to provide anesthesia distal to mid-thigh.	Supine with mild leg external rotation/50 mm 22 g short-bevel echogenic needle/20–40 mL Bupivacaine or Ropivacaine 0.25–0.5%.	High frequency (6–13 MHz) linear probe in parallel to the inguinal crease.
Adductor canal block	Anesthesia of saphenous nerve as it travels distally within adductor canal will result in block of sensory fibers to anteromedial knee and medial lower leg, foot, and ankle sensory block.	Surgeries of the medial knee when combined with associated knee blocks (IPACK, genicular nerve blocks, etc.) and lower leg, foot, and ankle when combined with the popliteal-sciatic nerve block.	Supine with mild leg flexion of knee with external rotation of leg/50–100 mm 22–17 g short-bevel echogenic needle/20–40 mL Bupivacaine or Ropivacaine 0.25–0.5%.	High frequency (6–13 MHz) or mid- (5–10 MHz) linear probe in transverse position over anteromedial mid-thigh.
Popliteal sciatic nerve block	Anesthesia of sciatic nerve (and terminal tibial and common peroneal nerves). This results in motor and sensory anesthesia of the lower leg below the knee with the exception of sensory innervation to the middle lower leg (saphenous nerve sensory input preserved during this block).	Surgeries below the knee (lower leg, ankle, foot) when combined with adductor canal block.	Supine, prone, or lateral position depending on proceduralist preference and familiarity/50–100 mm 22–17 g short-bevel echogenic needle/20–40 mL Bupivacaine or Ropivacaine 0.25–0.5%.	High frequency (6–13 MHz) or mid- (5–10 MHz) linear probe in transverse position over anteromedial mid-thigh.

Ankle blocks	Terminal branches of the lumbar and sacral plexus are targeted at the ankle to achieve sensory anesthesia of foot, while sparing motor function (blocks distal to associated muscle/tendon activators responsible for foot motor function). Five terminal branches blocked: tibial nerve, deep peroneal nerve, superficial peroneal nerve, sural nerve, and saphenous nerve. Note: One, several, or all nerves can be blocked depending on the nature of surgical procedure and anatomy of the incision/working area.	Foot surgeries, particularly ambulatory given motor sparing nature of blocks, for foot	Supine with block, pillow, or ramped blankets under calf to facilitate block access for ankle/50 mm 25–22 g short-bevel echogenic nerve stimulating needle/3–5 mL Bupivacaine or Ropivacaine 0.25–0.5% per nerve blocked.	High frequency (6–13 MHz) linear probe
Nerve block name	**Scanning placement and technique**	**Associated anatomical borders**	**Needle placement and path**	**Notes**
Femoral nerve block	With probe in line with the inguinal ligament scan medial and lateral to locate the femoral artery. Remember, within this region the ordering of structures from lateral to medial is **N**erve → **A**rtery → **V**ein → **E**mpty → **L**ymphatics (NAVEL). As such, the hyperechoic oblong shaped nerve should travel just lateral to the artery, deep to the fascia iliaca, and superficial to the iliopsoas muscle.	Superficial border-fascia iliaca, medial border-femoral artery, deep and lateral borders-iliopsoas muscle, associated structures-femoral artery.	Following anesthesia of skin 1 cm lateral to the ultrasound probe insert block needle in plane and visualize needle tip as it traverses in a lateral to medial path through the skin and fascia iliaca before popping adjacent to the femoral nerve. 1–3 cc of local anesthetic should be injected when adjacent to nerve to confirm perineural spread; Note, always aspirate prior to injection to reduce risk of intravascular injection.	Tape can be used to retract patient pannus in obese patients when access to the inguinal crease is limited by body habitus; When scanning, if 2 arteries present in view (femoral artery and profunda femoris) the probe should be moved proximally up the leg until the single femoral artery is visualized; The femoral nerve is widest and most superficial at the inguinal crease; Motor testing to confirm successful block involves active knee extension against resistance to evaluate for quadriceps motor weakness (femoral nerve); non-motor sparing block.

(continued)

Table 1 (continued)

Adductor canal block	With probe in transverse orientation over mid-thigh locate the femur and scan from lateral to medial until the sartorius muscle is located (roof of the adductor canal).	Adductor canal is a triangular tunnel formed by 3 muscles: Superficial border-sartorius muscle, medial border-adductor longus muscle, lateral border-vastus medialis muscle, associated structures-femoral artery, vein, saphenous nerve, and medial branches of medial femoral cutaneous nerve all travel distally down thigh in adductor canal.	Once sartorius muscle (hull shaped) is located in medial thigh locate pulsating femoral artery and hyperechoic saphenous nerve just lateral to artery (between sartorius and vastus medialis muscles and lateral to adductor longus). Following injection of local anesthesia 1–2 cm lateral to ultrasound probe, advance block needle in plane from lateral to medial towards hyperechoic saphenous nerve with careful attention to path of needle tip. 1–3 mL of local can be injected following negative aspiration around saphenous nerve to confirm spread around nerve and then administer incremental doses from 10 to 20 mL total within adductor canal.	Block of the saphenous nerve within the adductor canal should produce sensory anesthesia of medial lower leg, ankle, and foot, while affecting quadriceps muscle strength very minimally; However, with larger volumes can have retrograde spread up adductor canal to femoral triangle which can result in femoral nerve block.

Popliteal sciatic nerve block	With the probe in the popliteal crease in a transverse configuration identify the deeper popliteal artery and more superficial popliteal vein within the popliteal fossa (diamond shaped posterior aspect of knee formed by semimembranosus and semi-tendinosis muscles medially, biceps femoris laterally, and medial and lateral heads of gastrocnemius muscles caudally). The tibial nerve will appear as a round hyperechoic bundle superficial to the non-compressible femoral artery and lateral to tibial nerve is the hyperechoic and smaller common peroneal nerve. Glide proximally (cephalad) until the 2 nerves combine into the sciatic nerve.	In aforementioned position the sciatic nerve can be seen between laterally situated biceps femoris muscle and medially oriented semimembranosus muscles. The femur can be seen as the floor of the view and just deep to the popliteal artery and vein.	With probe in the popliteal crease in a transverse position anesthetize skin 2–3 cm laterally to transducer. In place, advance from lateral to medial until the block needle tip is adjacent to target sciatic nerve. Following negative aspiration administer 1–3 mL adjacent to sciatic nerve to confirm proper spread. Once confirmed, 5 mL incremental doses up to total volume of 20 mL can be delivered with needle tip repositioning as needed to facilitate adequate block spread.	When it is difficult to block the sciatic nerve prior to division into common peroneal and tibial nerves, or if visualization inadequate of combined sciatic nerve within the popliteal crease, individual nerve blocks can also be used at this level; Patient plantarflexion and dorsiflexion during scanning can aid in nerve visualization (during dorsiflexion common peroneal nerve becomes more superficial to probe and during plantarflexion tibial nerve becomes more superficial to probe); Given necessary compression of popliteal crease during this block, the popliteal vein is often compressed and inadequately visualized. This can result in inadvertent partial or total needle tip injection into the popliteal vein. Non-motor sparing block.
Ankle blocks	– **Tibial nerve**-with probe proximal (cephalad) to medial malleolus in transverse plane obtain view of posterior tibial artery and hyperechoic honeycomb lattice (tibial nerve) immediately posterior to tibial artery	– **Tibial nerve-**largest of the distal nerves and travels posterior to medial malleolus and enters the tarsal tunnel between digitorum longus and flexor hallucis longus muscles and just posterior to posterior tibial artery and vein within tarsal tunnel	Anesthetize skin just lateral to ultrasound probe and in plane while visualizing needle tip, place block needle just adjacent to desired ankle block nerve (see 2 prior columns for probe placement and anatomy). Following negative aspiration, inject 5 mL local anesthetic per desired nerve.	This block can be performed as a field block based on landmarks, nerve stimulator guided, or ultrasound guided depending on practitioner preference; Given superficial nature of nerves and ease of compressibility, blocks can be performed when anticoagulated if necessary.

(continued)

Table 1 (continued)

	– **Deep peroneal nerve**—with probe placed in the transverse plane obtain a view over extensor retinaculum and identify the anterior tibial artery and it's laterally adjacent deep peroneal nerve (often appears as a target with a hypoechoic core and hyperechoic rim)	– **Deep peroneal nerve—** nerve passes under extensor retinaculum at ankle between extensor digitorum longus and extensor hallucis longus muscles. The nerve can be seen laterally to the anterior tibial artery at anterior tibial surface in most individuals		
	– **Superficial peroneal nerve—**with probe placed in the transverse plane 5–10 cm proximal and just anterior to medial malleolus to locate the superficial peroneal nerve in the groove between anteriorly located extensor digitorum longus muscle and posteriorly located peroneus brevis muscle. Once identified, the probe can trace the nerve down/distal to identify distal ankle divisions for block, or block can occur more proximally as above	– **Superficial peroneal nerve**—Can be seen superficially in foot between peroneus brevis and extensor digitorum longus. The 2 cutaneous branches of this nerve travel superficial to extensor retinaculum and ultimately form sensory afferent signals from dorsal toes and feet other than between 1st and 2nd webspace (deep peroneal nerve distribution)		

	– **Sural nerve—**with the probe placed transversely just proximal and posterior to lateral malleolus locate the small saphenous vein and adjacent sural nerve located superficial to peroneus brevis fascia and achilles tendon. Slight distal scanning towards level of lateral malleolus can separate vein and nerve laterally away from achilles tendon for more optimal block plane	– **Sural nerve—**Just proximal and posterior to lateral malleolus locate the small saphenous vein and adjacent sural nerve located superficial to peroneus brevis fascia and achilles tendon		
	– **Saphenous nerve**—with lower leg in external rotation and transducer in transverse orientation over anteromedial lower leg proximal to medial malleolus identify the great saphenous vein over bony tibial shelf. Scanning proximally up tibia often improves nerve visualization next to greater saphenous vein.	– **Saphenous nerve**—In close proximity to the great saphenous vein, the saphenous nerve can be located in medial lower leg in the subcutaneous fat layer		

local anesthetic (Bupivacaine/Ropivacaine) provides anesthesia from the anterior thigh to medial and anterior knee, and extend along the medial leg to medial foot. Table 1 summarizes the block characteristics, patient positioning, supplies needed, scanning techniques, block needle trajectory, and high yield notes on this block.

Remember, anatomically the femoral triangle is bordered superiorly by the inguinal ligament, medially by the adductor longus muscle, and laterally by the medial border of the sartorius muscle. The floor of the triangle is lined medially by the pectineus and adductor longus muscles and laterally by the iliopsoas muscle. The superficial covering (roof) of the femoral triangle from superficial to deep is skin, subcutaneous tissue, superficial fascia, deep fascia (fascia lata) and fascia iliaca. As such, during a femoral nerve block at the level of the femoral triangle the needle must penetrate both the facia lata and the fascia iliaca in order to allow for local anesthetic spread around the femoral nerve.

Patient positioning Supine with ipsilateral leg externally rotated.

Probe positioning The ultrasound probe is placed in-line with the inguinal ligament. Scanning from lateral to medial the femoral artery is located as a key landmark for this block given its medial location to the femoral nerve (***Remember****, within the inguinal crease the ordering of structures from lateral to medial is Nerve → Artery → Vein → Empty Space → Lymphatics (NAVEL)*). As such, the hyperechoic oblong-shaped nerve should travel just lateral to the artery, deep to the fascia iliaca, and superficial to the iliopsoas muscle.

Local anesthetic Bupivacaine or Ropivacaine 0.25–0.5%.

Total volume of local anesthetic 20–40 mL

Pitfalls

- Placement of the probe can often be challenging in obese individuals with large pannus overlying inguinal crease. Tape can be used to retract patient pannus in obese patients when access to the inguinal crease is limited by body habitus.
- Partial or incomplete needle penetration through the fascia iliaca can result in incomplete femoral nerve block and care should be taken to confirm proper spread around femoral nerve after popping through the fascial layer.
- Femoral nerve blocks are more likely than adductor canal block to result in near or actual mechanical falls following surgery secondary to quadriceps motor weakness [4].

Clinical Pearls

- If two arteries are present in view (femoral artery and profunda femoris) the probe should be moved proximally up the leg until the single femoral artery is visualized prior to bifurcation.
- The femoral nerve is widest and most superficial at the inguinal crease.
- Motor testing to confirm successful femoral nerve block involves active knee extension against resistance to evaluate for quadriceps motor weakness (femoral nerve).
- Given anesthesia of motor branches of femoral nerve, a knee immobilizer should be applied post-op with patient instructions on weight bearing status printed and explained to the patient prior to home-going. Anesthesiologist-patient follow-up, either by phone or in person, should occur to confirm block resolution post-op.

2.1 Adductor Canal Nerve Block

Scenario

J.W. is a 56-year-old male PMH htn and hld who presents for (p/f) right-sided repair of a midfoot Lisfranc injury with fracture and ligamentous tear with orthopedic surgery. He has not had surgery in the past and his only medications are lisinopril 10 mg daily and atorvastatin 20 mg daily.

Questions (q) and Answers (a)

1. What are the anatomical borders that should be identified during an adductor canal block?
2. What nerve is blocked during an adductor canal block and what would you expect to see post-block?
3. What other blocks are paired with this block and what is the rationale for this combination?

3 Summary

Adductor canal block The adductor canal block involves blocking of the saphenous nerve (most distal sensory branches of the femoral nerve) to provide sensory blockade of the anteromedial knee and medial lower leg, foot, and ankle (Fig. 2). As it relates to surgeries of the lower leg, ankle, and foot, the adductor canal block is frequently paired with the popliteal-sciatic nerve block to provide complete sensory blockade distal to the knee (***Note****, see popliteal-sciatic block in next section for more details*). Table 1 summarizes key block characteristics, materials, patient positioning, scanning techniques, block needle trajectory, and high yield

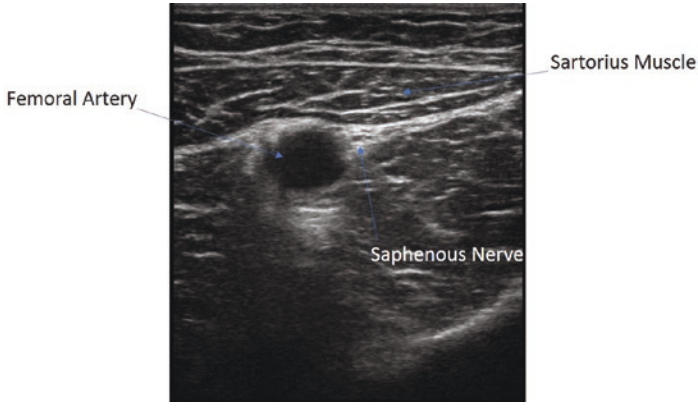

Fig. 2 Ultrasound view of the adductor canal nerve block

notes on this block. It is important to note that the adductor canal is a triangular tunnel formed by three muscles which is connected to and extends from the femoral triangle apex to the adductor hiatus. The boarders of this canal are composed superficially by the sartorius muscle, medially by the adductor longus muscle, and laterally by the vastus medialis muscle.

Patient positioning The patient is positioned supine with slight flexion of knee and external rotation of leg.

Probe positioning The ultrasound probe is situated in the transverse orientation over mid-thigh. After locating the femur, the probe is moved from lateral to medial until the sartorius muscle is located (roof of the adductor canal).

Local anesthetic Ropivacaine or Bupivacaine 0.25–0.50%.

Total volume of local anesthetic 20–40 mL.

Pitfalls

- Sensory anesthesia is limited to medial lower leg during ankle and foot surgery.
- Block needs to be combined with either select ankle blocks or more proximal sensory-motor blocks depending on surgery to be performed (see Table 1).

Clinical Pearls

- Assessment of block prior to anesthesia can be determined through testing of sensation pre- and post-block over the medial malleolus (saphenous nerve distribution).
- Less hamstring weakness occurs following an adductor canal block when compared to a femoral nerve block. Mild weakness is still possible, however, secondary to the potential for proximal spread of local anesthesia through the adductor canal during adductor canal block.
- Proximally the adductor canal begins at the junction point where the sartorius muscle and adductor longus muscle meet.

3.1 Popliteal-Sciatic Nerve Block

Scenario
R.R. is a 37-year-old male with past medical history of low back pain and former opioid abuse disorder currently on 16 mg/4 mg sublingual buprenorphine/naloxone daily for maintenance therapy presents following a traumatic trimalleolar ankle fracture. He has had several drug relapses in the past and is concerned about pain control following surgery and large pain medication requirements. He is otherwise healthy and previously was able to climb over four flights of stairs without chest pain, shortness of breath, or other issues.

Questions (q) and Answers (a)
1. How would you tailor this patient's peri-operative anesthetic plan given his previous opioid abuse disorder and current suboxone (buprenorphine + naloxone) prescription?
2. How would you manage his pain medications peri-operatively given the partial agonist properties of suboxone?
3. What regional block(s) could be employed to aid in peri-operative pain control?
4. What are the benefits of a combined regional and spinal anesthetic approach for surgeries of the ankle and foot?
5. What are some disadvantages to regional anesthesia?
6. What is a popliteal-sciatic nerve block and what nerves are targeted during this procedure?
7. What are the anatomical borders that should be identified by sonography during a popliteal-sciatic nerve block?

4 Summary

Popliteal-sciatic nerve block The popliteal-sciatic block is a peripheral nerve block which targets the sciatic nerve by anesthetizing its terminal branches, tibial and common peroneal nerves.

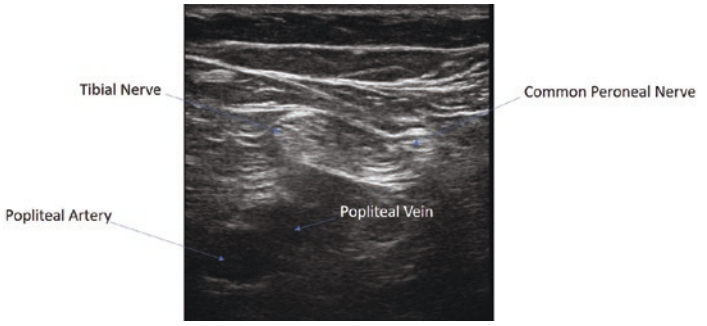

Fig. 3 Ultrasound view of popliteal-sciatic nerve block

Blockade of these nerves results in motor and sensory anesthesia of the lower leg except for sensory innervation to the medial leg (***Remember***—the saphenous nerve provides sensory input over the medial lower leg) (Fig. 3).

LA Ropivacaine or Bupivacaine 0.25% or 0.50%.

Total volume of LA for block of both nerves 20–40 mL.

Pitfalls

- Foot drop following popliteal-sciatic block (continuous or single shot) can increase fall risk and patients should be discharged with an ankle splint.
- Injection of local anesthetic into the popliteal vein can occur for two reasons during this block; (1) The popliteal vein is often compressed during the application of probe pressure while scanning in the popliteal fossa which makes avoiding this vascular structure difficult, and (2) If the block needle is partially or completely within the occult popliteal vein negative aspiration could be achieved secondary to decreased venous flow from the above mentioned probe compression of the vein.

Clinical Pearls

- This block can either be performed in the following positions: supine position with knee flexed and leg raised via stacked towels or block under calf; lateral decubitus position with leg extended; or prone position based on patient mobility and placement restrictions.
- Motor block can be evaluated by testing the patient's ability to conduct plantar flexion (posterior tibial nerve) and dorsiflexion (common peroneal nerve).
- More precise and complete block can be achieved with injection of local anesthetic (equal injection of local anesthetic divided between tibial and common peroneal nerves) just distal to the sciatic nerve bifurcation compared to pre-bifurcation [5].
- Continuous popliteal-sciatic nerve catheters provide reliable pain control post-operatively and are placed under ultrasound guidance prior to the bifurcation of the sciatic nerve in the popliteal fossa.
- Improved visual analog scale scores have been reported in patients undergoing outpatient foot and ankle surgery for patient with continuous infusions at 24- and 48-h post-op when compared to single shot alone [6].

4.1 Ankle Blocks

Scenario

J.W. is a 56-year-old male with bilateral (right worse than left) hallux valgus deformity refractory to medical management who presents for right-sided repair with orthopedic surgery. He has not had surgery in the past and his only medication is Tylenol 975 mg every 6 h as needed for discomfort of his feet.

Questions and Answers

1. What are the anatomical borders that should be identified during an ankle block?

2. What are some advantages of an ankle block compared to a more proximal regional nerve block?
3. What are some disadvantages of an ankle block compared to a more proximal block?

5 Summary

Ankle blocks aim to target one or more of the five nerves of the lower extremity; These five nerves include the saphenous nerve, the tibial nerve, the superficial peroneal nerve, the deep peroneal nerve, and the sural nerve. All except one of these nerves are terminal branches of the sciatic nerve [7].

In terms of sensory innervation for each of these five nerves:

- The tibial nerve innervates the sole and heel (Fig. 4)
- The saphenous nerve: A terminal sensory branch of the femoral nerve, covers the medial aspect of the lower extremity (Fig. 5)
- The deep peroneal nerve gives rise to the sensation between the first and the second toes (Fig. 6)
- The superficial peroneal nerve mainly contributes to the sensation of the dorsal foot (Fig. 7)
- The sural nerve provides cutaneous innervation to the lateral aspect of the foot (Fig. 8)

Overall, this regional technique is indicated in toe surgeries and operations that involve areas that are distal to the ankle. Several injections are required in an ankle block to cover all branches. Unlike other deeper lower extremity blocks, ankle block generally can be safely performed in fully anticoagulated patients. Absolute contraindications include patient refusal and localized infection/tissue damage at the injection sites.

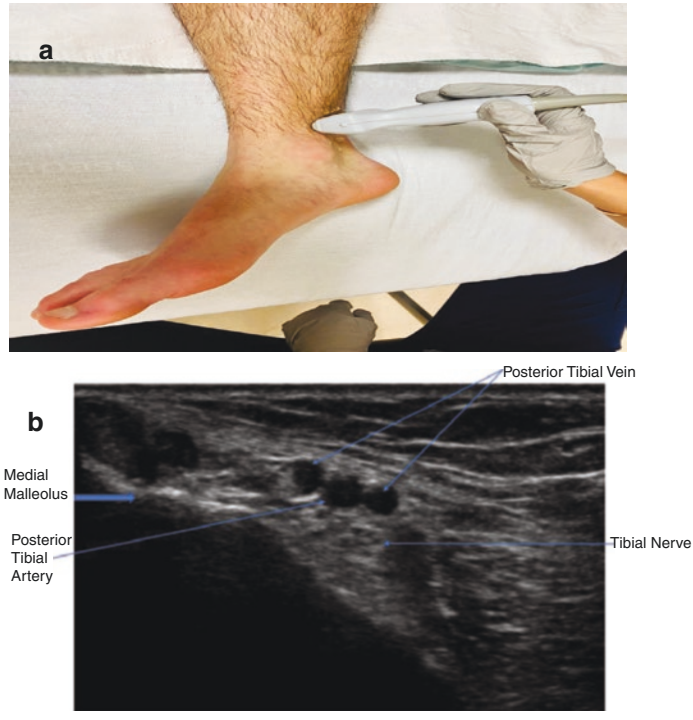

Fig. 4 (**a**) Ultrasound probe placement (upper image) and (**b**) ultrasound view (lower image) of the tibial nerve block at the ankle

Ankle blocks are very versatile blocks that can be achieved using any one or a combination of the following methods: anatomical landmarks, nerve stimulation, and ultrasound guidance. One may argue that ultrasound guidance is more advantageous over the other two because it helps avoid intravascular/intraneural injections and requires lower local anesthetic volume. Block techniques may also vary depending on the provider. Specifically, with anatomic landmarks, some providers may choose to inject local anesthetic solution starting from a point proximal and poste-

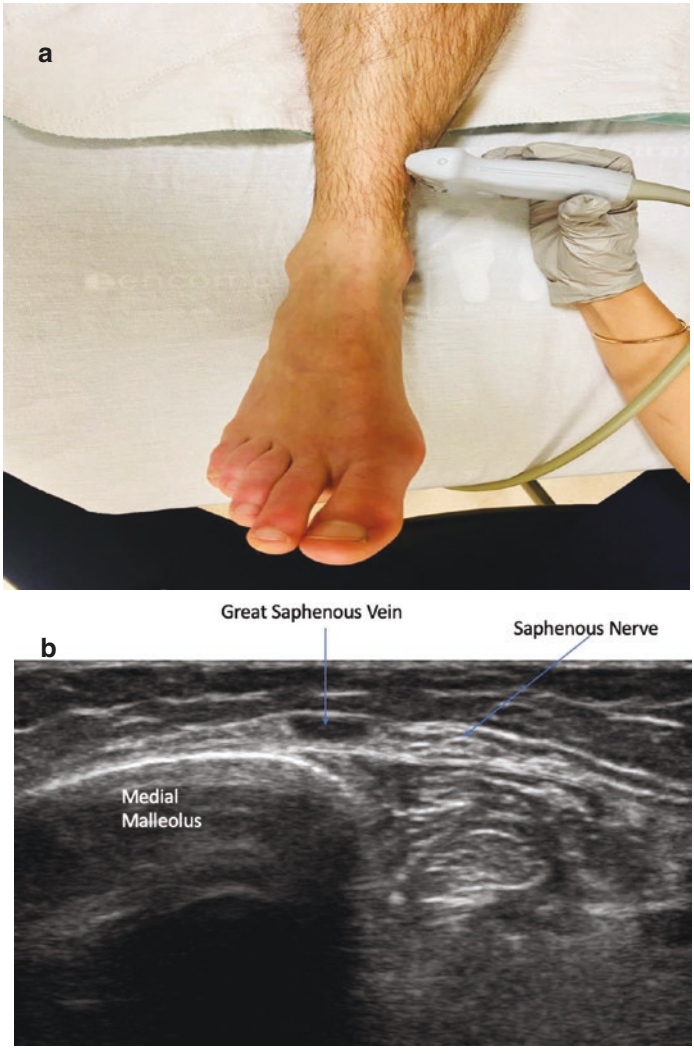

Fig. 5 (**a**) Ultrasound probe placement (upper image) and (**b**) ultrasound view (lower image) of the saphenous nerve block at the ankle

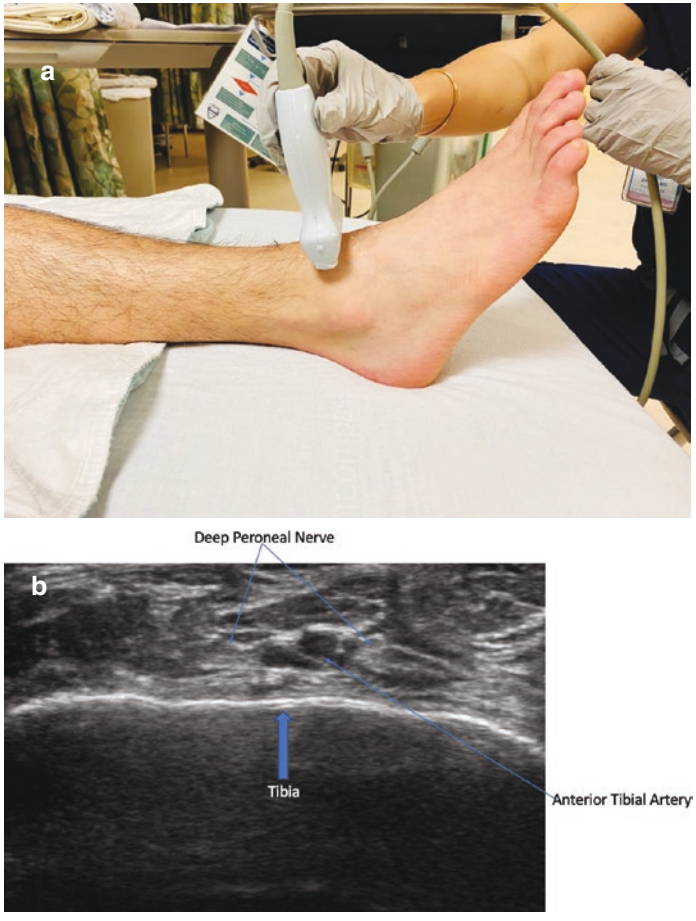

Fig. 6 (**a**) Ultrasound probe placement (upper image) and (**b**) ultrasound view (lower image) of the deep peroneal nerve block at the ankle

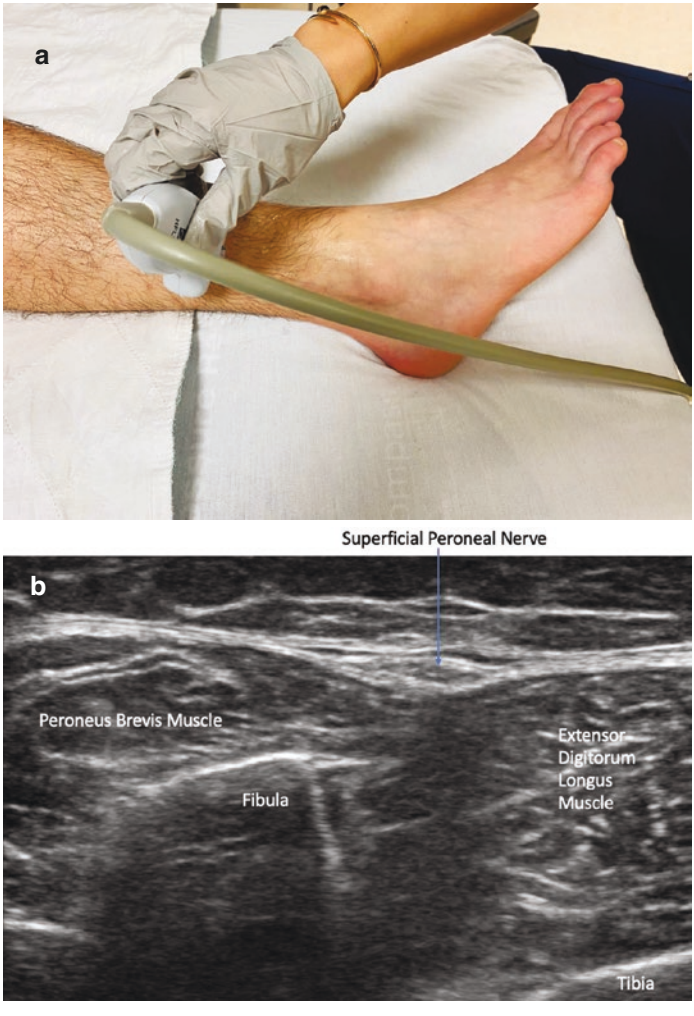

Fig. 7 (**a**) Ultrasound probe placement (upper image) and (**b**) ultrasound view (lower image) of the superficial peroneal nerve block at the ankle

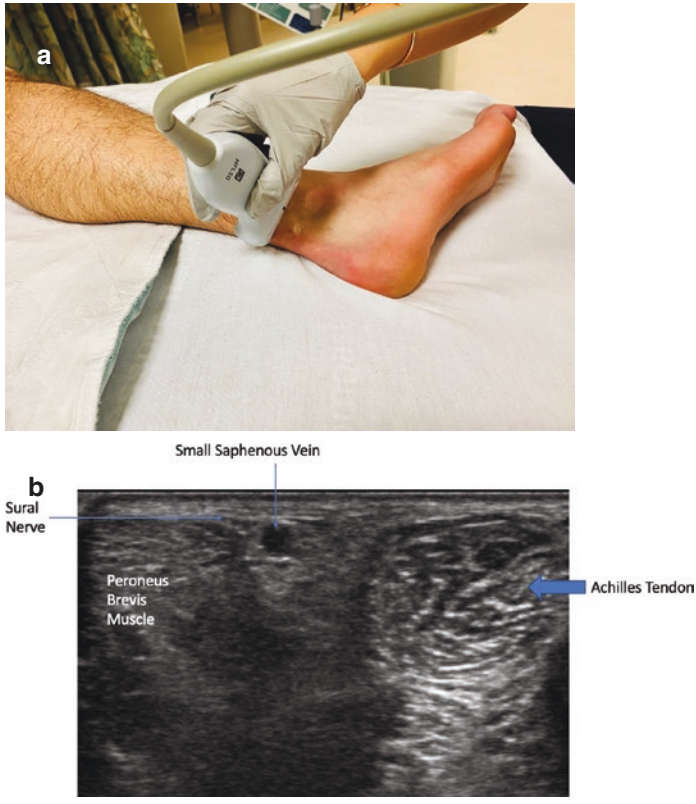

Fig. 8 (**a**) Ultrasound probe placement (upper image) and (**b**) ultrasound view (lower image) of the sural nerve block at the ankle

rior to the medial malleolus followed by continuation around the ankle circumferentially in the subcutaneous compartment. Others may use anatomic clues more precisely and block each nerve individually. For example, one would locate bony landmarks like the medial malleolus and palpate for the posterior tibial artery to locate the tibial nerve [8]. More reliable identification of specific vessels and tendons occur when one uses ultrasound soundwaves to guide ankle injections. Both in-plane and out-of-plane injec-

tions can be achieved easily since these nerves tend to be superficial, and the needle can be identified on the ultrasound imaging easily.

6 Summary

Ankle block Ankle blocks are indicated for surgeries involving areas distal to the ankle. An ultrasound guided ankle block usually requires multiple local anesthetic injections in order to anesthetize the nerves that provide both sensory and motor innervation of the distal foot. The five terminal branches are saphenous nerve, tibial nerve, superficial peroneal nerve, deep peroneal nerve, and sural nerve.

Patient positioning The patient is usually positioned in the supine position with operative foot elevated to allow for probe placement and injections (see Table 1 for positioning by block).

Probe positioning The ultrasound probe is placed at different locations along the ankle based on the nerve to be blocked (see Table 1 for probe placement by block). Linear probe is usually used.

Local anesthetic Ropivacaine or Bupivacaine 0.25–0.50%. Two percent lidocaine may be added for faster onset.

Total volume of local anesthetic 5 mL per nerve.

Volume may be increased for individual injections if certain areas of the foot is targeted. For example, 7 mL of local anesthetic can be given to target the sural nerve if lateral foot is the area of surgical interest, and one may consider omitting the saphenous nerve.

Pitfalls

- Ankle block will not provide motor paralysis to most of the leg, and patient movement during surgery may necessitate deep sedation or general anesthesia based on requirement of surgeon.

- Patients with peripheral vascular disease may be challenging, as their distal arteries are atherosclerosized and can be difficult to identify on ultrasound. One may use other structures such as bony landmarks and tendons for indications on the ultrasound.

Clinical Pearls

- Deep peroneal nerve testing involves sensory testing between first and second toe interspace.
- Superficial peroneal nerve testing can be achieved by testing dorsal foot sensory perception (except between first and second toes).
- Plantar sensory testing will allow for evaluation of adequate block of the tibial nerve.
- Lateral foot sensory testing will test for adequate block of the sural nerve.

Conflicts of Interest The authors declare no conflicts of interest.

Funding The authors have no sources of funding to declare for this manuscript.

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Acute Pain Management Protocol for Unilateral and Bilateral Chest/Thoracic Procedures

Dena Danji, Jacob A. Lambert, and Matthew B. Ellison

Abbreviations

ESPB	Erector spinae plane block
ICN	Intercostal nerve block
PSINB	Parasternal intercostal nerve block
PVB	Paravertebral block
SAB	Serratus anterior block
TEA	Thoracic epidural analgesia

Case Stem 1 Lobectomy

Patient is a 68-year-old male with past medical history of multiple cerebrovascular accidents for which he is currently on warfarin, chronic obstructive pulmonary disease, 30 pack year smoking, and squamous cell lung cancer presenting for left lower lobectomy.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_25

Questions/Answers

1. What regional techniques could you offer this patient?
   (a) ***Thoracic epidural analgesia (TEA)*** Considered the "gold standard" for post-thoracotomy pain management [1]. Options for epidural analgesia include opioids with or without local anesthetic that can supplement the intraoperative anesthetic management and for continued pain management post-operatively. Notably, patients who have received epidurals versus opioids alone were found to have decreased post-thoracotomy complications including atelectasis and pneumonia [2].
   (b) ***Paravertebral block (PVB):*** Targets intercostal nerves, dorsal rami, rami communicantes and sympathetic chain as they exit the vertebral column [3]. Thoracic paravertebral analgesia with catheters was found to be as effective as epidural analgesia in management of post-thoracotomy incisional pain and is associated with fewer hemodynamic changes [4, 5]. While not required, this block is almost always performed under ultrasound guidance utilizing similar views for ESPB. The needle is guided with the aim of contacting the transverse process, followed by "walking off" and inserting into paravertebral space, usually signified by a pop of crossing fascial plane, as well as identification by ultrasound. Local anesthesia is injected incrementally into the space either as single injection or with placement of catheter for continuous local administration [6]. Refer to Fig. 1.
   (c) ***Erector spinae plane block (ESPB):*** Recently introduced technique that describes injection into the interfascial plane deep to the erector spinae muscle and superficial to the tips of the thoracic transverse processes. While the exact mechanism is unknown, it is thought that the nerve block targets both the dorsal and ventral rami as they exit intervertebral foramina providing analgesia to the ipsilateral hemothorax [1, 7]. The analgesic coverage would make it an alternative to the PVB, and similarly, can be done as single injection or as a continuous infusion with catheter placement. Refer to Fig. 2.

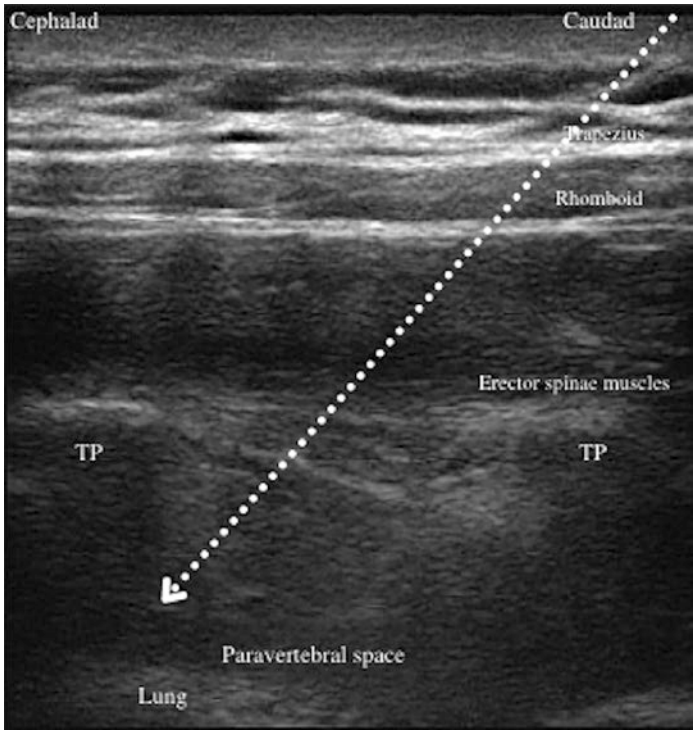

Fig. 1 Ultrasound image of paravertebral block in sagittal plane. Dotted line represents needle trajectory with arrow pointing to site of local deposition

(d) ***Serratus anterior plane block (SAB):*** Technique involving the injection of local anesthetic in the fascial plane deep to the latissimus dorsi and superficial to the serratus anterior muscle at the fifth rib in the mid-axillary line. This block provides dermatomal numbness from T2-T9 by targeting the associated intercostal nerves as they pierce the serratus anterior muscle. Continuous local anesthesia can be achieved with this technique by inserting a catheter into the space [8]. Refer to Fig. 3

(e) ***Intercostal nerve block (ICN):*** Intercostal nerve blocks can be performed intraoperatively by the surgeon under direct visualization or pre/post operatively by the anesthe-

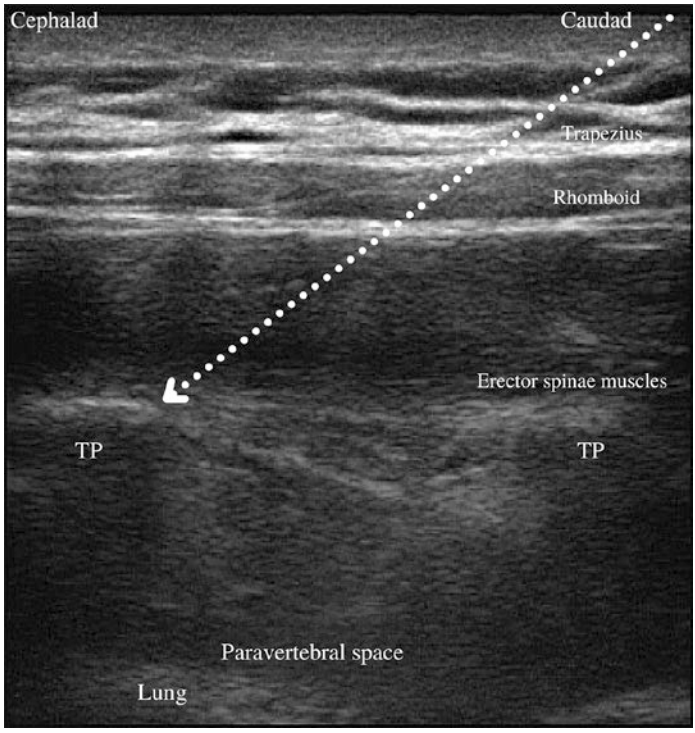

Fig. 2 Ultrasound image of erector spinae plane block. Dotted line represents needle trajectory with arrow pointing to site of local deposition

siologist. ICN blockade is achieved by injection in the subcostal grooves that spreads both distally and proximally. It's commonly performed at the angle of the rib or 6–8 cm from the spinous processes. Technique involves the needle to be angled 20 degrees cephalad until it contacts rib, at which point the needle is walked caudally until fascial give is encountered [9].

