UiT The Arctic University of Norway

Faculty of Health Science

Peripheral nerve blocks for shoulder surgery

Periclavicular approaches in the pursuit of a diaphragm-sparing technique

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A dissertation for the degree of Philosophiae Doctor - May 2021

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1 Acknowledgements

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2 Abbreviations

ASA	American Society of Anesthesiologists
CI	Confidence interval
CNS	Central nervous system
DSN	Dorsal scapular nerve
GA	General anaesthesia
HBE	Hypotensive and bradycardic events
IQR	Interquartile range
ISB	Interscalene brachial plexus block
LA	Local anaesthetic
LAST	Local anaesthetic systemic toxicity
LSIB	Lateral sagittal infraclavicular brachial plexus block
LTN	Long thoracic nerve
MEC	Minimum effective concentration
MEV	Minimum effective volume
MEV_{50}	Minimum effective volume in 50% of the patients
MEV_{95}	Minimum effective volume in 95% of the patients
MRI	Magnetic resonance imaging
NIRS	Near-infrared spectroscopy
NSAID	Non-steroidal anti-inflammatory drug
NRS	Numerical rating scale
OMEq	Oral morphine equivalent
PABA	Para-aminobenzoic acid
PACU	Post-anaesthesia care unit
PCA	Patient-controlled analgesia
PONV	Postoperative nausea and vomiting
$rScO_2$	Regional cerebral oxygenation
SCPB	Superficial cervical plexus block
SD	Standard deviation
SEM	Standard error of the mean
SSN	Suprascapular nerve
SSNB	Suprascapular nerve block
TCI	Target-controlled infusion

3 List of papers

This thesis is based on the following papers, which will be referred to by their Roman numerals:

I. Musso D., Flohr-Madsen S., Meknas K., Wilsgaard T., Ytrebø LM, Klaastad Ø. A novel combination of peripheral nerve blocks for arthroscopic shoulder surgery. Acta Anaesthesiol Scand 2017; Vol.61(9): p.1192-1202

II. Musso D, Klaastad Ø, Wilsgaard T, Ytrebø LM. Brachial plexus block of the posterior and the lateral cord using ropivacaine 7.5 mg/mL. Acta Anaesthesiol Scand. 2019 Mar; Vol.63(3): p.389-395

III. Musso D, Klaastad Ø, T Ytrebø LM. A combination of infraclavicular and suprascapular never blocks for total shoulder arthroplasty: a case series. Acta Anaesthesiol Scand. 2021 Jan; Vol.65(5): p.674-680.

4 Abstract

Background: Interscalene brachial plexus block is currently the gold standard for intraoperative and postoperative pain management in patients undergoing shoulder surgery. In expert hands, it has a very high success rate, but it is associated with a wide spectrum of block-related complications, with the risk of hemidiaphragmatic paresis of prominent interest. In study I, we hypothesized that the combination of superficial cervical plexus block, suprascapular nerve block and infraclavicular brachial plexus block would provide a good alternative to the interscalene block.

The total dose of local anaesthetic we used in study I was reasonably high, with the largest proportion used for the infraclavicular block. At this level, the subscapular, axillary and lateral pectoral nerves are the shoulder relevant nerves, which originate from the posterior and lateral cords. Hence, we speculated that blocking the medial cord may be unnecessary. Accordingly, we hypothesised that the dose for the infraclavicular block in the above-mentioned novel shoulder block combination could be significantly reduced by targeting the posterior and lateral cords.

The need for a diaphragm-sparing shoulder block is well acknowledged and alternatives to the classic interscalene block are currently being developed. In study III, we hypothesised that a combination of anterior suprascapular nerve block and lateral sagittal infraclavicular block of the posterior and lateral cords would provide effective postoperative analgesia for patients undergoing shoulder arthroplasty.

Methods: In study I, in an observational prospective case series, 20 adult patients scheduled for arthroscopic shoulder surgery received a combination of superficial cervical plexus block, anterior suprascapular nerve block, and lateral sagittal infraclavicular block. Primary aim of the

study was to find out how many patients could undergo arthroscopic shoulder surgery with this triple block, eventually supplemented by light propofol sedation, but without the need for opioids or artificial airway. In study II, in a dose-finding investigation, 23 patients received an infraclavicular block targeting the posterior and lateral cords with ropivacaine 7.5 mg/ml. Aims of the study were to estimate minimum effective volume in 50% (determined by the staircase up-and-down method) and 95% (estimated with logistic regression and probit transformation) of the patients (MEV_{50} and MEV_{95}). In study III, in an observational prospective case series, 20 adult patients scheduled for total shoulder arthroplasty received a combination of anterior suprascapular nerve block and lateral sagittal infraclavicular block of the posterior and lateral cords. Primary aims for this study were to document numeric rating scale (NRS) pain score and use of oral morphine equivalents (OMEq) during the first 24 hours after surgery. A secondary aim was to determine the incidence of hemidiaphragmatic paralysis, assessed by ultrasound before and 30 minutes after the blocks were performed.

Results: In study I, 95% of the patients underwent arthroscopic shoulder surgery with light propofol sedation, but without need for opioids nor artificial airway. In study II, we estimated that MEV_{50} and MEV_{95} were 7.8 ml and 9.0 ml, respectively. In study III, surgery was performed on 19 patients scheduled for total shoulder arthroplasty under general anaesthesia with a combination of anterior suprascapular and lateral sagittal infraclavicular block of the posterior and lateral cords. Median NRS (0-10) pain score 1, 3, 6, 8 and 24 hours postoperatively were 1, 0, 0, 0 and 3, respectively. During the first 24 postoperative hours, static median NRS was 4, maximum NRS was 6.5 and total OMEq consumption was 52.5 mg. Hemidiaphragmatic paralysis was diagnosed in one patient (5%).

Conclusions: The novel combination of superficial cervical plexus block, suprascapular nerve block and lateral sagittal infraclavicular block provides surgical anaesthesia and satisfactory postoperative analgesia in patients scheduled for arthroscopic shoulder surgery. MEV_{50} and

MEV_{95} to block the posterior and lateral cords at the infraclavicular level with a single injection of ropivacaine 7.5 mg/ml were 7.8 ml and 9.0 ml, respectively. The combination of anterior suprascapular and infraclavicular nerve block shows an encouraging postoperative analgesic profile with a relative low risk for hemidiaphragmatic paralysis after total shoulder arthroplasty.