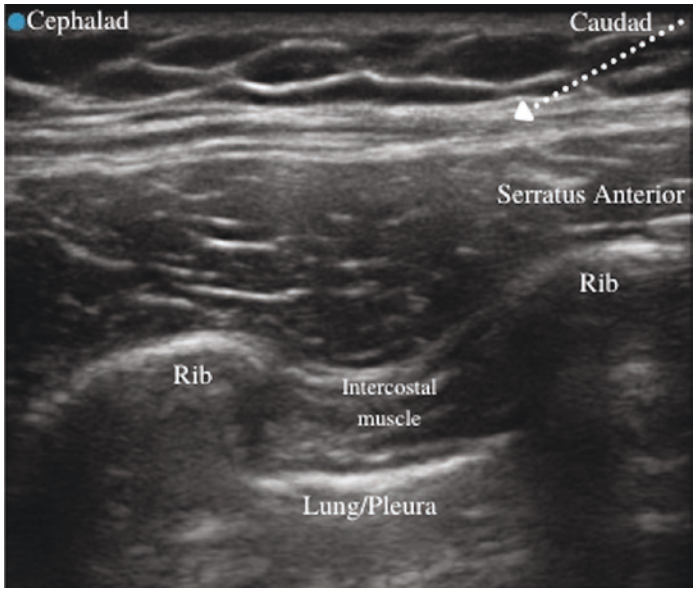

Fig. 3 Ultrasound image of serratus anterior plane block. Dotted line represents needle trajectory with arrow pointing to site of local deposition

2. Benefits and disadvantages of each?

	Advantages	Disadvantages
Thoracic Epidural (TEA)	• Post-thoracotomy patients have a decreased rate of pulmonary complications rate with TEA [1] • Decreased pain scores and opiate requirements • Decreased ICU stay • Earlier hospital discharge [6]	• Potential for hemodynamic instability • Difficulty of placement, failure rate of approximately 10% [10] • Restrictions on placement and removal of catheters in relation to anticoagulation

	Advantages	Disadvantages
Paravertebral block (PVB)	• Laterality, limiting analgesia to one side • Comparable pain scores with decreased adverse effects and increased success compared to TEA [10] • Greater hemodynamic stability, less nausea and urinary retention when compared to TEA [6] • Decreased failure rate than TEA [10]	• Follows neuraxial anticoagulation guidelines for placement and removal per ASRA • If using for sternotomy, would need bilateral blocks - increased risk for high local anesthetic plasma concentrations [6] • Risk for pneumothorax • May not be appropriate candidate for PVB if history of prior thoracotomy, as PVB space may be obliterated, putting patient at risk for dural/intrathecal injection [6]
Erector Spinae Plane Block (ESPB)	• Hemodynamic stability • Less difficult and improved safety profile compared to TEA (injection site distant from pleura and major vasculature) [6] • Significant cranial-caudal spread with single injection, estimated to be 2–3 levels above and below [1] • There is no formal classification as “deep” or “superficial” nerve plexus to apply ASRA anticoagulation guidelines, however there have been several studies that demonstrate the safety of ESPB in anticoagulated patients [11, 12]	• If using for sternotomy, would need bilateral blocks - increased risk for high local anesthetic plasma concentrations [6]
Serratus anterior plane block (SAB)	• Hemodynamic stability • High safety profile [6] • Equally efficacious in post-thoracotomy pain reduction with longer duration of action compared to intercostal nerve block [13]	• Risk of pneumothorax • Limited area of analgesia compared to other plane blocks and TEA

	Advantages	Disadvantages
Intercostal nerve block (ICN)	• Does not require ultrasound • Quick, easy to perform [9]	• Epidural analgesia superior to ICN [7] • Higher local anesthesia absorption, risk for LAST • Risk of pneumothorax estimated to be 1% • Technically more difficult to perform between T1-T7 due to scapula and rhomboid muscles [9] • Limited area of analgesia, requires additional injections

3. This patient was taking warfarin at home and has been admitted to bridge to a therapeutic heparin infusion. What are the implications for timing of regional block if this patient was to receive a TEA or PVB with continuous infusion via catheter?
   (a) Both TEA and PVB follow anticoagulation guidelines for neuraxial blocks. The American Society of Regional Anesthesia and Pain Medicine (ASRA) Evidence Based Guidelines published in 2018 recommend holding heparin for **4–6 h** prior to procedure, as well as verifying normal coagulation status, such as with PTT [14]. Considerations must also be taken for when heparin can be restarted after procedure, holding of heparin before catheter removal, as well as when to restart heparin after removal.
      (i) When to restart heparin after block? 1 h
      (ii) When to hold heparin ***before catheter removal***? 4–6 h and normal coagulation status
      (iii) When to restart heparin ***after catheter removal***? 1 h [14]
   (b) What if the patient was not admitted early to bridge to heparin and instead withheld warfarin 7 days prior to surgery?
      (i) ASRA recommends holding warfarin 5 days prior to procedure with normal INR values [14].
4. You opt to proceed with PVT with indwelling catheter placement. What local anesthetic would you choose and at what dose? What level?

(a) A single shot injection in the paravertebral space requires approximately 2 ml of local anesthetic per dermatome level of anesthesia if doing multiple injections. However, with a single injection, at least 10 ml is required to reach 5 dermatome levels. Local anesthetic infusion rate through an indwelling catheter is recommended at 0.1 ml/kg/h. The choice of local anesthetic has little literature supporting one over another, in addition to institutional differences in recommendation. Suggestions have been made in literature for 0.3% ropivacaine or 0.25% bupivacaine, with some indication that ropivacaine may be a superior option due to the tendency for bupivacaine to accumulate in a linear manner [15].

(b) The paravertebral space extends from T1-T12 [15]. This block can be completed at various levels depending on the surgical site. For the example incision in Fig. 4, a target of T6 is appropriate, with the option to block the surrounding dermatomal levels.

5. The patient is getting ready to be discharged and needs PVB indwelling catheter removed but has been on once daily dosing

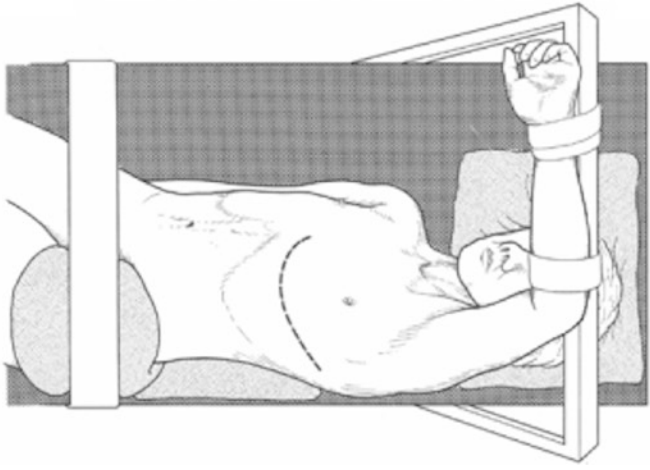

Fig. 4 The incision for an anterolateral thoracotomy extends from the midline along the anterior aspect of the fifth rib. It continues around the thorax to a point slightly caudal to the inferior angle of the scapula [16]

of enoxaparin for deep vein thrombosis prophylaxis. Does he need labs or to wait a certain number of hours prior to removal?

(a) The risk of epidural hematoma formation is increased with the removal of epidural catheters while receiving anticoagulation. It is recommended that prior to catheter removal, enoxaparin be held for 12 h [14].

Common Pitfalls

- Be aware of regional techniques that require holding of anticoagulation before procedures and holding post catheter removal, such as paravertebral blocks
- Discussion with the surgeon to confirm surgical approach to assure adequate pain control from the most appropriate regional block for the patient

Clinical Pearls

- Multimodal pain control with regional anesthesia leads to improved outcomes
- PVB and ESPB have similar analgesia coverage
- Comparison of TEA and PVB demonstrate decreased side effect and failure rate of PVB with no significant difference in pain scores [10]

1 Summary

There are many regional anesthesia techniques to apply in cases that require thoracotomy or chest wall reconstruction including TEA, PVB, SAB, ESPB and intercostal nerve blocks. Important considerations to keep in mind include anticoagulation status, site of incision, concern for hemodynamic instability, technical difficulty, user experience and if anticipating early discharge. Nonetheless, regional modalities play an important role in thoracic surgery to promote shorter hospital stays and decreased pulmonary complications.

Case Stem 2

Patient is a 23-year-old female with past medical history of asthma, pectus excavatum, and malnourishment with BMI 17 (48 kg) presenting for Nuss procedure.

Questions/Answers

1. What regional techniques would you offer the patient?
   (a) Thoracic epidural, paravertebral block, erector spinae plane block, serratus anterior plane block and intercostal nerve block are appropriate options for the incisions in a Nuss procedure as illustrated in Fig. 5.

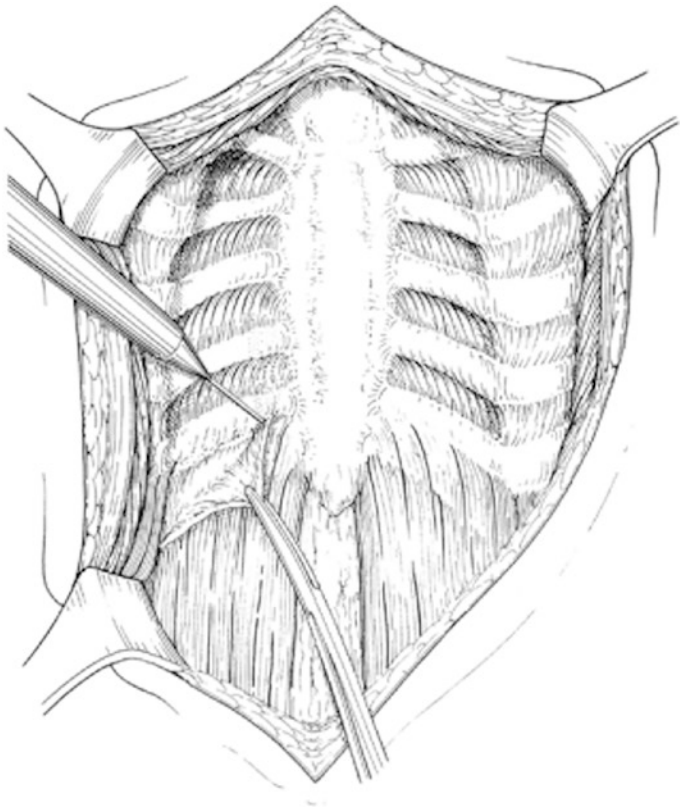

Fig. 5 The Nuss Procedure for Pectus Excavatum involves the insertion of a pre-curved bar under the sternum at, or slightly below, the level of the nipple [17].

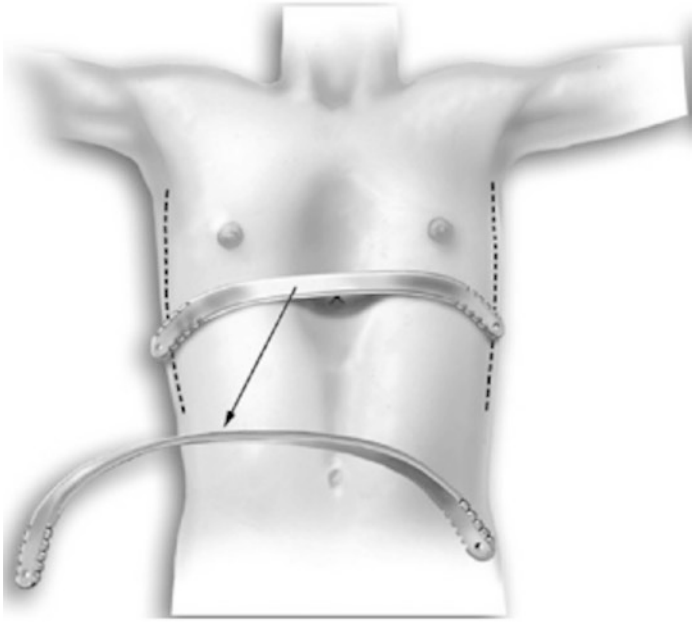

Fig. 6 The Modified Ravitch Operation for Pectus Excavatum requires a midline vertical incision from the manubrium to a level inferior to the xiphisternum in order to expose the sternum and costal cartilages [18]

2. On the day of surgery, the surgeon and patient are discussing possibly proceeding with the Modified Ravitch approach instead. How would this change your regional anesthetic plan?
   (a) Modified Ravitch repair involves a midline chest incision with sternotomy to allow for subperichondrial resection of costal cartilages as demonstrated in Fig. 6. Given the midline approach, SAP and ICN would not provide adequate coverage. TEA, PVB, ESPB, and parasternal intercostal nerve blocks would remain good options.
3. The patient and surgeon decide they will proceed with the Nuss procedure. The patient is agreeable for a thoracic epidural, what level would you ideally place it?
   (a) Discussion with the surgeon is important as the level of bar placement may vary per case, however placement around T6 is usually adequate [19].

4. What risks should you discuss as part of informed consent?
   (a) Epidural hematomas, epidural abscesses, permanent nerve injury, infection, cardiovascular collapse, LAST, failure of block, postdural puncture headache. Overall incidence of complications with thoracic epidural catheterization was found to be 3.1% in a retrospective study that analyzed over 4000 patients that received thoracic epidurals for abdominal or abdominothoracic surgeries [19].
5. You are called to the PACU as the patient was noted to have consistent hypotensive blood pressure readings averaging 80/50s. The surgeon is requesting the epidural infusion be shut off. After appropriate resuscitation and turning off the epidural infusion, the patient's blood pressure normalizes but she is now complaining of lateral chest wall pain. What rescue block could you offer this patient?
   (a) SAB, ICN, ESPB, PVB (assuming the patient has not received any anticoagulation)
   (b) It's also important to consider the total local anesthetic dose this patient has received in relation to her weight. Given her weight is 48 kg, consider low concentration of local anesthetic with an adjunct such as dexamethasone to prolong duration of action, while staying below total maximum local anesthetic dose.

Common Pitfalls

- Be aware of risk/benefit with various regional techniques, including potential for hemodynamic fluctuations with TEA. Consider rescue blocks given site of pain while staying within safe local anesthetic doses

Clinical Pearls

- TEA is considered the gold standard in many chest wall and thoracic surgeries as these patients were found to have decreased post-thoracotomy complications compared to patients who received intravenous opioids only [2].

- ESPB is a good alternative to TEA when anticoagulation may be considered an issue. While ESPB has not been formally classified as ESPB as a "deep" or "superficial" nerve plexus to apply ASRA anticoagulation guidelines, there have been several studies that demonstrate the safety of ESPB in anticoagulated patients and should be considered [11, 12].

2 Summary

Similar to the prior example, there is a wide overlap of regional techniques that apply to this case. As mentioned before, these procedures can be incredibly painful and adequate control of pain through a multimodal approach ultimately allows for adequate analgesia and faster recovery.

Case Stem 3 Minimally Invasive Mitral Valve Replacement
Patient is a 45-year-old female with past medical history of poorly controlled diabetes mellitus, myocardial infarction, hypertension, 10 pack-years of smoking, obesity, and coronary artery disease presenting for minimally invasive mitral valve replacement with mini-thoracotomy on cardiopulmonary bypass.

Questions/Answers

1. What regional techniques would you offer this patient?
   (a) Thoracic epidural, paravertebral block, erector spinae plane block, serratus anterior block, intercostal nerve block.
2. What level would you perform an ESPB for this patient?
   (a) As depicted in Fig. 7, mini-thoracotomy for minimally invasive mitral valve replacement typically is completed between intercostal spaces 3 through 5. ESPB at T4 would be adequate. It has been noted that ESPB provide coverage for an average of four dermatome levels above and six levels below injection site [21].

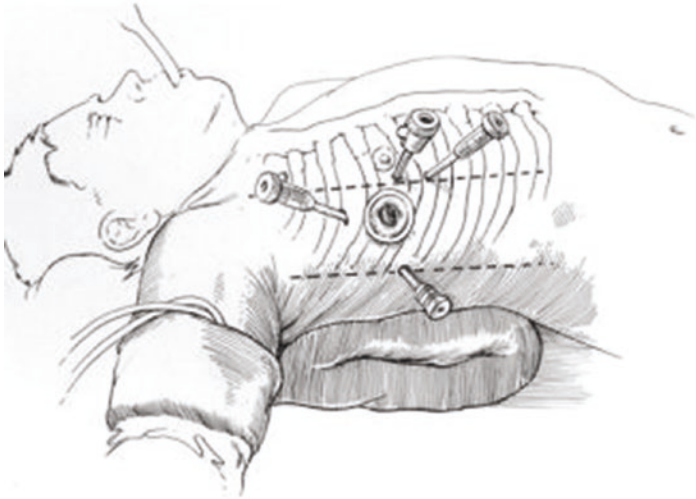

Fig. 7 Robotic mitral valve trocar and mini thoracotomy port placement in the third, fourth and fifth intercostal spaces [20]

3. What local would you use? How much would you bolus? Infusion?
   (a) A single shot technique with ropivacaine and bupivacaine is the most commonly utilized technique in literature, though other local anesthetics have been effective [22]. It has been shown that between 2.2 and 3.4 ml on average of local anesthetic are required to anesthetize one dermatome, with the possibility that concentration of local anesthetic plays some role. A bolus of 20 mL is the most commonly reported and demonstrates efficacy [21]. Catheter insertion for continuous infusion, in addition to a single bolus, as a part of multimodal anesthesia has been shown to improve opioid usage and improve post-operative outcomes [23].
4. Anticoagulation implications?
   (a) As mentioned earlier in this chapter, there is no formal classification for ESPB as a superficial plexus, deep plexus, or neuraxial. ASRA does recommend guidance

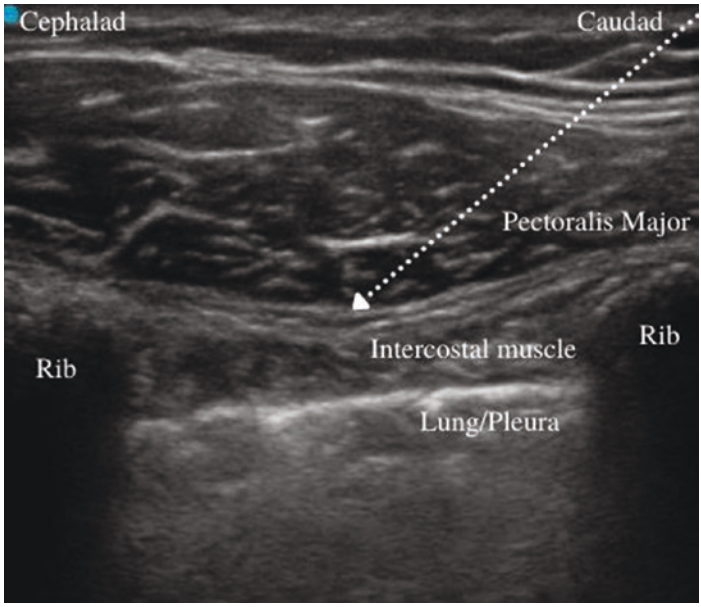

Fig. 8 Ultrasound image of parasternal plane block. Dotted line demonstrates needle trajectory with arrow pointing to site of local deposition

based on site vascularity, compressibility, and consequences of bleeding [6]. That said, there have been several studies that demonstrate the safety of ESPB in anticoagulated patients [11, 12].

5. Intraoperatively, the surgery converts from minimally invasive to open via a midline sternotomy. Postoperatively, you are called to the PACU as the patient is complaining of significant pain to her sternum. What rescue block can you offer the patient?
   (a) Parasternal intercostal nerve block (PSIN) aims to block the anterior branches of intercostal nerves that penetrate through the pectoralis major and intercostal muscles. As shown in Fig. 8, local anesthesia is administered between the pectoralis major and the intercostal muscle. Care must be taken to localize the needle during this block due to the

close proximity to the pleura to prevent pneumothorax. Other complications include hematoma, infection, nerve injury and local anesthetic systemic toxicity, given that the intercostal area is known for high uptake [6].

Common Pitfalls

- Cardiac surgery often utilizes systemic heparinization. If performing regional technique with anticoagulation restrictions such as PVB or TEA, be aware of timing block with surgery time to stay within ASRA guidelines
- Patients undergoing cardiac surgery may be more sensitive to hemodynamic changes with TEA; consider careful titration

Clinical Pearls

- Erector spinae plane blocks serve as a critical adjunct in cardiac surgery due to hemodynamic stability and demonstrated safety in anticoagulated patients [12].

3 Summary

Cardiac surgery's high-risk nature in and of itself lends an open door to a multimodal pain regimen to promote early extubation, reduce postoperative complications, minimize ICU stays and reduce overall cost of perioperative care [19]. Regional techniques that apply to cardiac surgery include neuraxial, chest wall plane blocks and intercostal blocks. Each has their own advantages and disadvantages and should be chosen specifically given surgical approach and patient history.

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Acute Pain Management Protocol for Breast Procedures, with and Without Reconstruction

Daniel Amor, Jordan Abrams, and Yan H. Lai

Case Stem

A 75 year old female, BMI 50, ASA 3 patient presents for a modified radical mastectomy with lymph node biopsy and breast reconstruction for breast cancer. Our patient has a past medical history of morbid obesity, OSA, atrial fibrillation, hypertension, and hyperlipidemia. She has completed a course of doxorubicin in anticipation of her surgery. Her home medications include carvedilol, atorvastatin, and rivaroxaban. On physical exam, you notice a mallampati 4 airway with a large neck, and on examination of her spine you notice what appears to be mild scoliosis. You are a resident at an academic hospital meeting the patient in the holding area prior to surgery. She is very afraid of postoperative pain and mentions she had terrible nausea after anesthesia for her cholecystectomy in the past. Her friend had a paravertebral block for a similar procedure and the patient is requesting if she could have one as well.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_26

Key Question 1: Describe the anatomy, techniques, benefits, and complications of TPVB for patients undergoing breast surgery. What unique benefits and risks do you see?

Breast cancer is the most common malignancy affecting women in the United States. Surgical resections are frequently complicated by poorly controlled pain as well as postoperative nausea and vomiting (PONV). Both of these complications lead to increased patient suffering as well as increased hospital length of stay and healthcare costs [1, 2]. In particular, mastectomy accompanied with reconstruction has been shown to be associated with higher pain scores compared to simple mastectomy alone [3]. Historically, thoracic paravertebral blocks (TPVB) have been considered the gold standard to provide anesthesia and analgesia to the chest wall. TPVB have been well studied in this surgical population and they can either be used as the sole anesthetic or as an adjunct for pain control [4]. TPVB involves injection of local anesthetic (LA) in a space proximal to the vertebral column and immediately lateral to where the spinal nerves emerge from the intervertebral foramina. Spread of LA into this area in cephalad and caudal directions results in sympathetic (an average of about eight dermatomes) and somatic nerve blockade (an average of about five dermatomes) in multiple contiguous thoracic dermatomes from the focus point of injection [5]. A provider may opt to perform a single injection, an injection at multiple levels, or the placement of a catheter for continuous infusion. For a mastectomy a typical level to insert the needle and inject LA is between T1-T5. Both landmark and ultrasound guided techniques for the block have been described.

TPVBs benefits [6]

- Superior pain relief as well as reductions in opioid consumption
- Decrease PONV by 18–26%
- Improved patient satisfaction, faster time to discharge, and decreased conversion of acute to chronic pain [6, 7].
- This patient has a history of OSA and obesity, putting her at an increased risk of postoperative respiratory obstruction and associated complications. TPVB has the potential to reduce her opioid consumption and mitigate these risks.

TPVB Complications

- Infection, bleeding and hematoma at puncture site, nerve damage, local anesthetic toxicity (LAST), pneumothorax, hypotension from sympathetic blockade, and extensive epidural or intrathecal spread such as a high spinal [8].
- Challenges for this patient include her high BMI and body habitus, as well as possible scoliosis. Special care must be taken with block placement to avoid any unintended trauma that could result in undesired complications.

Case

On further discussion with the patient, she mentions that she has only stopped her rivaroxaban for 48 h. Given this new information, you explain to her that it is not safe to proceed with a TPVB. The surgeon, frustrated with your decision, asks you why this patient cannot receive a block since many of her anticoagulated patients have received other blocks in the past.

Key Question 2: Describe the difference between deep and superficial regional nerve blocks and list the cessation timing for commonly used anticoagulants for neuraxial and peripheral nerve blocks based on the current 2018 American Society of Regional Anesthesia (ASRA) guidelines.

The most catastrophic hemorrhagic complication of TPVBs is a spinal hematoma caused by a non-compressible bleeding from needle trauma in the deep and vascular neuraxial space, resulting in potential spinal cord compression and permanent neurologic damage. This hemorrhage risk can be drastically elevated by recent intake of oral anticoagulants. Based on pharmacology of agents, published clinical evidence, and expert consensus, the ASRA guidelines provide cessation timing of anticoagulants to mitigate bleeding risks (see Table 1 below) [9]. However, American guidelines do not clearly delineate which blocks are deep or superficial. Nevertheless, clinical judgement and guidelines from other international societies do classify paravertebral blocks in the deep nerve block category (as compared to other brachial plexus or lower extremity nerve blocks). The approach to

Table 1 ASRA timing and cessation of anticoagulation therapy

Drug	Time to hold for deep/neuraxial blocks
Apixaban	72 hours (GFR dependent)
Argatroban	AVOID
Aspirin	No restrictions
Bivalirudin	AVOID
Cangrelor	3 hours
Cilostazol	2 days
Clopidogrel	5–7 days
Dabigatran	5 days (GFR dependent)
Enoxaparin prophylaxis BID	12 hours (GFR dependent)
Enoxaparin prophylaxis—q day	12 hours (GFR dependent)
Enoxaparin—therapeutic	24 hours (GFR dependent)
Heparin SC—high dose prophylaxis	12 hours
Heparin SC—low dose prophylaxis	4–6 hours
Heparin SC—therapeutic	24 hours
Rivaroxaban	72 hours (GFR dependent)
Warfarin	Ideally 5 days AND normal INR

Adapted from ASRA Evidence-Based Guidelines (fourth edition) [9]

nerve blocks and hemorrhagic complications should be based on site compressibility, vascularity, and consequences of bleeding should it occur [9].

Based on the current guidelines, in order to safely perform her TPVB our patient would need to have stopped rivaroxaban for at least 72 h. Similarly, a thoracic epidural would also not be considered safe.

Case

The patient is upset as she had been expecting TPVB. She asks if there is other PNB that would be safe. The surgical resident brings up that he has seen other anesthesiologists perform blocks for patients undergoing these procedures and wonders if she would be a candidate.

Key Question 3: Describe three alternative fascial plane blocks for chest wall and breast surgery and their efficacy compared to TPVBs.

Please refer to Fig. 1 below for the relevant anatomical correlation and needle localization for chest wall blocks (Fig. 1). Originally described in 2016, Erector Spinae Plane block (ESPB):

- Erector spinae muscle group in posterior thoracic wall: iliocostalis, longissimus, and spinalis. These muscles run parallel along the spinal vertebrae from skull to sacrum.
- ESP targets a potential space deep to the ESP muscle. Injection of LA in this space spreads cranio-caudally with the level

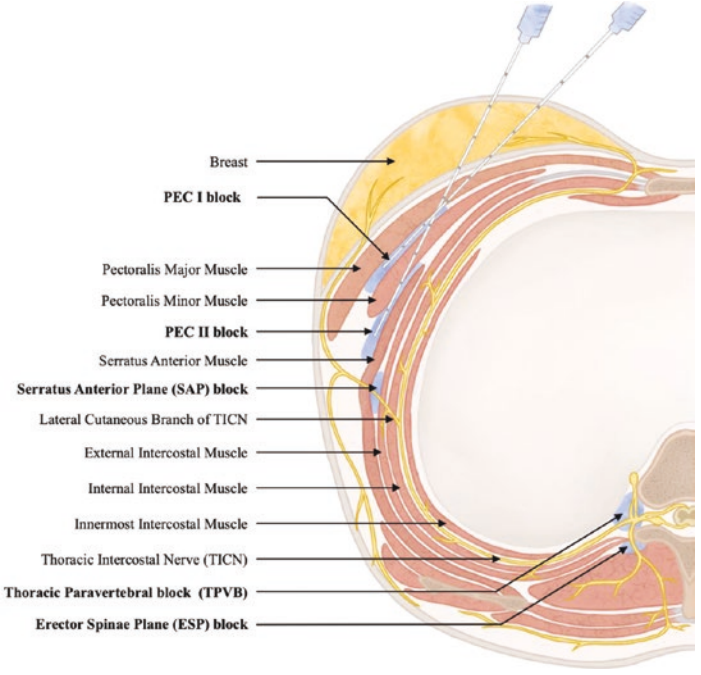

Fig. 1 Chest wall blocks and anatomy. (Illustrated by author Jordan Abrams, MD)

determined both by volume of injectate and the point of entry [10].
- ESP block targets the ventral and dorsal rami of spinal nerves and the rami communicantes of the sympathetic track [10].
- Although there is conflicting evidence between cadaver, imaging, and clinical studies, LA spread into the neighboring TPV space (and even neuraxial space) could account for analgesic efficacy that is similar to TPVB or possibly even thoracic epidural [11, 12].
- Rare and potential complications: pneumothorax, hemidiaphragmatic paralysis, and LAST.

Serratus Anterior Plane Block (SAPB)

- Lateral chest wall fascial plane block that involves deposition of LA at the mid axillary line either superficial (between latissimus dorsi and serratus anterior (SA) muscles) or deep to the SA muscle (between SA and rib).
- Targets the thoracic intercostal nerves that emerge around the SA muscle providing analgesia to the lateral part of the chest [13].
- Rare complications: pneumothorax and LAST.

PECS 1&2

- Interfascial plane blocks in the anterior and antero-lateral chest wall.
- PECS 1 involves depositing LA between the pectoralis major and pectoralis minor muscles to target the lateral and medial pectoral nerves (that originate from the brachial plexus) providing analgesia to the parts of the chest wall [14].
- PECS 2 (includes the PECS 1) LA between the pectoralis minor and SA muscle at the anterior axillary line, providing additional coverage to the lateral branches of intercostal nerves (T2-6) as well as the intercostobrachial, thoracodorsal, and the

long thoracic nerves [15]. Randomized controlled trial (RCT) in 2014 and 2016 found improved pain scores, opioid consumption, higher dermatomal spread, with the PECS 1&2 blocks when compared to TPVB [16, 17]. Because these injection sites are very close to mastectomy incision sites, LA can sometimes be seen to track along dissection planes and can interfere with surgery.

- Rare complications: intravascular injections (acromio-thoracal artery and cephalic vein), hematoma, LAST, and pneumothorax.

Case

After a discussion with the surgical team and patient, a decision is made to proceed with a PECS II block and informed consent is obtained. The patient receives the block uneventfully and the procedure commences. The medical student with you is curious if there are any other evidence-based practices that we can implement to maximize timely and optimal recovery.

Key Question 4: What interventions have been recommended for ERAS around breast reconstruction?

In 2017, the ERAS society published a list of 18 recommendations focusing on return to ambulation, normal bowel function, and superior pain control [18]:

- Regional anesthesia (RA) techniques were associated with decreased postoperative opioid use, decrease in PONV, constipation, and early mobilization [18].
- Providing multimodal analgesia including NSAIDs, gabapentinoids, and acetaminophen.
- Timely administration of antiemetics and consideration of using total intravenous agents (TIVA) as maintenance to reduce PONV
- Timely antibiotics and adhering to institutional redosing regimen
- Maintain hydration and euvolemia
- Avoiding intraoperative hypothermia by maintaining tempera-

tures >36 °C
- Frequent postoperative flap monitoring for 72 h

Case

A few years later you encounter the same patient in your preoperative clinic. She has developed a recurrence of her breast cancer and has been referred to you for preoperative optimization. She mentions that she came across an article in the news that these regional techniques have been associated with cancer recurrence.

Key Question 5: What is the evidence around cancer recurrence and the use of RA in breast cancer surgery.

Mortality from breast cancer is rarely associated with the primary tumor, and is typically secondary to recurrence which is estimated to affect 30% of patients [19]. For the last two decades, there have been ongoing controversy and conflicting evidence on the benefits of RA and the use of LA during surgical resection on future cancer recurrence when compared with GA alone. While some earlier studies showed a decreased recurrence with TPVB combined with GA versus patients undergoing GA without a block, they were limited in their design [19]. Several perioperative factors have been hypothesized to promote recurrence that should theoretically be counteracted by RA. First, surgical stress releases both proangiogenic and growth factors. These factors promoting both local and distant tissue growth, as well as depressing cell mediated immunity. RA have shown to mitigate surges in stress and release of these factors. Second, studies have demonstrated that volatile anesthetics may blunt a multitude of immune processes, and consequently may promote malignant cell growth. Third, LA may possess apoptotic properties in local and distant tissues. Lastly, opioid medications have been shown to inhibit both humoral and cellular immune function. The first large multicenter RCT was published in 2019 by Sessler and colleagues that evaluated cancer recurrence in a propofol and RA versus GA with sevoflurane [20]. This study looked at 2132 women across eight countries, and unfortunately found no difference in cancer recurrence over a 6 year period.

Before making a final decision on the effectiveness of RA on cancer recurrence more definitive trials need to be conducted. One thing that is certain is that RA does not appear to increase cancer recurrence. It seems however, that if there is a potential benefit of RA in suppressing tumor recurrence, it is not as large as once hoped.

1 Summary

Multiple nerve blocks have been studied to provide analgesia for breast surgery including thoracic epidurals, TPVB, ESPB, SAB, and PECS 1&2. It is important to be familiar with the pros and cons of each block.

- RA has been shown to offer multiple benefits including decreased pain scores, decreased opioid consumption, and decreased PONV.
- Earlier studies have shown a decrease in cancer recurrence in patients undergoing breast surgery associated with the use of RA, though more recent RCT have not proven this benefit.
- It is important to understand the ASRA anticoagulation guidelines for neuraxial, deep, and superficial nerve blocks to guide your clinical decision making and prevent undue harm to your patients.
- Being familiar with ERAS protocols for different surgeries and our role in certain interventions is important to provide the best quality of care.

Common Pitfalls

- Failure to establish strict follow up with all patients receiving regional blocks can lead to a delay in treatment on complications that may be missed by the surgical team.
- Failure to consider doing these blocks before surgery will prevent you from taking advantage of their analgesic benefits dur-

ing the procedure and lead to higher opioid use with resultant increase in PONV.
- Failure to educate patients and surgeons on the benefits of regional anesthesia for breast surgery may lead to a decreased adoption rate amongst your patient population.

Clinical Pearls

- Every hospital may have their own ERAS protocol. For instance, at our institution subcutaneous heparin is given preoperatively for cases involving flaps and this must be taken into account when choosing a regional approach.
- Provider expertise with various chest wall blocks is always a key factor in choosing what regional techniques should be offered.
- In patients with expected difficult pain control in the postoperative period (e.g. chronic pain history), a nerve catheter can always be considered.

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Acute Pain Management Protocol for Cardiac Procedures

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Abbreviations

ASRA	American Society of Regional Anesthesia and Pain Medicine
BMI	Body Mass Index
CABG	Coronary Artery Bypass Grafting
ERAS	Enhanced Recovery After Surgery
ESP	Erector Spinae Plane
ICNB	Intercostal Nerve Block
ICU	Intensive Care Unit
IIM	Internal Intercostal Muscle
IMA	Internal Mammary Artery
LAST	Local Anesthetic Systemic Toxicity
PIFB	Pectointercostal Fascia Block
PTPS	Post-Thoracotomy Pain Syndrome

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_27

PVB	Paravertebral Block
RCT	Randomized Controlled Trial
SAP	Serratus Anterior Plane
TTM	Transversus Thoracis Muscle
TTP	Transversus Thoracis Plane

1 Abstract References: [1–4]

Case Stem

A 65 year old, 120 kg (BMI 41), male with a past medical history of severe mitral regurgitation, chronic obstructive pulmonary disease, obstructive sleep apnea and type 2 diabetes presents for minimally-invasive mitral valve repair via right mini-thoracotomy [1–4].

Question

Is there a role for regional anesthesia in this cardiac surgery patient?

Answer

- Regional anesthesia techniques decrease duration of mechanical ventilation, postoperative opioid consumption, and postoperative pain scores [5, 6, 7].
- Regional anesthesia decreases intensive care unit (ICU) length of stay and overall cost of hospitalization without increasing cardiorespiratory morbidity or overall mortality rates [2, 8, 9].
- Improved postoperative thoracic analgesia is associated with increased functional residual capacity, improved ventilation:perfusion (V:Q) ratio by decreasing atelectasis, and allows for participation in pulmonary physiotherapy, all of which have shown to decrease postoperative pulmonary complications [10].
- Fascial plane nerve blocks have a high safety profile, making it ideal for operative cases requiring full heparinization for cardiopulmonary bypass which typically involves doses up to 30–40 units/kg given intravenously [11].

Question

What regional techniques can be considered for analgesia in a mini-thoracotomy? What anatomy utilizing ultrasound is pertinent to these nerve blocks for safe and appropriate performance? Which local anesthetic and dose can you consider for each block for effective postoperative analgesia?

Answer

- Serratus anterior plane (SAP)
- Performed ipsilateral to the operative site between the mid and posterior axillary line.
- Local anesthetic is deposited into the fascial plane between the latissimus dorsi and serratus anterior muscles (superficial plane technique) thus blocking the intercostobrachial, long thoracic, and thoracodorsal nerves as well as the lateral cutaneous branches of the intercostal nerves.
- The thoracodorsal artery travels with the thoracodorsal nerve and can also be located within the fascial plane between the latissimus dorsi and serratus anterior muscles.
- 0.2–0.4 mL/kg of 0.125–0.25% bupivacaine or 0.2–0.5% ropivacaine is recommended for postoperative analgesia [12].
- Intercostal nerve block (ICNB)
  - Performed ipsilateral to the operative site at the angle of the rib 6-8 cm from the spinous processes.
  - Local anesthetic is deposited within the subcostal groove allowing for both proximal and distal spread.
  - Block must be performed at multiple individual levels around the incision for adequate coverage.
  - High rate of systemic absorption due to nerve's proximity to vasculature resulting in relatively high blood levels of local anesthetic.