5 Introduction

5.1 Brachial plexus anatomy

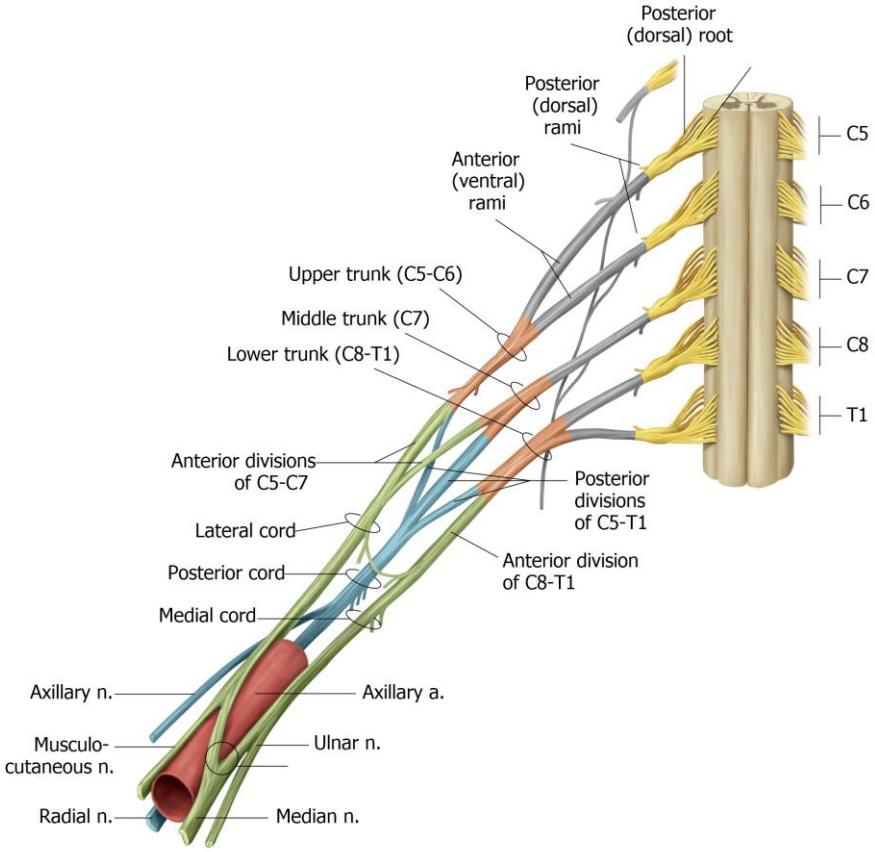

Figure 1 - Roots, trunks, and cords of the brachial plexus

Source: Gilroy et al., Atlas of Anatomy. All rights reserved. © Thieme 2018, www.thieme.com

The brachial plexus is a complex network of nerves that provides the innervation of the upper extremity and the pectoral girdle[1,2]. It originates in the ventral rami of the cervical spinal nerves C5-8 and the first thoracic spinal nerve T1, with some additional contributions from C4 and T2. The anterior ramus of C5, after receiving an anastomotic branch from C4, forms the superior trunk together with the anterior ramus of C6. The anterior ramus of C7 forms the middle trunk. The anterior ramus of T1, after receiving an anastomotic branch from T2, forms the inferior trunk together with the anterior ramus of C8. The roots of the brachial plexus and the trunks extend laterally from spinal cord to behind the clavicle, crossing the interscalene cleft, which is localized between the anterior and middle scalene muscles.

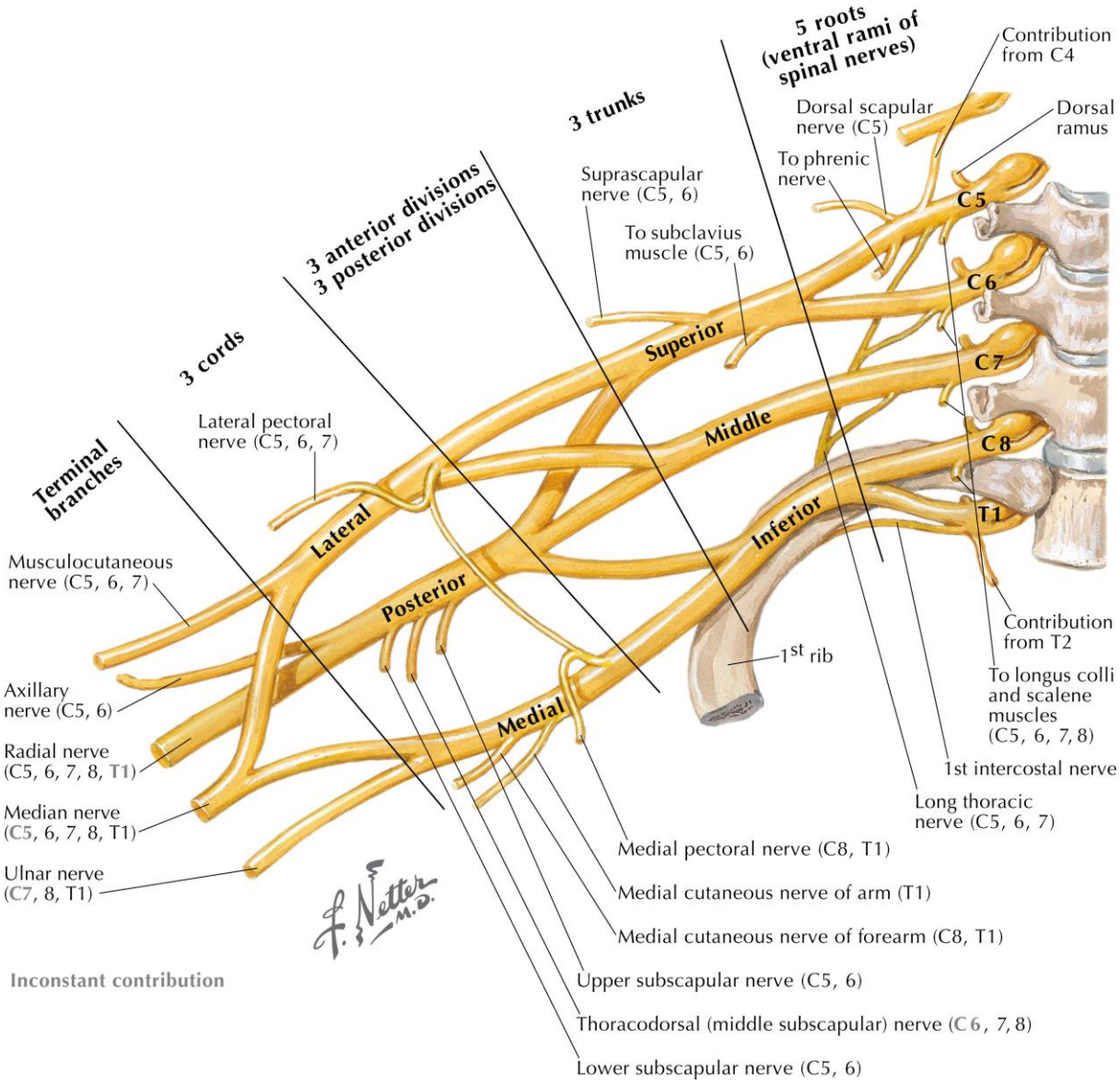

Figure 2 - The brachial plexus.

Source: netterimages.com

At this level, we can appreciate the phrenic, the long thoracic, the dorsal scapular, the subclavian and the suprascapular nerves, though the first nerve does not belong to the brachial plexus. The phrenic nerve originates from the C4 (C3-C5) root and innervates the ipsilateral half of the diaphragm. Its anatomy is described in an in-depth level later (see section 5.3). The long thoracic nerve arises from C5-C7 and innervates the serratus anterior muscle, pulling the scapula forward around the thorax. The dorsal scapular originates from C5 and innervates the rhomboid muscles, which retracts the scapula, and the levator scapulae, which lifts it. The

subclavian nerve arises from the superior trunk and innervates the subclavian muscle. Contribution of this nerve to the innervation of the clavicle is still a matter of debate[3]. The suprascapular nerve (SSN) derives from the upper trunk. It runs caudally, laterally and posteriorly towards the upper border of the scapula, lying superficially to the middle scalene muscle and deep to the trapezius muscle. It then passes through the suprascapular canal, below the superior transverse scapular ligament, and enters the supraspinous and infraspinous fossae. It innervates the supraspinatus and infraspinatus muscles, as well as most of the shoulder joint.