    Maximum local anesthetic doses should be calculated due to the rapid uptake and increased risk of local anesthetic systemic toxicity (LAST).
  - High rate of complications, such as pneumothorax and neurovascular injury, secondary to the nerves' proximity to

these structures. In addition, the need to perform repeatedly at multiple levels to maintain clinical effect has made these blocks fall out of favor.
  - 3–4 mL of 0.375% ropivacaine can be used per level for adequate postoperative analgesia [13, 14].
- Erector spinae plane (ESP)
  - Performed ipsilateral to the operative site 2.5 cm lateral to the spinous processes, most commonly at the fifth thoracic (T5) vertebrae level.
  - Local anesthetic is deposited deep to the erector spinae muscle overlying the posterior surface of the transverse process within the posterior chest wall [15].
  - Proposed mechanism involves blockade of both the dorsal and ventral rami of the thoracic spinal nerves [4].
  - Continuous nerve block catheter applications are common for prolonged local anesthetic infusions.
  - Demonstrated to lower postoperative pain scores and improve both time to first mobilization as well as time to thoracostomy tube removal [16].
  - 20 mL of 0.5% ropivacaine has been shown to be an effective dose for postoperative analgesia [4, 17].

Question

Do these regional techniques have any pitfalls?

Answer

- Variability in effectiveness due to the degree of spread which is influenced by the volume and location of the injection [18].
- Due to limitations of spread and location of injection, ancillary procedures, such as thoracostomy tube placement, may not be sufficiently covered and should be anticipated prior to selection of technique [18].

Case Stem (Continued)

Upon preoperative evaluation in the anesthesia clinic the patient endorses new onset exertional angina and is subsequently scheduled for coronary angiography. This study demonstrates severe multi-vessel atherosclerotic disease. His surgical plan is consequently changed to include coronary artery bypass grafting (CABG) with left internal mammary artery (IMA) and saphenous vein grafting along with his originally scheduled mitral valve repair, now via a median sternotomy.

Question

What are some considerations, specific to this patient and surgical plan, which may warrant further consideration of regional anesthesia?

Answer

- Median sternotomy, as a surgical approach, is associated with a high incidence of acute post-surgical pain (up to 49%) as well as chronic post-sternotomy pain (up to 30–50%) [19–22].
- Regional anesthesia may decrease the incidence of chronic post-sternotomy pain [23].
- Dissection of the IMA for CABG is associated with worse postoperative pain compared to median sternotomy alone. Prolonged sternal retraction causes soft tissue damage as well as direct damage to the intercostal and brachial nerve network. These factors lead to an increased risk of severe acute postoperative pain [24].
- The patient's underlying pulmonary disease puts him at increased risk of postoperative pulmonary complications such as prolonged intubation, reintubation due to respiratory failure, and pneumonia. Optimizing analgesia, while limiting opioid use, is imperative to improving overall hospital morbidity [10, 25].

Question

What chest wall anatomy is related to these surgical approaches?

Answer

- The intercostal nerves, originating from the anterior rami of the second through sixth thoracic spinal nerves (T2-T6) bilaterally, provide most of the sensory innervation to the thoracic wall [20].
- The thoracic intercostal nerves course from posterior to anterior, giving off a lateral cutaneous branch within the midaxillary line, and ultimately ending as an anterior cutaneous branch which lies between the pectoralis fasciae and the internal intercostal muscles [11] (Fig. 1).

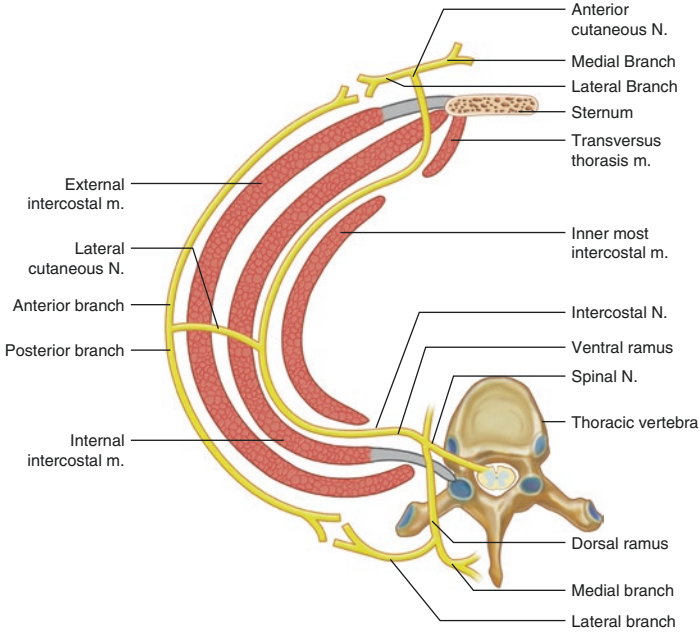

Fig. 1 Anatomical sketch of the thoracic nerves innervating the chest wall

Question

What regional techniques should be considered for analgesia with this patient? What anatomical landmarks are pertinent to identify via ultrasound for safe and appropriate performance of these nerve blocks?

Answer

- Pectointercostal fascial block (PIFB)
- Performed bilaterally, approximately 1 cm lateral from the sternum.
- Local anesthetic is deposited into the fascial plane between the pectoralis fascia and the internal intercostal muscle (IIM), blocking the anterior cutaneous branches of the intercostal nerves.
- The IMA lies deep to this plane between the IIM and transversus thoracis muscle (TTM).
- Long-acting local anesthetics, including bupivacaine and ropivacaine, can be considered.
- Cardiac surgery patients may be particularly sensitive to arrhythmias, therefore, ropivacaine may be preferred due to a more favorable safety profile with less cardio-selective properties than bupivacaine.
- The use of liposomal bupivacaine has been described and may be considered to extend the duration of analgesia.
- 40 mL of 0.25% bupivacaine split between both sides of the sternum, with a total of 2–4 injection sites, has been shown to be effective for postoperative analgesia [19].
- Transversus thoracis plane (TTP)
  - Performed bilaterally, approximately 2 cm lateral from the sternum.
  - Local anesthetic is deposited one plane deeper than the PIFB, between the IIM and the TTM, also anesthetizing the anterior cutaneous branches of the intercostal nerves [3].
    The TTM may be more difficult to visualize, due to its relative depth, making a TTP block more difficult to perform via ultrasound compared to PIFB.

  - Care should be taken to identify and avoid the IMA which lies within this plane, as damage could preclude use for bypass grafting and increase the likelihood of inadvertent intravascular injection.
  - 10–20 mL of 0.25% bupivacaine per side of the sternum has been shown to be effective for postoperative analgesia [20, 26, 27] (Fig. 2).
- The previously discussed nerve blocks, ICNB and ESP, can also be utilized for analgesia of a median sternotomy surgical approach if performed in bilateral fashion.

Question

What pitfalls must be considered with these nerve blocks in cardiac surgery patients?

Answer

- As with any regional procedure, identification of relevant anatomy and awareness of surrounding structures must be considered. In the above described blocks, care must be taken to avoid causing a pneumothorax, intravascular injection, and damage to the IMA as well as other cardiac structures.
- Due to the large volume of local anesthetic required for performing fascial plane nerve blocks, there is an increased risk of LAST; any arrhythmia may have significant hemodynamic consequences in the cardiac surgery patient.
  - Appropriate local anesthetic doses should be calculated for each patient prior to the performance of any regional anesthetic.
- Some anesthesiologists advocate for multiple injections at different levels with a smaller volume vs. one injection at a single level with a larger volume.
- Reliance on regional anesthesia techniques for the sole method of pain control may be inadequate, thus multimodal analgesia should be considered perioperatively when appropriate.
  - Recall in our patient a saphenous vein harvest is planned, therefore lower extremity pain is not uncommon. This will

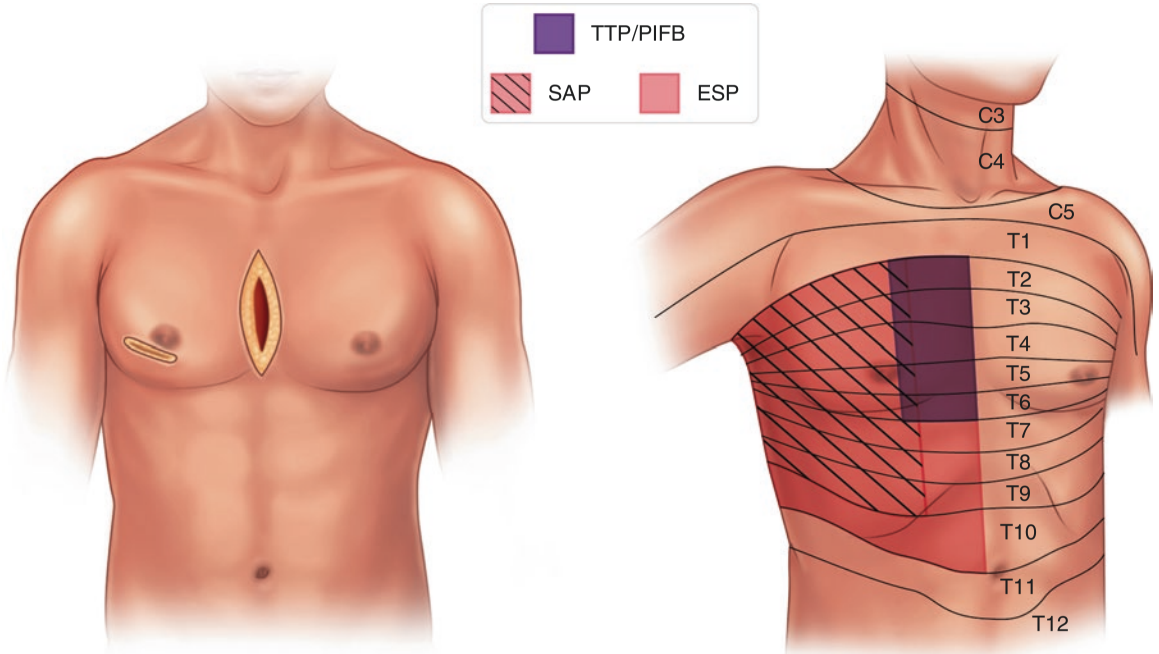

Fig. 2 (Left) Anatomical sketch depicting surgical incision sites, median sternotomy and right mini-thoracotomy. (Right) Anatomical sketch depicting location of dermatomal coverage by regional technique; coverage varies depending upon the volume of injectate and the site at which the injection is performed

be left untreated by any of the aforementioned chest wall regional procedures, hence must be anticipated independently.

Question

Would neuraxial anesthesia be an appropriate option for this patient? What about paraneuraxial anesthesia?

Answer

- Thoracic epidural and spinal anesthesia have been extensively studied in cardiac surgery patients.
- Thoracic epidural catheters historically have been the gold standard for postoperative analgesia in major open thoracic procedures [13, 28].
- Paravertebral block (PVB)
  - Performed approximately 2.5 cm lateral to the spinous process either unilaterally or bilaterally.
  - Local anesthetic is deposited into the paravertebral space once the superior costotransverse ligament is traversed.
  - A catheter for continued local anesthetic infusion may be placed for prolonged analgesia.
  - Local anesthetic may potentially spread medially to the epidural space causing hypotension.
  - 0.4 mL/kg of 0.375% bupivacaine with 0.0005% epinephrine as a single injection technique has shown clinically significant postoperative pain control [29, 30].
- Although benefits from the resultant sympathectomy have been reported, such as decreased incidence of arrhythmias and myocardial ischemia, the risk of devastating consequences from epidural hematoma formation in the setting of full heparinization has made neuraxial and paraneuraxial anesthesia uncommon in cardiac surgery. The risks likely outweigh the benefits given safer alternatives [31, 32] (Table 1).

Table 1 Summary of chest wall regional analgesia techniques [34]

Regional technique	Pertinent anatomy	Pitfalls
PIFB	*Nerve(s) blocked:* Anterior cutaneous branches of intercostal nerves Location: 1 cm lateral to sternum; fascial plane between pectoralis fasciae & IIMs	Pneumothorax, IMA injury, cardiac injury
TTP	*Nerve(s) blocked:* Anterior cutaneous branches of intercostal nerves Location: 2 cm lateral to sternum; fascial plane between IIM and TTMs	Pneumothorax, IMA injury, cardiac injury
SAP	*Nerve(s) blocked:* Intercostobrachial, long thoracic, thoracodorsal nerves & lateral cutaneous branches of the intercostal nerves Location: Mid/posterior axillary line; fascial plane between the serratus anterior & latissimus dorsi muscles (superficial plane)	Pneumothorax, "winging" of the scapula
ICNB	*Nerve(s) blocked:* Intercostal nerves Location: Angle of the rib 6–8 cm from the spinous processes	Pneumothorax, neurovascular injury, LAST
ESP	*Nerve(s) blocked:* Dorsal & ventral rami of spinal thoracic nerves Location: 2.5 cm lateral to spinous process; fascial plane between erector spinae muscle & transverse processes of vertebrae	Pneumothorax
PVB	*Nerve(s) blocked:* Dorsal & ventral rami of spinal thoracic nerves, sympathetic ganglion & rami communicantes (somatic & sympathetic nerves) Location: 2.5 cm lateral to spinous process; within wedge-shaped paravertebral space	Pneumothorax, epidural spread, hematoma formation

- The American Society of Regional Anesthesia and Pain Medicine (ASRA) has established evidence-based consensus guidelines to encourage safe and quality care in patients receiving antithrombotic or thrombolytic therapy and regional anesthesia [33].

Clinical Pearls

- Regional anesthesia has been shown to be a valuable tool perioperatively in cardiac surgery and may lead to decreased postoperative opioid consumption, improved postoperative respiratory parameters including oxygenation as well as a decreased incidence of post-thoracotomy pain syndrome (PTPS) [1, 2, 6, 11, 15, 23, 35, 36, 37].
- The effectiveness of fascial plane nerve blocks for analgesia depends upon the degree of physical spread [11, 12].
- The use of long acting local anesthetics and catheter techniques allow for prolonged analgesia and may aid in expediting key postoperative events such as extubation and removal of thoracostomy tubes [2, 6].
- Newer chest wall and fascial plane nerve blocks may be a safer alternative to traditional neuraxial and paraneuraxial techniques in the setting of cardiac surgery. Technical knowledge and a thorough understanding of anatomy, anticoagulants, and patient risks are vital to the safety and success of performing these nerve blocks [5, 11], [19, 38–41].

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Acute Pain Management Protocol for Gastrointestinal Procedures

Tolga Suvar and Henry R. Govekar

Colon and rectal surgery is one of the oldest subspecialties in the field of general surgery. The American Society of Colon and Rectal Surgeons was initially established in 1899 to promote research and advancement of the field. Over the next 20 years the American Medical Association established the Section on Proctology and the University of Minnesota initiated the first training program. As we entered into the late 1920's to early 1930's, the innovation of different instruments and techniques led to more intricate surgery. In the Post-Graduate Medical Journal from August of 1936, Frankis Evans M.B, BS, D.A, anesthetist of St Marks Hospital, discussed "Anesthesia in rectal Surgery." In this, he divided the methods of anesthesia into three groups based on the different areas of colon and rectal surgery. The three groups are the same as what we describe today: spinal, general and local anesthesia. The optimal anesthetic is decided collaboratively with the surgeon and the anesthesiologist, considering all options that are pertinent to the patient's risk factors and the nature of the sur-

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_28

gery. A spinal anesthetic may be a good choice for an outpatient surgery being the primary anesthetic, whereas the epidural anesthesia may serve as postoperative analgesia with general anesthesia being the primary anesthetic.

In the early 2000's Kehlet developed the first multimodal enhanced recovery program for colorectal surgery [1]. Enhanced recovery after surgery (ERAS) protocols consist of recommendations for preoperative and postoperative care with a large focus on the optimal analgesia for each case. Despite ERAS protocols, patients still experience moderate to severe pain after open and minimally invasive surgery. In a paper by Lindberg et al. in 2020, the authors concluded that "There is a need for effective and individualized analgesia after colorectal surgery, since the individual pain response to surgery is difficult to predict." [2].

Case 1

56 year-old male (BMI 42) with a PMH of DM, HTN and HLD presents with rectosigmoid cancer at 15 cm from anal verge. Patient has a past surgical history of a laparoscopic cholecystectomy. The pre-operative staging workup shows no evidence of metastatic disease. The surgeon plans for a robotic possible open low anterior resection which will take 3–4 h. What regional anesthesia block options would you consider?

Answer There are several ways to deliver postoperative analgesia to this patient. One of the ways is bilateral peripheral nerve blocks. Peripheral nerve block in general is an effective alternative to neuraxial analgesia when the patient has contraindications such as anticoagulation, or bleeding diathesis, patient refusal, or infection over the injection site.

Generally speaking for colorectal surgery, the patient is supine in the operating theatre and the easiest nerve block will be TAP, rectus sheath block, or lateral quadratus lumborum block, since the TAP approach is most accessible in this position compared to the blocks requiring access to the posterior elements of the spine. These blocks are also associated with relatively lower risk of severe complications, nonetheless, only offers somatic pain control.

On the other hand, emerging fascia plane blocks such as erector spinae blocks and paravertebral blocks that are placed closer to the neuraxis, can be associated with higher effectiveness with various degree of visual pain control, in addition to somatic pain control. They may also at higher risk of severe complications, including pneurmothorax in paraverteral blocks.

The most complete block will be offered by a neuraxial anesthetic, generally an epidural anesthetic to the low thoracic region (approximately T8 entry) will allow blockade of the sensory, motor, and sympathetic nerves if the patient does not have contraindications to a neuraxial anesthetic.

After a detailed discussion with the patient on the risks and benefits, the patient agreed to preoperative TAP blocks for the robotic procedure, but would like to have epidural analgesia postoperatively if the surgery becomes an open procedure or much more extensive than planned.

Two hours into the procedure, the surgeon needed to convert from robotic to an open procedure via a large midline laparotomy incision because of local tumor invasion. Postoperatively the patient had severe pain in PACU. You decided to perform a thoracic epidural anesthesia. At what level would you perform the epidural anesthesia, and why?

1 Discussion

1.1 Open Surgery/Minimally Invasive Surgery

The optimal anesthetic delivered for gastrointestinal procedures ensures a perioperative plan to mitigate pain and reduce adverse effects, while enhancing recovery after surgery. There is utility in minimally invasive surgery to reduce the surgical stress burden and postoperative pain associated with gastrointestinal procedures. Aggressive use of multimodal analgesics with regional or neuraxial anesthetics reduce the common postoperative side effects including nausea, vomiting, opioid intolerance, postoperative bowel dysmotility, with reduced hospital stays. Minimally invasive procedures in junction with appropriate regional

anesthetic technique may allow for procedures to be performed in an outpatient setting and implement rapid rehabilitation recovery programs, associated with substantial cost savings to the patient and the healthcare system.

Laparoscopic versus open surgery for rectal cancer has been widely studied in multicenter randomized control trials (CLASICC, COLOR II, ACOSOG Z6051, ALaCaRT) [3–6]. The trials were all designed to evaluate laparoscopic versus open colorectal surgery, and laparoscopy showed slight decrease in length of stay but complications and long term outcomes were comparable. Robotic surgery versus laparoscopic surgery has been studied, and outcomes have also been quite comparable. The decision to choose between the different modalities is based on surgeon experience and patient factors. The robotic platform for minimally invasive surgery is becoming the preferred approach for its improved visualization and dexterity.

Peripheral nerve blocks are suitable for uses in minimally invasive surgery and when neuraxial anesthesia is contraindicated due to infection or coagulopathy. Paravertebral blocks offer both somatic and sympathetic blockade, preserving the hemodynamic changes often seen with epidural and spinal anesthesia. The quadratus lumborum (QL) block is an interfascial plane nerve block performed by depositing local anesthetic to the thoracolumbar fascia, a space which is bordered by posterior extension of the abdominal wall muscle fascia, the quadratus lumborum, psoas major, and the erector spinae muscles. Transversus abdominal plane (TAP) and rectus sheath blocks can be performed for umbilical, abdominal, and midline surgeries. Rectus sheath blocks target the terminal branches of the 9th, 10th, and 11th intercostal nerves between the posterior rectus sheath and rectus abdominal muscles. In contrast, TAP blocks target innervation of the abdominal wall where the nerves arise from the anterior rami of spinal nerves T7 to L1. The two methods for performing TAP blocks are the subcostal approach and the classic TAP blocks. These nerves are targeted by depositing local anesthetics between the transversus abdominus and internal oblique muscles by ultrasound guidance. A subcostal TAP block is performed inferior to the costal margin, aiming to target the intercostal nerves at T6–9 between

Table 1 Block type, patient positioning, equipment, local anesthetic amount

Block type	TAP/ Rectus Sheath	Quadratus Lumborum Block	Paravertebral Block	Erector Spinae Block
Patient position	Supine	Supine or Lateral	Sitting or prone or lateral	Sitting or prone or lateral
Equipment	High-frequency (13 MHz) linear probe 21 or 22 gauge 4 in needle	5–13 MHz curvi-linear or linear probe, depending on body habitus and quadratus lumborum block type, respectively	5–13 MHz curvi-linear or linear probe, respectively 21 or 22 gauge 4 in needle	5–13 MHz curvi-linear or linear probe, respectively 21 or 22 gauge 4 in needle
Local anesthetic amount	20–30 mL on each side (bilateral)	20-30 mL on each side (bilateral)	20–30 mL on each side (bilateral)	20–30 mL on each side (bilateral)

rectus abdominis and transversus abdominis muscle. The main difference between the QL block and the TAP blocks, is that QL blocks have visceral coverage, whereas TAP blocks do not. The erector spinae plane block is another type of interfascial block used to provide analgesia for a variety of surgical procedures. Similar to other interfascial nerve blocks, a single shot or catheter technique can be used to provide a greater duration of analgesia. Ultrasound is used for the dorsal and ventral rami of the spinal nerves to achieve a multi-dermatomal sensory blockade of the thoracic or abdominal walls (Table 1).

1.2 Anorectal

For Anorectal procedures intraoperative anesthesia has the options of general anesthesia and spinal anesthesia. If a spinal anesthesia is chosen, Perianal and rectal procedures will require a spinal block height to the level of the L1 and L2 vertebral bodies to

Table 2 Factors for spread of local anesthetic solution

Factors proposed for the spread of local anesthetic solution within the subarachnoid space
Characteristic of local anesthetic solution
Baricity
Local anesthetic dose and concentration
Volume
Patient characteristics
Age, weight, height, gender, pregnancy, position
Technique
Site of injection
Speed of injection
Barbotage technique
Direction of needle bevel
Addition of adjuvants

achieve satisfactory blockade. The baricity of the injectate also plays a role in the spread and distribution of local anesthetic in the intrathecal space pertinent to the surgical position (Table 2). Baricity is defined as the ratio of density of the solution in relation to density of the cerebral spinal fluid (CSF). For anorectal procedure Hyperbaric solution would be indicated in a patient in the sitting patient, while hypobaric solution has a role in the jackknife position, and isobaric solution when the patient is in horizontal solution [7]. Consideration for patient positioning is a factor in the spread of local anesthetic as gravity influences the distribution throughout the CSF.

It is also common practice to provide sedation to patients receiving regional and neuraxial anesthesia for patient satisfaction [8].

The anesthesiologist must remain cautious when the surgeon requests steep Trendelenburg positioning after receiving spinal anesthesia, for concerns of a high spinal or total spinal where the anesthetic affects the spinal nerves above T4 or intracranial spread of local anesthetics results in loss of consciousness, respectively. The management of high spinal or total spinal are listed in table below:

The dose (concentration by volume) of local anesthetics will increase the duration of the spinal block [9]. Contrary to spinal anesthesia, the location of the epidural block is the most impor-

tant determinant of spread of the block and the dose has less effect on duration of surgical anesthesia. An epidural catheter for lower abdominal surgery will require placement to the approximate level of T12. The spinal nerves and the autonomic nervous system when blocked with epidural analgesia, offer differential blockade to sensory, motor, and sympathetic nerve function (Fig. 1).

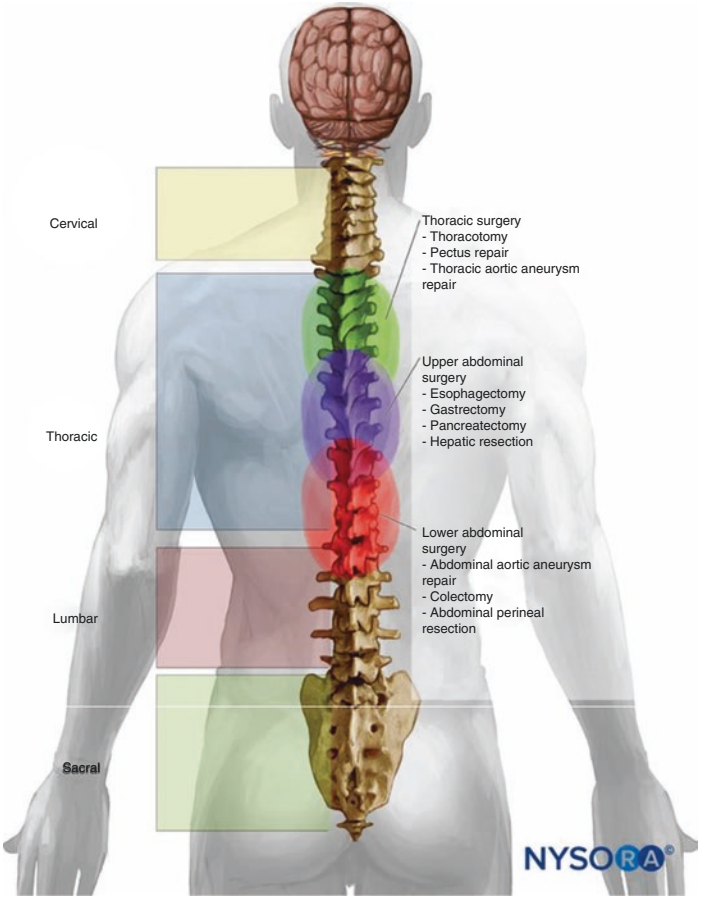

Fig. 1 The highlighted red overlying the vertebrae represents the required placement for epidural catheter for its intended level of analgesia [Source: NYSORA.COM]

Maintaining a constant dose but changing the volume of local anesthetic during an epidural block will result in greater block spread. The duration of two dermatome regression and complete resolution can be found in Table 3. The effects of local anesthetics do not terminate abruptly, but rather it recedes gradually. Anesthesiologists are in control of the duration and extent of spinal and epidural blocks. While considering all factors discussed above, spinal anesthesia and epidural anesthesia each have their own advantages and disadvantages making the selection between the two an important factor for the anesthesiologists. A summary of the differences between spinal and epidural anesthesia can be seen in Table 4.

There is an important difference to be noted between intraoperative surgical anesthetic cases and analgesia which is intended for the postoperative course. Mainly, a spinal anesthetic is a primary (surgical) anesthetic delivered for intraoperative case whereas regional nerve blocks are meant for postoperative analgesia. Epidural analgesia can provide intraoperative surgical anes-

Table 3 Duration of Local Anesthesia for Epidural Blockade

Drug	Two dermatome regression (min)	Complete resolution (min)
Chlorprocaine 3%	45–60	100–160
Lidocaine 2%	60–100	160–200
Mepivacaine 2%	60–100	160–200
Ropivacaine 0.5–1%	90–180	240–420
Bupivacaine 0.5–0.75%	120–240	300–460

Table 4 Differences between Spinal and Epidural Anesthesia

Spinal anesthesia	Epidural anesthesia
Takes less time to perform	Lower risk of Post Dural Puncture Headache
Rapid onset	Less hypotension
Improved Sensori-Motor blockade	Ability to extend the block with a catheter

Table 5 Surgical and postoperative analgesia

Surgical anesthesia	Postoperative analgesia
Epidural anesthesia	Paravertebral block
Spinal anesthesia	Erector spinae block
	Quadratus lumborum block
	Transversus abdominis plane block
	Rectus sheath block
	Pudendal nerve block

thesia, or used for postoperative analgesia. The different nerve blocks are organized in Table 5.

A pudenal nerve block serves as a postoperative anesthetic indicated for many anorectal procedures. As with most regional anesthetics, absolute contraindications include patient refusal and infection at the site of needle insertion. Relative contraindications for this peripheral nerve blockade are coagulopathy, neuropathy, systemic infection, and neuromuscular disorders. For performing a pudendal nerve block, the patients are placed in the prone position with the hips on a towel roll or premanufactured bump. The blockade is accomplished using a mixture of 20 cc of 0.5% lidocaine with 20 cc of 0.25% Marcaine. The mixture was injected peripheral to the ischiorectal fat starting at the anus. We use 30–40 cc of solution total with injections fanning out lateral, anterior and posterior to the anus. This is directed toward the ischial tuberosity and advanced to the level of the levator muscles. The injection blocks the terminal nerve endings of the sphincters and anus without the need to directly block a specific nerve structure as done in spinal anesthesia (Fig. 2).

This technique is effective for anorectal surgery including fistulotomy, hemorrhoidectomy and excision of skin tags. As documented by Nystrom in their article titled Local perianal block for anal surgery, “The anaesthesia is adequate when the sphincter is relaxed and can be dilated without pain [10]. Because the patient is awake, the surgeon needs to work gently and the operations will take a longer time. This is readily balanced by the much quicker turnover between cases. We found that one operation per hour was easily achieved.”

Fig. 2 Asterisks represent the location of the pudendal nerve

2 Summary

Regional anesthesia is a key component in ensuring a patient's pain control is adequate after a major abdominal or anorectal surgery. Laparotomy and port site incisions can be a major contributor to postoperative pain and most patients will benefit from peripheral nerve blocks to the abdominal wall. Spinal and epidural anesthetics allow the surgeon to operate without the need for general anesthesia, while pudendal nerve blockade and other aforementioned interfascial nerve blocks allow the patient to recover with minimal post-operative discomfort.

Common Pitfalls

- Laparoscopic and robotic procedures have the risk of conversion to open procedure
- Nerve blocks require a team of proficient regionalists who are adept at utilizing ultrasound and are well versed in understanding anatomy
- Inability to perform block

Clinical Pearls

- Pudenal blocks can provide adequate postoperative anaglesia for short anorectal operations
- Spinal anesthesia allows surgeons to avoid general anesthesia for more complex anorectal surgeries where relaxation and visualization are crucial

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Acute Pain Management Protocol for Urological Procedures: Kidney, Bladder, Prostate

Poonam Pai, Jordan Abrams, and Yan H. Lai

Case Stem *A 55-year-old man with a BMI of 28 (weight of 60 kg) presenting for an elective total laparoscopic nephrectomy for treatment of his primary renal cell carcinoma. His past medical history includes pulmonary embolism (after a long-haul travel). His medications include aspiring 81 mg and rivaroxaban (which he had stopped three days ago). Patient complains of mild fatigue prior to detection of cancer and started taking ginseng and claims that his energy levels are phenomenal. His electrocardiogram was notable for NSR. Patient also takes 24 mg of suboxone for history of opioid addiction which he stopped 3 days ago. A recent stress echocardiogram demonstrated left ventricular hypertrophy, moderate pulmonary hypertension, an ejection fraction of 45%. On exam, patient was noted to have a mallampati II airway and adequate mouth opening.*

Patient had a prior abdominal surgery for which he had received an epidural and says that helped him a lot with postoperative pain. The patient requests an epidural for this procedure as he thinks his kidney tumor is big and there is a higher chance of the laparoscopic procedure being converted to open. Your medical student has just finished his OB rotation and had

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_29

seen women on the labor floor receive an epidural for pain control, and wonders if this is the same.

Key Question 1 Can an epidural be considered as a regional anesthetic technique to this patient? How is it different from neuraxial techniques that are offered to parturients?

Epidural anesthesia may be used a sole anesthetic or as an adjunct to general anesthesia (GA) for procedures involving the lower abdomen, lower limbs, pelvis and perineum. Table 1 lists a number of urologic procedures where an epidural might be beneficial [1].

Dermatome is defined as an area of skin supplied by a specific nerve root. In the context of spinal anesthesia, certain procedures mandate a certain dermatomal level to obtain surgical anesthesia. Figure 1 lists the required dermatomal level for genitourinary procedures.

There are several benefits of using an epidural in comparison to GA. Some benefits of thoracic epidural analgesia are listed in Table 2.

Use of epidural intraoperatively provides not only analgesia but controlled hypotension, contributing to reduced blood loss and thereby transfusion requirements [2–4].

Although GA is required for nephrectomy due to patient positioning for the procedure, the use of a midthoracic epidural with a T6 sensory level will be appropriate for analgesia for laparoscopic and potential open surgical incisions [1].

Similarly, epidural is the standard technique for labor analgesia in parturient. It can be used for managing pain during labor, delivery and post-partum period. One of the main advantages of an epidural is the ability to retain the sensation of uterine contraction while maintaining adequate pain control allows the parturient

Table 1 Urogenital surgeries where epidural might be beneficial [1]

Cystectomy
Nephrectomy
Ureteral repair
Prostatectomy
Pelvic exenteration

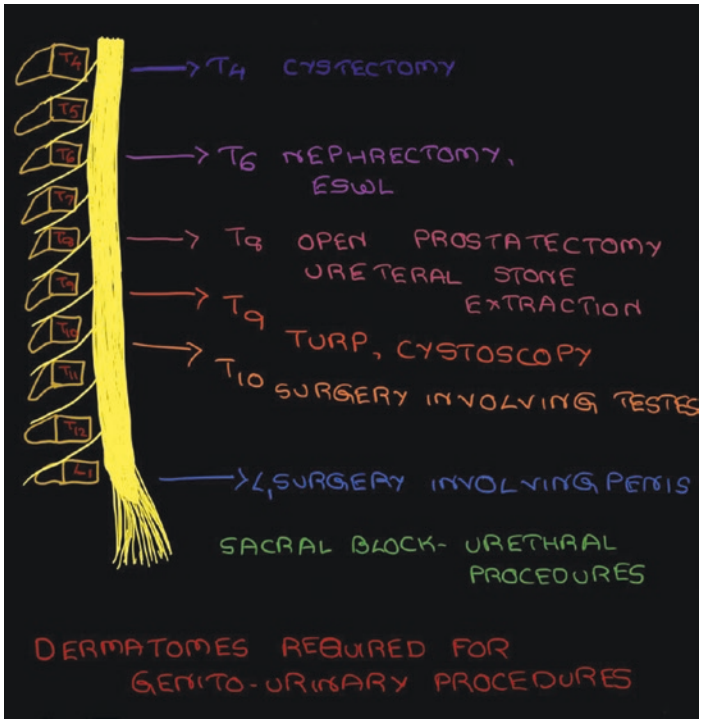

Fig. 1 Sensory level required for genitourinary procedures

Table 2 Benefits of thoracic epidural anesthesia and analgesia [2]

Superior perioperative analgesia
Decreased postoperative pulmonary complications
Decreased duration of postoperative ileus
Decreased duration of mechanical ventilation
Improved post-operative cognition
Reduced blood loss, transfusion requirements
Reduced incidence DVT
Reduced surgical stress response

to push during labor. It also allows for complete motor blockade of lower extremities up to the level of T4 if a cesarean section is necessary. The use of neuraxial anesthetics (epidural and spinal anesthesia) helps to avoid GA in the laboring patient [5, 6].

The use of epidural in parturient is somewhat different than patients undergoing nephrectomy because of the concomitant use of GA. GA is avoided in parturient because of increased aspiration risk with changes in the esophageal sphincter tone, possible difficult airway with more airway edema and mucosal vascularity and friability during pregnancy.

Case *The patient insists on an epidural due to his history of addiction. The surgeon tells you that there is a low probability that he might need to convert to open and is concerned that an epidural might hinder patient's ability to get out of bed given his prior history of PE and facilitate discharge as he plans on discharging the patient on postoperative day 1 (POD1) if the surgery is uneventful and fears that an epidural might add to the length of stay.*

Key Question 2 What other regional anesthetic techniques can be offered to this patient for analgesia that share similar analgesic efficacy as an epidural?

Paravertebral block (PVB) is an excellent regional anesthetic (RA) technique for primary or adjunct analgesia for thoracoabdominal surgeries. It is often considered when an epidural is contraindicated. Paravertebral block (PVB) involves injecting local anesthetic (LA) into the paravertebral space to block the spinal nerves that exit the intervertebral foramen. The paravertebral space communicates with the epidural space and PVB demonstrates similar efficacy in terms of analgesia when compared to epidural anesthesia [7].

The paravertebral space is defined:

- anterolaterally by parietal pleura
- posteriorly by superior costotransverse ligament
- medially by vertebrae and intervertebral foramina
- superiorly and inferiorly by heads of the ribs

Within this space, the spinal root emerges from the intervertebral foramen and divides into dorsal and ventral rami. The sympathetic chain lies in the same fascial plane, just anterior to the intercostal nerve and communicates with it via the rami communicantes. Hence, PVB produces unilateral sensory, motor and sympathetic blockade [8].

Besides similar analgesia profiles, hypotension is less likely with PVB because sympathetic block is rarely bilateral. Also, urinary retention is rare in PVB unlike neuraxial techniques. When performed correctly, complication and failure rates are low [9].

Case *You begin to discuss about PVB. The patient suddenly remembers that during his PE work up, they found him to have APLA syndrome. He denies any bleeding/clotting symptoms and states that he was cleared by his hematologist with his rivaroxaban (stopped 3 days ago) and ginseng (took last night) regimen. The platelet count during pre-operative work up done at the hematologist's office was 70,000 and normal coagulation (INR, PT, PTT) profiles.*

Key Question 3 Would the history of APLA syndrome and the cessation timing of anticoagulants change your plan for PVB?

Anti-phospholipid antibody syndrome (APLA) is considered to have a multifactorial etiopathogenesis and its classification depends on the clinical manifestations such as thrombotic APLA, characterized by venous, arterial, or microvascular thrombosis; and is characterized by multiorgan failure resulting from microthrombi. The prevalence of APLA is estimated to be 50 per 100,000 population, and a female-to-male ratio of 5:1. Considering the characteristic hypercoagulability, attention should be given to the occurrence of thrombotic complications while also considering the possibility of perioperative bleeding [10].

Evidence has shown that patients who consume herbal medications such as ginseng have increased chances of bleeding, and concurrent use of oral anticoagulants may exacerbate the risk of hemorrhage. It is often recommended that herbal medications be

discontinued in anticipation of surgery to avoid increased perioperative bleeding [11, 12]. Even though the cessation of rivaroxaban (3 days) is appropriate for placement of neuraxial or PVB anesthetics, the concomitant use of ginseng complicates the clinical picture and could increase risks of catastrophic epidural hematoma.

Case *The surgeon wants to proceed with the surgery as the hematologist has cleared the patient and bleeding in surgical area can be controlled easily under direct vision. There is blood available in case of hemorrhage. After placement of monitors, administration of mild sedatives, and performing a procedural timeout, your fellow begins to scan the patient's back with an ultrasound transducer to confirm thoracic spine anatomy. Fellow notices that patient has thoracic kyphoscoliosis/ spine deformity that would make PVB extremely challenging even under ultrasound guidance. You consider deferring PVB technique to avoid any bleeding complications or block failure. The fellow is back from an international regional anesthesia conference and heard about an erector spinae (ESP) block. The fellow suggests placing an ESP block instead of a PVB. On the other hand, you are more familiar with the Quadratus Lumborum block (QLB). The surgeon is also curious if transversus abdominis plane (TAP) blocks will cover the incisions, how long these blocks will last, and if they will hinder discharge.*

Key Question 4 What are the different abdominal fascial truncal block techniques that are appropriate for this patient?

The relevant anatomy, fascial block techniques and the correlative targets, and needle trajectory of abdominal truncal techniques are shown in Fig. 2.

Case *The medical student recently finished his surgery rotation and heard about how ERAS protocols in abdominal surgeries help better patient outcomes and asks you if they are any different when it comes to kidney surgeries especially in this patient with APLA syndrome and history of PE.*

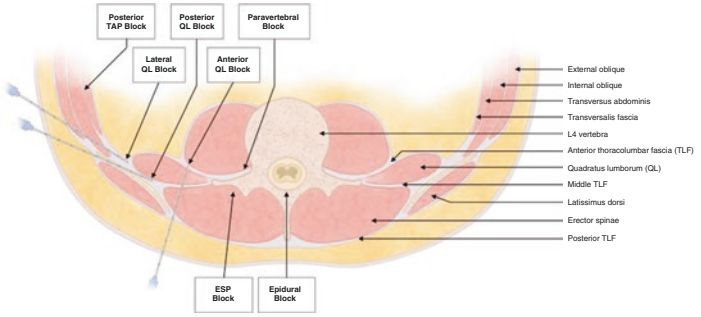

Fig. 2 Needle trajectory, targets, and relative anatomy of abdominal truncal techniques. Illustrated and labelled by author Jordan Abrams, MD

Key Question 5 What is the ERAS protocol for kidney surgeries? Is the ERAS protocol any different for this patient?

While limited studies are published on enhanced recovery after surgery (ERAS) implementation of laparoscopic nephrectomy and cystectomy, improved patient reported outcomes have been reported during early phases of recovery. There are many institutional variations but most protocols focus on multimodal analgesia with emphasis on regional anesthesia techniques, adequate hydration, PONV control, early mobilization. Some examples include reduced duration of fasting with pre-operative carbohydrate loading, intraoperative fluid maintenance of 3 ml/kg/h, with endpoint urine output of 0.5 ml/kg/h, and non-opioid analgesics such as acetaminophen, ketorolac, or tramadol [17].

In a patient with APLA syndrome, primary prophylactic strategies include:

- Prevention of perioperative thromboembolism, including use of intermittent pneumatic compression devices, early mobilization, and plans for postoperative anticoagulation
- Maintenance of perioperative normothermia is crucial in reducing blood loss and transfusion requirements [10].

Case *You induce general anesthesia and position the patient in lateral decubitus for the surgery and for the QL block. The sur-*

geon says he is running behind his schedule and asks if the block can be done after closure of skin. You explain why you would like to perform the block prior to surgical incision.

Key Question 6 What is pre-emptive analgesia?

- Any treatment that prevents establishment of central sensitization caused by incisional and inflammatory injuries. Surgical incision triggers an inflammatory reaction to damaged tissues that induces central sensitization of pain pathways.
- Crile in 1913 described the term and introduced use of regional techniques to prevent post-operative pain.
- Antinociceptive protection provided by pre-emptive treatments should extend into the postoperative period to effectively cover the inflammatory phase [18].
- Conflicting evidence on true mechanism or benefits of pre-emptive analgesia [19]

Case *Your team performs QLB and patient underwent laparoscopic nephrectomy uneventfully. The next day, you are seeing the patient on the floors. The patient is very happy and reports zero pain. However, he is unable to lift his leg on the side of the surgery. The surgeon is concerned that this might interfere with early mobility and discharge. He thinks your block might be the reason behind this.*

Key Question 7 What is the complication from the regional technique used that might have caused the leg weakness? What is the reason behind it?

See the complication section under QLB in Table 3. Complications associated with abdominal wall blocks are rare. A thorough history and physical exam will help ascertain the reason behind the lower extremity weakness. Surgical causes and positioning injuries should be ruled out.

Flexion of the hip and knee extension is provided by: Psoas muscle (L1–3 spinal nerves innervation), iliacus (femoral nerve),

Table 3 Comparison between ESP, QL and TAP blocks [13–16]

Type of Block	ESP	QL	TAP
Clinical indications	Analgesia with wide coverage for major thoracoabdominal procedures (mastectomy, rib fractures, heart surgery, lung surgeries).	All abdominal surgeries requiring visceral analgesia and abdominal wall incisions as high as T6.	Commonly performed when infraumbilical anterolateral abdominal analgesia is desired (colorectal, hernia repair, cesarean section).
Needle entry and approach	After selecting the target transverse process for the block, place the transducer in a paramedian sagittal orientation, approximately 2 cm away from the midline (spinous processes), and try to visualize the transverse process. Target is injection of local anesthetic in the plane deep to the erector spinae muscles and superficial to the transverse processes, to achieve a craniocaudal distribution along several vertebral levels. Needle insertion target for T5-T8 paraspinal levels for abdominal and T3-4 for thoracic procedure	(1) Lateral QLB or type 1 QL (QL1)—Linear transducer placed in the axial plane in the midaxillary line and moved posteriorly until the posterior aponeurosis of the TAP muscle becomes visible. The target is between the taper of fascia transversalis and the lateral margin of the QL muscle. (2) Posterior QLB or QL2—Linear transducer placed in the axial plane in the midaxillary line and moved posteriorly. Posterior to the QL muscle, outside the middle layer of the TLF. (3) Anterior QLB or QL3 or trans muscular QLB—Curved array transducer placed in the axial plane with target anterior to the QL muscle, between the QL and the psoas major muscles.	(1) subcostal—Linear transducer placed alongside the lower margin of the rib cage. The target is the fascial plane between the posterior rectus sheath and the TAP muscle. (2) TAP—Linear transducer placed on the midaxillary line axially between the subcostal margin and the iliac crest. The target is the fascial plane between the internal oblique (IO) and the TAP muscles. (3) Ilioinguinal/Iliohypogastric—A linear transducer is placed medial to the anterior superior iliac spine pointing toward the umbilicus. The target is the same fascial plane at the level of the deep circumflex iliac artery.

(continued)

Table 3 (continued)

Type of Block	ESP	QL	TAP
Contraindications	Patient refusal, active infection over site of infection, LA allergy.	Patient refusal, active infection over site of infection, LA allergy, known bleeding diathesis.	Patient refusal, active infection over site of infection, LA allergy.
Type of probe, needle and local anesthetic volume	Linear or curved **Needle:** 22-gauge, 5-10 cm short bevel **Local anesthetic volume:** 20–30 ml of LA each side with the concentration of 0.2–0.5% ropivacaine or 0.25–0.5% bupivacaine recommended.	Liner or curved **Needle:** 22-gauge, 5-10 cm short bevel **Local anesthetic volume:** 20–30 ml of LA each side with the concentration of 0.2–0.5% ropivacaine or 0.25–0.5% bupivacaine recommended.	Liner or curved **Needle:** 22-gauge, 5-10 cm short bevel **Local anesthetic volume:** 20-30 ml of LA each side with the concentration of 0.2–0.5% ropivacaine or 0.25–0.5% bupivacaine recommended.
Position	Sitting, lateral decubitus or prone	Supine with a lateral tilt, lateral decubitus, sitting, or prone	Lateral decubitus position, supine.
Potential complications	LAST, infection at the needle insertion site, vascular puncture, pleural puncture, pneumothorax, and failed block. Motor weakness may occur when the LA spreads to the lumbar plexus when performed from the lower thoracic or lumbar area.	LAST, possible to needle trauma to intra-abdominal structures such as the kidney, liver, and spleen if unfamiliar with ultrasound anatomy. Possible lower extremity weakness from lumbar plexus spread.	LAST, hematoma, possible needle trauma to intraabdominal structures such as liver, intestine and vascular structures.
Dermatome	At T4 level-T2 to T10 At T7 level, upper thoracic to L2-3	T4 to T12-L1; blocks the anterior and the lateral cutaneous branches of the nerves	T10–L2 (higher if subcostal)

Benefits with mechanism of action	Somatic and visceral analgesia due to diffusion of LA anteriorly to the ventral and dorsal rami of spinal nerves. Sensory block of the anterior, posterior, and lateral thoracic and abdominal walls Utilized for management of acute and chronic pain syndromes of the chest and abdomen	Somatic as well as visceral analgesia due to potential paravertebral and epidural spread. All the different QLB have different patterns of LA spread according to clinical and cadaver studies. Paucity of evidence recommending one approach over the other for different surgical populations. Anterior QLB may result in LA spread to the lumbar plexus resulting in prolonged unilateral lower extremity weakness, delaying mobilization and hospital discharge. There is a risk of direct needle trauma because of close proximity to the pleura and kidney. The risk of bleeding based on QLB approaches are not yet known. It is recommended that, for all approaches, the American Society of Regional Anesthesia and Pain Medicine guidelines for deep peripheral blocks be followed.	Somatic analgesia targeting intercostal nerves (T10-L2), the subcostal nerve (T12), and the Ilio-hypogastric and ilioinguinal nerves (L1) located in the TAP plane. TAP block might be insufficient to cover higher abdominal or ports needed in nephrectomy cases.

and quadriceps femoris muscles (femoral nerve). LA might spread to the lumbar plexus or to the femoral nerve via the transversalis and iliacus fascia within the psoas compartment. An unwanted femoral nerve block has been reported as a possible complication of all QL blocks (but especially with QLB 3). The lower extremity weakness may last for 12-18 hours depending on the volume and concentration of local anesthetic used. This complication should be considered when performing the block, especially in the setting of day-case surgery [20, 21].

1 Summary

- Multiple nerve blocks have been studied to provide analgesia for urologic surgeries including thoracic epidurals, TPVB, ESPB, QL, and TAP blocks. It is important to be familiar with the advantages/benefits and disadvantages/risks of each block.
- Being familiar with comparative block anatomy is helpful in selecting the appropriate technique.
- RA has been shown to offer multiple benefits.
- It is important to understand the ASRA anticoagulation guidelines for neuraxial, deep, and superficial nerve blocks to guide clinical decision making.
- Being familiar with ERAS protocols for different surgeries and our role in certain interventions is important to provide the best quality of care.

Common Pitfalls

- Failure to establish strict follow up with all patients receiving regional blocks can lead to a delay in treatment on complications.
- Failure to consider performing blocks before surgical incision will prevent one from taking advantage of their analgesic benefits during the procedure and lead to higher opioid use with

resultant increase in postoperative nausea and vomiting and adding to length of stay.
- Failure to educate patients and surgeons on the benefits of regional anesthesia for urologic surgery may dampen benefits and enthusiasm of an ERAS protocol. RA for kidney surgery has been shown in several studies to provide a multitude of benefits for patients postoperatively.

Clinical Pearls

- Institutions vary greatly with ERAS protocols. Type of procedure must be considered when choosing a regional approach.
- Provider expertise with different blocks is a key factor in choosing regional techniques.
- In patients with expected difficult pain control in the postoperative period (e.g., chronic pain history), a nerve catheter can always be considered.

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Acute Pain Management Protocol for Biliary-Hepatic, Spleen, Pancreatic Procedures

Elizabeth Cooney Reyes, Claire Marie Bentley, Hong Wang, and Pete Pelletier

Case Stem

The patient is a 65-year-old male who has pancreatic cancer and is scheduled for robotic and possible open pancreatectomy, splenectomy, and possible hepatectomy. The patient's endoscopic ultrasound and fine needle aspiration show a mucous neoplastic cyst. The CT image showed a 5.3 × 4.1 pancreatic body lesion. The patient admits to weight loss but denies any abdominal pain, nausea, fever, or chills. The medical history includes colitis, chronic obstructive pulmonary disease (COPD), diabetes mellitus type II, deep vein thrombus (DVT), hemochromatosis carrier, hyperlipidemia, and depression. His surgical history includes cholecystectomy and pancreaticoduodenectomy for pancreatic cysts. His medications include: albuterol sulfate (inhalational), aspirin, bupropion, cetirizine, cholecalciferol, dexlansoprazole, digoxin, escitalopram oxalate, folic acid, insulin glargine (subcutaneous injection), lipase-protease-amylase, mesalamine, metoprolol succinate, montelukast, multivitamin, novolog flexpen, pravastatin, and pyridoxine. He is allergic to erythromycin, penicillin, sulfa, and morphine.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_30

His body mass index is 19.16 kg/m2. He has 26 pack-year smoking history and requires home oxygen (O2) 2 l/min. Selective Preoperative Laboratory test: Hemoglobin: 11.0 g/dl, Platelet: 100 k/ul, Normal liver faction, hemoglobin A1C: 10, PO2: 69 mmHg with room air, Lactate: 1.2 mmol/L, INR: 1.5.

1 Incisions for Robotic and Open Pancreatectomy and Splenectomy

Open pancreatectomy incision can be midline vertical (Fig. 1a) or bilateral subcostal incision (Fig. 1b). The robotic approach includes 4-5 incisions for camera and assistant ports and one midline incision for extraction (Fig. 1c).

1.1 Any Difference in Postoperative Pain?

The midline vertical incision involves multiple dermatoses (T6-T12) and will likely have the most severe postoperative pain. Bilateral subcostal incision involves dermatoses T6-T8 and the resultant pain likely affects the pulmonary function more, increasing the incidence of postoperative pulmonary complications. The robotic approach has the least somatic pain among the above three incisions, but the visceral and referral pain can still be considerable.

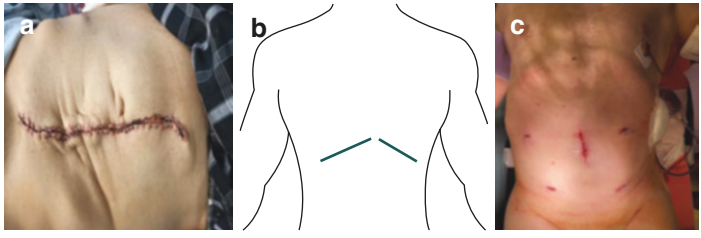

Fig. 1 Incisions for robotic and open pancreatectomy and splenectomy. (**a**) Midline vertical; (**b**) Bilateral subcostal; (**c**) Robotic approach

1.2 What Type of Regional Blocks Can we Use?

The type of block to use will depend on the patient's condition and surgical procedure. Traditionally, thoracic epidural analgesia is the mainstay for abdominal, especially open, procedures. Bilateral paravertebral blocks and other peripheral nerve blocks such as erector spinae plane (ESP), transversus abdominal plane (TAP), and quadratus lumborum (QL) blocks (see the section below) have been used for patients who have absolute or relative contraindications of epidural analgesia. This may include patient refusal, history of back surgery, local infection at the catheter insertion site, and allergy to epidural agents.

1.3 What Are the Concerns for Selecting a Different Type of Block?

- Efficacy of the block
- Contraindications of the individual block
- Potential hemodynamic changes from the block
- Coagulation issues due to the patient condition or surgery
- Continuous infusion (catheter) vs single injection
- The dermatoses and the size of the incision
- Surgical site infection

2 What History of this Patient Should we Be Concerned about for Postoperative Analgesia?

- History of COPD and home O2
  - Effective postoperative analgesia will facilitate deep breathing and reduce the risk of postoperative pulmonary complication.
- History of DVT
  - Epidural analgesia may have some benefits for reducing postoperative DVT incidence.

- The patient's preoperative coagulation profile: platelet count is 100 k/u, INR 1.5
  - The surgical procedures may further reduce the coagulation function.
- Hypotension resulted from perioperative bleeding.
  - Sympathetic block induced by neuraxial analgesia may exacerbate hypotension and require additional volume resuscitation.
- Possible hepatic resection
  - Extensive hepatic resection affects liver function. Several blocks listed above are volume-dependent and require a significantly larger quantity of local anesthetics. To avoid the risk of local anesthetic toxicity, the choice of the block and the required amount of local anesthetic should be carefully considered.
- Robotic approach vs open laparotomy
  - Most of the pain from the robotic approach can be effectively managed with single injection blocks while the open laparotomy often requires catheter infusion for a longer duration's analgesia.

2.1 What Factors Should we Consider when Choosing a Single Shot Injection or Catheter Infusion?

- Time consumed performing the block: Single < Catheter
- Risk of deep tissue bleeding: Single < Catheter
- Risk of infection: Single < Catheter
- Post-operative block management: Single < Catheter
- Catheter-related complications: Single < Catheter
- Duration of the block: Single < Catheter
  - The duration of the single injection can be prolonged by the addition of other agents such as dexmedetomidine, dexamethasone, or magnesium.

– Liposomal bupivacaine (exparel) has been approved for TAP blocks but has not been approved for paravertebral, ESP, and QL blocks although some recent studies have successfully used exparel for QL blocks.

Summary Epidural analgesia was not considered in this patient due to the borderline coagulation status (platelet count is 100 k/u, INR 1.5) and the potential massive blood loss during surgery. The patient received bilateral ESP catheters instead of bilateral ESP single shots. This decision was made because of the anticipated difficulty of the surgery, and the increased likelihood of the surgeon converting to an open procedure due to the patient's history of multiple abdominal surgeries.

3 Ultrasound Guided Regional Anesthesia Technique and Surgical Approach

The following section will group and summarize the techniques according to the surgical approach.

3.1 Laparoscopic Approach

3.1.1 Transversus Abdominal Plane (TAP) Block

The TAP block has become increasingly popular in recent decades as ultrasound technology has improved [1]. Through point-of-care ultrasound, providers can easily locate and inject a local anesthetic into a plane between the transversus abdominis and internal oblique muscles [2]. Variable approaches to the TAP block have different dermatomal coverage, the TAP block selectively provides analgesia to thoracolumbar spinal nerves in the T6-T12 range of distribution corresponding to the anterolateral abdominal wall. As a result, the TAP block has become a preferred modality of postoperative pain management for minimally invasive hepatobiliary, pancreatic, or splenic surgeries (i.e. robotic or laparoscopic).

Pros

- Like many blocks, it reduces the need for postoperative opioid analgesia
- It can be performed percutaneously by an anesthesia provider preoperatively or intraoperatively by a surgeon from inside the abdominal wall [3]

Cons

- Due to this block's reliance on anesthetic extravasation within the TAP, the anatomic variance between patients within this potential space can potentially increase outcome variability relative to other blocks which isolate individual nerves [1]

How To

- TAP blocks were historically performed as landmark-guided procedures. The plane would be accessed by inserting a needed through the triangle of petit and advancing until both fascial layers of external and internal oblique muscles were penetrated and the provider felt a loss of resistance. Colloquially this technique was known as a "double pop."
- Landmark-guided approaches are no longer indicated for TAP blocks and providers are encouraged to use ultrasound instead. This provides greater assurance of block placement and reduces the risk of penetrating trauma to underlying structures [1]
- Use the following steps to appropriately identify the TAP [1]:
  - Using a linear probe (or curvilinear probe to accommodate for depth), locate the rectus abdominus muscle at the xiphoid process and follow it along the costal margin until the linea semiluminaris becomes visible laterally.
  - Just medial to this linea semiluminaris, a local anesthetic can be injected into the plane between the rectus abdominus and transverse abdominus to perform a subcostal TAP block.

  - Continue moving the probe inferolateral until it rests between the iliac crest and costal margin.
  - 3 distinct muscle layers should be visible at this time: external oblique, internal oblique, and transversus abdominus.
  - At the midaxillary line, the TAP can be found between the internal oblique and transversus abdominus and is the site of injection for the lateral TAP block.
  - From a posterior approach, the TAP exists between the internal oblique and the transversus abdominus and extends adjacent to the quadratus lumborum.
- These TAP block variations can be performed to further localize the portion of the abdominal wall being anesthetized.

3.2 Open Approach

3.2.1 Thoracic Epidural

Thoracic Epidurals (TE) have long been established as a cornerstone in perioperative care for open abdominal surgery. In these cases, TE catheter placement offers superior perioperative analgesia and patient satisfaction compared with systemic opioids or more peripheral regional techniques (i.e. TAP, QL, PVL, ESP blocks). Beyond its analgesic properties, TE has been shown to be beneficial for multiple physiologic processes.

Pros

- Decreases risk of postoperative pulmonary pneumonia—likely due to improved cough and earlier extubation and mobilization [4]
- Decreases adverse perioperative cardiac events—likely due to better pain control and attenuation of the neurohumoral stress response (provided by the segmental temporary sympathetic block) [5, 6]
- Improves postoperative intestinal mobility—which may be in response to the decreased sympathetic tone, attenuated intesti-

nal neuroinflammatory processes, and reduced systemic opioid analgesia requirements [7, 8]
- Reduces post-operative respiratory failure after major abdominal surgery in high-risk patients [9]

Cons

- Serious, but rare, complications include: epidural hematoma, epidural abscess, meningitis, subdural injection, high spinal, cardiovascular collapse
- Mild to moderate procedural complications: back pain, postdural puncture headache, pneumocephalus
- Increased contraindications exist for TE placement than for superficial plexus blocks, limiting its safe use in many patient populations
- Requires careful risk-benefit analysis prior to initiation of TE in each individual case

Midthoracic epidural catheter placement from T5 to T8 is appropriate for most upper abdominal procedures. At these levels, there is lumbar and sacral nerve root sparing which decreases the risk of urinary retention and lower extremity motor deficit. Common hepatobiliary procedures supplemented with TE include pancreatectomy and hepatectomy. The changes in coagulation for uncomplicated minor liver resections are brief so TE can be performed preoperatively. However, the close patient monitoring required in post-operative management must be considered. Neurologic exams should be performed daily while the catheter is still in place to assess for early signs of cord compression. The prothrombin time and platelet count should also be monitored post-operatively and prior to epidural catheter removal. With protracted coagulopathy, epidural catheter removal might be delayed or, alternatively, there may be a need to administer fresh frozen plasma prior to epidural removal [10].

While there are various techniques for thoracic epidural placement (the two most common described are the paramedian

approach and midline approach), the paramedian approach will be discussed below. Midline insertion can be more challenging as the spinous processes of T4–T9 is more acutely caudally angled. The paramedian approach offers a larger intervertebral opening into the epidural space than the midline approach too. The supraspinous and interspinous ligaments are midline structures that are not traversed in the paramedian approach. Instead, the epidural needle penetrates paraspinal muscle before reaching ligamentum flavum [9, 11, 12].

How To

- Use the following steps to properly place TE via paramedian approach:
- Palpate desired spinous process (depending on surgical incision) starting from T7 (approximately at the level of the inferior edge of the scapula) or counting each spinous process from C7
- Localize skin ~1-1.5 cm lateral and ~ 1 cm caudad to the inferior aspect of the superior spinous process
- Insert the needle through localized skin with a slight angle (10-15 degrees) toward the midline and cephalad direction
- Once the lamina is reached with the needle, slightly back out and redirects in a cephalad and medial direction before reinsertion. Continue this process until loss of resistance is achieved

The procedural complications highly specific to TE are rare but can result in serious injury. Thus, understanding the conditions that may predispose certain patient populations to these complications is paramount in deciding whether the patient is a candidate for the procedure.

Absolute contraindications include patient refusal and severe coagulation abnormalities. Most other pathologic conditions are relative/controversial contraindications and require thorough risk-benefit analysis prior to initiation of epidural placement. Some of the relative contraindications to TE placement include thrombocytopenia (etiology, platelet function, bleeding history, and the

trend must be taken into account, but most sources suggest platelets <70,000-100,000 mm^3 as the contraindication cut-off), anticoagulation status (anticoagulant must be held within the time frame specified in the safety profile for each drug prior to TE placement), and elevated intracranial pressure. Ultimately, a risk-benefit analysis, with particular emphasis on patient preferences, comorbidities, and the type and duration of surgery, should be done prior to the initiation of thoracic epidural placement [11].

3.2.2 Erector Spinae Plane (ESP) Block (Fig. 2)

Bilateral erector spinae plane (ESP) blocks can provide diffuse analgesic coverage, like TE, adequate for open abdominal surgery. ESP block is a newer interfascial anesthetic technique and covers somatic and visceral pain by affecting the ventral rami and rami communicantes as local anesthesia spreads to the paravertebral space. When performed bilaterally it has been demonstrated to be comparably effective to thoracic epidural analgesia [13, 14].

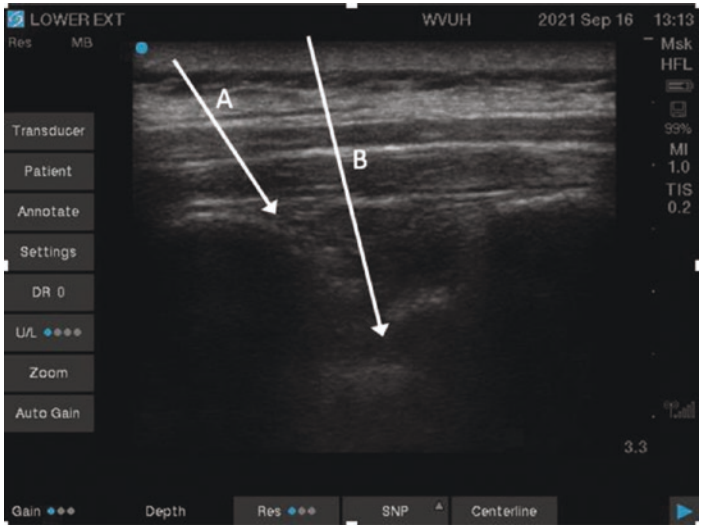

Fig. 2 Ultrasound image for Erector Spinae plane (A) and Paravertebral (B)

The erector spinae consists of three distinct muscles arranged in parallel along the spine: spinalis, longissimus, iliocostalis. The ESP block is the technique of injecting local anesthesia deep to the erector spinae muscle, allowing for volume-dependent longitudinal diffusion within the plane across several vertebral levels. The mechanism of action possibly comprises anterior diffusion into the paravertebral space and more likely by interfascial spread where the spinal nerves bifurcate into anterior and posterior rami [14]. These branches provide unilateral innervation to the anterolateral and posterior abdominal walls, respectively, making this block a strong option for those undergoing open abdominal procedures.

Pros

- Easy to perform
- Lower pain scores and opioid requirements for abdominal surgery [15]
- Complications are rare
- Provides somatic and visceral pain coverage (unlike TAP blocks)
- Lower risk of serious injury compared to TE or Paravertebral Block
- Increased candidates for thoracic ESP block, compared to neuraxial anesthesia, without concern for coagulopathy

Cons

- Procedural risks, although rare, like pneumothorax or local anesthetic toxicity
- Thoracic ESP block is a newer block so efficacy, mechanism of action, and clear indications less understood

How To

- Use the following step to properly locate the erector spinae plane [14]:

- *Palpate the spinous process of T7 (approximately at the level of the inferior border of the scapula)*
- *Using a linear ultrasound probe in the parasagittal orientation, scan until the transverse process of T5 can be visualized underneath 3 layers of muscle (from superficial to deep: trapezius, rhomboid major, erector spinae).*
- **Above T5, the trapezius, rhomboid major, and erector spinae muscles can be visualized as superficial to transverse processes. Below T5, only the trapezius and erector spinae muscles are visualized.*
- *Advance the needle in-plane in a cranial to caudal direction through each muscle layer until the transverse process of the desired level is reached, gently aspirate and inject a saline bolus. Observe dissection of the plane confirming proper needle placement.*
- *Aspirate and inject 20-30 ml of local anesthetic (since interfascial plane blocks require volume) bilaterally for adequate spread (consider patient weight and drug to prevent exceeding maximum total dose).*

The ESP block has multiple advantages superior to other regional techniques. Its safety profile is one of them as it has a low risk of damage to other underlying structures. While catheters can be placed bilaterally for continuous infusions, it can also be performed as a single shot using long-acting local anesthetic thus minimizing the risk of infection [14, 15]. The ESP block is newer, so more research would benefit our full understanding of the block's mechanism of action and clear indications.

3.2.3 Paravertebral Block (Fig. 2)

The thoracic paravertebral block (PVB) involves injecting local anesthesia along the thoracic vertebrae where the spinal nerves exit the intervertebral foramen in the thoracic paravertebral space (TPVS). This produces ipsilateral segmental somatic, and sympathetic nerve blockade by direct effect on the nerves in the TPVS, and extravasation into the intercostal space laterally and the epidural space medially. The TPVS is bound anterolaterally by the pleura, medially by the vertebrae and intervertebral foramen, and

posteriorly by the transverse process and superior costotransverse ligament [16, 17]. The TPVS consists of adipose tissue within which contains: the spinal (intercostal) nerve, the dorsal ramus, intercostal vessels, rami communicantes, and the sympathetic chain [17, 18]. The dermatomal distribution after large volume single injection is less predictable, so multiple small volume single injections at contiguous thoracic levels is preferable. Also, since the nerve blockade is unilateral, thoracic PVB should be performed bilaterally for adequate analgesia for open abdominal surgery.

Pros

- Lower pain scores and opioid requirements
- Complications are rare
- Hypotension is rare, even after bilateral injection [18]
- Provides somatic and visceral pain coverage

Cons

- Serious adverse effects, although rare, include: pleural puncture, pneumothorax, nerve injury, local anesthetic toxicity
- Considered a deep plexus block, like TE, so more relative contraindications exist than for superficial plexus blocks, limiting its safe use in many patient populations [18]
- Requires careful risk-benefit analysis prior to initiation of in each individual case

How To

- Use the following steps to perform TPV block under ultrasound guidance [16, 18]:
- *While there are various approaches to performing TPV block (with and without ultrasound using surface landmarks), we will describe one method, similar to the ESP block discussed above, using the ultrasound in parasagittal orientation*

- *After palpating spinous process of desired level, place probe there and scan laterally until the transverse process can be visualized*
- *Advance the needle in-plane in a cranial to caudal direction towards the inferior edge of the transverse process of the desired level. Traverse the superior costotransverse ligament into the TPVS. Aspirate and inject saline to confirm the location*
- *Aspirate and inject the local anesthetic. Block should be performed bilaterally. Consider at multiple levels (3-4 ml per injection) for adequate and more predictable spread. Consider patient weight and drug to prevent exceeding the maximum total dose.*

3.2.4 Quadratus Lumborum (QL1, QL2, QL3) Block

The quadratus lumborum block (QLB) is a newly described ultrasound-guided fascial plane block where local anesthetic is injected adjacent to the quadratus lumborum, anesthetizing the thoracolumbar nerves. Unlike TAP blocks which only provide somatic analgesia, QLBs provide somatic as well as visceral analgesia of both the abdominal wall and the lower segments of the thoracic wall. As such, QLBs are very useful in providing analgesia for abdominal surgeries, especially when neuraxial analgesia is not an option for patients. QLBs provide visceral analgesia due to their paravertebral and possibly epidural spread. The present evidence suggests that the different variants of QLB have different analgesic effects and mechanisms of action, but largely provide sensory blockade of T7–L2 dermatomes. In particular, the "QL3" and "QL2" may result in wider and longer sensory blockade compared to the TAP nerve block [19].

Pros

- Provides somatic and visceral analgesia, unlike TAP block
- Lower pain scores and opioid requirements

Cons

- More technically challenging procedure
- Serious complications exist from direct needle trauma like: kidney puncture, pleural puncture, vessel injury leading to retroperitoneal hemorrhage
- Possible local anesthetic extension to the lumbar plexus could result in lower extremity motor blockade, potentially delaying post-operative mobilization. Lower limb weakness has been reported after use of all quadratus lumborum block approaches [19, 20]
- Contraindicated in anticoagulated patients as it is considered a deep plexus block

How To

- Use the following steps to perform the QL block [19–21]:
- *The patient can be positioned supine with a lateral tilt, lateral, sitting, or prone. This is largely determined by patient mobility and planned needle trajectory*
- *If the patient is in lateral decubitus position, place probe at the midaxillary line in axial orientation and identify the three muscle layers of the lateral abdominal wall between the subcostal margin and ipsilateral iliac crest. Then move posterior-laterally until the transversus abdominis muscle ends, and where the internal and external oblique will form the aponeurosis of the quadratus lumborum. Further posterior-laterally, the QL muscle will come into view with the latissimus dorsi lying superficially to the QL.*
- *Here the "Shamrock Sign" can be visualized (the stem represents L4 transverse process and the three leaves are the quadratus lumborum (with its attachment to lateral edge of TP), the erector spinae posteriorly, and the psoas anteriorly).*
- *Use color doppler to identify lumbar arteries posterior to the QL muscle or any other large vessels prior to needle insertion.*

- *The following are described using an in-plane approach:*
- *For the lateral QLB or "QL1" block, the needle is directed anterior to posterior towards the injection site: the junction of the tapered abdominal muscles and the lateral border of the QL muscle.*
- *For the posterior QLB or "QL2" block, the needle is directed anterior to posterior (or vice versa) towards the injection site: posterior surface of the QL muscle, in the fascial plane between the QL muscle and the latissimus dorsi.*
- *For the transmuscular/anterior QLB or "QL3" block, the needle is directed anterior to posterior (or vice versa) towards the injection site: anterior to the QL muscle, between the QL and psoas major muscles.*
- *Aspirate and inject normal saline to confirm correct needle placement.*
- *Aspirate and inject local anesthetic bilaterally for adequate spread. Consider patient weight and drug to prevent exceeding maximum total dose.*

The indications for QLBs, are shared with those of TAP blocks, with the added benefit of providing visceral analgesia. While all QL block approaches have been shown to provide adequate analgesia, each has their own benefits and risks. The lateral QLB ("QL1") can potentially compromise visceral coverage with less spread to the paravertebral space. On the other hand, performing the anterior QLB ("QL3") block can be more technically challenging with higher risk for needle trauma to kidney, pleura, or vasculature resulting in retroperitoneal bleeding.

Absolute contraindications to performing a QLB include those for all blocks like patient refusal, local infection over needle insertion site, and allergy to agent as well as those specific to deep plexus blocks like therapeutic anticoagulation. Possible relative contraindication to performing a QLB would be difficult identifying structures given possible anatomic abnormalities or larger body habitus [20, 21].

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Acute Pain Management Protocol for Hernia Repair: Umbilical, Inguinal, Femoral Hernia

Rutuja Sikachi and Yan H. Lai

Case Stem

You are an anesthesia resident assigned to the pediatric room today. Your first case is a five-year-old, 15 kg, male child planned for open umbilical hernia repair. He is in a preoperative holding area with his mother. He appears calm and watches his favorite cartoon on mobile phone. Mother reveals that he was born full term and it was normal delivery without any complication. She noticed a small but growing bulge from his umbilicus that is more prominent when he is crying. All growth milestones have been normal and he is up to date on his immunizations. The child has few teeth but none loose and had milk at 10 pm last night. Surgeon mentioned that after surgery they are going home. Mother prefers general anesthesia but she is concerned about managing his operative pain at home and wants to know about her options.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_31

Key Question 1 How do you approach a mother's concern? Is there any regional anesthesia (RA) technique which can be offered for this patient?

A multimodal approach should be implemented for analgesia. Oral, intravenous, rectal acetaminophen and NSAIDS are helpful perioperatively if indicated. Surgeon should also be encouraged to infiltrate wound area with LA. Nevertheless, regional anesthesia (RA) should be considered as an adjunct to general anesthesia (GA) or as a primary anesthetic. The decision to utilize various RA techniques (neuraxial or peripheral nerve blocks (PNB)) depends on patient and surgeon preference, as well as other absolute or relative contraindications:

- Absolute: local anesthetic (LA) allergy and patient refusal.
- Relative: active infection, anticoagulation or bleeding disorders for deep blocks, pre-existing neurological deficits, and inability to cooperate.

A spinal anesthetic can be employed for this procedure but we should consider patient preference (mother prefers GA) and our child's ability to cooperate. Inevitably, heavy sedation or GA would have to be administered for the spinal anesthetic. On the other hand, a bilateral rectus sheath block (RSB) as a supplement with GA can provide adequate analgesia for this particular case.

Key Question 2 How is RSB helpful in this procedure? Describe anatomy of RS and technique for block. What are possible complications associated with this block? Can this block be used for any other procedures?

For open umbilical hernia repair, incision is made in the infraumbilical region. Rectus abdominis muscles originate from pubic symphysis and pubic crest and insert on xiphoid process and 5–7th costal cartilage. Two muscles are separated by linea alba and covered by anterior and posterior rectus sheath. Both layers of sheaths are derived from aponeurosis of three abdominal wall muscles, namely external oblique (EO), internal oblique (IO), and transversus abdominis (TA) [1]. RSB targets the anterior cutaneous

branches from the ventral rami of T7-T12 that pass through the posterior rectus sheath space. This space is continuous and allows for spread of LA in cephalad and caudal direction. This space also contains superior and inferior epigastric arteries and veins and lymphatic vessels [1].

In the supine patient, the linear ultrasound transducer is placed horizontally at the level or just above the umbilicus. Once layers of abdominal musculature and boundaries of rectus muscles are identified, LA is deposited between rectus muscle and posterior rectus sheath [2]. Complications include peritoneal puncture, bowel or visceral perforation, major vessel puncture (mesenteric, inferior epigastric artery), and retroperitoneal hematoma [2].

RSB can be successfully used as sole analgesic or as supplemental strategy combining with other abdominal wall interfascial plane blocks in procedures involving midline or other areas of abdominal incisions [2]:

- Periumbilical procedures such as pyloromyotomy, duodenal atresia repair
- Open abdominoplasty
- Laparoscopic and robotic surgeries involving multiple port placement (general and urological).

Case *In the holding area, the surgeon examines the child and identified an additional inguinal hernia repair on the right groin. He plans to repair that with an open approach. In addition to the RSB, he inquires about other blocks that will help manage pain without too much opioids postoperatively since he wants to avoid constipation when the child is recovering at home.*

Key Question 3 What is inguinal hernia? How are they repaired? What type of anesthesia techniques can be used for these cases?

Inguinal hernia (IH) occurs when intraabdominal contents like fat or intestines protrude through weakness in the lower abdominal wall in the inguinal or groin area. Worldwide, more than 20

million groin hernia repairs are performed annually [3, 4]. IH is repaired with mesh in tension free manner, either by open technique or laparo-endoscopic technique. In laparoscopic technique, 3 ports are created amongst which one is usually at the umbilical region [3, 4].

Open approach surgeries can be performed under:

- General (GA)
- Neuraxial and paravertebral: spinal, epidural and paravertebral blocks
- LA infiltration: surgeon infiltrative field blocks targeting ilioinguinal and iliohypogastric nerves as well as skin or subcutaneous wound infiltration
- Ultrasound (US) guided peripheral nerve block (PNB): TAP, II/IH, or QL blocks
- Combination techniques: GA + neuraxial, GA + LA, GA + PNB, neuraxial + LA, PNB + LA

Benefits of RA: less postoperative pain, reduced incidence of nausea, vomiting, and urinary retention, faster mobilization, earlier discharge, lower hospital costs [3, 4]. Success rate of RA techniques is higher with ultrasound guided techniques than with landmark techniques.

Key Question 4 Besides RSB, highlight various abdominal fascial plane blocks that can be utilized for groin hernia repair surgery.

II/IH block [5, 6]

- Indicated for open inguinal surgeries: inguinal hernia repair, femoral hernia repair, orchiopexy, varicocele repair, hydrocele repair and laparoscopic repairs
- Anatomy: Both Ilioinguinal (II) and iliohypogastric (IH) nerves are derived from lumbar plexus, particularly the L1 primary ventral ramus. L1 enters the upper part of psoas major where II and IH nerves branch out. These nerves emerge at the

lateral border of psoas major and pass anterior to quadratus lumborum (QL) muscle. At the lateral border they pierce lumbar fascia and run in between the IO and TA muscles. II nerve enters the inguinal canal along with spermatic cord or round ligament and supply skin of upper medial thigh in both sexes, upper part of scrotum, root of penis in males and skin of mons pubis and labia majora in females. IH nerve branches into lateral and medial cutaneous branches at the iliac crest. Lateral cutaneous branch supplies gluteal skin while medial cutaneous branch supplies skin above inguinal ligament and suprapubic region.