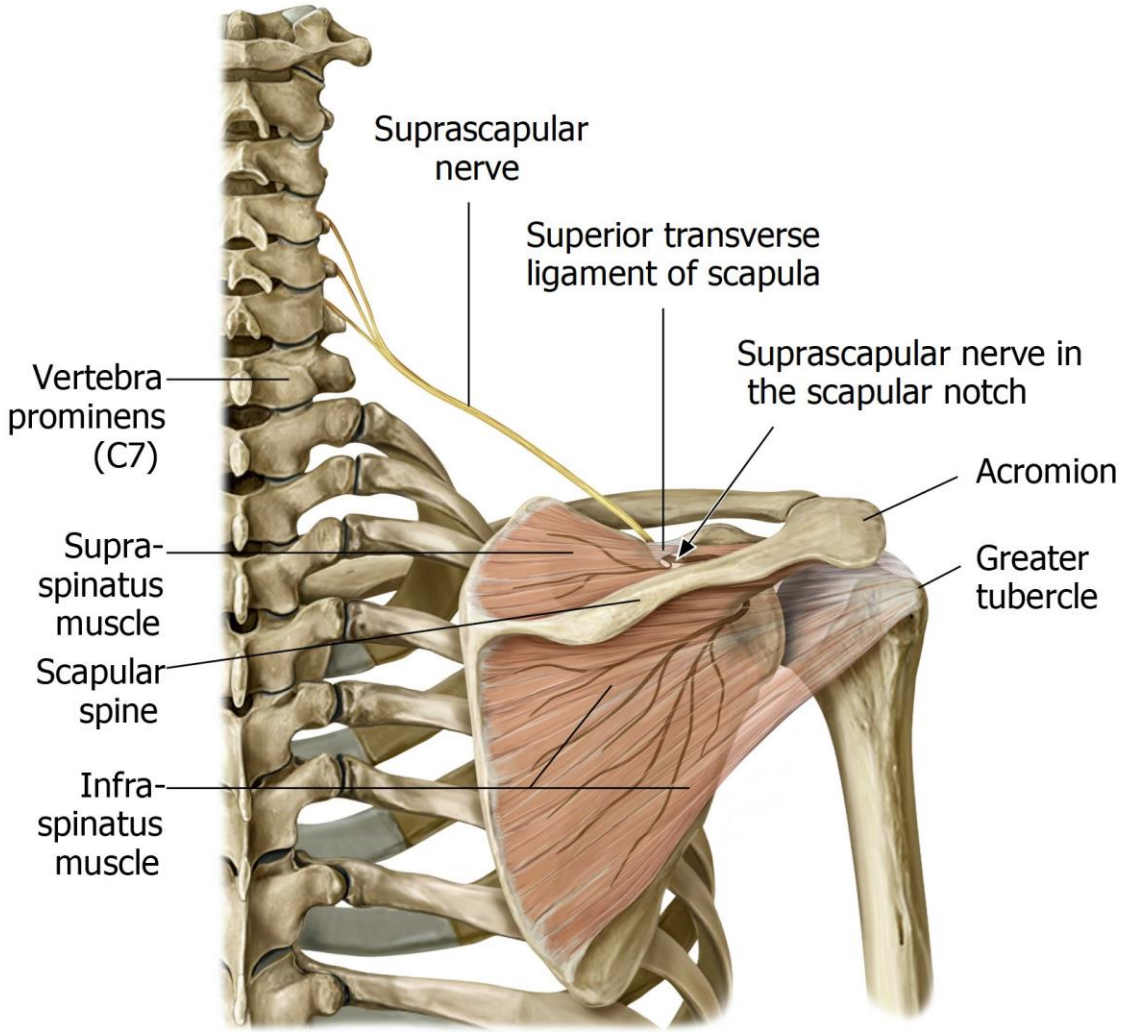

Figure 3 - Posterior view of the right shoulder, showing the suprascapular nerve and its course.
Source: Gilroy et al., Atlas of Anatomy. All rights reserved. © Thieme 2018, www.thieme.com

At the level of the clavicle, each trunk splits into two branches, the anterior and the posterior divisions, and reorganise to form the three cords, below the clavicle.

The anterior divisions of the upper and the middle trunk merge to form the lateral cord. The posterior cord originates from posterior divisions of all three trunks. The medial cord originates from the anterior division of the inferior trunk. The divisions and the cords of the brachial plexus extend from behind the clavicle to the medial part of the axillar cavity.

The three cords give rise to collateral branches and terminal nerves.

Three nerves originate from the lateral cord: lateral pectoral nerve (a collateral branch, innervating the pectoralis major muscle), the musculocutaneous (a terminal nerve, innervating the flexors of the elbow and the anterolateral skin of the forearm) and part of the median nerve (a terminal nerve, innervating most the flexors of the forearm, the thenar eminence, the lumbrical 1-2, as well as the skin of the lateral 2/3 of the hand, volarly, and the tips of the digits 1-4).

Three collateral nerves originate from the posterior cord: the upper subscapular (innervating the subscapular muscle), the thoracodorsal (innervating the latissimus dorsi muscle) and the lower subscapular nerves (innervating the subscapular and teres major muscles). The posterior cord terminates in two nerves: the axillary (innervating the teres minor and deltoid muscles, as well as part of the skin overlying the latter) and the radial nerve (mostly innervating the extensor muscles of the arm and forearm and the skin of the posterior aspect of the hand and forearm).

Five more nerves originate from the medial cord, three of which are collateral ones: the medial pectoral nerve (innervating the major and minor pectoral muscles), the medial cutaneous brachial and the medial cutaneous antebrachial nerves (innervating the medial skin of the arm and forearm, respectively); two of which are terminal ones: the ulnar nerve (innervating some

of the flexors of the forearm, and most of the intrinsic muscles of the hand, as well as medial volar skin of the hand) and part of the median nerve.

Anatomical variations are common and have been found in up to 50% of the subjects[4-6]. These variations can take place anywhere, from the roots to terminal branches. Knowledge about interindividual anatomic variations is crucial for the understanding of why a peripheral nerve block may develop unexpected patterns or fail, even in trained hands.

5.2 Innervation of the shoulder

5.2.1 Cutaneous innervation

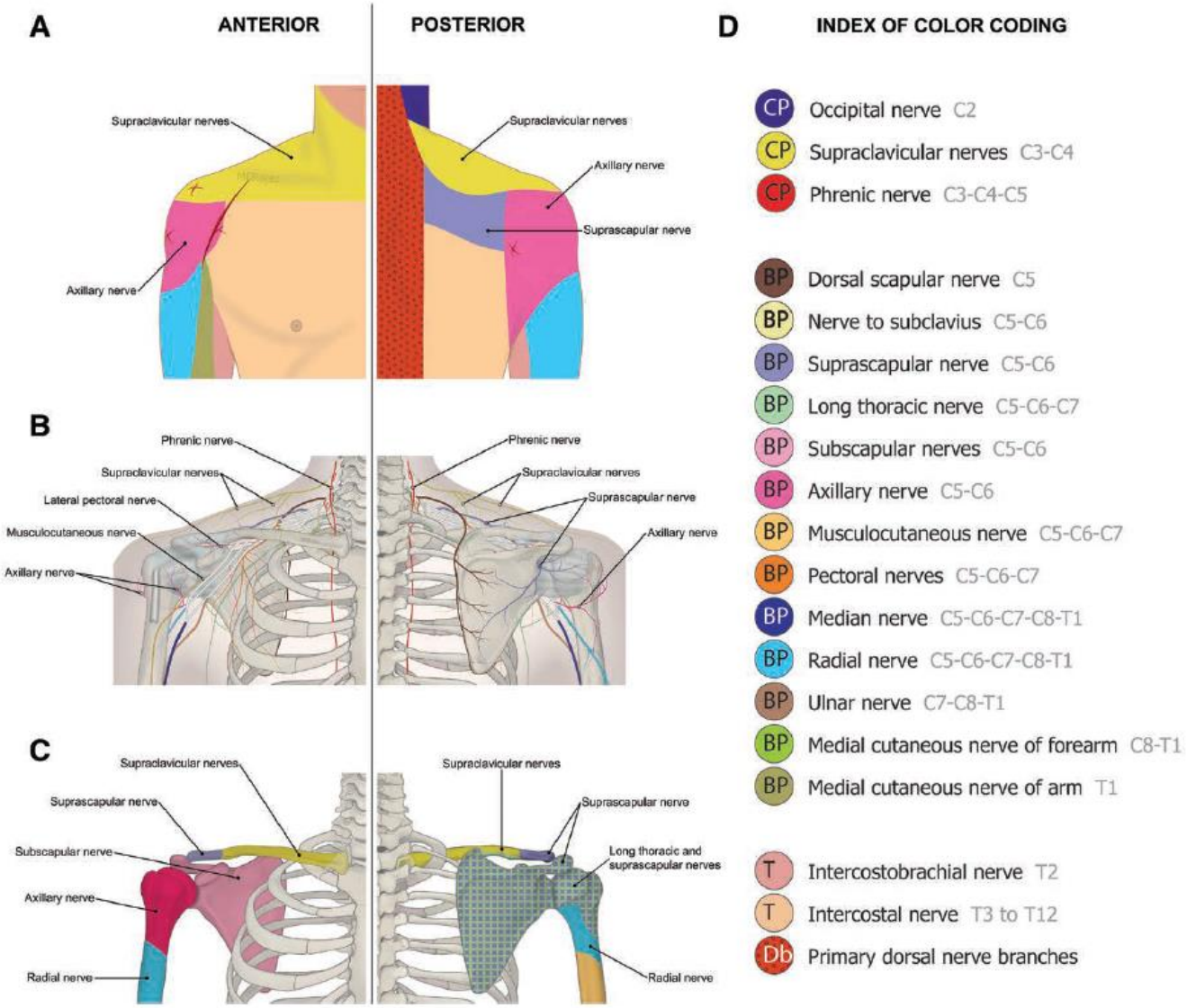

Figure 4 - Innervation of the shoulder.

Source: El-Boghdadly et al. 2017, Anesthesiology[7]

A. Cutaneous innervation with incision areas (indicated with red crosses and line). B. Nerve paths. C. Ostetome map

The cutaneous innervation of the shoulder is mainly provided by the supraclavicular nerves and the axillary nerve[8]. The first of these are not derived from the brachial plexus, but arise from the superficial cervical plexus (C3-4).

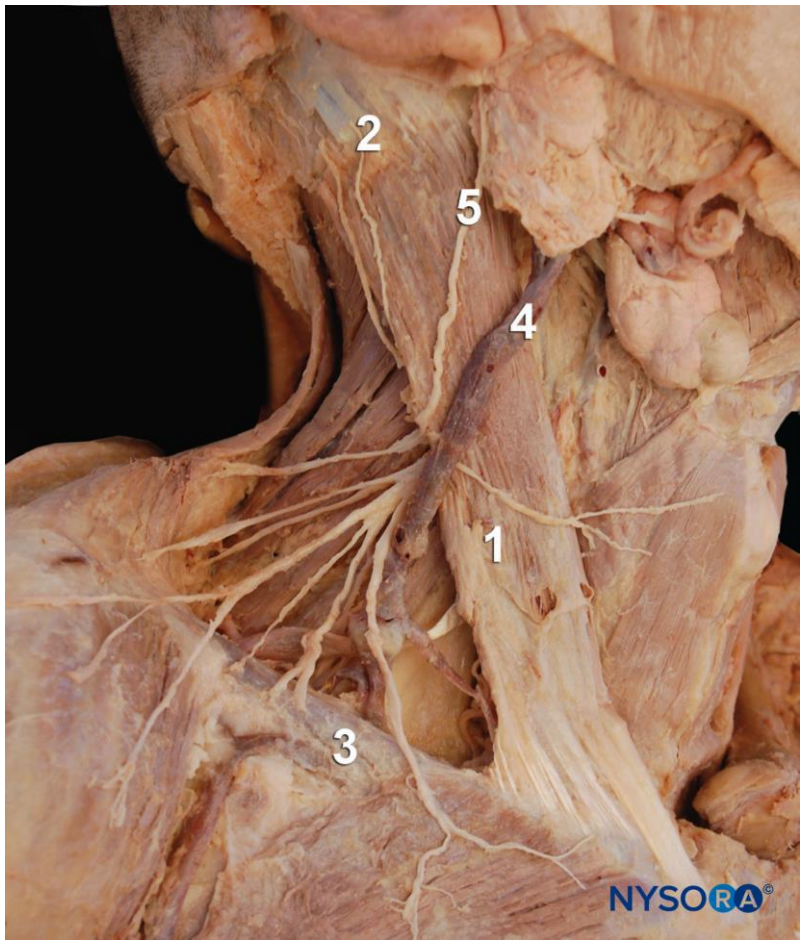

Figure 5 - The supraclavicular nerves.

Source: NYSORA.com

1: Sternocleidomastoid muscle. 2: Mastoid process. 3: Clavicle. 4: External jugular vein. 5: Greater auricular nerve. Supraclavicular nerves are seen crossing the clavicle.

The supraclavicular nerves (medial and lateral) innervates the cape-shaped region of skin overlying the shoulder and the lateral part of the neck. More specifically, they innervate the skin in the homonymous area, in addition to the first two intercostal spaces, anteriorly, and the skin of the upper and posterior parts of the shoulder. These nerves may have a role in the innervation of the clavicle as well, but their importance is a matter of debate[3]. The upper lateral brachial cutaneous nerve, a branch of the axillary nerve (terminal branch of the posterior cord), innervates the lateral side of the shoulder and the remaining skin overlying the deltoid muscle. The medial side of the arm is innervated by the intercostobrachial nerve (from the 2nd and 3rd intercostal nerves), proximally, and the medial brachial cutaneous nerve (originating from the medial cord), distally.

5.2.2 Deep innervation

The shoulder joint is mainly innervated by the suprascapular and the axillary nerve, but receives contributions from the subscapular and the lateral pectoral nerves[9,10]. As previously mentioned, the suprascapular nerve derives from the upper trunk. The axillary and the subscapular nerves are derived from the posterior cord of the brachial plexus, whereas the lateral pectoral nerve originates from the lateral cord.