- Technique: In supine position, a linear transducer is placed along a line between umbilicus and anterior superior iliac spine (ASIS). Once peritoneum and muscular layers are identified, transducer is moved towards the iliac crest maintaining orientation till all three abdominal muscles (EO, IO, TA) and two nerves are identified. Nerves appear as hypoechoic structures lying between IO and TA muscles. Needle is inserted in plane to transducer and directed medial to lateral with 10–20 ml of LA injected.

TAP Block [6, 7]

- Same indication as II/IH plus open appendectomy, laparoscopic cholecystectomy, laparoscopic nephrectomy, minor colorectal surgery, renal transplant surgery.
- Anatomy: TA forms the innermost layer of the muscular layer of the abdominal wall. Unlike II/IH blocks that targets lower abdominal wall (umbilicus or lower), TAP fascial planes can be found in the entire abdominal cavity. This plane exists in between IO and TA muscles. Branches from ventral rami of T7-T12 and L1 together form upper and lower TA plexus. These supply anterior abdominal wall and parietal peritoneum.
- Technique: Patient is supine and transducer placed transversely between costal margin and iliac crest. After identification of

EO, IO, TA, and peritoneum, the transducer is moved posteriorly towards midaxillary line. A needle is inserted in-plane to place the needle tip between the IO and TA muscles and 20-30 ml of LA is injected.

Subcostal TAP block [6, 7]

- Variation of TAP used to cover higher abdominal incisions (T6-T9 intercostal nerves).
- Place US Transducer in the subcostal area, lateral to rectus sheath and parallel to subcostal margin. After identifying lateral aponeurosis of RS, EO, IO, TA, and peritoneum, needle is inserted in plane from the lateral border of the rectus muscle and away from the midline. LA is injected in between the IO and TA muscle plane.
- Subcostal TAP would have suboptimal coverage for an inguinal or femoral hernia.

QLB [8]

- All abdominal surgeries involving anterior abdominal wall, open or laparoscopic: appendectomy, cholecystectomy, large bowel resection, cesarean section, abdominal hysterectomy, open prostatectomy, renal transplant, nephrectomy, abdominoplasty, iliac crest bone graft, ileostomy, exploratory laparotomy with midline incisions
- QL muscle spans from iliolumbar ligament and iliac crest to 12th rib and transverse processes of the L1 to L5 lumbar vertebrae. It is invested by thoracolumbar fascia (TLF) which divides into anterior, middle and posterior layers. These layers form the basis for variations of QLB. QLB provides wider coverage than any other abdominal wall fascial plane blocks and may potentially covers both somatic and visceral analgesia from T4 to L1. 20-30 ml of LA is needed for each side of the abdominal wall.

- *QL1 (lateral):* Starting with patient supine and a TAP view, slide US Transducer posteriorly to locate posterior aponeurosis of TA muscle. LA is deposited deep to aponeurosis, superficial to TLF at lateral margin of QL muscle. This variation covers lateral cutaneous branches of IH, II and subcostal nerves T12-L1. This is the easiest and safest to perform.
- *QL2 (posterior):* From QL1 view, move transducer further posteriorly until the entire QL muscle is located. LA is deposited in the posterior part of QL muscle where it intersects with the middle layer of TLF. Block is easier to perform with patient in lateral decubitus position.
- *QL3/Transmuscular QLB (anterior):* A curvilinear transducer might be needed to visualize deeper structures. From QL2 view, adjust depth to visualize the psoas major (PM) muscle deep to the QL muscle and erector spinae muscles posteriorly. Together with the transverse process of L4, these form the 'Shamrock' sign. LA is deposited between QL and PM. This variation provides not only somatic but visceral analgesia from T4 to L1. Lower extremity weakness and increased risk of falls due to LA spread to the lumbar plexus is possible with QL3.

Key Question 5 What is the key difference between TAP and QL blocks [6–8]**?**

- QL blocks have a more widespread dermatomal coverage and longer lasting analgesic effect compared to TAP.
- TAP: somatic coverage of 1–2 dermatomal spread from injection site (range: T8-L1)
- QL: somatic and visceral coverage from T4-L1 (especially QL2 and QL3).
- Both blocks can be performed accurately and easily with US guidance.
- QL1 has similar efficacy to TAP but likely more spread.
- QL2 and QL3 are shown to provide better pain control than TAP and QL1, but risks of unilateral lower limb weakness, LAST, failed block are higher.

Case *You decide to perform RSB and bilateral QLB for this child. You use a total of 50 ml of bupivacaine 0.5% for this 15 kg child. Within 20 minutes of beginning of surgery, ECG shows supraventricular tachyarrhythmia with hypotension.*

Key Question 6 What are possible complications involved with fascial plane blocks? What precautions can be taken to prevent complications?

Complications with all abdominal fascial plane blocks:

- Injury to nearby solid organs (peritoneum, bowel, kidney, colon, spleen, liver, etc.…)
- Injury to vessels.
- Infection and neurologic complications (weakness, falls, nerve injury)
- High volume LA deposition in neurovascular intermuscular planes can increase risk of LAST.

Prevention with performing any nerve or fascial blocks:

- Calculate dosing based on lean body weight and toxic doses of LA.
- LA injected slowly in aliquots of <5 ml with gentle aspiration in between.
- US guidance and visualization of vital structures and LA delivery and spread [9].
- Addition of intravascular marker in LA (epinephrine to identify absorption with vasocontriction to slow vascular uptake of LA)
- Clear labeling of syringes

Key Question 7 What is LAST? Describe the various risk factors and clinical presentations associated with this condition. Summarize management and resuscitation of this complication.

LAST is a life-threatening adverse event with an incidence currently estimated to be 0.03%, or 0.27 episodes per 1000 PNB [10]. Multiple risk factors associated [10]:

- Highly vascular sites chosen for injection (i.e., tracheal, intercostal, caudal, etc.)
- High volume injected
- Multiple PNBs in the same patient at same time
- Tumescent anesthesia with high doses of LA.
- Vulnerable population: neonates, elderly, parturient, severe organ dysfunction

Clinical presentation [10]:

- Neurotoxicity:
  - Awake patients: tinnitus, metallic taste, and circumoral numbness, sensory and visual changes,
  - Under GA: muscular activation, seizures, status epilepticus.
- Excitatory phase followed by depressive phase: loss of consciousness, coma and respiratory arrest.
- Cardiovascular: arrhythmias and negative inotropy.

Management [10, 11]:

- Use the ASRA checklist [11]
- Stop LA injection and start resuscitation.
- Start 1.5 ml/kg bolus of 20% intralipid intravenously followed by infusion at rate of 0.25 ml/kg/min. If no improvement, load-

ing dose can be repeated two more times or infusion rate can be doubled. Maximum dose is 12 mg/kg.
- Secure airway and avoid hypoxia, hypercarbia and acidosis with possible seizure.
- Treat seizures with benzodiazepines and avoid propofol (cardio-depression agent).
- Start ACLS when indicated but:
  - Use epinephrine in lower 1 mcg/kg bolus doses.
  - Lidocaine is contraindicated.
  - Use Amiodarone is a first line antiarrhythmic agent for ventricular dysrhythmia
- Early consideration should be given to cardiopulmonary bypass for circulatory support.

1 Summary

- Multiple fascial plane blocks have been studied to provide analgesia for hernia surgeries including lumbar epidurals, IL/IH blocks, TAP, and QLB. It is important to be familiar with the dermatomal coverage, advantages/benefits, and disadvantages/risks of each block.
- Being familiar with comparative anatomy is helpful in selecting the appropriate block.
- RA has been shown to offer multiple benefits including decreased pain scores, decreased opioid consumption, and decreased postoperative nausea and vomiting.
- It is important to understand the ASRA guidelines for prevention and management of LAST.

Common Pitfalls

- Failure to match the location of hernia with the type of fascial plane blocks may result in inadequate coverage. Inappropriate examples include RSB for inguinal hernia or unilateral II/IH for midline incisions.

- Failure to educate patients and surgeons on the benefits of regional anesthesia for hernia surgery may dampen benefits and enthusiasm for acceptance.
- Failure to consider weight-based dosing of LA may increase risk for LAST, especially in vulnerable populations

Clinical Pearls

- Provider expertise with various abdominal wall blocks is always a key factor in choosing what regional techniques should be offered.
- In patients with expected difficult pain control in the postoperative period (i.e., chronic pain history), a nerve catheter can always be considered.

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Acute Pain Management Protocol in Major Vascular Procedures

Ailan Zhang and Jeff L. Xu

Case Stem

A 70-year-old man presented at the emergency room with severe abdominal pain radiating to the back. His medical history was positive for hypertension, coronary artery disease, and severe chronic obstructive pulmonary disease (COPD) that required home oxygen therapy but no past abdominal surgical history. Physical examination revealed a distended abdomen with a pulsatile mass in the central abdomen. Enhanced computed tomography (CT) scans revealed a ruptured infrarenal abdominal aortic aneurysm with 68 mm in transversus diameter without involvement of celiac trunk. Comprehensive metabolic panel results showed mild renal impairment with a serum creatinine of 1.4 mg/dL and an estimated glomerular filtration rate (eGFR) 52 mL/min. Given the patient's comorbidity, emergency endovascular aortic repair (EVAR) was performed under local infiltration with sedation. The anesthesiologist partner reached out to the regional anesthesia team and asked, "Can you do any nerve blocks instead of local infiltration?"

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_32

An abdominal aortic aneurysm (AAA) endovascular graft was deployed just below the renal arteries to both common iliac arteries. However, digital subtracted angiography (DSA) showed an endo-leak that was not able to be fixed. The patient became hypotensive and tachycardiac despite a blood transfusion, and was intubated immediately. Conversion to open repair from EVAR was performed under general anesthesia. Midline laparotomy was made to expose the infrarenal aorta. A synthetic tube graft was completed by primary end-to-end anastomosis of the aorta. Patient remained intubated after surgery and was transferred to the ICU. An acute pain management team was consulted for post-operative analgesia.

Afterwards, the chair of Department of Anesthesiology approached the regional anesthesia team about developing anesthesia and post-operative analgesic protocols for EVAR and open repair.

Questions and Answers

1. **How are aortic aneurysms and aortic dissection classified?**
   (a) Classification of an AAA is based its location and relationship to the renal and visceral arteries [1].
   - Infrarenal AAAs are the most common: they develop in the infrarenal abdominal aorta and arise 1 or 2 cm distal to the renal vessels. Endovascular aneurysm repair (EVAR) or open repair are normally used to treat infrarenal AAAs.
   - Juxtarenal AAA is an aneurysm that extends to but does not involve the renal orifices.
   - Suprarenal AAA is less common with fewer than 10% of cases.
   - If the aneurysm involves the visceral vessels but is still limited to the abdomen, it is a pararenal (renal artery involvement) or a paravisceral (renal and visceral artery involvement) AAA. Due to complicated anatomy, open repair is often performed in such AAAs. Currently, EVAR for AAAs involving the visceral aorta has been

used given the evolving technique and design for aorta branches.
- AAA may extend into the iliac arteries unilaterally or bilaterally.
- Less than 10% of patients with an AAA may have a popliteal aneurysm.

(b) When the aneurysm involves both the abdominal and thoracic aorta, the Crawford classifications [2] are used to describe a thoracoabdominal aortic aneurysm (TAAA).
- Type I TAAA is a thoracic aneurysm; this is distal to the left subclavian artery and above the renal arteries.
- Type II TAAA starts distal to the left subclavian artery but involves the entire aorta (and/or iliac arteries).
- Type III TAAA starts from the sixth intercostal space and extends down to the renal arteries.
- Type IV TAAA starts from the 12th intercostal space to the iliac bifurcation.
- Type V TAAA starts from the sixth intercostal space, involving the celiac and superior mesenteric origin, and extends to just above the renal arteries.

(c) There are two classification systems to describe aortic dissection. The Stanford Classification was introduced by Daily et al. in 1970 based on the origin of the entry tear alone. DeBakey et al. later described the intimal tear and the extent of aorta involved in the dissection. Most providers use Stanford type A or B to describe the presentation and direct treatment because the origin of the entry tear is the key predictor of early outcome [3].
- A Stanford type A dissection originates in the ascending aorta, and therefore encompasses DeBakey type I and II dissections.
- A Stanford type B dissection originates in the descending aorta distal to the origin of the left subclavian artery, and encompasses DeBakey type IIIa and IIIb dissections.

2. **What are the risk factors for AAA formation and rupture?**
   (a) **The main risk factors identified in the formation of aortic aneurysms** [4].
   - Age: 50 years older of age for men and 60-years older of age for women.
   - Sex: Four times higher in men than women.
   - Smoking history: Strongest modifiable risk factor.
   - Presence of AAA in first-degree relative: Four times higher in patients with family history.

   (b) **Major risk factors for aneurysm rupture** [5].
   - Aneurysm diameter and rate of growth: Absolute aneurysm size is the most important predictor of aneurysm rupture.
   - Sex: Women with AAA have a higher rate of rupture than men with AAA [6–8].
   - COPD and low forced expiratory volume in 1 s.
   - Current smoking status.
   - Elevated mean arterial pressure.
3. **What is involved in perioperative assessment?**
   (a) **History**: Patients with aortic disease often have multiple comorbidities. Review and assess functional capacity and reserve of each organ system, including:
   - Coronary artery disease
   - Cerebrovascular disease
   - Pulmonary history as well as smoking status and COPD with or without home oxygen therapy
   - Renal disease
   - Liver disease
   - Chronic pain history, including opioid tolerance
   - Substance abuse history.

   (b) **Risk Factor Modifications** [4]
   - Cessation of smoking is associated with a reduced rate of aneurysmal growth.
   - Optimize blood pressure and cholesterol level.

(c) **Laboratory Exams**
- A complete blood count (CBC) should be done to identify anemia and thrombocytopenia, which may need to be corrected preoperatively.
- Comprehensive metabolic panels should be included to reveal evidence of renal insufficiency and/or liver dysfunction.
- Coagulation studies will reveal coagulation status, especially for patients on anticoagulants or antiplatelet medications.

(d) **Imaging Studies**
- Magnetic resonance angiography or CT imaging study: including precise
- measurement of aneurysm size, evaluation of surrounding tissues and structures, and ability to evaluate iliac and femoral arteries for aneurysmal or occlusive disease.

4. **What are the indications for AAA and TAAA repair?**

When aneurysms are identified, active medical treatment should be started to reduce the rate of aneurysm expansion and decrease the risk of aneurysm rupture. An elective intervention is needed to prevent rupture.

(a) **AAA**: According to two large randomized trials [9, 10], the annual risk of rupture of AAAs increases when the aneurysm's diameter is over 5.5 cm. Aneurysms ruptured at smaller sizes in women than in men [6–8]. The rate of aneurysm expansion is another important predictor of rupture [11]. Therefore, elective intervention should be considered for AAAs of 5.5 cm in men and 5.0 cm in women, growth of >0.5 mm in 6 months regardless of absolute size, or due to symptoms from the aneurysm compression on adjacent structures.

(b) **TAAA**: The indications for repair of asymptomatic TAAAs have been extensively debated with the advocating elective intervention at anywhere from 5 to 10 cm. All symptomatic TAAAs regardless of the size or anatomic extent should be treated.

5. **AAA and TAAA repair: endovascular, open or hybrid?**

There are three options for AAA and TAAA repair: traditional open surgical repair, endovascular aortic aneurysm repair (EVAR), and a hybrid approach [12–15]. Successful repair of a complex AAA or TAAA requires detailed planning based on anatomic and patient comorbidity. Surgical approach and perioperative anesthesia management will dramatically impact both short- and long-term outcomes.

(a) **Open repair** has been the gold standard for decades, especially for patients with complex anatomy and limitations in using endovascular repair. Current providers are considering other operative interventions given this method's challenges in post-operative care and complications for the patient.

(b) **Endovascular aneurysm repair** is a less invasive procedure and has become the standard of care given its lower morbidity and mortality compared with open repairs. The conventional EVAR is suitable for infrarenal aneurysms. Fenestrated endograft and branched endograft have extended the EVAR to juxtarenal, pararenal/paravisceral AAA, TAAA, and aortic dissection [16–18]. However, the use of EVAR is limited by access difficulties, severe calcification, and presence of thrombosis.

(c) **Hybrid repairs** have been chosen for patients who are not good candidates for a thoracotomy given significant comorbidities [19]. Visceral branches and renal arteries are debranched and bypassed with a synthetic tube graft through laparotomy and an endovascular graft is deployed in the thoracoabdominal aorta to exclude the aneurysm. The potential advantages of hybrid approach include avoiding a thoracotomy, single-lung ventilation, cardiac

pulmonary bypass, and aortic cross-clamping; this then minimizes pulmonary complications and ischemic time for each visceral organ and spinal cord [14, 20]. Publication for hybrid AAA repair is limited [15], yet is considered less invasive than conventional open repair and an alternative to overcoming difficult anatomical cases.

6. **In an EVAR, where are the vascular access sites?**
   (a) **The common femoral artery** provides adequate vascular access for deployment of an endograft for most patients. The incision is made at the level of the inguinal ligament to expose the femoral artery. Alternatively, percutaneous access of the femoral artery with a percutaneous closure devices has also become increasingly popular [21] (Fig. 1).
   (b) **The iliac artery** is an option if the femoral artery is suboptimal for access. The iliac artery may be exposed by a retroperitoneal approach with incision above the inguinal ligament [21] (Fig. 1).
7. **In an EVAR, what primary anesthesia techniques can we use?**
   (a) **General anesthesia**: Intravenous induction with endotracheal intubation. Anesthesia is maintained with either volatile anesthetics or total intravenous anesthesia.
   (b) **Regional anesthesia with sedation**
      - **Neuraxial block:** A combination of epidural and sedation with propofol, midazolam, or dexmedetomidine. The epidural catheter is placed between L3 and L5. A sensory block level at T10 can be established with bupivacaine or ropivacaine [22]. However, patient's anticoagulation status may limit the use of neuraxial technique.
      - **Deep peripheral nerve block:** Combination of low thoracic paravertebral or lumbar plexus block and sedation with propofol/midazolam ± dexmedetomidine. A

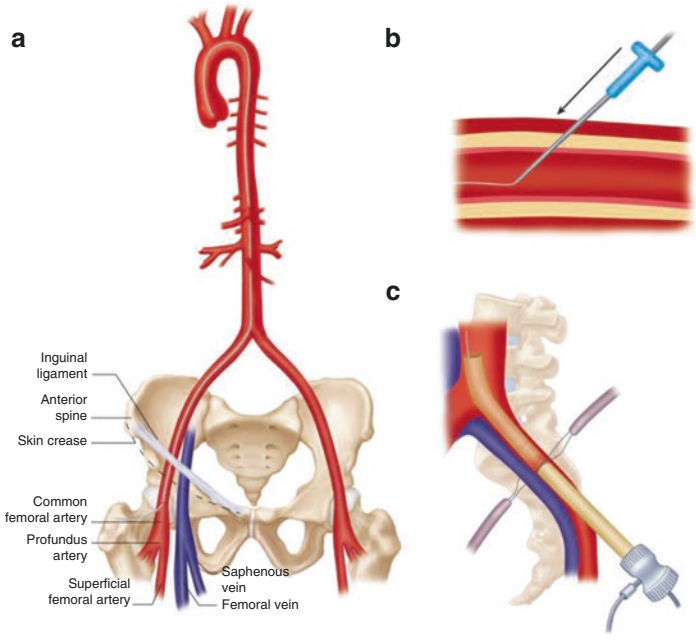

Fig. 1 Vascular access for endovascular repair. (**a**) Common femoral artery access. (**b**) Percutaneous access of the femoral artery. (**c**) Retroperitoneal approach access of iliac artery [21]. (Atlas of Cardiac Surgical Techniques. Elsevier, Inc; 2019. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

bilateral low thoracic paravertebral or lumbar plexus block between T12 and L2 can achieve analgesia for bilateral femoral artery exposure [23]. Similar to the neuraxial block, patient's anticoagulation status must be considered.

- **Peripheral nerve block:** Combination of transverse abdominis planet (TAP) and femoral branch of genitofemoral nerve (GFN) has shown analgesia efficacy for femoral endarterectomy [24], femoral artery access of the extracorporeal life support [25], and inguinal hernia repair [26]. To avoid neuraxial and deep plexus blocks,

a combination of TAP and femoral branch of GFN has been used successfully during EVAR for AAA in our institution. However, a RCT is required to confirm the efficacy of this technique (Fig. 2).

(c) **Local infiltration by surgeons:** Skin infiltration with local anesthetics by surgeon, and sedation with propofol or midazolam.

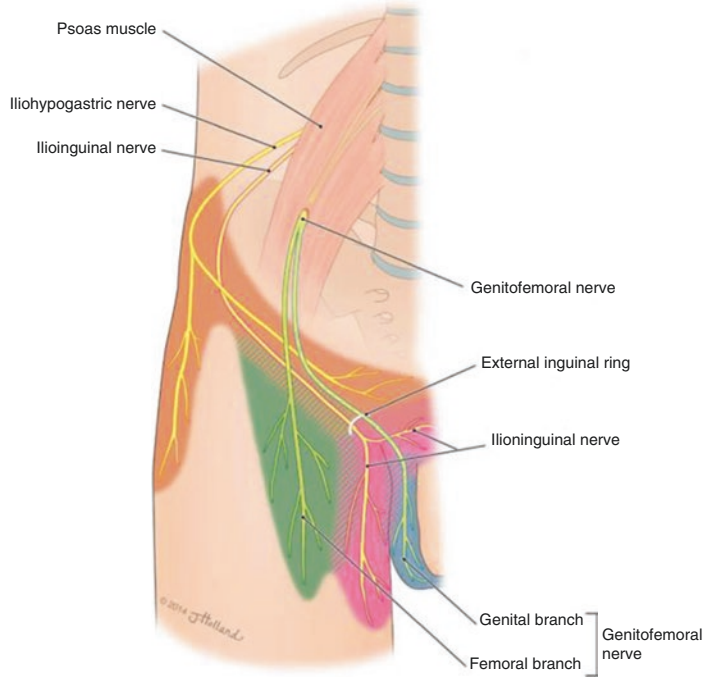

Fig. 2 Illustration of the GFNs and their dermatomes. The GFN forms from L1 and L2 roots, pierces through the psoas muscle, and bifurcates into the genital and femoral branches. The genital branch runs along the ilioinguinal nerve through the inguinal canal and innervates the medial aspect of the thigh and scrotum. The femoral branch then pierces the fascia lata, runs within the femoral sheath, and innervates the anterior aspect of the upper thigh [27]. (Clin Anat. 2015;28(1):128–35. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

8. **In an elective EVAR, does anesthesia mode affect the outcome? General anesthesia (GA) or local anesthesia (LA)?**

   The choice of anesthesia often is based on the preference of the operating surgeon and the experience of the anesthesiologist. Recent systemic reviews and meta-analyses show that LA provided satisfactory and comparable perioperative outcomes with patients who received GA. There was no difference in cardiac or renal complications between GA and LA. Patients with LA had shorter total surgical time and hospital stay [28].

9. **In an emergency EVAR of a ruptured AAA, does the type of anesthesia matter?**

   The use of LA for EVAR of a ruptured AAA has been performed widely in the UK. Recently, studies have shown that the mortality rate is lower than the patients who received GA for ruptured AAA [29, 30]. Hypotension, especially low systolic blood pressure, is strongly and independently associated with 30-day mortality [30]. The potential causes of poorer outcomes with GA are associated with a loss of vascular tone and hypotension while LA has less hemodynamic change. However, more RCT studies are required to assess the outcome and benefits of LA for EVAR of a ruptured AAA.

10. **In an open aortic aneurysm surgical repair, what approaches are normally used?**

    (a) **For AAA repair:** The surgical approach depends on the proximal (and to a lesser degree, distal) extent of the aneurysm. Three approaches normally are used: retroperitoneal, transabdominal, and wide transverse.

    - **The transabdominal approach**: Midline abdominal incision. Patient is placed in supine position to allow wide access to the peritoneal and retroperitoneal cavities as well as to the supra-celiac aorta down to the bilateral iliac arteries; this is preferred during emergency ruptured AAA repair or suspected aortoenteric fistula (Fig. 3) [31].

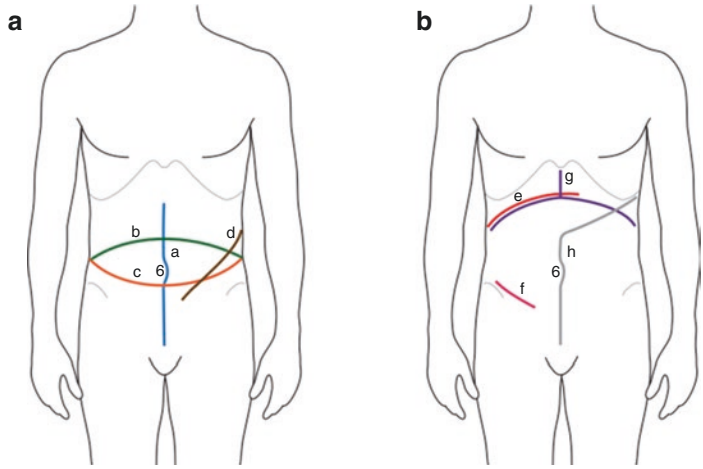

Fig. 3 Abdominal incisions on a supine patient. (**a**) *a*—midline incision; *b*—supraumbilical transverse ("frown") incision; *c*—infraumbilical transverse ("smile") incision; *d*—left flank retroperitoneal incision. (**b**) *e*—right subcostal incision; *f*—right lower quadrant "transplant" incision; *g*—Chevron incision; *h*—thoracoabdominal incision [31]. (Rutherford's Vascular Surgery and Endovascular Therapy. Ninth Edition ed.: Elsevier Inc; 2019. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

- **The wide transverse approach:** Chevron incision. Patient is placed in supine position to allow wide access to the peritoneal and retroperitoneal cavity, which is preferred if the AAA involves the supra-celiac aorta but extends less to distal part (Fig. 3) [31].
- **The retroperitoneal approach** [32]: Left flank retroperitoneal incision. Patient is placed in the right lateral decubitus position with the aid of a kidney rest to lift the flank to allow access to the supra-celiac aorta while limiting access to the peritoneal cavity and right iliac artery. The incision starts in the tenth intercostal space at the posterior axillary line, extends on abdomen parallel to the lateral boarder of the left rectus muscle, and terminates below the umbilicus at the level of distal aneurysm (Fig. 4).

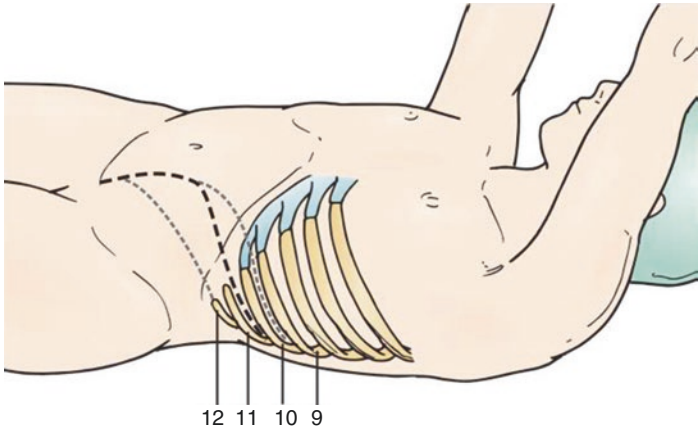

Fig. 4 Incision for retroperitoneal aortic exposure. Alternative incisions are shown in gray [32]. (Rutherford's Vascular Surgery and Endovascular Therapy. Ninth Edition ed.: Elsevier Inc; 2019. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

(b) **For TAAA open repair:** For access to the thoracic and abdominal aorta, patient is placed in the right lateral decubitus position with the table broken at the waist. The surgical approach depends on the proximal and distal aneurysm [33].

- Posterolateral thoracotomy through the sixth or fifth intercostal space is preferred when access is needed to the descending thoracic aorta, distal arch, and left subclavian.
- A thoracotomy incision is carried across the costal margin and proceeds inferiorly to the left of midline then to just below the level of the umbilicus for the retroperitoneal approach (Fig. 5).

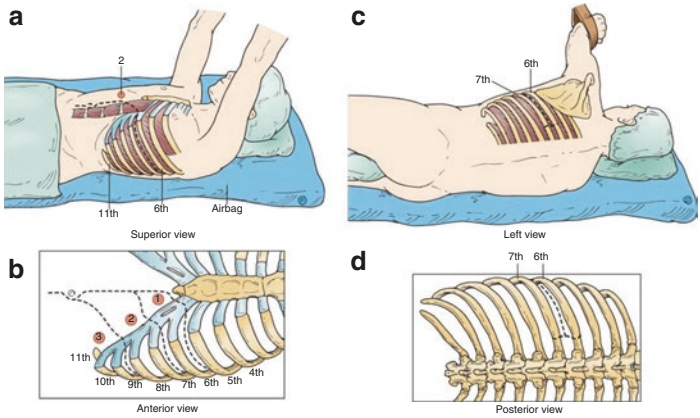

Fig. 5 Incision for TAAAs. (**a**, **b**) Superior and anterior view of the incision. (**c**, **d**) Left and posterior view of the incision [33]. (Rutherford's Vascular Surgery and Endovascular Therapy. Ninth Edition ed.: Elsevier Inc; 2019. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

11. **In an AAA /TAAA open surgical repair, what RA techniques with or without catheter placement can we use for different incisions? What are the benefits and risks?**
    (a) **The midline or wide transverse abdominal incision**
    - **Epidural Analgesia:** Epidural analgesia is normally used in combination with GA in open AAA or TAAA for intraoperative and postoperative analgesia. A low thoracic epidural catheter is placed before induction of general anesthesia. Depending on the incision, the intervertebral space between T8 and T10 is often chosen for AAA open repair while T6-T8 is chosen for TAAA.
    - In addition, epidural anesthesia can be used as a primary anesthesia for AAA open repair. However, it is only considered in high-risk patients who may develop severe respiratory complications with GA. Meecham

et al. [34] reported combined epidural anesthesia and bilateral transversus abdominis plane block catheter for open AAA repair in an awake patient who had poor respiratory function and high risk of bullous rupture during positive pressure ventilation.

- **Benefits:** Epidural analgesia provides a superior block of somatic and visceral pain. In one case, adding an epidural analgesia to GA significantly decreased the postoperative pain scores, respiratory failure, myocardial infarction, and ICU length of stay [35]. Sympathectomy from epidural analgesia results in vasodilation and increased visceral perfusion. Retrospectively, a study by Bardia et al. [36] showed that a combined epidural anesthesia and GA was associated with lower odds of 30-day surgical reintervention, postoperative bowel ischemia, and pulmonary complications. Compared to open AAA repair, TAAA open repair will need a left thoracotomy, which causes greater pain and post-operative pulmonary complications. As such, Monoaco et al. has shown that thoracic epidural analgesia was effective in reducing post-operative pain and that the systemic effects from epidural analgesia may reduce post-operative complications [37].
- **Risks and limitations**: Due to sympathetic blockade, a high dose of epidural analgesia may produce dramatic reduction of cardiac preload with significant decrease of cardiac output and reflex tachycardia after aortic cross-clamp release. Incremental dose titration with minimal hemodynamic changes is recommended while using epidural analgesia. Some investigators suggest that the administration of epidural local anesthetics can be started after aortic cross-clamp release and hypotension is resolved. Intraoperative heparinization is normally performed in open AAA/TAAA repair during cross-clamping of arteries. Epidural techniques are

also associated with an increased risk of epidural hematoma when intravenous heparinization is applied [38–40].

- **Ultrasound guided transversus abdominis plane (TAP) block, rectus sheath (RS) block and quadratus lumborum (QL) block**
  - **Transversus abdominis plane (TAP) block** is an interfascial plane between the internal oblique muscle (IOM) and transversus abdominis muscles (TAM), which contains the T6–L1 thoracolumbar nerves [41]. TAP blocks can be used for pain control from the surgeries derived from the abdominal wall. Local anesthetics spread from different approaches are variable. A midaxillary TAP block or lateral TAP block [41, 42], subcostal TAP block [43], and other approaches have been descripted in TAP block family [44, 45].
  - **Rectus sheath (RS) block:** The aim of a RS block is to target the terminal branches of the T9–11 intercostal nerves, which run between IOM and TAM, to penetrate the posterior wall of rectus abdominis muscle and terminate in an anterior cutaneous branch that supplies the skin of the umbilical area [46]. A RS block with catheter has been used in laparotomy, and is another option for midline incision [47].
  - **Quadratus lumborum (QL) block:** The QL muscle lies dorsolateral to the psoas major muscle. A QL block potentially blocks both the anterior and the lateral branches of the thoracoabdominal nerves.

    Lateral QL block: Local anesthetic is deposited at the lateral border of the QL muscle. This approach was also described as posterior TAP block in the literature [41, 48, 49] (Fig. 6), and can produce a sensory block of the lateral cutaneous branches of T6-L1.

Posterior QL block: Local anesthetic is injected between the QL and erector spinae muscles. Patient can be placed in a lateral decubitus position with the block side up. The needle is introduced in a posterior to anterior direction and advanced to the posterior surface of the QL muscle. A posterior QL block spreads along the posterior fascia of QL muscle, extends to the TAP, and nearly 50% the injection may extend to the anterior aspect of the QL muscle [48] (Fig. 6).

Anterior QL block: Local anesthetic is injected between the QL muscle laterally and the psoas major muscle; LA may spread to the lumbar nerve roots and branches in addition to the thoracic paravertebral space [48, 50–52] (Fig. 6).

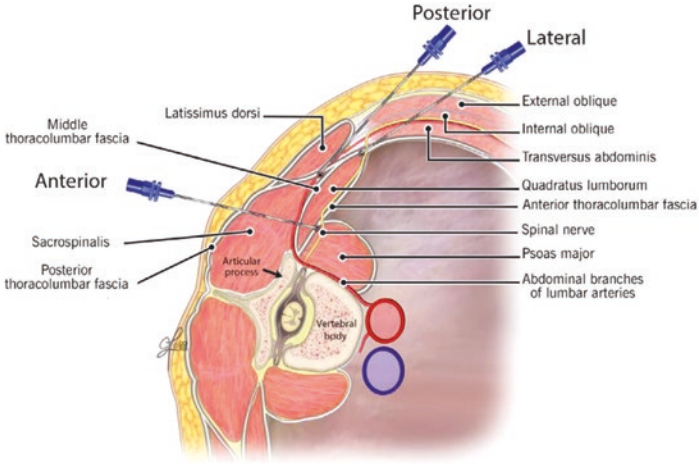

Fig. 6 Nomenclature and trajectory of needle for all three approaches to a QL block [53]. (Atlas of Ultrasound-Guided Regional Anesthesia. Elsevier, Inc.; 2019. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

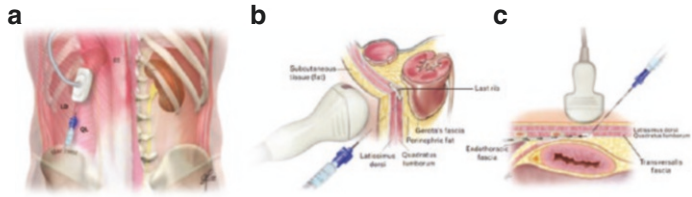

Fig. 7 Anterior subcostal QL block. (**a**) Transducer position for the subcostal, paramedian sagittal oblique approach relative to the erector spinae muscle, the latissimus dorsi muscle and the quadratus lumborum muscle. (**b**) Sagittal section demonstrating the position of the ultrasound probe relative to the kidney, perinephric fat, and last rib. (**c**) The needle trajectory and dye spread in cranial direction anterior to the transversalis fascia and the endothoracic fascia [54]. (Eur J Anaesthesiol. 2017;34(9):587–95. Adaptations are themselves works protected by copyright. Authorization has been obtained from the owner of the copyright)

Anterior subcostal QL block: Local anesthetic is injected between the QL muscle and the anterior layer of the thoracolumbar fascia (TLF). Significant spread from T6 to L1 nerve roots and paravertebral space and anterior to the psoas muscle was observed [54] (Fig. 7).

- **Benefits:** TAP and QL blocks effectively block the somatic pain originating from an abdominal incision**.** Both blocks have been used for open AAA repair [55–58] for post-operative analgesia. Preincisional TAP blocks as a preemptive analgesia may not improve post-operative pain scores; however, it may carry some benefits of reducing intraoperative opioid consumption [59, 60]. A post-operative TAP block has provided satisfactory analgesia and enhanced recovery in major open abdominal surgery, during which epidural analgesia was relatively contraindicated [61]. Continuous TAP and QL block infusions are considered only one component of multimodal analgesia and have provided analgesic benefits in patients undergoing

open AAA repair or other abdominal surgeries without epidural analgesia [62–68]. However, there is not adequate evidence of other outcome measures such as the effect of the time to extubation or postoperative cardiac and pulmonary complications.

– **Risk and Limitations:** For surgeries with significant visceral pain, a TAP is inferior to epidural analgesia [69]. Bilateral QL blocks may cause hypotension in open AAA repair given the sympathetic block from the bilateral paravertebral spread of local anesthetics [70]. Compared with a lateral QL block, posterior and anterior QL blocks may cause anterior spread to lumbar plexus, which is associated with high incidence of muscle weakness in the quadriceps after a QL block [71, 72]. Extensive cephalad spread after QL is rare; however, unilateral upper extremity weakness and sensory blockade as well as Horner's syndrome was reported in a patient who received a QL block after cesarean delivery [73]. There is also a risk of local anesthetic systemic toxicity because both TAP and QL blocks normally require appropriate volumes of local anesthetics to achieve a blockade. Moreover, it is still unclear if the anterior QL block should be considered as a deep nerve block.

(b) **Left flank retroperitoneal incision or posterolateral thoracotomy incision**

- **Paravertebral Block (PVB) with/without catheter placement**: Paravertebral space (PVS) is a wedge-shaped compartment lateral to the vertebral body where the spinal nerves emerge from the intervertebral foramina. PVS communicates laterally with intercostal space and medially with epidural space. Injection of local anesthetics in PVS produces segmental and ipsilateral somatic and sympathetic nerve

blockades [74, 75]. One previous cadaver study showed that the dermatomal distribution following a single injection of a large volume local anesthetic is unpredictable, and instead multiple injections of small volumes are preferred if several ipsilateral thoracic dermatomes are desired [76, 77]. However, a recent randomized controlled trial (RCT) study has shown that an ultrasound-guided single injection of PVB provided equivalent dermatomal distribution and duration of analgesia compared with the multiple-injection PVB [78].

- PVB is normally performed by landmarks or a thoracoscope or is ultrasound-guided (USG) [74]. Recent studies show that USG techniques have a higher success rate and better perioperative analgesia, and are more effective, more reliable, and safer than other techniques [79, 80]. There are different approaches for an USG thoracic paravertebral block [75, 81]. Many techniques, such as the parasagittal approach at the rib or transverse process [81], transverse approach at intercostal, transverse process approach, the interior articular process [82, 83], and PVB catheter placement under direct vision [87, 88] have been used for PVB.
- PVB is considered a safe and reliable technique in cardiothoracic surgery, especially in thoracic surgery[77, 84–88]. PVB is feasible for TAAA open repair or type B aortic dissection, which normally require unilateral thoracotomy. Unilateral PVB catheters can be placed either preoperatively or postoperatively [84, 89, 90]. The American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition) on RA in patients receiving antithrombotic or thrombolytic therapy remain the same for PVBs as neuraxial blocks [91]. Therefore, it is necessary to evaluate CBC and coagulation studies before PVB/

catheter placement or removal and coordinate the timing for intraoperative full heparinization.