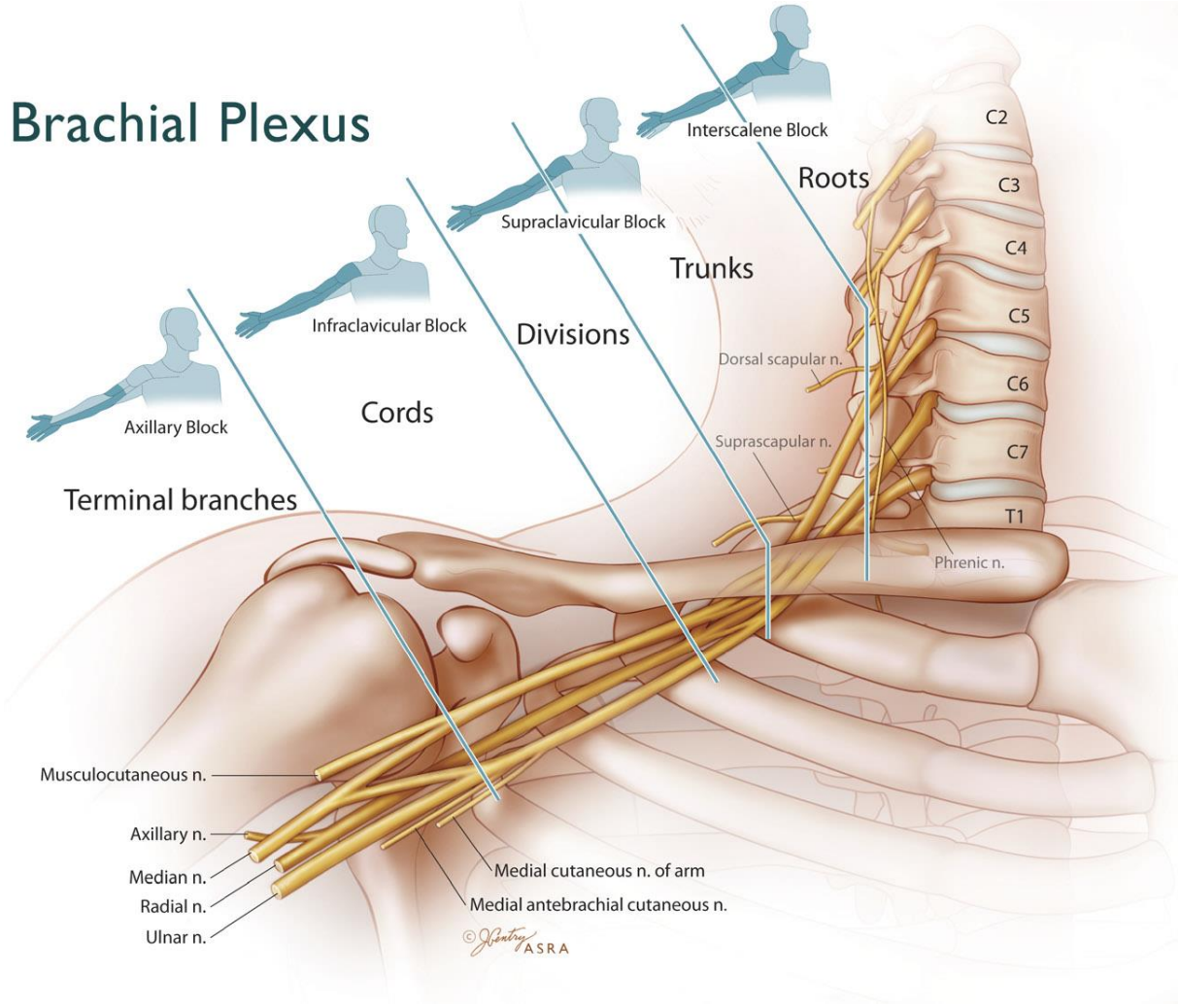

Figure 6 - Idealised brachial plexus and different block approaches.

Source: Neal et al. 2009, RAPM[11]

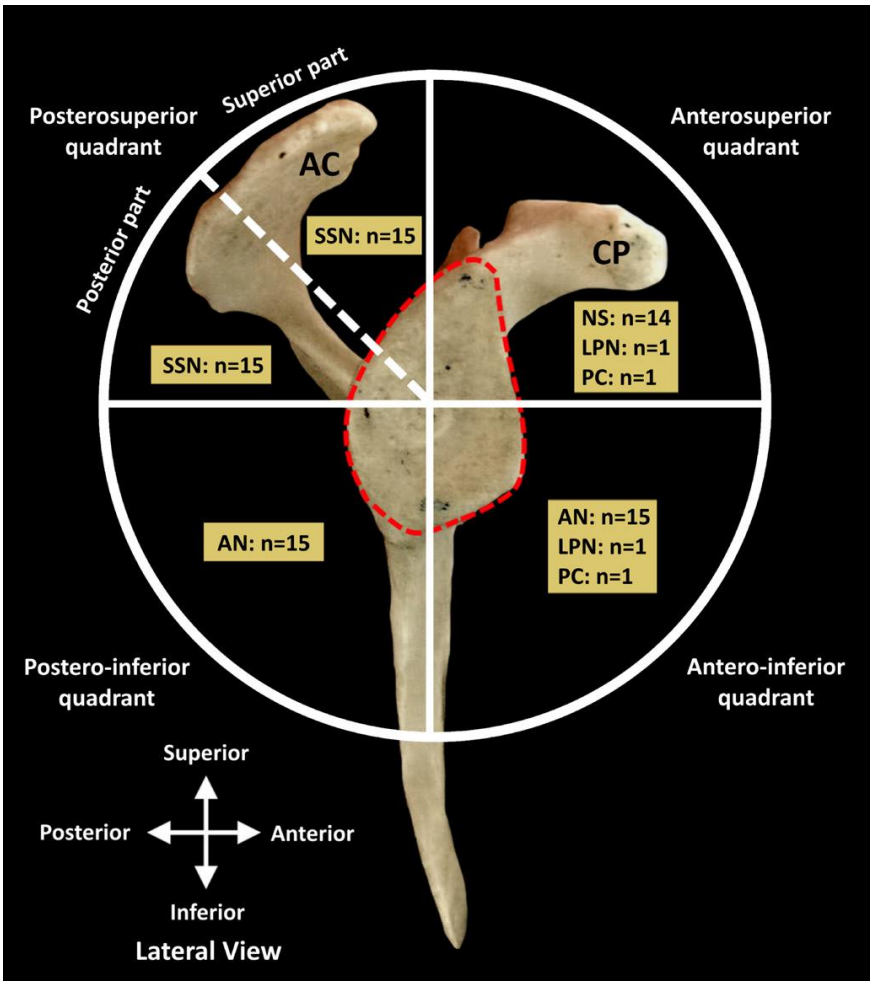

Figure 7 - Innervation of quadrants of the glenohumeral joint.

Source: Tran et al. 2019, RAPM[10]

AC = acromion, CP = coracoid process, SSN = suprascapular nerve, AN = axillary nerve, NS = subscapular nerve, LPN = lateral pectoral nerve, PC = posterior cord

The suprascapular nerve innervates the posterosuperior part of the glenohumeral joint, while the axillary nerve provides sensory branches to the inferior quadrants and the subscapular nerve supplies the anterosuperior aspect. The lateral pectoral nerve and branches from the posterior cord may provide the anterior quadrants, but their contribution is not consistent[10]. One more nerve, the musculocutaneous, originates from the lateral cord and may supply the innervation of the shoulder joint, but its contribution may be very small or completely absent[8].

The acromioclavicular joint is innervated by branches of the lateral pectoral nerve and the acromial branches of the suprascapular nerve[10].

5.3 Anatomy of the phrenic nerve

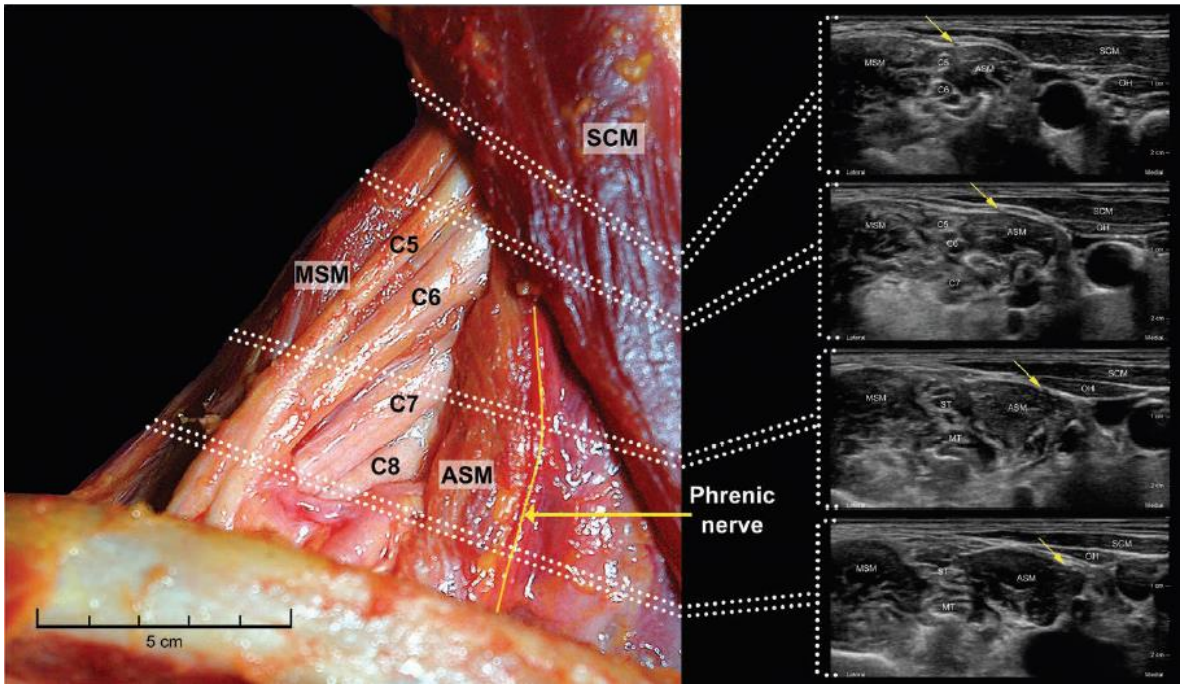

Figure 8 - Cadaveric (left) and sonographic (right) images showing the course of the phrenic nerve.

Source: El-Boghdadly et al. 2017, Anesthesiology[7]

SCM = sternocleidomastoid muscle, MSM = Middle scalene muscle, ASM = Anterior scalene muscle, C5-8 = nerve roots, OH = Omohyoid muscle. ST = Superior trunk, MT = Middle trunk, yellow arrows/line = Phrenic nerve

The anatomy of the phrenic nerve is crucial to understand its involvement in upper extremity nerve blocks and the rationale for the strategies to avoid it. The phrenic nerve mainly originates from C4, but it also receives contributions from C3, C5 and the cervical sympathetic ganglia or the thoracic sympathetic plexus[12]. The nerve forms at the upper lateral border of the anterior scalene muscle and descends on the anterior surface of this muscle in medio-lateral direction, lying deep to the prevertebral fascia. Its course is in proximity to the brachial plexus, initially lying 18 to 20 mm medial to the anterior ramus of C5 at the level of the cricoid cartilage (C5-6) and diverging 3 more millimetres for every centimetre in a distal direction[13]. Anatomic variations are frequent, with an accessory phrenic nerve present as often as in 60 to 75% of individuals and providing independent contribution to the phrenic nerve[7]. These fibres originate primarily from C5 and run together with the subclavian nerve, the ansa cervicalis or the nerve to the sternohyoid[14]. The contributions may emerge from any of the above-mentioned nerves

to form an accessory phrenic nerve, joining the main nerve at a variable location along its course[15,16].

5.4 Microanatomy and physiology of peripheral nerves

5.4.1 Peripheral nerve anatomy

The membrane of the nerve cells and the axons consists of a phospholipid double layer housing several proteins, including the ion channels[17]. Myelinated nerve axons are surrounded by other cells, called Schwann cells, that wrap around the axons forming the myelin sheath. Lengthwise, this sheath is punctuated by gaps, called nodes of Ranvier. The nerves of most interest for regional anaesthesia are myelinated, whereas autonomic and some nociceptive afferent fibres lack the myelin sheath.

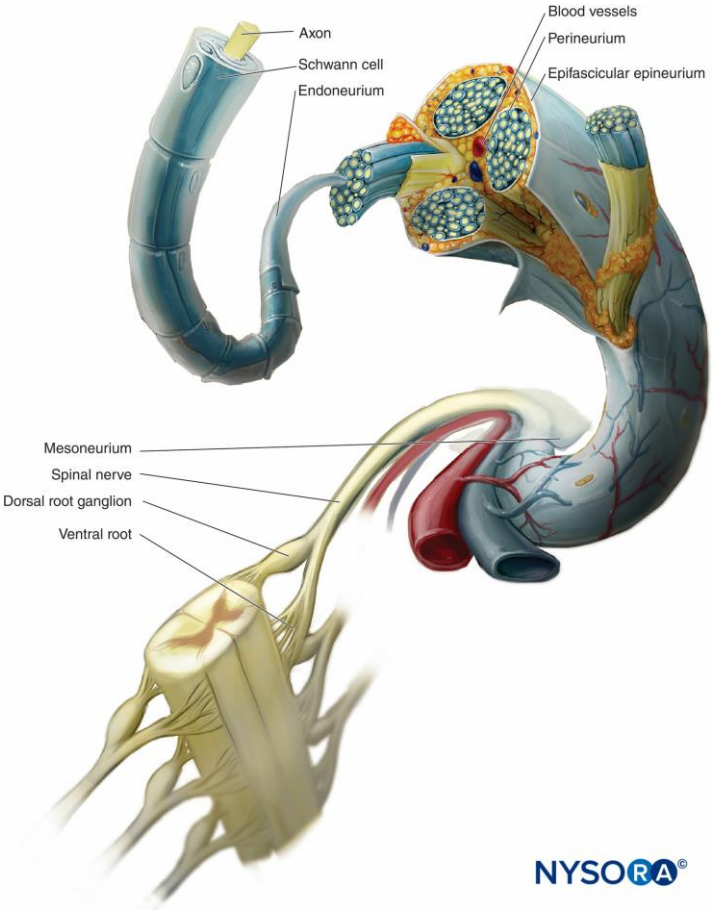

Figure 9 - Peripheral nerve anatomy.

Source: NYSORA.com

The nerve fibres are encased in a loose connective tissue, the endoneurium, consisting of glial cells and fibroblasts together with blood capillaries. These fibres are surrounded by a dense connective tissue, the perineurium, forming a structural unit known as the fascicle. The fascicles are grouped, along with blood vessels, by a thicker layer of connective tissue, the epineurium, forming the nerve. A mixed peripheral nerve consists of individual nerves surrounded by a fascia. These are the structures that need to be penetrated by the local anaesthetic in order to bind to the sodium channels and block nerve conduction.

The nerves are classified by their diameter, which roughly corresponds to the degree of myelination and speed of impulse conduction.