- **Benefits:** Continuous PVB was as effective as a thoracic epidural in analgesia after a thoracotomy. PVB significantly reduced opioid requirement and improved patient satisfaction after surgery [87, 90, 92, 93]. A recent study also shows that preoperative PVB combined with GA in patients undergoing cardiac surgery contributed to reduced intra and post-operative opioid consumption, and early tracheal extubation [84]. Compared with thoracic epidural, PVB is associated with a reduced incident of hypotension and urinary retention due to unilateral sympathectomy and less motor blockade, and an intraoperative PVB injection decreased opioid administration without causing hypotension [89]. PVB has also been shown to reduce the incidence of pulmonary complications compared with systemic analgesia after thoracotomy [92]. One recent retrospective study has shown effective analgesia for post-operative thoracotomy pain and fewer pulmonary complications in patients who underwent open TAAA repair with intraoperative high-dose heparin [94]. Moreover, PVB was able to preserve the ability to monitor neurologic function after surgery and early detection of late onset paraplegia after open TAAA repair [88]. The efficacy of PVB in preventing post-thoracotomy chronic pain syndrome still needs more clinical trials [74, 85, 95].
- **Risk/limitation:** Significant medial/epidural spread of local anesthetics after a large-volume paravertebral injection may result in hemodynamic and neurologic change [76]. PVB is associated with the risk of dural puncture, inadvertent vascular puncture, pleural puncture, and pneumothorax [96]. USG PVB minimizes the risk of pleural puncture and pneumothorax [97]. Given full heparinizа-

tion for aortic cross clamping or cardiopulmonary bypass during aortic aneurysm or dissection open repair, PVB use in these surgeries still controversial, and the risk of a paravertebral hematoma and consequent neuropathy is theoretically increased [84].

- **Ultrasound guided erector spinae plane (ESP) block/catheter placement:** An ESP block was introduced by Forero et al. that administrated LA between the thoracic transverse process and erector spinae muscle [98]. The extent of LA spread in anatomic cadaver and magnetic resonance imaging studies are variable based on the different volumes and levels chosen. There are multiple levels of cranio-caudal spread in the fascial plane underneath the erector spinae muscle, anterior spread into the paravertebral space, posterior spread to the dorsal ramus of spinal nerve, lateral spread to the intercostal space and medial spread to the epidural space [99–102]. The mechanism of ESP is still controversial [103]. There are different approaches to perform thoracic ESP blocks, such as the parasagittal approach [98], transverse approach [104], and bilateral ESP block with a single needle entry [105].
- An ESP block with/without catheter placement is feasible for TAAA open repair that requires thoracotomy. Unilateral single level at T5 or bi-level at T4 and T6 can be chosen for a thoracic ESP block with catheter placement [106–108].
- Recently, continuous bilateral ESP blocks either at T8 or T9 were used in open AAA repair and abdominal surgery [109–111], which showed adequate pain control without complications. However, the efficacy of ESP blocks for post-operative analgesia after laparotomy needs further RCT studies.

- The ESP block is considered one of the peripheral regional analgesia techniques for cardiovascular surgery and is associated with a lower risk of hematoma compared to PVB or thoracic epidural analgesia, which was reported in a patient on dual-antiplatelet therapy or heparinization during cardiovascular surgery without complications [112, 113]. However, further studies are still needed to evaluate the safety profile of ESP in vascular surgery with full heparinization.
  - **Benefits:** A continuous ESP block provides effective analgesia after thoracotomy, decreases postoperative opioid consumption, and assists rapid mobilization; this is a great alternative to thoracic epidural analgesia or PVB, where these have failed, or in the presence of anticoagulation [106, 107, 112, 114–121]. Compared to thoracic epidurals and PVBs, ESP blocks target the relatively superficial plane and the needle does not enter the paravertebral space, which carries a lower risk of epidural hematoma and pneumothorax [122]. Bilateral ESP blocks have been reported in open abdominal surgeries to show effective postoperative analgesia [109, 123–125] yet there are limited case reports evaluating the efficacy of a continuous ESP block for open AAA repair [110, 111].
  - **Risk/limitations:** ESP is a relative safer option for thoracic surgery. However, pneumothorax has been reported [126, 127]. A bilateral ESP block is not comparable to other fascial plane blocks given their variable clinical and anatomical effects. Lower extremity motor weakness and hypotension were observed after a bilateral ESP block, which may result from epidural spread or anterior spread of local anesthetics [128–130].

12. **For ascending aortic dissection repair, what surgical approach is normally used? What regional technique can be used for post-operative analgesia?**
    (a) Median sternotomy is the common approach for Type A aortic dissection. Nowadays, upper mini sternotomy has been used frequently; this not only provides adequate exposure for total arch replacement and aortic root repair, but also has been shown to be beneficial for earlier extubation, post-operative pain, and shorter ICU stay [131, 132].
    (b) Inadequate pain control from a sternotomy may result in shallow breath and ineffective cough, which prolong recovery and cause pulmonary complications.
    (c) Sternum and anteromedial chest are innervated by T2-T6 anterior cutaneous branches of the intercostal nerves, which travel in the intercostal space between the internal and innermost intercostal muscle then ascend through the internal intercostal and pectoralis major muscle to innervate the anteromedial region of the chest. The internal mammary artery runs between the internal intercostal and transverse thoracis muscles [133]. In recent years, there are two fascial plane blocks that can target the anterior branches of intercostal nerves.
        - **Deep parasternal intercostal plane (PIP) blocks** were introduced by Ueshima et al. in 2015 as transversus thoracic muscle plane blocks (TTP) [134–136]. Local anesthetics are injected into a deep fascial plane between the transversus thoracic muscle and internal intercostal muscle between the third and fourth ribs lateral to the sternum.
        - **Superficial parasternal intercostal plane (PIP)** blocks are described as pecto-intercostal fascial blocks in previous literature [137]. Local anesthetics are injected into the superficial plane between the ribs and internal intercostal muscles.

(d) Two recent prospective RCT studies investigated the efficacy of deep and superficial PIP blocks for post-operative pain management in patients with sternotomy in cardiac surgery. The authors have shown that a pre-operative deep PIP block provided effective analgesia. Compared with the control group, the deep PIP block significantly reduced pain scores and post-operative 24-h opioid consumption [138]. The post-operative superficial PIP block also offered effective analgesia and a significant reduction in pain scores. There was a decline in post-operative 48-h opioid consumption in patients who received superficial PIP block; however, the reduction was not statistically significant [139]. Bilateral ESP block with/without catheter technique has been used for post sternotomy pain control, resent studies show the analgesic effectiveness seems promising.

13. **For descending aortic dissection, what surgical approaches are used? What regional technique we can use for post-operative analgesia?**

(a) **Thoracic endovascular aortic repair (TEVAR):** TEVAR is currently the consensus treatment of choice for descending aortic dissection given its lower operative mortality and morbidity [140]. The femoral artery either is accessed by a cut-down or percutaneous device [21]. The primary anesthesia for TEVAR is similar to AAA EVAR, GA, or sedation with regional anesthesia or local infiltration. A combination of TAP and the femoral branch of the genitofemoral nerve block may provide post-operative analgesia if the cut-down approach is used for TEVAR.

(b) **Open repair**: Because of the significant advancements in TEVAR and endovascular technology, open surgical repair of descending aortic dissection has become increasingly rare and is reserved only for a select group of patients. A left anterolateral thoracotomy is often performed in open repair with or without cardiopulmonary bypass [141, 142]. Given the full heparinization during

the procedure, the neuraxial or deep plexus technique should be avoided due to high risk of epidural hematoma. A continuous unilateral ESP block with catheter is feasible for open descending aortic dissection.

14. **Is continuous wound infusion for open vascular repair surgery safe and effective?**
    (a) Continuous wound infiltration (CWI) with local anesthetics have recently been reintroduced as integral parts of multimodal analgesia for postoperative pain control. The catheter, with multiple and laterally aligned holes designed for an even spread of the local anesthetics and available on the market, is normally placed at the end of surgery by surgeons without significant increases in the time of the procedure. The catheter can be placed for all different incisions, such as midline abdominal, thoracotomy, or sternotomy incisions [143–145].
    (b) There are two potential mechanisms for analgesic effect of CWI: blockade of pain transmission from nociceptive receptors of the wound surface and inhibition of regional inflammatory response to injury [146, 147].
    (c) Paraincisional subcutaneous CWI of ropivacaine was reported for patients undergoing open AAA repair. CWI's analgesia effect is still controversial [148]. Several studies have found that CWI might have a detrimental effect on the wound healing [149] and an increased risk of wound infection [150].
    (d) Regardless, the heterogeneity of results in a reduction in pain and opioid consumption has been observed with CWI, and can thus be included in the multimodal analgesia regimen for postoperative pain when other options are contraindicated [151].

1 Summary

A summary of regional anesthesia in major vascular surgeries can be found in Table 1.

Table 1 Regional anesthesia in major vascular surgeries

Type of surgery	Surgical incision/ approach	Primary anesthesia	Regional anesthesia techniques for analgesia
1. Abdominal Aortic Aneurysm			
Endovascular Aortic Aneurysm Repair (EVAR)	Unilateral or bilateral small incisions at the level of inguinal ligament	GA	May not be needed
		Sedation + RA (TAP + GFN, or LP vs. low thoracic PVB if not contraindicated)	May benefit from RA
		Sedation + LI	May not be needed
Open Repair	Midline transabdominal approach	GA	TAP/QL/ESP/RS, or epidural if not contraindicated
	Wide transverse approach		TAP/QL/ESP, or epidural if not contraindicated
	Retroperitoneal approach		ESP, or PVB vs. epidural if not contraindicated
Hybrid Repair	Unilateral or bilateral small incisions at the level of inguinal ligament	GA	May not be needed
	Midline transabdominal approach		TAP/QL/ESP/RS, or epidural if not contraindicated
2. Thoracoabdominal Aortic Aneurysm			
Thoracic Endovascular Aortic Aneurysm Repair (TEVAR)	Unilateral or bilateral small incisions at the level of inguinal ligament	GA	May not be needed
		Sedation + RA (TAP + GFN, or LP vs. low thoracic PVB if not contraindicated)	May benefit from RA
		Sedation + LI	May not be needed

Table 1 (continued)

Type of surgery	Surgical incision/ approach	Primary anesthesia	Regional anesthesia techniques for analgesia
Open Repair	Posterolateral thoracotomy + midline abdominal incision	GA	ESP, or PVB vs. epidural if not contraindicated
Hybrid Repair	Unilateral or bilateral small incisions at the level of inguinal ligament	GA	May not be needed
	Midline abdominal incision		TAP/QL/ESP/RS, or epidural if not contraindicated
3. Ascending Aortic Dissection			
Open Repair	Sternotomy	GA	Superficial PIP +/- Deep PIP, or ESP
4. Descending Aortic Dissection			
Thoracic Endovascular Aortic Repair (TEVAR)	Unilateral or bilateral small incisions at the level of inguinal ligament	GA	May not be needed
		Sedation + RA (TAP + GFN, or LP vs. low thoracic PVB if not contraindicated)	May benefit from RA
		Sedation + LI	May not be needed
Open Repair	Thoracotomy	GA	ESP

GA general anesthesia, *RA* regional anesthesia, *LI* local infiltration, *TAP* transversus abdominis plane, *QL* quadratus lumborum, *LP* lumbar plexus, *RS* rectus sheath, *GFN* genitofemoral nerve, *ESP* erector spinae plane, *PVB* paravertebral block, *PIP* parasternal intercostal plane

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Acute Pain Management Protocol in Minor Vascular Procedures

Ashley Shilling, Matthew Thames, and Michael Glick

Case
A 65 year old male with a past medical history of poorly controlled type 2 diabetes mellitus (TIIDM), hypertension (HTN), chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF), and end stage renal disease (ESRD) presents for a right arm arteriovenous (AV) fistula creation in the distal forearm.

What anesthetic techniques would you consider for this procedure?
Due to the patient's comorbidities, a general anesthetic does confer an increased risk for complications, particularly related to the cardiac and pulmonary systems. Creation of an AV fistula is typically too invasive to be performed under sedation alone but can frequently be accomplished under a regional nerve block with monitored anesthesia care (MAC).

Rationale Poorly controlled diabetes and hypertension are among the most common causes of ESRD. These conditions may also predispose the patient to coronary artery disease (CAD) which may be undiagnosed or unrecognized. Thus, with multiple

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_33

comorbidities, the risk of undergoing general anesthesia may be higher than in the general population [1]. In addition to the avoidance of general anesthesia, regional anesthesia may improve patient satisfaction and confer some benefits in surgical outcomes.

Durable vascular access for hemodialysis is a critical issue for end-stage renal disease patients. An autologous arteriovenous (AV) fistula is considered the best option for chronic hemodialysis when compared to AV grafts. Unfortunately, graft failure is common as is the inability to actually perform an autologous AV fistula due to lack of target vessels.

Research focusing on anesthetic techniques has demonstrated benefits of regional anesthesia when compared to both general anesthesia and local anesthetics (Table 1). Patients receiving AV fistula creation under brachial plexus block show both venous and arterial dilation [2–4]. When used for AVF surgery, brachial plexus blocks show higher radial artery blood flow and AVF blood flow when compared to local infiltration techniques. Early studies suggest brachial plexus blocks may reduce the risk of thrombosis following AV procedures [3, 5]. Studies demonstrate that regional anesthesia and immediate preoperative ultrasound is a useful strategy for improving site selection, increasing fistula prevalence over AV grafts, as well as improved graft survival [6–8]. Other studies show anti-spasmodic effects of regional anesthesia [9]. A recent literature review noted possible improvements in failure rates for vascular access placed under regional anesthesia when compared to general anesthesia as well as increased AVF placement over AV graft [10].

Table 1 Benefits of regional techniques in AV fistula creation

Vasodilation by sympathectomy
Decreased thrombosis of fistula
Improved AV fistula site selection
Increased prevalence of AV fistula over AV graft
Avoidance of general anesthesia
Post-operative pain relief
Decreased recovery times
Improved graft survival

Clinical Pearl
Regional anesthetic techniques confer many benefits for patients undergoing AV fistula creation.

Techniques Brachial plexus blocks—The brachial plexus is primarily formed by C5-T1 nerve roots and can be targeted at multiple levels. As the most proximal of conventional options, an interscalene block is performed at the level of the nerve roots, typically visualizing C5 and C6. While useful for shoulder analgesia, this block is rarely appropriate for other procedures of the upper extremity as it does not reliably cover C7-T1 and therefore may spare the forearm and hand. Proceeding distally, supraclavicular blocks are performed at the level of the trunks or divisions (Fig. 1), infraclavicular blocks at the level of the cords (Fig. 2), and axillary blocks at the level of terminal nerve branches (Fig. 3).

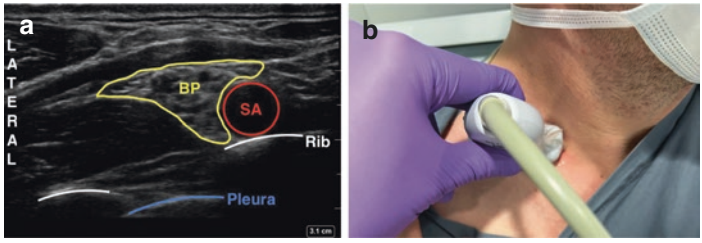

Fig. 1 (**a**) Ultrasound image of supraclavicular approach to brachial plexus nerve blocks. *BP* Brachial plexus, *SA* subclavian artery. (**b**) Ultrasound probe placement to obtain supraclavicular view

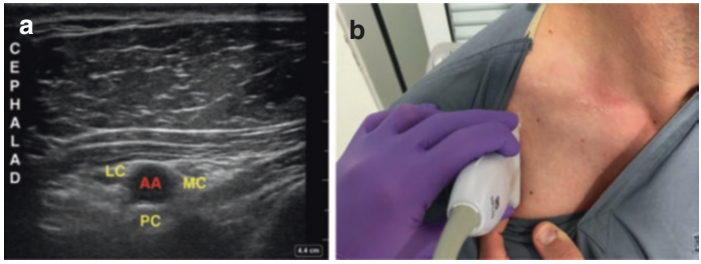

Fig. 2 (**a**) Ultrasound image of infraclavicular approach to brachial plexus nerve blocks. *AA* axillary artery, *LC* lateral cord, *MC* medial cord, *PC* posterior cord. (**b**) Ultrasound probe placement to obtain infraclavicular view

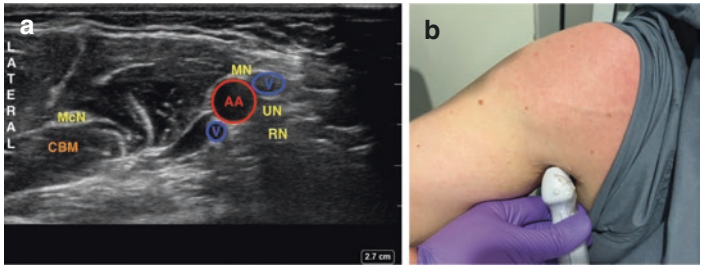

Fig. 3 (**a**) Ultrasound image of axillary approach to brachial plexus nerve block. *AA* axillary artery, *V* vein, *MN* median nerve, *UN* ulnar nerve, *RN* radial nerve, *McN* musculocutaneous nerve, *CBM* coracobrachialis muscle. (**b**) Ultrasound probe placement to obtain axillary view

Selection from among these three blocks may be dependent upon the specifics of surgery, patient anatomy and comorbidities, and also upon the experience or preference of the anesthesiologist. For a distal forearm fistula, a supraclavicular or infraclavicular brachial plexus block would be reliably sufficient, covering C6–C8 dermatomes.

Choice of local anesthetic Please refer to previous chapters regarding local anesthetic specifics. When using a nerve block as the primary anesthetic, a concentrated local anesthetic with medium to long-acting duration is preferred so that lasting vasodilating effects can be maximized. Common choices include 0.5% Ropivacaine and 0.5% Bupivacaine. These provide dense blocks that prevent limb movement and minimize surgical stimulation with increased patient comfort and decreased anesthetic requirements to that of anxiolysis. Additionally, long-acting local anesthetics may prolong the sympathectomy effects of a brachial plexus block which may further improve AV fistula or graft survival as noted above. Examples of shorter-acting local anesthetics include 2% Lidocaine and 1.5% Mepivacaine. These medications set up quickly but are of shorter duration compared to longer-acting local anesthetics like Bupivacaine and Ropivacaine. Longer acting LAs can take upwards of 30 min to achieve surgical anes-

thesia, but also provide a block duration of greater than 10 h even without additives.

Common Pitfalls

The patient states that he last took rivaroxaban 1 day prior for stroke prevention related to atrial fibrillation. Is he still a candidate for regional anesthesia?

Plan Anticoagulation is common in the vascular surgery population and can be an impediment to regional anesthetic techniques. This should always prompt careful consideration. Novel oral anticoagulants such as rivaroxaban and apixaban can be especially vexing due to a lack of readily available assays to monitor coagulation status. Depending upon the indication, patients are often instructed to hold anticoagulation prior to scheduled procedures, but communication and compliance are imperfect. With direct visualization of any potential complications, the surgeon may still be comfortable operating upon an anticoagulated patient, but the anesthesiologist must be cautious to not take undue risk as complications from block procedures may remain occult until significant progression. The American Society of Regional Anesthesia (ASRA) has developed consensus guidelines to help guide best practices related to procedural interventions on the anticoagulated patient [11]. Generally, procedures are categorized as neuraxial, deep blocks, or superficial blocks to reflect the variable nature of both site compressibility to terminate a bleed as well as the severity of potential consequences of a bleed. While neuraxial techniques represent both a noncompressible site and a potentially severe degree of a bleeding complication, most peripheral nerve blocks arguably fall into the superficial category and present a favorable risk/benefit profile even in the absence of fully reversed anticoagulation. In the setting of an anticoagulated patient, one may opt for a supraclavicular or axillary approach as those sites are very superficial as opposed to an infraclavicular block where the artery lies deep under the pectoralis muscles. Table 2 shows some common anticoagulants and their hold time prior to certain blocks.

Table 2 Common anticoagulants and recommended hold time prior to neuraxial/deep blocks

Warfarin (Coumadin)	5 days + INR within normal range
Apixaban (Eliquis) or rivaroxaban (Xarelto)	72 h
Clopidogrel (Plavix)	5–7 days
Enoxaparin (Lovenox) therapeutic	24 h

Clinical Pearl
When determining the anesthetic plan for a patient on anticoagulation, one must look at the risk/benefits of general anesthesia compared to regional anesthesia and specifically if the regional technique is considered superficial, deep, or is neuraxial.

Common Pitfalls
Patient states that he is currently an everyday smoker and has recently been placed on continuous oxygen of 3 L. He is attached to pulse oximetry on room air and his SpO_2 reads 85%. He is not in respiratory distress. 3LNC brings him up to 91%. Does this information change your anesthetic plan?

Plan Brachial plexus nerve blocks, depending on the site of blockade, can cause ipsilateral phrenic nerve paralysis. The origins of this effect are anatomical in nature as the phrenic nerve crosses the brachial plexus in the cervical region in the area of the anterior scalene muscle. Table 3 demonstrates odds of developing phrenic nerve paralysis following nerve block. Figure 4 demonstrates the proximity of the phrenic nerve to the brachial plexus at the interscalene approach to the brachial plexus nerve block. COPD can be considered a relative contraindication to some nerve blocks as risk of respiratory failure increases with severity of lung disease. One absolute contraindication to proximal brachial plexus blocks would be contralateral phrenic nerve paralysis. Infraclavicular or axillary approaches to brachial plexus block are the safest in avoiding phrenic nerve blockade. In this complex

Table 3 Odds of developing ipsilateral phrenic nerve paralysis following brachial plexus block

Interscalene	Supraclavicular	Infraclavicular	Axillary
~100%	~50%	~1–3%	~0%

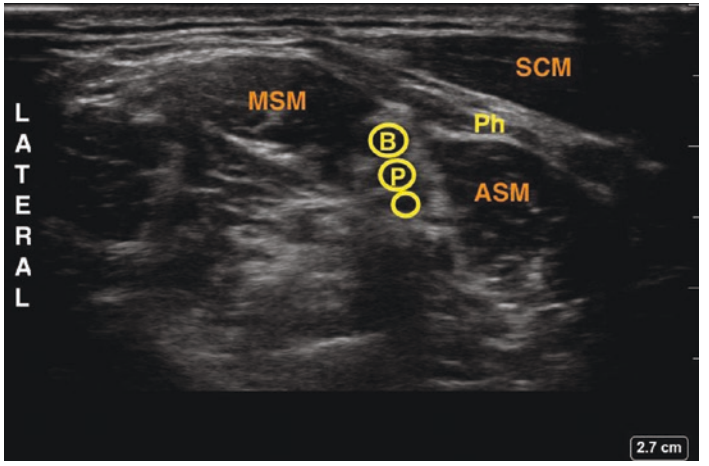

Fig. 4 Ultrasound image of interscalene approach to the brachial plexus nerve block. *MSM* middle scalene muscle, *ASM* anterior scalene muscle, *SCM* sternocleidomastoid muscle, *BP* brachial plexus, *Ph* Phrenic nerve

scenario, an axillary block (with attention to blocking the musculocutaneous nerve) would arguably be the safest as it removes the risk of phrenic complications and is more compressible than the infraclavicular approach to blocking the brachial plexus.

Clinical Pearl

Phrenic nerve paresis is a common risk of interscalene brachial plexus block and decreases as the brachial plexus approach moves more caudal.

Common Pitfalls

Prior to the block, the surgeon performs an ultrasound of the upper extremity and states that there is no viable site in the fore-

arm for the fistula. The plan is now for an antecubital or upper arm graft.

Plan Of note, a brachial plexus block may actually dilate vessels and help in the identification of target vessels that were not evident prior to the PNB [6, 9]. Nonetheless, as surgical plans change, anesthesiologists must adapt their plan as well. Aside from the interscalene block, other brachial plexus blocks mentioned reliably cover C6–8 dermatomes. C5 is rarely needed for procedures below the shoulder. One potential shortcoming of a brachial plexus block is failure to block the upper medial arm. Lack of coverage here can cause patient discomfort when surgical work is within this area. Frequently, addition of a supplemental block is needed to cover this area. The intercostobrachial (ICB) nerve is a branch of the second intercostal nerve originating from the T2 level. It travels through the serratus anterior and travels superficially. It can be blocked by ultrasound using a PECs II approach, or can also be blocked by a subcutaneous injection in the midaxillary line (Fig. 5).

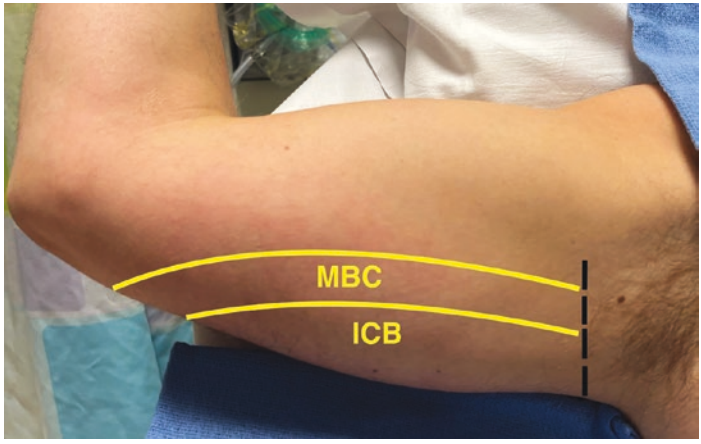

Fig. 5 Approximate distribution of *MBC* medial brachial cutaneous and *ICB* intercostal brachial nerve. Dashes—approximate line of cutaneous infiltration to anesthetize skin

Conclusion The patient is counseled on the risks and benefits of regional versus general anesthesia for the antecubital graft. The patient wishes to proceed with a brachial plexus block. The infraclavicular view is the optimal view of patient's anatomy. Brachial plexus block is performed at this site with 20 mL of 0.5% Ropivacaine and an additional 10 mL of 1.5% mepivacaine is injected in the upper arm to block the intercostobrachial distribution. The patient undergoes repeat ultrasound prior to surgery which now demonstrates improved vascular targets. He is administered Propofol at 30 μg/kg/min and is calm and comfortable. His pulmonary function is preserved as well. The patient undergoes successful AV fistula creation using the regional technique as the primary anesthetic.

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Acute Pain Management Protocol for Spine Procedures

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Case Stem

A 51-year-old 100 kg male (BMI 38 kg/m^2) presented to the clinic for evaluation of lower back pain for which he was mainly seeking care from a chiropractor. He has a past medical history of hypertension, type 2 diabetes mellitus, obstructive sleep apnea and anxiety/depression. He works as an independent contractor and on a roof tiling job and states to have fallen off a ladder 8 months prior and continues to have difficulty with activities of daily living. His home medications include duloxetine, nifedipine, atorvastatin, clonazepam, furosemide, lisinopril, metformin and oxycodone.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_34

Physical exam findings

- Vital signs: BP 158/96 mmHg, HR 99 bpm, RR 18/min, T 37.0 °C.
- Airway: Mallampati 2, normal dentition, no limitation of neck movement, clear bilateral lungs, heart regular rate and rhythm.
- Exam: There are no sensory or motor deficits on neurological exam. Limited range of motion of neck with extension.
- CBC: Hgb 12.4 g/dL, Platelet 395,000/μL, BMP: Na^+ 142 mEq/L, K^+ 3.8 mEq/L, BUN 14 mg/dL, Cr 0.68 mg/dL, Glu 123 mg/dL.
- Radiographs and MRI lumbar spine revealed anatomic narrowing indicating degenerative lumbar spinal stenosis.

Question 1 *A lumbar laminectomy for spinal stenosis is indicated for this patient. The patient does not want to take opioids as his brother developed opioid addiction after his surgery and underwent rehabilitation. He wants to discuss other options for pain management. What do you tell him? What are some of the intraoperative non-opioid based analgesic strategies for patients undergoing spine surgery?*

Answer: Postoperative consumption of opioids increases the risk of dependence [1–3]. Regional anesthetic techniques used alone or in combination with general anesthesia offer the opportunity to limit postoperative opioid use by modifying perioperative analgesia [4, 5]. Amongst the neuraxial techniques included are standard spinal and epidural anesthesia or intraoperative intrathecal administration of opioids [6–8]. Spinal anesthesia is more commonly used than epidural anesthesia. Some of the regional anesthesia techniques that have recently surfaced include the erector spinae plane (ESP) block, thoracolumbar inter-fascial plane (TLIP) block and multifidus cervicis plane (MCP) block [9–11] Table 1.

Table 1 Summary of neuraxial and regional analgesia techniques for spine surgery

Regional technique	Pertinent anatomy	Pitfalls
Spinal	Neuraxial technique	Hematoma, hypotension, urinary retention, motor weakness and sensory changes
	Location: Lumbar region using midline or paramedian approach; local anesthetic is deposited into the subarachnoid space	
Epidural	Neuraxial technique	Hematoma, motor weakness and sensory changes, urinary retention
	Location: Thoracolumbar region; local anesthetic is deposited into epidural space	
ESP	Nerve(s) blocked: Dorsal and ventral rami of spinal thoracic nerves	Pneumothorax
	Location: 2.5 cm lateral to spinous process; local anesthetic is deposited into fascial plane between erector spinae muscle and transverse processes of vertebrae	
TLIP	Nerve(s) blocked: Medial, intermediate, and lateral branches of lumbar dorsal ramus	Hematoma, intravascular injection
	Location: Lateral to lumbar transverse process; local anesthetic is deposited into multifidus-longissimus thoracis plane	
MCP	Nerve(s) blocked: Medial branches of the dorsal rami of C4–T4 spinal nerves	Injury to artery of dorsal ramus, intrathecal injury
	Location: Posterior cervical region; local anesthetic is deposited into fascial plane between the multifidus cervicis and semispinalis cervicis muscles	
TAP	Nerve(s) blocked: Anterior rami of spinal nerves T7–L1 spinal nerves	Intraperitoneal injection/bowel perforation
	Location: Lateral to the linea alba; local anesthetic is deposited into plane between internal oblique and transversus abdominis muscles	

ESP: Erector Spinae Plane; *TLIP*: Thoracolumbar Inter-facial Plane; *MCP*: Multifidus Cervivis Plane; *TAP*: Transversus Abdominis Plane

Question 2 *Why are local anesthetic-based techniques such as epidurals, field blocks or peripheral nerve blocks that are considered mainstay for multimodal analgesia under-utilized in spine surgery?*

Answer: The reasons that local anesthetic-based techniques are considered unsuitable for patients undergoing spine surgery are multifactorial [12, 13]:

1. Lack of anatomically amenable blocks.
2. Concerns from surgical colleagues regarding interference of these blocks with intraoperative neuro monitoring (IONM).
3. Concern regarding interference with early postoperative neurological assessments should there be an unanticipated motor weakness or sensory changes.
4. Risk of infection of an indwelling epidural or peripheral nerve catheter which will be directly in the surgical field.
5. May not be utilized in prolonged, complex procedures.
6. Absolute contraindications such as severe spinal stenosis precluding proper needle placement in the lumbar area.

Question 3 *What are the other reasons that general anesthesia is preferred for spine surgery?*

Answer: General anesthesia continues to be the most common anesthetic for spinal surgeries for the following reasons [12, 14]:

1. Placing patients in the prone position necessitates securing the airway with an endotracheal tube to prevent airway compromise.
2. Extensive surgeries of greater duration can be performed due to ability to titrate the anesthetic as needed as well as rendering the patient motionless throughout the entire procedure.
3. Greater patient acceptance and overall satisfaction.

Question 4 *What are the disadvantages of general anesthesia for spine surgery?*

Answer: General anesthesia gives rise to several unwanted complications and side effects. Hemodynamic instability from both induction medications and inhaled anesthetics is more common, as well as an increase in intraoperative blood loss [12]. There is also a nearly 30% increased incidence of postoperative nausea and vomiting after the use of inhaled anesthetics [15]. Another factor is the increased need for rescue analgesics with difficulty optimizing multimodal treatments without use of opioids [16]. Postoperative cognitive dysfunction may also be a cause for concern in older populations, increasing in-hospitals stays and resultant morbidity and mortality [17, 18].

Question 5 *What are the qualities of an ideal nerve block technique?*

Answer: An ideal nerve block technique for spine surgeries is the one that has no impact on neurophysiological monitoring, does not mask the postoperative neurological assessment and does not cause urinary retention.

Question 6 *What are the advantages of spinal or epidural anesthesia?*

Answer: There are several known short-term benefits of neuraxial anesthesia for spine surgery. Spinal anesthesia permits spontaneous ventilation in the patient, leading to decreased risk of atelectasis. There is also significantly less postoperative nausea and vomiting, decreased incidence of intraoperative hypertension and tachycardia as well as reduced analgesic requirements in the post-anesthesia care unit. Due to the reduction in these complications, patients have a shorter length of hospital stay and thus reduced morbidity and mortality [12, 14, 19].

Question 7 *What are the disadvantages of neuraxial anesthesia for spine surgery?*

Answer: Neuraxial blocks provide reliable analgesia, however, they carry multiple disadvantages for spine surgery [12, 20–22]:

1. Neuraxial block techniques are not site specific, contributing to increased chance of errors.
2. Hypotension is a common side effect, especially in the elderly population.
3. The risk of transient urinary retention is higher in patients receiving a neuraxial block, increasing the risk of bladder infection.
4. Patients who have spine fractures, spine instability, sepsis or prior spine surgery have less success rates.
5. There is an increased risk of neuraxial hematomas.

Question 8 *Are there any nerve blocks that can be performed for lumbar spine fusion with posterior approach?*

Answer: Both ESP blocks and TLIP blocks can be performed for lumbar spine fusion. Studies have shown that it can be used in multimodal analgesia practice to reduce opioid consumption and relieve acute postoperative pain in patients undergoing open lumbar decompression surgery [23, 24]. It has also been shown to improve patient satisfaction compared with standard analgesia in lumbar spine surgery patients [25]. However, the studies have not paid much attention to the effect of ESP block on early out of bed activity and hospital stay in patients with lumbar spine surgery [9, 26].

Question 9 *What is the anatomy of ESP block?*

Answer: The idea of this block is that a needle is inserted off the midline of the spine and is advanced until it meets between the erector spinae muscle and the thoracic transverse process [27] (Fig. 1). Due to its position and its unique quality of injectate infiltrating the paravertebral space, it can also be considered as a paravertebral block. Studies currently are unclear about the mechanism of the ESP block as studies fail to show a vertebral spread

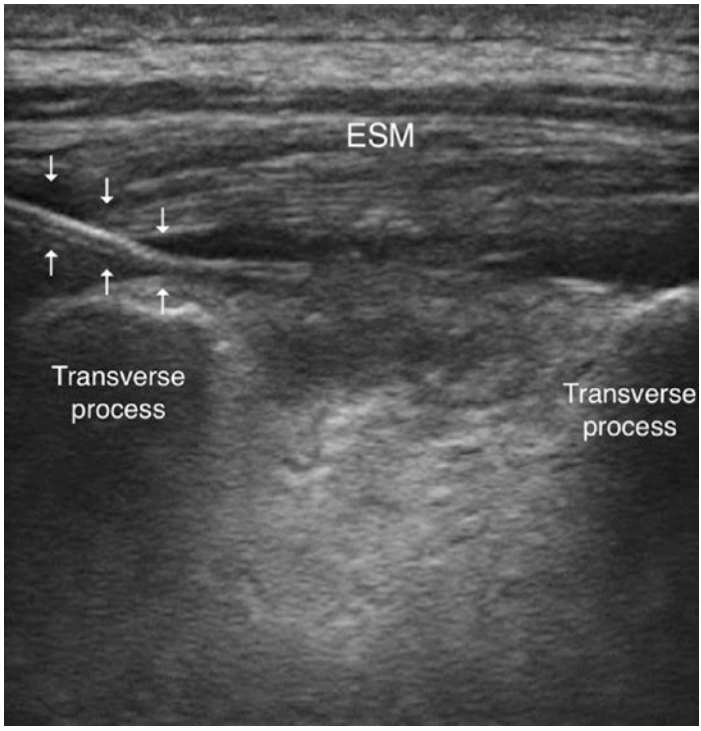

Fig. 1 Ultrasound depiction of correct needle placement underneath the erector spinae muscle (ESM) lifting off the transverse process. Solid white arrows: fascial plane deep to erector spinae muscle [27]

and some demonstrate a lateral spread toward the lateral cutaneous nerve [28].

Question 10 *What are the disadvantages of ESP block?*

Answer: The disadvantages of the ESP block lie in the spread of anesthetic. The injectate can spread to the ventral rami which may interfere with intraoperative neurophysiological monitoring, and immediate neurological examination postoperatively [29]. In addition, local anesthetic is washed out during the surgical procedure and can spread into the epidural space extending anesthetic effects into undesired areas [30].

Question 11 *Is there any method to avoid catheter at the surgical site?*

Answer: Low thoracic erector spinae single injection or catheter has been shown to result in spread as low as L5 [31]. It is reported to be an easier method of accessing lumbar erector spinae plane as compared to direct lumbar erector spinae plane injection and is also remote from the surgical site [32].

Question 12 *How is the ESP block performed?*

Answer: The patient is positioned prone with pillow under the abdomen and arms resting over the head symmetrically. A wide scan is performed with a view of several centimeters laterally, low lumbar in the caudad direction and cephalad until rib/pleura are visible (T12). The midline and costotransverse junction are marked bilaterally 2.5 cm off midline. Using a 25 G needle, 1% lidocaine 3–5 mL is infiltrated to provide analgesia for skin puncture if the patient is awake. This needle is aimed at the caudad edge of the transverse process. After skin infiltration a catheter needle is advanced at the same angle under ultrasound guidance to touch the caudad edge of the transverse process. 0.5 mL of saline boluses are used to identify the spread. If the needle is in correct position, there will be lifting of the erector spinae with the bolus. High volume (25–30 mL) of local anesthetic is needed to open the space. The needle is flattened to thread catheter within the erector spinae plane as much as possible. The catheter is carefully and thoroughly secured [27].

Question 13 *What is the dose of local anesthetic for ESP block?*

Answer: Programmed intermittent boluses of 0.2% ropivacaine 10 mL every 90 min or 20 mL every 3 h with 2–5 mL as needed every hour is the usual dose for ESP blocks. 0.25% bupivacaine can also be used [33, 34].

Question 14 *What is TLIP block? What is the advantage of TLIP block in the intraoperative and postoperative period?*

Answer: The TLIP block is a fascial plane block which interrupts transmission along the dorsal primary rami of thoraco-lumbar nerves. Local anesthetic is injected between multifidus and longissimus muscle planes. This block provides the advantage of good analgesia while having no impact on intraoperative neurophysio-

logical monitoring. In addition, regarding postoperative recovery, there is no impact on immediate neurological examinations postoperatively nor movement as there is no motor blockade [35]. The TLIP block is also useful if one tissue plane has more edema and becomes difficult to access and visualize [35].

Question 15 *What nerve block can be performed for lumbar spine fusion with anterior or lateral approach?*

Answer: Transversus abdominis plan (TAP) block, unilateral ESP block or unilateral low paravertebral blocks can be performed for lumbar spine fusion with anterior or lateral approach. TAP blocks are used for postoperative pain management in laparoscopic or open abdominal surgeries. Unilateral ESP block is a paraspinal fascial block (as described in the earlier sections of this chapter) that can be used for surgeries involving anterior, posterior and lateral thoracic and abdominal areas [29]. Paravertebral nerve blocks target the space lateral to where the spinal nerves emerges from the intervertebral foramina, providing a large unilateral somatic and sympathetic block [36].

Question 16 *How and why would a TAP block be beneficial for patients undergoing anterior or lateral spinal fusions?*

Answer: Anterior and lateral lumbar interbody fusion is usually associated with a considerable amount of post-operative pain. The use of a TAP block is normally used for abdominal procedures like cholecystectomies [37]. However, since they include the intercostal nerves, subcostal nerve and iliohypogastric and ilioinguinal nerves they can provide a widespread analgesia that would counteract pain observed with spinal fusion [38]. The block also allows for good analgesic spread between the vertebrae [39].