Fibre	Diameter (μm)	Conduction speed (m/s)	Sensitivity to block	Myelination	Anatomic location	Function
A-α	15-20	80-120	++	+++	Muscles and joints	Motor Proprioception
A-β	8-15	80-120	++	+++	Muscles and joints	Touch Pressure Proprioception
A-γ, A-δ	3-8	4-30	+++	++	Muscle spindles Sensory roots Afferent peripheral nerves	Pain Temperature Touch/Motor
B	4	10-15	++++	+	Preganglionic sympathetic	Autonomic – preganglionic
C	1-2	1-2	++++	-	Postganglionic sympathetic Sensory roots Afferent peripheral nerves	Pain Temperature Touch

Table 1 - Different nerve types. Characteristics and sensitivity to local anaesthetics

Table adapted from: Hugh C. Hemmings B, Egan TD. Pharmacology and Physiology for Anesthesia: Foundations and Clinical Application[17]

5.4.2 Electrophysiology

The axonal membrane is relatively impermeable to sodium ions, but selectively permeable to potassium ions[17]. The Na^+/K^+-pump exports sodium and imports potassium in order to establish and maintain a concentration gradient across the membrane. The higher concentration of intracellular K^+, together with the greater membrane permeability to these ions, creates a relatively negative electrical potential intracellularly of around -70 mV.

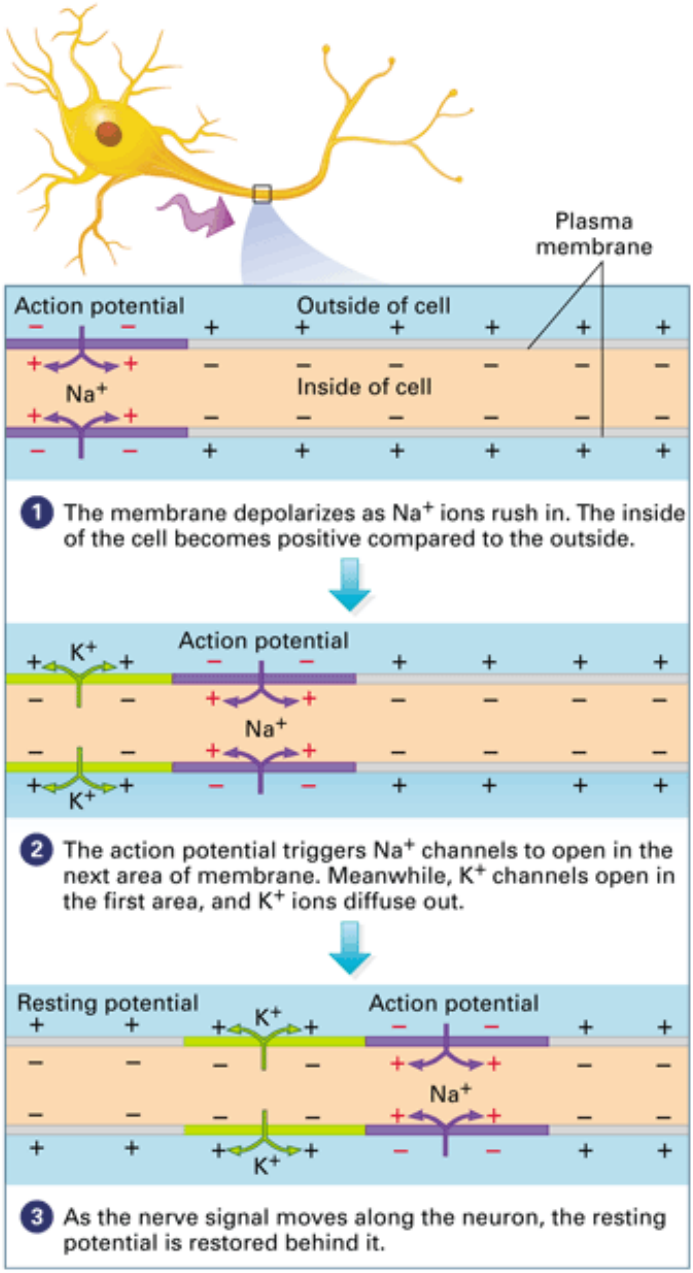

Figure 10 - Action potential and transmission of the nerve signal along the axon.

Source: open source https://bodell.mtchs.org/OnlineBio/BIOCD/text/chapter28/concept28.2.html

Neurons are activated by chemical, molecular, thermal or mechanical stimuli into electrical potential by the influx of cations inside the cell. When the stimuli are strong enough they cause a depolarisation of the neural membrane via the opening of Na^+-channels, letting these cations flow inside the cell and invert the membrane potential (to approximately +20 mV). The sodium ions diffuse along the axon and depolarise the adjacent membrane by triggering additional Na^+-channels. The original resting potential is restored by outflow of K^+ and further action of the Na^+/K^+-pump, exporting sodium and importing potassium. During this phase the membrane is in a refractory period and the impulse can only propagate in anterograde direction. In myelinated axons, the myelin serves as insulation and depolarisation takes place at the level of the nodes of Ranvier, providing a faster, saltatory conduction.

5.5 Local anaesthetics

5.5.1 General properties and pharmacodynamics

The molecule of all local anaesthetics consists of 3 components[18,19]:

- A (lipophilic) aromatic ring
- An intermediate chain (amide or ester)
- A terminal amine

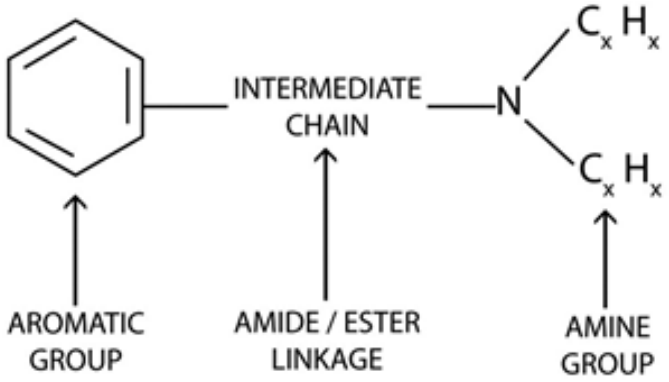

Figure 11 - Local anaesthetic structure and its main components.
Source: Culp et al. 2011, J Vasc Interv Radiol[20]

The aromatic ring is important for the lipidic solubility. This property is crucial for the diffusion of the molecule across the nerve membrane and correlates with the potency of the local anaesthetic (LA). The higher the liposolubility, the greater the proportion of the administered dose can enter the neurons. The intermediate chain dictates the pathway of metabolization, which has implications for the pharmacokinetic profile and the allergy potential. The amine group is a proton acceptor, providing the potential for both charged (hydrophilic) and uncharged (hydrophobic) isoforms and hence the source of amphipathic nature of the local anaesthetics.

Local anaesthetics are drugs that suppress the action potential by blocking the Na^+-channel. This mechanism of action accounts for both their analgesic effects and for their systemic effects. The local anaesthetics bind to the Na^+-channel in its open form from the inside of the cell, hence the importance of the lipid solubility. Intracellularly, the molecules diffuse in an aqueous environment, hence the importance of the amphipathic nature.