Question 17 *Is there a nerve block that can be performed for cervical spine surgery?*

Answer: The MCP block can be performed to provide analgesia for cervical spine surgery. It is performed with ultrasound guidance. Local anesthetic is infiltrated between the fascial plane of the multifidus cervicis and semispinalis cervicis muscles bilaterally. This block selectively acts on the medial branches of the dorsal rami of spinal nerves from C4 to T4 [40]. The other approach is intra-semispinal fascial plane (ISP) block which is useful in elderly

patients as multifidus muscle is difficult to visualize in elderly patients. In this block, local anesthetic is injected between the semispinalis cervicis and semispinalis capitis muscles which are easier to locate using ultrasound. The blocks are performed at the C5 level; the needle traverses through five layers of cervical muscles. Both MCP and ISP blocks provide coverage from C3 down to the T1-T4 levels [41].

Clinical Pearls

- Regional anesthesia has been shown to decrease pain during the postoperative period and thus lowers opioid consumption in patients undergoing spine surgeries and significantly increases patient satisfaction.
- Spinal and epidural anesthesia provide less complications when compared to general anesthesia, such as decreased postoperative nausea and vomiting and reduced hospital stay.
- There are multiple techniques available depending on surgical approach, offering the options of ESP, TLIP, TAP and MCP blocks.
- Given variations to each technique, a trained anesthesiologist with an understanding of ultrasound technology as well as a thorough understanding of the fundamentals of anatomy are vital to a successful nerve block.

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Must-Known Special Considerations for Acute Pain Management in Pediatric Patient Population

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1 Introduction

With the advent of ultrasonography, the popularity of regional anesthesia has grown immensely; this is largely due to a significant improvement in the safety profile for regional anesthetic techniques afforded by the visualization of anatomy and key vascular structures during procedures. Historically, the caudal block, a form of neuraxial blockade, has been the gold standard in children due to the ease of placement, low complication rate, and efficacy. Peripheral nerve block techniques performed using landmark techniques were associated with more complications and were less dependable; therefore, they were rarely used in the pediatric population. However, the use of ultrasonography has allowed for

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_35

the routine use of peripheral nerve blocks which were once considered dangerous in children presenting an alternative to neuraxial techniques [1, 2].

In this chapter, we will address the following regarding considerations for regional anesthesia in children:

1. Risks and benefits of placement of peripheral nerve blocks in an awake or sedated child as compared to children under general anesthesia
2. Dosing of local anesthetics—types of local anesthetics that should be used or considered in children
3. LAST and its presentation in children especially children who have received blocks under general anesthesia
4. The use of adjuncts (clonidine, dexmedetomidine and steroids) along with local anesthetics in children-benefits such as extension of block duration and density of block-sensory vs. motor; elimination of the need for catheter placement (infectious risks and longer block time and hospitalizations); risks of adjuncts

The chapter will be divided into three categories: truncal blocks, upper extremity and lower extremity blocks. Each section will have a case stem, followed by PBLD style questions focusing on highlights and special considerations in children.

2 Special Considerations for Regional Anesthesia in Children

While it is considered safer to perform blocks on adults who are awake and mildly sedated, additional factors must be considered in the pediatric patient, including the age, cognitive development, and social development of the child. Generally, children are often not cooperative and require sedation and/or general anesthesia with peripheral IV placement and other invasive procedures. These difficulties can be further exacerbated by separa-

tion anxiety and the unfamiliar environment of the hospital. In 2012, the pediatric regional anesthesia network (PRAN) conducted a multi-center study comparing blocks performed in children who were awake, sedated, or under general anesthesia. Of the 14,917 neuraxial and peripheral nerve blocks in the study, 95% were performed under general anesthesia and resulted in no deaths, cases of paralysis, or serious sequelae lasting longer than 3 months. Postoperative neurological symptoms occurred at a rate of 0.93/1000 (confidence interval [CI], 0.7–1.2) under general anesthesia and 6.82/1000 ([CI], 4.2–10.5) in sedated and awake patients. This study highlights the fact that sedated or awake children are more likely to move during regional procedures, increasing the risk of an adverse event; this makes performing the block under general anesthesia the safest option in this patient population. However, in older children, particularly teenagers, it is possible to perform nerve blocks safely with sedation, as these patients are appropriately cognitively developed to follow commands and cope with the experience of undergoing such a procedure. If general anesthesia is required, it can be induced via standard inhalational induction or IV induction with propofol, however it is worth noting that if a nerve stimulator is being used to improve block efficacy, muscle relaxation should be avoided [3, 4].

As blocks in children are usually performed after induction of general anesthesia, the purpose of block placement is primarily for the reduction of intra/post-operative opioid requirements and improvement of post-operative pain control. The exception to this is the use of spinal anesthesia in premature neonates to avoid general anesthesia, which is associated with an increased incidence of post-op apnea, bradycardic episodes, and need for post-operative intubation in this age group. Single shot spinal blocks are performed with the infant awake and held in either a sitting or lateral decubitus position by an experienced individual; the success rate of this procedure is particularly dependent on the proper positioning of the infant [5].

3 Upper Extremity Blocks

Case Stem
Fifteen-year-old otherwise healthy male who presents for ORIF of right distal radius and ulna fracture.

Which peripheral nerve blocks are commonly used for surgery on the upper extremity?
Supraclavicular nerve block
Infraclavicular nerve block
Axillary nerve block
Interscalene nerve block

For surgical procedures involving the upper extremity such as the arm, forearm, and wrist, blocking the brachial plexus is the most effective means of providing postoperative analgesia. The roots of the brachial plexus consist of the anterior divisions of C5–C8 and T1 spinal nerves. These nerve roots then pass out of the intervertebral foramina, over the superior aspects of the transverse processes, and run downward in the neck towards the first rib. These roots will join and divide to form trunks, divisions, cords, and then finally the terminal branches.

The supraclavicular nerve block is often referred to as the spinal for the arm, as it provides coverage for most if not all surgical procedures involving the upper extremity including shoulder procedures. This procedure blocks the brachial plexus at the level of the divisions. Supraclavicular nerve blocks are performed by placing the ultrasonography probe above the clavicle and visualizing the brachial plexus lateral to the subclavian artery and above the first rib. Local anesthetic is then injected below and above the brachial plexus. Despite providing excellent analgesia, supraclavicular nerve blocks are not the most common upper extremity blocks performed in younger children undergoing surgery given the increased risk of pneumothorax due to the closer proximity of the cervical pleura [1, 6].

Infraclavicular nerve blocks serve as a popular alternative to supraclavicular nerve blocks, as this block is performed at the level of the cords but is still associated with similar risks to the supraclavicular nerve block such as pneumothorax, infection, nerve damage and intravascular injection [6].

Axillary nerve blocks are the most commonly placed peripheral nerve blocks placed in children, as they are placed at the level of the axilla, avoiding any risk of pleural puncture. Axillary nerve blocks block the terminal branches of the brachial plexus including the radial, ulnar, and median nerves with the exception of the musculocutaneous nerve (which must be blocked separately at the body of the coracobrachialis muscle) and provide effective coverage for surgeries involving the forearm, wrist, and hands. Common surgical procedures such as ORIF of wrist fractures, excision of ganglion neuromas, and sarcoma of upper extremity are effectively covered by axillary nerve blocks [7].

Interscalene nerve blocks provide coverage for the roots of the brachial plexus and are often used for surgeries involving the shoulder and clavicle. This block is rarely performed in children due to difficulty in providing coverage for C8-T1 as well as increased risks of inadvertent vertebral artery puncture, transection of the spinal cord, high spinal due to spread of local anesthetics in the epidural space, spinal, and subarachnoid space. Interscalene blocks are associated with 100% blockage of the phrenic nerve, which can result in ipsilateral diaphragmatic paresis and/or paralysis; which can cause significant respiratory depression in neonates, infants and toddlers who are more diaphragm dependent. Also, the lung apices are more cranially located anatomically in infants, which increases the risks of pneumothorax. This block has also been reported to result in increased risk of laryngeal nerve blockade, which can result in ipsilateral vocal cord paralysis with increases in airway resistance for younger children [1, 8].

What are the different techniques used to perform these brachial plexus blocks in children and how does the use of ultrasonography aid in the placement of these blocks?

Brachial plexus blocks are routinely placed using real time ultrasonography especially in children due to the close proximity of vascular structures to the apices of the lung and vertebral bodies. Landmark techniques for brachial plexus nerve block placement have been associated with an increased risk of vascular puncture with inadvertent intravascular injection, pneumothorax, vertebral

body laceration, inadvertent injection in the epidural and spinal space. Real time ultrasonography has been used with nerve stimulation technique particularly for axillary and musculocutaneous nerve block placements with increased accuracy when compared to each technique alone [9].

4 Blocks for Lower Extremity Surgery

Case Stem
Twelve-years-old male with a past medical history significant for ADHD (attention deficit hyperactivity disorder), anxiety, constipation, dysuria with gross hematuria, pervasive developmental disorder (PDD), Von Willebrand disease and Charcot-Marie-Tooth disease complicated by bilateral cavovarus feet with chronic pain who now presents for bilateral cavovarus foot reconstruction.

What are the different options for postoperative pain management in this patient in terms of regional anesthesia? Which peripheral nerve blocks would you use and why and which local anesthetics and dosage would you use?
For surgeries of the lower extremity different options for postoperative analgesia include:

A. Peripheral nerve block catheters (single shot or catheters).

B. Neuraxial techniques such as lumbar epidural.

Innervation for the lower extremity is provided by the lumbar and sacral plexus. The lumbar plexus formed from L1 to L4 nerve roots provides innervation for most of the lateral and anterior thigh and proximal knee as well as the medial aspect of the ankle. The femoral, lateral femoral cutaneous, and obturator nerves are branches from the lumbar plexus. The sacral plexus is formed from the anterior rami of L4, L5, S1, S2, and S3 and provides innervation to the posterior thigh and lower leg and most of the ankle. The sacral plexus gives rise to the sciatic nerve, the largest nerve in the body [10].

The sciatic nerve can be blocked proximal (sub-gluteal and gluteal) and distally (popliteal and ankle). This nerve is most

commonly blocked at the level of the popliteal fossa, a technique referred to as the popliteal sciatic nerve block. At the level of the popliteal fossa, the sciatic nerve is divided into two branches, the anterior tibial and common peroneal nerves, both of which can be blocked 5–10 cm above the popliteal crease. This nerve block is typically performed with the patient in the supine position with the knee of the affected leg elevated and flexed to allow for easy to the popliteal fossa. The US probe is placed in the popliteal fossa and advanced cephalad until both nerves are adjacent to each other and the needle is placed lateral to the thigh and used to place local anesthetics around both nerve branches. Either Ropivacaine or Bupivacaine can be used and doses 2–3 mg/kg with 20–40 mL used for popliteal sciatic nerve block. It is recommended that more dilute local anesthetics such as Bupivacaine 0.25% and Ropivacaine 0.1–0.2% are used for younger children due to smaller total body weight and concerns for local anesthetic toxicity, whereas 0.5% of either of these local anesthetics can be used for older children and teenagers.

For the proximal sciatic (gluteal or sub-gluteal) approach, the patient is placed in the lateral position with the surgical side up. Given that this block is usually done under general anesthesia, this approach is less desirable and usually only used if the popliteal approach cannot be accessed or is not effective such as in the case of surgeries above the level of the knee such as for rotationplasty [1, 11].

4.1 Ankle Block

The ankle block can be used for surgeries involving the ankle, but this block does not provide any analgesia proximal to the ankle such as in the case of tourniquet placement, which can be managed effectively under general anesthesia. During ankle block placement, the posterior tibial, deep peroneal, superficial peroneal, saphenous, and sural nerves are blocked. Usually, 2–5 mL of local anesthetics are deposited for each of these nerves based on the weight of the child [12].

4.2 Lumbar Plexus

The lumbar plexus is composed of the T12-L5 nerve roots and branches include the femoral, lateral femoral cutaneous, and obturator nerves, which innervate the upper thigh, anterior aspect of the knee and the medial aspect of the ankle. For procedures involving the ankle, the sensory component of the femoral nerve is often blocked at the level of the thigh and/or above the knee [13].

4.3 Femoral Nerve Block

The femoral nerve block is the most commonly performed PNB for lower extremity due to ease of placement as most providers are familiar with this procedure. This nerve block provides analgesia to proximal hip, anterior thigh and medial aspect of the ankle and is often used for knee arthroscopies or ankle surgeries. This nerve block is commonly performed at the level of the inguinal ligament with the nerve being lateral to the artery and vein with ultrasonography. If a nerve stimulator is used in addition to ultrasonography, then quadriceps contraction should be obtained prior to injecting the local anesthetics [11].

4.4 Adductor Canal Block

An alternative option for post-operative analgesia in pediatric patients undergoing knee and/or ankle surgery is the adductor canal block, as it blocks sensory innervation to the medial aspect of the ankle without causing motor weakness in the quadriceps muscle, which is commonly associated with femoral nerve block placement [1].

4.5 Saphenous Nerve Block

The saphenous nerve is the sensory component of the femoral nerve after it enters the adductor canal, and it provides sensory innervation to the medial aspect of the ankle.

This nerve block is placed with the patient in the supine position with the anterior rotated laterally. The nerve is often visual-

ized as either superior and lateral to the artery or within the aponeurosis between the sartorius and vastus medialis muscles. There is a 10% failure rate associated this block placement, which is undesirable for blocks done in children under general anesthesia. For this reason, the adductor canal nerve block is a more popular alternative [11].

How would your choice of PNB placement change if this procedure was for periacetabular and/or femoral osteotomies instead?

For more proximal procedures such as periacetabular and/or femoral osteotomies that often include the hip, lumbar plexus nerve block placement provides the most complete ipsilateral blockade. This nerve block is considered to be more challenging when compared to other blocks such as femoral or adductor canal nerve blocks as this block involves accessing the psoas compartment. Given this increased depth and close proximity to the spinous process and branches of the aorta as well as other visceral structures such as the kidney and bowel, lumbar plexus block placement has been associated with inadvertent visceral and arterial perforation, intravascular injection with high uptake due to large volumes of local anesthetics used for PNB placement, LAST, epidural and/or spinal anesthesia, profound hypotension, and hematoma in the psoas compartment [13].

This block placement is often painful and requires increased sedation in adults and is usually placed following the induction of general anesthesia in children. Due to high risks associated with LP placement, this block is often performed with the use of real time ultrasonography in conjunction with nerve stimulation. Following induction of general anesthesia, the patient is placed in lateral decubitus position with the surgical side up. Both the iliac crest and spinous processes are identified and marked 4–5 cm from the spinous process in older children and teenagers. The classic US guided technique used is referred to as the shamrock technique where the US probe is placed at the level of the iliac crest perpendicular to the spinous process until the quadratus lumborum muscle is identified superior to both the psoas muscle and the transverse process. The lumbar plexus is then identified within the body of the psoas muscle, and a needle is advanced until quadriceps contraction is elicited.

Pro tip: Place hand over the patellar for the ipsilateral side to determine if there is patellar snap or contraction. If only uses nerve stimulator, set the nerve stimulator to a higher frequency such as 1.5 mA and once quadriceps contraction is obtained, then turn the dial and lower the amplitude to 0.5 mA prior to inject local anesthetics. Make sure there is still muscle contraction prior to injection of the local anesthetics, as the needle can move during placement. If using nerve stimulation in conjunction with US guidance, the nerve stimulator can be set at a lower number such as 0.5 mA just for confirmation prior to injection.

4.6 Fascia Iliaca Block

The fascia iliaca (FI) block serves an alternative to lumbar plexus block placement as it blocks the femoral, obturator and lateral femoral cutaneous nerves (LFCN). This block is traditionally done by finding the fascia illicia and iliacus muscle and injecting inferior and lateral to the fascia iliaca and often requires a higher volume in order to be effective. Given the variable path of the LFCN below the inguinal ligament particularly in children and so the supra-inguinal approach to the FI block is becoming more popular, as there is more coverage of the LFCN. The patient is placed in the supine position with the groin and inguinal crease exposed. The probe is placed longitudinal and medial to the ASIS. The internal oblique and transversus abdominis muscles are identified in addition to the iliacus muscle. The needle is inserted and transducer advanced caudad to cephalad until the tip of the needle is identified below the FI and above the iliacus muscle prior to injecting local anesthetics. However there is limited date in for the use of these blocks in pediatric patients [14].

4.7 Neuraxial Blockade

Lumbar epidural has been the gold standard for management of postoperative pain due to decreased need for intraoperative and postoperative opioids, which results in a lower incidence of uri-

nary retention, ileus and reduced hospitalization stay. As in the case with PNB placement, lumbar epidurals are placed without any difficulty in children under general anesthesia using landmark technique.

What are the advantages and disadvantages of a peripheral nerve block placement compared to a neuro-axial block such as an epidural?

Advantages

Unilateral blockade.
Avoid instrumentation of the neuraxiom that increases the risks of epidural abscess or hematoma in high-risk patient population.
Can be safely performed in patients on anti-coagulants.
Avoid side effects associated with epidural blockade such as urine retention requiring placement of a Foley catheter, bowel incontinence, and opioid induced pruritis and nausea.

Disadvantages

Higher risk of nerve damage and intravascular injection.
Incomplete sensory coverage.
Requires more than more PNB catheters to provide similar coverage with one epidural catheter.

Is catheter placement superior to single shot? Why or why not?

Single shot blocks are often placed for same day outpatient surgeries. With the addition of adjuncts such as precedex and clonidine, single shot blocks using bupivacaine can last for 24–48 h [15].

5 Truncal Blocks: Anterior Trunk

Case Stem
Six-year-old male with renal insufficiency due intermittent ureteropelvic junction obstruction and antenatal hydronephrosis is scheduled for right robotic assisted laparoscopic pyeloplasty. He has GERD which is well controlled and hypotonia. His parents are extremely concerned with post-operative pain. They had heard from a family member whose child had a similar procedure and who did well with a block, therefore, they asked surgeon for a block. Anesthesia team was consulted for pain management strategies and block placement options.

What are the different options for post-operative pain management this patient? Neuraxial vs PNB?
Abdominal surgeries are probably amongst the most common surgical procedures performed in the pediatric population and encapsulate a variety of surgical subspecialities including general surgery, urology and gynecology, making truncal blocks the most common blocks performed in children. Neuraxial blocks such as the caudal block remain the gold standard in this patient population, but as regional anesthesia techniques are further developed, peripheral nerve blocks are emerging as viable alternatives to neuraxial blocks [16].

5.1 Neuraxial Blocks: Block Type and Dosing

Neuraxial techniques such as lumbar epidural catheter placement and single shot caudal blocks are options for post-op pain control. As these patients are usually discharged after 24–48 h, epidural catheter placement has become a less popular option due to prolonged hospitalization associated with epidural catheter placement. As a result, a single shot caudal block is the most commonly neuraxial technique utilized. Single shot caudal block can be performed after induction of anesthesia in the lateral decubitus position, using an angiocath, with either landmark or ultrasound guidance and a loss of resistance technique. EKG monitoring should be continuous

during placement. Administration of a test dose is an important step in the procedure as it is useful for early detection of intravascular injection, which is crucial in patients under general anesthesia. Bupivacaine and ropivacaine are the most commonly used local anesthetics for this block due to their longer duration of action. Bupivacaine 0.25% with epinephrine 1:200,000 is the most used formulation and is often diluted to 0.125% with epinephrine 1:400,000. Dilution of bupivacaine also allows for the administration of a larger volume of anesthetic, allowing for a higher dermatomal spread. Ropivacaine 0.2% is the second most used commonly used formulation; care must be taken to add epinephrine 1:200,000 or 1:400,000 to allow for detection of intravascular injection. A common adjunct used to extend the duration of the caudal block as well as to increase dermatomal coverage to reach the abdominal dermatomes is the addition of an alpha agonist such as clonidine or dexmedetomidine. The use of clonidine was prevalent until the past few years; but it is now being superseded by dexmedetomidine which has been shown to be eight times more specific to alpha 2 receptors than clonidine and have an improved analgesic effect. The addition of clonidine or dexmedetomidine has resulted in the reduction of caudal catheter placement [1, 15, 17].

What are the disadvantages to neuraxial blocks?

Neuraxial blockade is associated with complications such as urinary retention, leg weakness and constipation. These symptoms are especially noticeable in children >4 years old, therefore, it is important to discuss these risks in detail with parents. For this reason, peripheral nerve block placement would be a great choice for children <4 years of age [18].

Which PNBs could be used and why? What are the efficacy and duration of these blocks? Coverage area for blocks?

In this case, where the procedure will be performed via laparoscopic assistance, the locations of the incisions for port and camera placement are key in selecting the correct block. Typically, there will be an umbilical incision made for placement of the camera along with two to three additional incisions in the upper and lower abdomen, necessitating coverage of the anterior abdominal wall and the umbilicus. For coverage of umbilical port site,

rectus sheath block would offer complete coverage of the umbilicus, which is often the area associated with the most pain. Transversus abdominus plane (TAP) block and quadratus lumborum (QL) blocks are also options for this procedure, as both would provide anterior abdominal coverage [16, 19].

5.2 TAP Blocks vs. QLB

Although TAP blocks were first described as a landmark technique by Rafi in 2001, it is now exclusively performed under ultrasound guidance due to concerns for vascular injuries such as epigastric artery laceration and bowel perforation. The abdominal wall consists of three muscle layers: external oblique, internal oblique and transversus. TAP blocks are performed in the supine position, with the target being the plane between the transversus abdominis and internal oblique muscles. In children, this block is usually performed after induction of general anesthesia in order to avoid the risk of excessive movement and inadvertent injury to abdominal structures. Bilateral TAP blocks should be performed for coverage of abdomen. Another alternative PNB would be QL blocks. US guided QL1 blocks provide excellent abdominal wall coverage, but do not reliably cover the umbilicus incision site, therefore, it is recommended to perform bilateral rectus sheath blocks in addition to QL1 [20].
Other common abdominal procedures in children that benefit from these types of blocks include umbilical hernia repair, epigastric/inguinal hernia repairs, laparoscopic appendectomy, laparoscopic cholecystectomy, exploratory laparoscopy or laparotomy. Procedures that can benefit from a caudal neuraxial technique include circumcision, hypospadias repair, meatoplasty, and inguinal hernia repair [1, 16].

6 Posterior Trunk: Spine/Back

Case Stem
Thirteen-year-old female with a PMH significant for asthma controlled on albuterol as needed and idiopathic scoliosis is scheduled for posterior spine fusion from T3 to L3. Imaging of the

spine shows significant lumbar curve with a Cobb angle >40°. She has never had anesthesia in the past and there is no family history of anesthetic complications. Her parents are extremely worried about pain and wanted to discuss options for post-operative pain control.

What are the considerations for regional anesthesia in this patient population?

With any regional technique, the patient must be first assessed for any absolute contraindication to regional anesthesia such as bleeding disorders, infections at the targeted site, hemodynamic instability, or patient/guardian refusal. Preoperative considerations include the patient's past surgical history (especially with regards to prior spine surgeries), the use of intraoperative neuromonitoring, duration of the planned intervention, anticipated blood loss, and patient and surgeon preference.

Pediatric anatomic and physiologic variation (as compared to adults) should also be considered; this is especially significant with neuraxial approaches. Remember that the conus medullaris is located at the L3 vertebral level in infants and children up to 1 year of age, as compared to L1 in adults. Additionally, the dural sac ends at S3–S4; more caudal than in adults where it ends at S2. Less densely packed epidural fat (allowing for easier catheter advancement and greater anesthetic spread) and a nonmyelinated spinal cord in neonates allow for the use of lower concentrations of local anesthetics; concurrently increased cardiac output leads to increased systemic absorption; therefore, maximum anesthetic dosage is usually lower as compared to adults. Finally, the incomplete fusion and ossification of the vertebrae in younger children make ultrasound imaging easier but increase the risk of trauma during block placement [21].

Further considerations in the setting of scoliosis include the etiology and the extent of disease. Patients with idiopathic scoliosis are less likely to have other medical problems and are at a lower risk of respiratory complications when compared to those with neuromuscular, myopathic, or mesenchymal etiologies. The degree of scoliosis is especially important in the context of respiratory function; a Cobb angle of >60° is associated with restrictive respiratory pathophysiology secondary to mechanical

limitations. From a cardiovascular perspective, scoliosis has been associated with congenital heart disease and the presence of concomitant connective tissue disorders (such as Marfan syndrome) can also predispose patients to cardiovascular pathologies. In addition, extreme and longstanding cases of scoliosis can result in pulmonary hypertension and right ventricular dysfunction [10].

Most nerve blocks for posterior spine fusion surgeries in children are done under general anesthesia following induction, establishment of peripheral IV and arterial line access and patient positioning. Although the final positioning will depend on the technique and approach (sedated vs. awake), many of the techniques discussed below are most conveniently performed in either lateral decubitus or prone position.

How is post-op pain managed?

Given the complex nature of the surgery these patients are often under the care of multiple treatment teams, including pain management specialists. Posterior spinal fusion is one of the most painful procedures performed on children and adolescents, making the management of postoperative pain in this patient population particularly challenging [22]. A multimodal and protocolized approach is often employed, with protocols varying by institution. Although no common, best practice, approach has been defined, protocols generally include patient-controlled analgesia (PCA) with either hydromorphone or morphine, along with scheduled dosing of acetaminophen, ketorolac, and benzodiazepines to relieve muscle spasms [10, 22]. Specific PCA programs also vary by institution and include both basal-bolus and bolus only approaches. Although opioids can provide effective pain control, their use is often complicated by nausea, ileus, pruritus, and the risk of respiratory depression; therefore, regional anesthetic techniques can be very useful in improving patient comfort and satisfaction after these procedures.

What blocks can be done with these cases?

Innervation of the structures affected by posterior fusion surgery is provided by the posterior rami of the spinal nerves, allowing for both neuraxial and peripheral regional approaches.

Arguably the simplest of these blocks is the intrathecal (IT) injection of morphine which can be performed after the induction of general anesthesia prior to surgical incision or intraoperatively by the surgical team. Dosing strategies range with 5–20 μg/kg with a maximum of 1 mg, with a similar incidence of nausea, pruritus, and respiratory depression when compared to opioid PCA. Doses greater than 20 μg/kg have been associated with an increased incidence of significant respiratory depression and should be avoided. Although IT administration of opioids significantly reduces intraoperative and postoperative opioid use, the analgesic effect wanes about 24 h after injection. Therefore, especially in longer procedures, it may be most beneficial to have the surgeon administered IT morphine immediately prior to wound closure. Given the duration of IT morphine, the patient will need an opioid PCA postoperatively with demand dosing only, as IT morphine will serve effectively as the basal rate for the first 24 h. A basal rate may be safely added after the 24 h period has passed [22].

An alternative neuraxial approach, which overcomes the temporal challenges of intrathecal morphine injection, is the use of epidural catheters. Epidural catheter placement is usually performed intraoperatively by the surgical team at the end of the procedure and is an option used by some institutions to facilitate postoperative management. In comparison to IT morphine, epidural catheter placement is less commonly utilized given issues with management of catheters placed in surgical site. No specific guidelines on placement are available, therefore local practice varies. The catheters are inserted at the incision site and advanced cephalad, and (if 2 catheters are used) caudal about 5 cm (to ~T5 and ~L2). Epidural catheters have been shown to offer improved pain control when compared to PCA alone. However, use of these catheters can be complicated by hypotension, urinary retention, and lower extremity weakness, resulting in difficulty with performing neurological evaluations [22].

Given the challenges with neuraxial blocks, peripheral nerve blocks are now emerging as an effective alternative for postoperative pain control. The most utilized peripheral nerve block techniques are single shot Erector Spinae Plane (ESP) blocks and

Paravertebral Blocks (PVB). These blocks are usually performed prior to incision to provide intra-operative analgesia, reduction of opioid requirement and avoid concerns with postoperative anatomical distortion and contamination of the surgical site [22].

PVBs are performed by injecting anesthetic into the paravertebral space; a triangular shaped area bordered by the vertebral body, the costotransverse ligament, and the parietal pleura. Although the cephalad extent of the paravertebral space is not defined; its caudal boundary is located at T12 due to the origin of the psoas major muscle. The paravertebral space contains the intercostal nerves, the sympathetic chain, and the posterior rami of the spinal nerves and is continuous with the epidural space medially and the intercostal space laterally, making it an attractive target for a regional anesthetic technique [23]. Both ultrasound and landmark techniques have been described. In the landmark technique the needle is inserted 1–2 cm (about 0.8 in.) lateral to the midline and advanced until transverse process is contacted, then the needle is repositioned to advance 1 cm (about 0.4 in.) below the transverse process and a bolus of 0.3–0.5 mL/kg of 0.25% bupivacaine is injected [23]. The PVB has mostly been used in thoracic and abdominal surgeries but has been recently suggested to improve postoperative opioid requirements and shorten hospital stay in vertebral body tethering procedures [21, 24]. However, because of the proximity of the paravertebral space and the pleura, the paravertebral block should only be done by, or under the supervision of, an experienced pediatric regional anesthesiologist given the risk of pneumothorax. Additional complications of PVB include hypotension and inadvertent epidural or intrathecal injection.

Presenting itself as an attractive alternative to PVB, the ESP block is a relatively novel technique (developed in 2016) which involves anesthetic injection into the musculofascial plane between the erector spinae muscle and transverse processes [25, 26]. Studies suggest that injection into this space results in transforaminal, epidural, and intercostal spread of the local anesthetic over several spinal levels, although the exact mechanism of action is unknown and studies have demonstrated conflicting results [27–29]. The block can be performed via a parasagittal, transverse, or lateral-transverse subcostal (aka Aktsu) approach prior to incision [30]. There are also

reports of intraoperative ESP catheter placement under direct visualization by the surgical team [31]. Bupivacaine or ropivacaine at 0.25–0.5% is the anesthetic of choice, with one case series suggesting that volumes of 0.5 mL/kg of 0.25% bupivacaine (to a maximum of 20 mL) provide satisfactory analgesia without affecting motor function [30]. Unfortunately, given the recent emergence of this technique randomized control trial evidence for use in pediatric spine surgery is not currently available. However, case reports suggest the technique is effective in decreasing pain and opioid requirements in a variety of pediatric surgeries [30, 32] and in adult spine surgery patients [25, 33]. Advantages over paravertebral blocks include relative ease of placement and lower probability of complications such as pneumothorax and subarachnoid injection. Given these benefits, as evidence of clinical efficacy accumulates, the ESP block may emerge as the technique of choice for regional anesthesia in pediatric spine surgery.

Finally, techniques are being developed that target the branches of the posterior rami as they course through the paraspinal musculature. These include the Thoracolumbar Interfascial Plane Block (TLIP), which involves injecting local anesthetic between the multifidus and longissimus muscles, and the Multifidus Cervices Plane Block which is designed for analgesia in cervical surgeries [34]. Although these blocks are unlikely to provide analgesia to the vertebral bodies, they may be a useful addition the regional anesthesiologists armamentarium for the postoperative management of this patient population.

What is the role of adjuvant agents in this patient population?

Most peripheral nerve blocks using bupivacaine or ropivacaine last about 16–24 h. One approach for extending block duration is continuous peripheral nerve blockade via catheter placement. However, catheters have a high rate of failure, expose the patient to additional complications, and require significant additional resources for maintenance and follow-up. Therefore, there has been a considerable interest in the use of adjuvants that can prolong block duration and efficacy [15].

The oldest of these agents is epinephrine, which has been shown to increase block duration by about 1 h, likely due to local

vasoconstriction via alpha1 adrenergic activity. This vasoconstriction has the theoretical benefit of reducing the risk of systemic local anesthetic toxicity, but at the risk of possibly exacerbating local neurotoxicity; More recent and more efficacious peripheral nerve block adjuvants include the alpha-2 agonist dexmedetomidine and the glucocorticoid dexamethasone [15].

Dexmedetomidine is hypothesized to exert its effects through the inhibition of nucleotide-gated channels that mediate the restoration of resting membrane potentials post depolarization. Administration of ~50 μg of dexmedetomidine in adult patients increased the duration of brachial plexus blocks by about 4–8 h. Adverse effects can include bradycardia, hypotension, and sedation [15]. In a 2016 meta-analysis of pediatric patients 0.3–1 μg/kg of dexmedetomidine used as an adjunct in a variety of peripheral nerve blocks was found to increase block duration and improve analgesia with no serious adverse events or complications reported [17].

Dexamethasone's exact mechanism of action is unknown but may be related to activation of neuronal membrane glucocorticoid receptors which increase inhibitory ion channel expression; it may also limit inflammatory processes and localized vasodilation. Co-administration of 4–8 mg of dexamethasone increases block duration by 8–24 h when injected with long-acting local anesthetics such as bupivacaine. Intravenous administration of dexamethasone has been associated with is a transient increase in blood glucose levels; theoretical concerns regarding susceptibility to wound infection or delayed healing have not supported by randomized control trials [15]. Decadron has been safely used in peripheral nerve blocks in children without any effects on wound healing [35].

It is important to note that there are no published clinical trials with regards to the use of these adjuvants with paravertebral or erector spinae blocks in pediatrics.

What is LAST and how is it managed?

LAST stands for Local Anesthetic Systemic Toxicity and describes the neurological and cardiovascular sequela of a toxic dose of a local anesthetic agent. Given the immaturity of the blood-brain barrier, longer elimination half-lives of local anesthetics, and the

fact that the volume of distribution of infants is greater than that of adults, the pediatric patient population is at a higher risk. LAST presents with the following: dizziness, lightheadedness, visual and auditory disturbances, muscle twitching/tremors, and generalized convulsions leading to arrythmia and cardiovascular collapse. Unfortunately, as many regional blocks are placed under general anesthesia in the pediatric population, the first sign of toxicity may be an abnormal heart rhythm, hypotension and cardiac arrest. Therefore, it is suggested that the less toxic agents (ropivacaine and/or levobupivacaine) be used in pediatric patients and that a careful and conservative approach be taken in calculating maximum doses (with a further 50% reduction in maximum dose for neonates). If LAST is suspected the anesthetic injection should be aborted, call for help while initiating BLS/ACLS protocols and aggressive resuscitation. Seizures should be managed with benzodiazepines (avoiding propofol in the setting of possible hemodynamic instability) and intralipid should be rapidly administered. Initial intralipid bolus of 1.5 mL/kg should be delivered over 1 min with the concurrent initiation of a continuous intralipid infusion at 15 mL/kg/h. The bolus dose can be repeated 2 more times at 3 min apart if cardiovascular instability continues; in this setting the infusion rate can be doubled and continued until adequate circulation is restored or until the maximum cumulative dose of 12 mL/kg is exceeded. Epinephrine at doses <1 μg/kg can be used to maintain blood pressure. Treatment should be continued until response is achieved and ECMO can be considered if the patient does not respond to lipid therapy [36].

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Must-Known Special Considerations for Acute Pain Management in Geriatric Patient Population

Thomas Halaszynski

Case Stem

A 75-year-old female presented to the emergency room (ER) complaining of severe right hip pain after tripping (unwitnessed) over a raised door jam in her home. Patient denies loss of consciousness prior to and following the trauma. She has no other reported injuries. She has a history of hypertension, gastrointestinal reflux disease, osteoporosis, transient ischemic attack (remote history), and 50 years smoking. Patient's family states that she has intermittent periods of forgetfulness in recent years. Her medications include: 10 mg/day of lisinopril, omeprazole 20 mg/day, and aspirin. Patient complaining of severe hip pain during examination and her right leg is shorter than the left and is externally rotated. ER vital signs and laboratory results are heart rate 101, 24 respiratory rate, 190/98 blood pressure, temperature 36.4 °C, and saturation of 97% on 2 L nasal canula; normal electrolytes/coagulation studies.

1. What are some typical conditions of the geriatric hip fracture patient and the common approach of optimizing patient care?

   Treatment of hip fractures in elderly patients remains a public health priority and both orthopedic surgeons/anesthesiologists agree that these injuries should be treated with sur-

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_36

gery in an expedient manner [1]. There are special considerations from the perioperative perspective in this patient population including osteoporosis, pre-existing arthritis, age-related influences/compromise of homeostasis, patient activity level, state of health and medical co-morbidities further contributing to the type of surgery and anesthesia to be performed. Open reduction and internal fixation versus arthroplasty remain the two major categories of treatment. Indications and treatment algorithms remain controversial, but an overall goal is early mobilization and prevention of morbidity/mortality where the use of regional anesthesia can aid in this effort [1].

2. What is the prevalence of hip fractures and general epidemiology factors contributing to this health issue?

Despite the rise within the aging population of the US along with a simultaneous increase in activity levels of this population, there has been a decline in hip fractures over the past decade [1, 2]. Decreased use of estrogens along with the use of bisphosphonates have contributed to this change, especially in women. In the US, it is estimated that by 2030 the prevalence of hip fractures will increase to 289,000/year and number of hip fractures among men projected to increase by 52%, making these injuries a significant public health concern [2]. However, hip fracture rates in Japan and China have increased secondary to a rise in the elderly population and lifestyle changes such as urbanization, and hip fractures in women occur at the highest rate in Norway, Sweden, Denmark, and Austria [2].

The rise in people older than 65 years of age will increase by over 80% and 90% of hip fractures occur in patients older than 65 [2, 3]. The distribution of hip fracture types has changed with a steep rise in the number of unstable extracapsular fractures (intertrochanteric (IT)/subtrochanteric hip fractures) while the number of intracapsular hip fractures (femoral neck fractures) has remained stable [3]. Pertrochanteric fractures (region surrounding the greater/lesser trochanters) accounts for approximately 50% of all hip

fractures in the elderly (due in part to osteoporosis), but the underlying reasons are not entirely understood [3, 4].

3. What are the financial burdens to the healthcare system associated with hip fractures?

   The expense of treating a hip fracture patient in the US is known with the average patient spending approximately $40,000 in the first year (direct medical costs) and approximately $5000 in each following year [1]. By 2050, there will be an estimated 3.9 million hip fractures worldwide (700,000 in the US) amounting to over $15 billion per year in medical costs [1]. Despite this financial burden, including hospital costs, rehabilitation, and nursing care, there remains a 21–30% risk of mortality within the first year of sustaining a hip fracture in the elderly; a risk up to 3× higher in men when compared to women [5, 6].

4. Why should perioperative regional anesthesia be considered in the elderly and what are the unique characteristics to be taken into consideration for this patient population?

   People over 65 years of age represent a fast-growing segment of society and these older individuals have surgery more frequently than younger age-group populations [1]. Therefore, all healthcare providers, especially anesthesiologists, are increasingly focused on providing targeted and effective management of perioperative pain in older adults [7] secondary to a host of factors needed to be considered in all patient populations including:
   (a) Advances in anesthetic and surgical techniques
   (b) Improved understanding of the pathophysiology of pain
   (c) Development of new opioid and nonopioid analgesic medications
   (d) Increased incorporation of regional techniques (reduce or eliminate reliance on traditional opioid analgesics) during the perioperative period
   (e) Novel methods of drug delivery.

5. What are some preoperative analgesic options for those older patients following hip trauma/fracture?

Despite the reports of moderate-to-severe pain, many elderly patients presenting with hip fractures often receive little or no analgesic therapy in the preoperative period. Regardless of the presenting complaints, age appears to be a factor since these older patients are less likely to receive analgesic interventions when compared with younger patients. Concerns for opioid related side-effects (i.e., sedation, confusion, etc.), evidence of chronic/acute preexisting confusion or dementia, inability to perform adequate pain assessments, and/or avoiding confusing the history and diagnosis are factors that often contribute to compromising pain management preoperatively.

Analgesic options can include:

(a) Non-opioid medications (acetaminophen, nonsteroidal anti-inflammatory drugs, local anesthetic infiltration)
(b) Opioid analgesics (most often intravenous; but intrathecal or patient-controlled analgesia also)
(c) Regional techniques (neuraxial, peripheral nerve/nerve plexus blocks—femoral nerve blockade, fascia iliac and obturator nerve blocks, paravertebral or lumbar plexus block, transversus abdominis plane block, etc.) [8]

Regarding regional options and peripheral nerve/nerve plexus blockade, the decision should take into consideration the health status, operation being performed, and expertise of the perioperative pain management providers of these older patients. Therefore, regional/peripheral nerve blockade options in these elderly patients need to be assessed according to patient-and-type-of-surgery and geared toward regional pain medicine choices that target the surgical site to better ensure safe interventional options and to conduct evidence-based decisions [8, 9].

6. What special considerations, multidimensional aspects, and consequences of aging among older individuals need to be addressed towards maximizing "multimodal" perioperative pain management and what are the differences in chronologic and physiologic age?

(a) Chronologic and physiologic factors of aging (chronologic age: actual number of years of age; physiologic age: functional capacity or reserve within organ systems defined in pathophysiologic parameters)
(b) Age-related changes in physiology, pharmacodynamics, and pharmacokinetics (Table 1)
(c) Altered responses to pain among the elderly along with difficult pain assessment in certain individuals (i.e., patients with cognitive dysfunction)
(d) Increased prevalence of chronic medical conditions
(e) Higher degrees of acute and chronic pain (including acute-on-chronic pain)
(f) Higher rate of arthritis (chronic and acute exacerbations of arthritis)
(g) Osteoporotic fractures (esp. of the spine that therefore warrants *targeted* pain assessments)
(h) Higher frequencies of cancer pain and pain from acute medical conditions (example: ischemic heart disease, herpes zoster, peripheral vascular disease)
(i) Medications used in the treatment(s) of comorbid diseases along with an increased risk of drug-to-drug and disease-to-drug interactions.
(j) Older individuals are adopting more active lifestyles (predisposes them to trauma and orthopedic injuries).

Chronologic component of aging can be divided into 2 groups: the "young old" (65–80 years of age) and the "older old" (greater than 80 years of age). Physiologic reserve describes the functional capacity of organ systems to compensate for stress and traumatic injuries/derangements [10]. When present, comorbid disease states such as diabetes mellitus, arthritis, renal insufficiency, ischemic heart disease, peripheral vascular disease, declining cognition, chronic obstructive pulmonary disease (COPD), etc. can decrease a patient's physiologic reserve making it challenging to recover from traumatic or surgical injury and possible higher incidence of morbidity and mortality [11].

Table 1 Physiologic changes associated with effects of aging along with medication dosing considerations

Physiologic process	Magnitude of changes	Variable pharma-kinetic and -dynamic consequences	Dosing strategy considerations
Physiologic central nervous system changes *(CNS: central nervous system)*			
Cerebral blood flow volume and metabolism	↓ 20%	↓ distribution to the CNS	Little evidence of net effect on overall drug dose
	↓ 20%	↓ potential volume in the CNS	
Active blood–brain barrier transport (efflux)	Drug-specific ↓	↑ apparent volume in the CNS	↓ bolus dose during drug titration
			↓ maintenance dose
Pain threshold sensitivity	Little change	↑ apparent sensitivity of the CNS	Need for titration is unchanged (necessary)
Concentration response to opioids	↑ 50% for several opioids	↑ response to opioids	↓ bolus dose during titration
			↓ maintenance dose
Physiologic hepatic and renal changes (*M6G: morphine-6-glucuronide; M3G: morphine-3-glucuronide)*			
Liver			
Liver size	↓ 25–40%	↓ hepatic clearance of high-extraction drugs	Minimal effect on drug IV bolus dose
		↓ hepatic clearance of some low-extraction drugs and equivocal for others	↓ maintenance dose (potential for changes in oral bioavailability)
Hepatic blood flow	↓ 25–50%		
Phase I (i.e., oxidation)	↓ 25%		
Phase II	Little change		
Kidney			

Table 1 (continued)

Physiologic process	Magnitude of changes	Variable pharma-kinetic and -dynamic consequences	Dosing strategy considerations
Nephron mass	↓ 25–35%	↓ clearance of drugs (little effect on opioids, esp. parent compound)	↓ maintenance dose (renally cleared drugs)
		↓ clearance of some active metabolites (e.g., M6G)	Assume and monitor for accelerated accumulation of polar active (e.g., M6G) or toxic (e.g., M3G, nor-pethidine) metabolites
Renal blood flow	↓ 10%/10 years		
Plasma flow at 80 years of age	↓ 50%		
Glomerular filtration rate	↓ 30–50%		
Creatinine clearance	↓ 50–70%		
Physiologic cardiovascular along with physiologic body changes			
Cardiac output	↓ 0–20%	↓ central compartment volume	Use smaller initial bolus dose
		↑ peak concentration of drug after bolus	Use slower injection rate (potential for change in clearance along with oral bioavailability and potential for change in cerebral effects)
Fat	↑ 10–50% followed by a ↓	Drug-specific changes can be seen in distribution volume	Drug-specific (dose based on total body weight and/or lean body weight)

(continued)

Table 1 (continued)

Physiologic process	Magnitude of changes	Variable pharma-kinetic and -dynamic consequences	Dosing strategy considerations
Muscle mass and blood flow	↓ 20%		
Plasma volume	Little change		
Total body water	↓ 10%	↓ distribution volume (water-soluble drugs)	
Plasma albumin	↓ 20%	↑ free fraction of drug	Potential for change in clearance and oral bioavailability
			Potential for change in cerebral effects
Alpha-1 glycoprotein	↑ 30–50%	Variable hepatic clearance of high-extraction drugs	
		↑ hepatic clearance of low-extraction drugs	
		↑ cerebral uptake of drugs	

7. What are the key advantages of choosing local and regional anesthesia (LRA) over a general anesthetic (GA) technique in the geriatric patient population?

   It has been accepted that LRA will provide added perioperative pain control; in addition, LRA can also positively influence and effect morbidity and mortality [12]. Regional anesthesia (peripheral nerve or neuraxial) is a key component of developing and implementing an anesthetic pathway that has shown improved *immediate* surgical outcomes [12, 13]. An anesthetic pathway incorporating regional provides evidence of positively influencing morbidity and mortality of several common surgeries, but also proves advantageous as pain control in the postoperative period can often be challenging [13].

8. Decision has been made to place an ultrasound-guided sciatic nerve block as part of the anesthetic plan. However, viewing the sciatic nerve proves difficult due to target nerve depth. What can be done to improve the target nerve view at this increased depth and what role if any does a coupling medium (i.e., ultrasound gel) play?

   A lower frequency ultrasound is selected to increase depth of penetration when typical linear array ultrasound penetration is insufficient to visualize target structures. However, using lower frequency/longer wavelengths yields a lower resolution of the image since resolution is proportional to the wavelength of the imaging wave. A coupling medium should always be used between the skin and transducer interface. Ultrasound gel displaces air since even a small/thin air layer may reflect the ultrasound wave and therefore, hinder the wave penetration into tissue [14].

9. Can regional anesthesia during major joint replacement surgery influence passive-range-of-motion following surgery?

   Regional during joint replacement surgery permits for improved joint flexibility that could last for several months due to several regional anesthesia advantages including improved surgical operating conditions, earlier and more enthusiastic physical therapy/rehabilitation, and lowered perioperative pain scores [15, 16].

10. How does regional anesthesia impact upon postoperative cognition of the geriatric patient following major joint replacement surgery, and when compared to general anesthesia, what are the findings related to postoperative cognitive dysfunction (POCD)?

    POCD can be very debilitating, a risk factor for long-term cognitive deterioration, and can result in higher mortality in the geriatric surgical patient [8]. However, for a host of yet to be fully investigated hypothesis, evidence is inconclusive and does not find a long-term cognitive difference for POCD in the elderly surgical patient whether undergoing regional or general anesthesia [8, 9].

11. What are the factors affecting postoperative pain (intensity and/or duration) and what single variable associated with older patients appears the most important in determining the degree of pain relief following administration of opioid medications?
    (a) Culture or race
    (b) Gender
    (c) Personality
    (d) Age
    (e) Nature/type/extent/site of surgery
    (f) Opioid pharmacodynamics
    (g) Psychological factors
    (h) Substance abuse or opioid tolerance
    (i) Body size (lesser influence)
    (j) Opioid pharmacokinetics (lesser influence)

    Age appears to be the most important variable determining degree of pain relief after opioid analgesic administration [17]. Advanced age alters opioid dose response revealing that there is a negative correlation between age and opioid consumption (i.e., strong correlation between increasing age and both efficacy and duration of pain relief) [17, 18]. The proposed reasoning for reductions in opioid dose requirements with advanced age are reflected by age-dependent reductions in volume of clearance and distribution (pharmaco-dynamics and -kinetics) yielding in higher serum levels along with enhanced clinical effects [18]. Additional factors leading to an enhanced opioid plasma concentrations include:
    (a) Age-related reductions in plasma albumin resulting in increased fraction of active/unbound opioid
    (b) Reductions in central nervous system (CNS) activity and pain input can reduce both perception of pain and pain processing
    (c) Reductions in hepatic enzymes/hepatic blood flow can result in prolonged opioid elimination half-life
12. What are the major Nervous System function physiological changes associated with aging and considerations for effective regional anesthesia/analgesia?

Aging results in anatomical and biochemical changes of the brain, spinal cord, and peripheral nervous system (PNS) that result in qualitative and quantitative alterations in function [19, 20] (Table 1). Advancing age can be associated with:

(a) Decreased brain volume (manifestation of the loss of neurons)
(b) Reduction in cerebral white matter nerve fibers (declining number of cholinergic and dopaminergic neurons)
(c) Morphologic changes in neuronal fibers (results in fewer synaptic contacts and neuroreceptor concentrations)
(d) Deterioration and decreases in number of myelinated nerve fibers (large, myelinated fibers are particularly affected resulting in atrophy along with degenerative changes to the myelin)
(e) Spontaneous remyelination efforts and rate of reappearance of proteolipids and myelin basic proteins are slowed
(f) Levels of acetylcholine and dopamine neurotransmitters decline
(g) Aging can result in an extraneuronal accumulation of amyloid (underlies neurocognitive dysfunction)
(h) Alterations in brain phospholipid associated with changes in second messengers (i.e., diacylglycerol)
(i) Cerebral electrical and metabolic activity are decreased (anatomic, structural, and biochemical changes)
(j) Degenerative changes in the myelin sheaths of nerve fibers of the central nervous system (CNS) and PNS can result in changes of nerve conduction velocity and disrupt timing of neuronal circuits
(k) Decreased spinal cord volume and degeneration of the bony spinal canal.

Somatic nervous system (SNS) changes of the PNS associated with aging include: (1) peripheral nerve deterioration; (2) dysfunction of genes responsible for myelin sheath protein components; (3) decreased myelinated nerve fiber conduction velocity; (4) motor and sensory discriminatory changes in the feet; and (5) changes in sensation (i.e., pain, touch). The autonomic nervous system (ANS) of the PNS

experiences age-related changes characterized by (1) limited adaptability to stress; (2) decreased basal activity of the parasympathetic nervous system and overall net *activation* of the sympathetic nervous system; (3) decreased baroreflex sensitivity; along with (4) slowing and weakening of homeostatic functions. NOTE: increase in sympathetic tone in older patients should be considered when choosing an anesthetic with sympathomimetic properties (such anesthetics may be poorly tolerated by those with cardiovascular disease).

13. What are the Neurocognitive effects of anesthesia/analgesia on the geriatric patient population?

    Risk factors associated with the development of negative cognitive influence include: (1) increased age; (2) level of patient education; (3) preexisting pain; and (4) use of certain preoperative medications (opioids, ketamine, and benzodiazepines). Following the negative consequences of perioperative delirium (should they develop), some patients may go on to experience postoperative cognitive dysfunction (POCD) [21]. POCD is very common and older patients are at a higher risk of POCD after major noncardiac surgery than are younger patients [22].

    Perioperative evaluation should consider PNS and CNS changes that can influence functional outcomes during the recovery phase following surgery and anesthesia. Neurologic dysfunction of aging can produce altered pharmacodynamics and result in increased sensitivity to anesthetic medications (signs and symptoms of altered reflexes, deterioration of gait and mobility, altered sleep patterns, impairment of memory and intellect, and decrements of the senses). Acute cognitive impairment (perioperative delirium and POCD) in elderly patients can increase postoperative morbidity, present with difficult pain management scenarios, impair postoperative rehabilitation, prolong hospital stays, and increase mortality (i.e., higher mortality if POCD persists into the postoperative period) [21]. Delirium can occur in up to 80% of elderly postoperative patients and can be influenced by: (1) type and extent of surgery; (2) perioperative anesthesia and analgesic needs of the patient; (3) type of pain therapy administered; (4) more common with emergency, trauma, and major surgery [22].

14. What are the major Cardiovascular physiological changes associated with aging and considerations for effective regional anesthesia/analgesia?

    Morphological and functional changes of the cardiovascular system associated with aging include (Table 1):

    (a) Reduction in left ventricular compliance
    (b) Generalized hypertrophy of the left ventricular wall
    (c) Fibrotic changes of the heart
    (d) Decreased myocardial compliance
    (e) Increased stroke volume
    (f) Elevated diastolic and systolic blood pressure.

    Elderly patients can present with cardiac pathology including: (1) moderate to severe coronary artery disease; (2) valvular heart disease; and (3) conduction defects (can increase risk of postsurgical morbidity and death) [23]. In the absence of coexisting disease, effects of aging on cardiac output will typically have minimal influence of the resting individual, but functional changes can become evident with stress and effort-dependent stress. Anesthetics and anesthesia technique can interact with a patient's preexisting cardiovascular disease in a manner that may be unfavorable such as: patients with a fixed cardiac output (i.e., aortic stenosis) may not tolerate a decrease in systemic vascular resistance associated with neuraxial anesthesia. This hemodynamic variability, in the setting of regional, can often be overcome with careful/titration use of vasopressors along with titration of neuraxial anesthesia with an epidural or spinal catheter.

    Regional anesthesia that complements multimodal analgesic therapies and effectively manages postoperative pain (with or without continuous local anesthetic infusion) can influence perioperative cardiac morbidity and mortality by mitigating myocardial dysfunction if catecholamine levels associated with stress and pain are reduced. Regional anesthesia will typically provide superior analgesia compared to systemic opioids. Peripheral nerve blocks and neuraxial anes-

thesia in the elderly can provide: (1) preemptive analgesia; (2) reduce the side-effects or eliminate the need for general anesthesia (or completely avoid it in certain surgical settings); (3) reduce sympathetic stimulation and stress responses associated with surgery; and (4) directly inhibit transduction, transmission, and conduction of nociception from surgical trauma site(s). An additional factor to consider is the duration of postoperative analgesic needs since surgery pain, associated surgical stress, and effects on the cardiovascular system do not always subside until days following surgery. Therefore, an effective regional technique (i.e., continuous catheter) may provide sustained benefits by reducing postsurgical pain and its associated sympathetic and neuroendocrine stress responses. However, patients with coexisting cardiovascular disease may also be treated with anticoagulants or antiplatelet medications, so careful attention should be paid to this issue prior to the administration of certain regional peripheral (i.e., deep blocks) and neuraxial techniques.

15. What are the major Pulmonary physiological changes associated with aging and considerations for effective regional anesthesia/analgesia?

    Airway manipulation can be avoided and respiratory parameters of lung function including respiration rate, tidal volume, respiratory drive (effort), and end-tidal carbon dioxide concentration can be preserved if surgical anesthesia can be achieved with regional modalities. Functional and structural changes, as well as physiologic changes in response to hypoxemia and hypercarbia, along with increased sensitivity to the respiratory depressant effects of anesthetic agents/opioids can influence the pulmonary system and explain respiratory compromise/complications among the elderly [24] in the perioperative period including: (1) elastic recoil of the lung parenchyma decreases in a fashion that functionally resembles emphysema; (2) less efficient alveolar gas exchange due to a loss of alveolar surface area and collapse of small airways; (3) compliance of the chest wall decreases (can lead to increased work of

breathing and increased risk for respiratory failure). There are reductions of functional residual capacity (FRC) created by experiencing surgery, supine positioning, and influence of general anesthesia that may persist for 7-to-10 days following surgery in all patients [25]. FRC and closing volume gradually increase with age, and by age 45, closing volume exceeds FRC in the supine position [24]. Vital capacity can be reduced by 25–50% due to inadequate pain management (i.e., splinting); and systemic opioids can lead to alterations in tidal volume and respiratory rate and impair clearing of secretions (altered cough mechanics). Elderly individuals also have decreased responsivity to hypoxia and hypercapnia, as well as a greater incidence of COPD and obstructive sleep apnea (OSA) [24, 25]. All the above factors make opioid-sparing approaches to postoperative pain desirable and effective regional techniques may be beneficial in providing superior postoperative pain control with opioid-sparing effects.

Attention to type of sedation used during regional blockade placement should always be considered given the increased sensitivity to opioids and benzodiazepines in the elderly, in addition to the decreased responses to hypoxemia and hypercapnia and the increased incidence of OSA in this population. When comparing regional versus general anesthesia/analgesia in elderly patients undergoing lower extremity orthopedic surgery have shown: (1) older patients experience fewer hypoxic events with epidural and regional anesthesia (using local alone) when compared to systemic opioids; (2) general anesthesia in older patients results in lower PaO_2 levels (postoperative day 1) compared to epidural and regional anesthesia; and (3) respiratory complications are less frequent comparing general anesthesia with postoperative intravenous morphine analgesia versus general anesthesia with postoperative epidural analgesia. Elderly patients have an increased sensitivity to the respiratory depressant effects of neuraxial opiates, and therefore should be used with caution.

1 Summary

Clinical Pearls for effective perioperative management along with considerations for regional anesthesia/analgesia in the geriatric patient:

- Pain thresholds to a variety of noxious stimuli are altered in older individuals (older patients have a reduction in pain tolerance)
- Patient-controlled analgesia (PCA), regional, and epidural analgesia are more effective in elderly patients than other conventional (PO and IM) opioid analgesics
- Physiologic changes associated with aging can vary markedly among older patients
- Administration of pain medications along with local anesthetics warrants a decrease in dose (maintenance and/or bolus) required for analgesia to reduce risk of increased plasma drug accumulation/accumulation of active metabolites
- Aging is associated with a shift in balance within the autonomic nervous system toward a predominance of sympathetic tone (i.e., considerations with sympathomimetic medications)
- Geriatric patients are more likely to have neurologic, pulmonary, cardiovascular diseases, and decreased reserve capacity that can lead to complications, therefore, targeted peripheral nerve and nerve plexus blockade in geriatric patients can be used to minimize potential postoperative complications
- There are established clinical practices and theoretical indications regarding administration of safe/effective regional blockade for elderly hip fracture patients, however, a lack of consistency among investigators/studies has prevented development of strong recommendations to guide or offer a regional technique(s) providing the best advantages for elderly patients undergoing hip surgery
- Advancing age, level of patient education, and evidence of preexisting cerebral vascular disease are strong predictors of perioperative delirium
- Studies of older hip fracture patients who received a femoral nerve block for perioperative analgesia, in addition to regularly scheduled nonopioid analgesics, were less likely to develop postoperative delirium, were able to sit up at the bedside

sooner, and required no supplemental opioid analgesics compared to patients administered ***only*** nonopioid analgesics
- Nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 (COX-2) inhibitors in elderly patients requires cautious (esp. longer-term use) administration; acetaminophen may be the preferred nonopioid analgesic
- Age-related decrease(s) in opioid medication requirements in the geriatric patient are related heavily to changes in pharmacodynamics
- Regional, peripheral nerve and nerve plexus blockade for elderly hip surgery patients may allow for reductions of adverse side effects compared to other conventional pain management strategies (intramuscular, oral, and parenteral analgesics or neuraxial blockade)
- There are age-related decreases in opioid requirements and significant interpatient variability in pain tolerance
- Peripheral nerve and nerve plexus blockade have proven to be as effective and gaining popularity in the elderly since incidence of potential side effects compared with neuraxial techniques may be less
- Pain assessment and evaluation of management in older patient's present problems arising from differences in (1) reporting mechanisms; (2) cognitive dysfunction; (3) end-organ impairment/compromise (affecting medication metabolism and excretion); (4) variations in medication tolerance and abuse; and [5] inherent difficulties in pain assessment
- Elderly patients often describe pain as being less intense and often provide atypical descriptions of perioperative pain (for example—reported frequency and description of intensity)
- Peripheral nerve blockade compared favorably with neuraxial analgesia (i.e., lumbar epidural) for hip surgery with little differences in pain scores at rest, however, complications such as hemodynamic variability, nausea/vomiting, urinary retention and bowel dysfunction, increased dynamic pain scores (i.e., movement, rehabilitation) and an increased need for supplemental opioid analgesics for break-through pain occurred more frequently with neuraxial analgesia
- In the acute pain setting, unidimensional measurements of pain (Verbal Rating Scale [VRS] and Numerical Rating Scale

[NRS] provide the best validity) should be used in older patients
- Acute pain undertreatment is more likely to occur in cognitively impaired older patients (obtaining a history regarding patient past experiences with pain can be challenging in those with cognitive impairment/decline)
- Dosage of intravenous opioid medications may be reduced in elderly hip fracture patients when they receive "procedure-specific" regional techniques for perioperative pain management. In addition, optimal "target-specific" regional and potential to reduce negative cognitive effects is possible by incorporating regional anesthesia "procedure-specific" pain therapy
- Paramedian (vs. midline) approach may facilitate needle placement into the epidural or subarachnoid space in those with age-related changes of vertebral anatomy (i.e., L5–S1 vertebral interspace is typically the largest intervertebral location to target for neuraxial blockade)
- Intrathecal morphine at a dose 200 μg (or below) can be a useful adjunct for pain management following surgery with acceptable risk(s) of respiratory depression
- There is evidence suggesting that peripheral nerve blockade effects can be prolonged in some elderly patients (reducing/eliminating opioid medications for breakthrough pain), therefore, such patients should be counseled appropriately regarding this effect(s), and plans are necessary to ensure that older patients have appropriate assistance if peripheral nerve blocks are to be used
- Unlike neuraxial anesthesia, it may be safe to perform some peripheral nerve/nerve plexus blockade in heavily sedated or anesthetized patients without any apparent increased risk of neurological injury. Therefore, in elderly patients who could experience pain/discomfort with positioning may receive heavy sedation or general anesthesia without great concern for significant neurologic injury
- Incidence of cancer is typically higher in elderly patients. Some evidence (i.e., animal and retrospective human studies) has suggested that regional may attenuate the immunosuppressive effects of surgery, anesthesia, along with perioperative pain that could improve patient long-term outcomes.

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Must-Known Special Considerations for Acute Pain Management in Trauma and Non-OR Patients

Brett Simmons and Nicole Hollis

Case Stem

A 33-year-old male patient arrives in the emergency room after extraction from a motor vehicle crash. The patient was a restrained passenger in a vehicle that struck a tree at approximately 45 mph. He has received 1 L of intravenous fluids during transport, along with an unknown amount of IV morphine. After a negative FAST exam and trauma survey, a thorough evaluation by the ED and trauma staff reveals a head laceration and diffuse tenderness and bruising over the right lateral chest wall. Vital signs are now in the normal range except for a blood pressure of 144/82 and a heart rate of 102. The patient has a GCS of 15 and complains of sharp pain along the right chest. A cervical collar immobilization device is in place. Imaging reveals non-displaced fractures of ribs four through six in the right mid-axillary line. The regional anesthesia service is consulted for assistance with pain management.

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J. Li et al. (eds.), *First Aid Perioperative Ultrasound*,
https://doi.org/10.1007/978-3-031-21291-8_37

Questions and Answers

1. What is the impact of trauma in the United States?

   Among those less than 45 years old, trauma is the leading cause of death. In 2011, inpatient care for trauma patients exceeded $30 billion, and the economic burden of trauma is estimated at $500 billion annually. The most common causes of trauma include falls (47%) and motor vehicle crashes (7%). Trauma due to violent assault is more common in those 18–44 years old. The extremities are disproportionately affected in trauma. With the use of modern military armor, more battlefield participants are surviving with higher rates of extremity injuries. The rate of extremity injury in motor vehicle crash survivors is also high [1].
2. What types of injuries can be treated with regional anesthetic techniques?

   Peripheral nerve blocks can be performed for almost any painful extremity injury. These blocks usually spare systemic side effects and are site-specific. Furthermore, there is strong evidence that regional anesthesia may decrease length of stay in the ICU and hospital. For upper extremity injuries, brachial plexus blocks (interscalene, supraclavicular, infraclavicular, and axillary approaches), as well as blockade of individual nerves and digital blocks distally, can be performed. For lower extremity injuries, blockade along the femoral and sciatic nerves and their branches are commonly performed, though other blocks can be useful for select patients. Truncal blocks, such as thoracic epidurals, paravertebral, erector spinae plane, and transversus abdominal plane blocks, and less commonly performed serratus plane, PECS, and intercostal blocks may also be part of the regional anesthesiologist's toolkit.
3. Why are multimodal regimens that include regional anesthesia techniques often preferred over intravenous opioids?

   The most common method of treating pain in trauma patients continues to be intravenous opioids. However, opioids carry a significant adverse effect profile, including: pruritus, immunosuppression, respiratory depression,

hypotension, delirium, constipation, nausea and vomiting, and increased length of hospital stay. Opioids may interfere with the ability to perform neurologic assessments, and potentially lead to addiction. Multimodal regimens for pain treatment have several advantages over opioid-based therapy and are becoming standard of care for both surgical and trauma patients. Along with other IV and oral medications, including ketamine, NSAIDs, acetaminophen, dexmedetomidine, and gabapentin, both neuraxial and regional techniques have important roles in reducing trauma pain in appropriate patients. A reduction in opioid use also decreases the need for intensive monitoring, which may confer a cost savings for health systems with high staffing outlays.

4. What patients are candidates for Neuraxial blocks versus Peripheral nerve blocks?

   Often, a thoracic or lumbar epidural, or single-injection spinal can provide effective analgesia for proximal traumatic injuries. In fact, a thoracic epidural is considered the gold standard for chest and abdominal analgesia. However, there are several limitations to neuraxial procedures. An infrequent but catastrophic complication of neuraxial anesthesia is spinal hematoma. Many trauma patients are coagulopathic due to blood loss, hypothermia, sepsis, or liver injuries. Perioperative thromboprophylaxis and widespread use of anticoagulation agents further complicate neuraxial patient selection and procedural timing. Current guidelines are readily available and suggest avoiding neuraxial procedures, including epidural catheter removal, when the INR exceeds 1.4. Epidurals are generally avoided in patients with significant head or spine injuries as neurologic evaluation can be complicated. Finally, neuraxial local anesthetics often cause sympatholysis and hypotension. Patients who are underresuscitated or hypotensive at baseline may not be ideal candidates for neuraxial analgesia, although vasopressors can be utilized to counteract these effects to an extent. Peripheral nerve blocks offer an option to provide excellent analgesia for trauma patients when neuraxial anesthesia is contraindicated.

5. Who should receive a continuous catheter versus a single-injection block?

   Pain associated with trauma is often severe and longstanding, and development of chronic pain is common after trauma caused by musculoskeletal injury. Whereas ropivacaine or bupivacaine single-injection blocks often provide 16–24 h of analgesia, continuous nerve block catheters can substantially prolong the duration of pain relief. While nerve block catheters are typically removed within 5–7 days due to the risk of infection, some have been left in for weeks. Patients who require repeated procedures, such as skin grafting, debridements, or serial fracture repairs, and those with more complex injuries, are likely to benefit from continuous nerve block catheters. Studies have consistently demonstrated a catheter-specific complication rate under 5% at 8 days, and catheter infection rates of 0–3%. When multiple catheters are utilized in polytrauma patients, care must be taken to ensure that local anesthetics in the plasma do not reach toxic levels. While continuous infusion catheters have several advantages for analgesia, many patients, such as those expected to be discharged quickly, those with sepsis or an active infection in the vicinity of the block, or those unable to tolerate a catheter, are better suited for single-injection blocks [2].

6. Can peripheral nerve blocks be performed in the field or Emergency Department (ED)?

   While anesthesiologists are the most qualified physicians to perform nerve blocks, they are rarely able to attend to patients in the emergency department. However, studies have shown that regional anesthesia performed in the ED decreases length of stay and improves clinical flows [3]. Some blocks, such as fascia iliaca blockade for hip fractures, can be relatively safely performed without ultrasound guidance. Digital blocks, sciatic, interscalene, and others have been successfully performed in the field for pain control prior to arrival at a hospital. New technologies, such as handheld ultrasonography, may also increase trauma patient access to timely regional anesthetics.

7. What blocks are appropriate for shoulder reduction?

   Dislocated shoulders are common in trauma patients, and shoulder reductions are often performed in the emergency department. IV sedation is routinely employed to provide muscular relaxation, but carries risks of gastric aspiration, respiratory depression, hypotension. An interscalene approach to the brachial plexus block effectively anesthetizes the superior trunk and offers an excellent alternative to sedation. The pulmonary status of the patient must be understood, as an interscalene block often affects the phenic nerve resulting in ipsilateral diaphragmatic paralysis. Nonetheless, the risks of hypotension, aspiration, and apnea are minimized with this approach. Monitoring costs and emergency room length of stay are reduced when an interscalene block is employed compared to procedural sedation [4].

8. What blocks are appropriate for digital amputation or replantation?

   Amputation injuries can be classified as guillotine (clean cut), crush, avulsion, and surgical. Clean cut amputations carry the best prognosis for functional recovery. Surgical amputations are often performed when distal tissues have no chance of survival (due to ischemia, temperature injuries, infection, etc.). When multiple digits are to be replanted, the thumb is given first priority as it is responsible for 40% of hand function. Warm ischemia permitted time for digits is approximately 12 h, while icing can increase this time to beyond 30 h.

   Single-injection blocks are highly beneficial for surgical amputations, which are often short procedures. Digital replantations are often time-consuming, often taking up to 18 h for multiple replants. This limits the utility of single-injection nerve blockade for replantation procedures. However, it is well-established that regional anesthesia will reduce the surgical stress response and decrease the likelihood of vasospasm and thrombosis in the affected digits. For this reason, a general anesthetic combined with a continuous nerve block catheter is often the best option. For upper extremity digital replantations, a brachial plexus or forearm

catheter not only improves pain control, but also establishes a chemical sympathectomy, which inhibits neurogenic vasospasm. While catheters placed anywhere along the brachial plexus can produce hand analgesia, interscalene blocks often fail to anesthetize the inferior trunk, and catheters at the axilla are prone to dislodging. Thus, supraclavicular or infraclavicular catheters are often placed. Finally, patients undergoing a digital replantation are usually subsequently anticoagulated for several days. Placing perineural catheters in anticoagulated patients remains somewhat controversial but is no longer contraindicated.

9. What are some regional anesthetic considerations for patients with burns?

   Depending on the location and depth of the burn, burn injury pain can be highly variable. When peripheral nociceptors are destroyed, pain transmission is blunted. However, nociceptors that are not destroyed transmit the painful stimulus immediately and can stimulate a secondary hyperalgesia. Furthermore, burn patients often undergo multiple rounds of procedures, including debridement, dressing changes, and skin grafting. Peripheral nerve blocks are effective for treating burn-related superficial pain, when used correctly. They can reduce opioid consumption and decrease exposure to repetitive general anesthetics. However, there are numerous challenges to utilizing regional anesthesia in these patients. Burn patients are susceptible to infections due to an altered immune response and skin compromise. The placement of a nerve block catheter through burned skin is contraindicated. For deep burns likely to require multiple procedures, single-injection techniques are of little benefit. Continuous nerve block catheters are often a better choice, as local anesthetic boluses can be administered prior to anticipated painful procedures.

   Approximately 10% of burn patients also have other traumatic injuries, and many present with burns at multiple anatomic locations [5]. Placement of multiple peripheral nerve catheters is not uncommon. In these cases, care must be taken to avoid systemic toxicity from the local anesthetics.

10. What blocks are appropriate for patients with acute hip fractures?

    Acute hip fractures are associated with severe pain, reduced quality of life, and long-term functional impairment. Perioperative delirium is also common in elderly hip fracture patients. It is prudent to minimize opioid use in these patients. Several studies have been published suggesting that regional anesthesia should be initiated as soon as possible in these patients. Femoral nerve blocks or fascial iliaca blocks will cover the majority of the pain at this site but are insufficient for complete surgical analgesia. Even a lumbar plexus block will spare the articular branches from the sacral plexus and input from the sciatic nerve. Thus, open reduction internal fixation of hip fractures are most commonly performed with neuraxial anesthesia, but there are several advantages to also placing a continuous catheter at a proximal femoral nerve location for postoperative pain control [6].

11. What blocks are appropriate for patients with rib fractures?

    Rib fractures are a common source of trauma-related pain, and account for more than 10% of trauma-related hospital admissions. Although pneumothorax and lung contusion are often associated with rib fractures and are independent causes of morbidity, significant pain worsens pulmonary status by limiting patients' ability to breathe adequately. Even in rib fracture patients without an oxygen requirement, shallow tidal breathing can lead to subsequent atelectasis and increase the risk of pneumonia [7]. In most rib fracture patients, operative fixation is not necessary and deferred.

    There are several options for effective analgesia involving regional anesthesia. Thoracic epidurals are highly effective, especially when the fractures are bilateral. Other regional anesthesia techniques that can be utilized for rib fractures include paravertebral catheters, erector spinae plane catheters, or serratus anterior catheters.

12. What peripheral nerve blocks are appropriate for patients with chest tubes?

    Similar to the treatment of rib fracture pain, the anesthesiologist has many options for treating pain arising due to chest

tubes, which can be debilitating. Chest tubes are often placed following chest injuries or surgeries in the thoracic cavity to facilitate healing and prevent pneumothorax. Thoracic epidurals, paravertebral blocks, erector spinae plane blocks, serratus anterior plane blocks, intercostal blocks, and intrapleural blocks have all been successfully utilized for treating chest tube pain. When not contraindicated, thoracic epidural analgesia can be highly effective when bilateral chest tubes are placed in trauma or post-surgical patients. Thoracotomy and chest tube-related pain has a high incidence of evolving into chronic pain [8]. Regional anesthesia techniques can decrease the probability of developing chronic pain following incisions or injuries to the chest wall [9].

13. What peripheral nerve blocks are appropriate for penetrating abdominal trauma?

    Penetrating abdominal traumas are common and often require a surgical laparotomy after transport to a medical center. The anterior rami of T7 through L1 innervate the abdominal wall. These sensory fibers travel between the second and third muscle layers in the chest and abdomen (between the internal oblique and transversus abdominis muscles) and ultimately terminate at the midline. Although the thoracic epidural has been considered the gold-standard block for the abdomen, more recently, paravertebral, erector spinae plane, transversus abdominis plane, and rectus sheath blocks have increased in popularity due to their improved safety profiles. Abdominal compartment syndrome is intra-abdominal hypertension leading to organ dysfunction. Truncal regional anesthesia can improve the prognosis in abdominal compartment syndrome by increasing abdominal wall compliance [10].

14. Should peripheral nerve blocks be performed on patients with concern for compartment syndrome?

    Acute compartment syndrome (ACS) is excessive pressure within a closed compartment which impedes circulation and tissue function within the affected space. Trauma is a leading cause of ACS, with fractures of the tibia and forearm (areas packed with muscles) representing common injuries associ-

ated with ACS. Higher risk categories for compartment syndrome include tibial plateau fractures, crush injuries, and prolonged extrication. An emergent fasciotomy is the definitive treatment, as ischemia, myonecrosis, hyperkalemia, and even death can result if not performed within 3–6 h.

ACS has traditionally been diagnosed on the basis of paresthesia with pain out of proportion to the injury. This had spurred fears among both surgeons and anesthesiologists of regional techniques masking ACS pain and delaying the diagnosis of ACS. The vast majority of case reports to date have suggested that ACS after nerve blockade leads to breakthrough pain, which may aid the early diagnosis of ACS [11]. Furthermore, compartment pressure monitoring can routinely be performed for high-risk trauma patients. One consideration when performing regional blocks in trauma patients at risk for ACS may be the use of dilute local anesthetic solutions to allow for breakthrough pain. Although large scale studies are still needed, continuous nerve block catheters are now considered safe and effective in patients at risk for ACS. Catheters can be adjusted, left dry, stopped, or bolused as appropriate for the clinical setting [12].

1 Summary

In addition to enhancing the comfort of trauma patients, techniques employed by the regional anesthesiologist reduce opioid requirements, shorten ED and hospital stays, reduce costs, and improve patient satisfaction with the healthcare system. Often, there are numerous modality options for treating a trauma patient's pain, and it is up to the regional anesthesiologist to determine the optimal regimen. Ultimately, the decision of whether to utilize a regional anesthetic is made in a multidisciplinary approach after a complete assessment of patient factors and the nature of the injury, in consultation with other providers. Table 1 summarizes the most common regional treatment modalities based on the location of injury.

Table 1 Regional anesthesia techniques for traumatic injuries

Trauma location	Regional anesthetic technique options
Upper extremity trauma	• Brachial plexus blocks
	– Interscalene approach
	– Supraclavicular approach
	– Infraclavicular approach
	– Axillary approach
	• Digital block
Lower extremity trauma	• Femoral nerve block
	• Sciatic nerve block
	• Lumbar plexus block
	• Fascia iliaca block
	• Ankle block
Truncal trauma	• Thoracic epidural
	• Paravertebral block
	• Erector spinae plane block
	• Transversus abdominal plane block
	• Quadratus lumborum block
	• Serratus plane block
	• PECS block
	• Intercostal block

Common Pitfalls

– Local anesthetic systemic toxicity (LAST) occurs when plasma levels of local anesthetics reach a toxic concentration. Care should always be taken to avoid exceeding the maximum safe dose of regional anesthetic, especially when performing two or more blocks on the same patient, administering bolus doses, and/or using high infusion rates of concentrated drugs. Blocks associated with high risk of LAST include: paravertebral, intercostal, intrapleural, epidural, and brachial plexus blocks. The clinical manifestation of LAST classically involves seizures, loss of consciousness, and cardiovascular complications (most commonly bradycardia). When suspected, treatment involves cessation of local anesthetic injection, circulatory support (with avoidance of vasopressors other than low-dose epinephrine), and lipid emulsion therapy.

- Failure to consider a patient's coagulation status or anticoagulant medications prior to performing a neuraxial block significantly increases the risk of epidural or spinal hematoma and serious complications. Strict guidelines are readily available and periodically revised. In general, neuraxial blockade is contraindicated with an INR >1.4.

Clinical Pearls

- Trauma is a leading cause of hospitalization and death in the United States
- Pain is often underappreciated and undertreated in trauma patients as life and limb-saving treatments are prioritized over pain management.
- Regional anesthetic techniques, including neuraxial analgesia and peripheral nerve blocks, can decrease opioid requirements, minimize opioid-related side effects, and decrease overall morbidity.
- Well-established guidelines exist to identify candidates for neuraxial blocks. When neuraxial or other deep blocks are contraindicated, there are often reasonable alternative blocks to consider. For patients not suitable for, or amenable to, regional techniques, multimodal regimens are often advantageous to opioid-based therapy.
- Effective regional anesthesia for digital reimplantation may improve graft success rates.
- There are many special considerations in burn victims. Continuous nerve block catheters are especially beneficial in this population.
- Regional analgesic methods for treating rib fracture pain directly improve respiratory status, decrease opioid-related respiratory depression, and reduce the risk of pulmonary complications.
- Peripheral nerve blocks may reduce the incidence of delirium, chronic post-traumatic pain, and post-traumatic stress disorder (PTSD), although more research is needed.
- With modern diagnostic and monitoring tools, peripheral nerve blocks are safe and effective for patients at risk for acute compartment syndrome.

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https://doi.org/10.1007/978-3-031-21291-8

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