Only a very small fraction of the local anaesthetic reaches the membrane, even when placed close to the nerve, because of several factors[17,19]. Both the chemical and the pharmacological variables of the molecule are involved, together with the local environment where the injection takes place. The local anaesthetic diffuses along a concentration gradient, meaning that the outer bundles of a mixed nerve are blocked first and the outer surface of the nerve is blocked before the core. The speed of diffusion is influenced by the concentration of the drug, its degree of ionisation, its hydrophobicity, the anatomical structures surrounding the nerve and the nerve itself. The concentration and the volume are important variables as well. The potency of a local anaesthetic can be expressed as the minimum effective concentration (MEC) to achieve a complete block. The volume is also important as a critical minimum length of a nerve must be blocked to prevent regeneration of the action potential in an adjacent node of Ranvier[17].

5.5.2 Pharmacokinetics

The plasma concentration of local anaesthetics is determined by both the pharmacokinetics of the local anaesthetic and patient-related factors, such as age, body size, local anatomy and organ function[17,19].

Absorption is the most important pharmacokinetic step to consider, since it is the one that the anaesthetist can influence, whereas distribution, metabolism and excretion are patient-related. The absorption of local anaesthetic is dependent on: site of injection, dose, physiochemical properties of the molecule and eventual use of adjuvants. An injection in a more vascularized area results in a higher plasma concentration in a shorter time. As a general rule, one can expect a decreasing plasma concentration if the injection is performed intravenously, intrapleural, intercostal, caudal, epidural, brachial plexus, femoral, sciatic and subcutaneously, which reflects the vascular supply to these tissues[17,19]. The plasma concentration is usually proportional to the total dose, irrespective of the concentration used or the speed of injection[17]. Furthermore, more lipid-soluble molecules are generally absorbed slower than more hydrophilic agents, probably because of segregation in lipophilic tissues[17].

The distribution is proportional to the lipid solubility of the drugs and the vascularisation of the organs. LAs are rapidly distributed to brain, heart, liver and lungs, and slower to muscles and fat tissue. The patient's age and cardiovascular status influence tissue blood flow[19].

The metabolism of local anaesthetics is hepatic and dependent on liver blood flow. Esters are hydrolysed by plasma esterases to para-aminobenzoic acid (PABA), which may cause allergic reactions in susceptible individuals. Amides are metabolised by the liver and do not produce PABA as a metabolite and therefore very rarely cause allergic reactions[17,19]. The metabolic rate varies between the different agents (prilocaine > lidocaine > mepivacaine > bupivacaine)[17,19].

In patients with hepatic or renal dysfunction, the elimination is slower and the risk for systemic toxicity is subsequently higher.

5.5.3 Local anaesthetic systemic toxicity (LAST)

The limiting factor for the application of local anaesthetics is their toxicity. This usually results in cardiovascular and neurological symptoms. In appropriate situations, the local anaesthetics are relatively safe, but local or systemic toxicity may emerge from unintended intravascular, intrathecal or intraneural injection or from situations leading to higher systemic absorption.

The direct cardiotoxicity is mediated by decreased conduction in Purkinje fibres and cardiomyocytes due to prolonged recovery time and via a mechanism that acts on the Ca^{++}-channels, reducing the influx of this ion into the cell and the release from the sarcoplasmic reticulum[17]. There is an action even on the vascular system, through effects on the vascular smooth muscles, which leads to vasoconstriction, at low concentrations, and vasodilation, at higher concentrations. Pharmacokinetic properties affect toxicity as well. More potent, lipophilic local anaesthetics, such as tetracaine and bupivacaine, are more cardiotoxic than less lipophilic substances such as procaine and lidocaine.

The clinical presentation is highly variable and LAST should be suspected whenever an unexpected clinical or physiological change occur after the administration of a local anaesthetic drug[21]. The classical clinical presentation of LAST progression of symptoms after injection of local anaesthetics, progressing through CNS excitatory symptoms, CNS-inhibition, cardiovascular excitation that may evolve into cardiovascular inhibition and circulatory collapse. However, in clinical practice, the presentation may debut later and show only cardiovascular signs and symptoms.

Local anaesthetic blood levels in the brain initially block cortical inhibitory pathways and may therefore cause excitatory signs and symptoms, such as perioral paraesthesia, metallic taste, visual and auditive changes, muscle twitching, mental status alterations such as anxiety and ultimately seizures. Increasing blood concentrations of local anaesthetics may cause CNS depression such as sedation, somnolence, coma and respiratory depression.

Cardiovascular symptoms may occur together or after CNS-symptoms, or as the only manifestation. Initial sympathetic activation may lead to tachycardia or hypertension. However, symptoms of cardiovascular inhibition may dominate, with bradycardia and hypotension. Direct cardiotoxicity can evolve into ventricular arrhythmias and asystole.

The total dose of local anaesthetics should be the lowest required to achieve the desired effect and duration. As an indicative guide, a plethora of maximum recommended doses appears in several publications. However, it is important to keep in mind that they should be treated as rough guidelines, since they are not evidence based and they do not distinguish between site of injection, technique and patient factors (extremes of age, end organ dysfunction, pregnancy, metabolic disturbances) that may increase the risk of toxicity[21].

5.6 Role and history of nerve blocks

A nerve block is an interruption of electric signals travelling along a nerve, usually achieved by injection of local anaesthetic in proximity to a nervous structure. The anatomic structure to categorise and distinguish central from peripheral nerve blocks is the intervertebral foramen. Nerve blocks are used to provide surgical anaesthesia, intra- and postoperative analgesia, as well as a method for invasive non-surgical pain treatment. It offers the benefits of lighter general anaesthesia or awake surgery and grants superior pain management compared to the use of systemic analgesic drugs[22-25]. Furthermore, patients receiving peripheral nerve blocks

spend shorter time in the post-anaesthesia care unit (PACU), receive less opioids and carry a lower risk of postoperative nausea and vomiting (PONV)[26].

In the very beginning, peripheral nerve blocks were performed by using superficial anatomical landmarks and a technique based on needle-induced paraesthesia. In the 1970's the electrical nerve stimulator was introduced, giving the clinicians the possibility to confirm the needle position in proximity to the target nerves with more objective findings, namely the contraction of pertinent muscles. Even though the first descriptions of ultrasound use can be dated as early as around the 1990's[27-29], its clinical routine use was introduced around year 2000. Ultrasound guidance allowed the operator to visualise in real time relevant anatomical structures, the actual nerve target and the spread of LA.

5.7 The interscalene block and the rationale for a diaphragm-sparing shoulder block

The interscalene brachial plexus block (ISB) is currently the gold standard for intraoperative and postoperative pain management in patients undergoing shoulder surgery. It was first described by Winnie in 1970[30], who performed the block using a landmark-based technique. Through the years, this block has undergone several technical refinements, from one of the first descriptions with help of ultrasound in the 1970's[31], to more modern approaches. The injection of local anaesthetic is performed at the level of the interscalene cleft and the LA spreads from distal roots/proximal trunks level and follows the distribution of the upper dermatomes of the brachial plexus (around C5-C7), with variable involvement of the supraclavicular nerves of the cervical plexus (C3-4), depending on the technique used. The ISB usually spares the lower trunk (30-50%)[32], resulting in unanaesthetised ulnar, cutaneous brachial nerve of the arm and forearm. In expert hands, it has a very high success rate[33], but may cause a wide spectrum of

complications and undesired side effects[34-37]. The risk of neurological complications, particularly concerning the phrenic nerve[38-40], due to its proximity to the injection site, has encouraged the development of alternative peripheral block methods for shoulder surgery[41,42]. Shoulder surgery results in the highest pain score within orthopaedic surgery and, in absence of regional anaesthetic techniques, the consumption of opioids may be as high as the one recorded after thoracotomy[43].

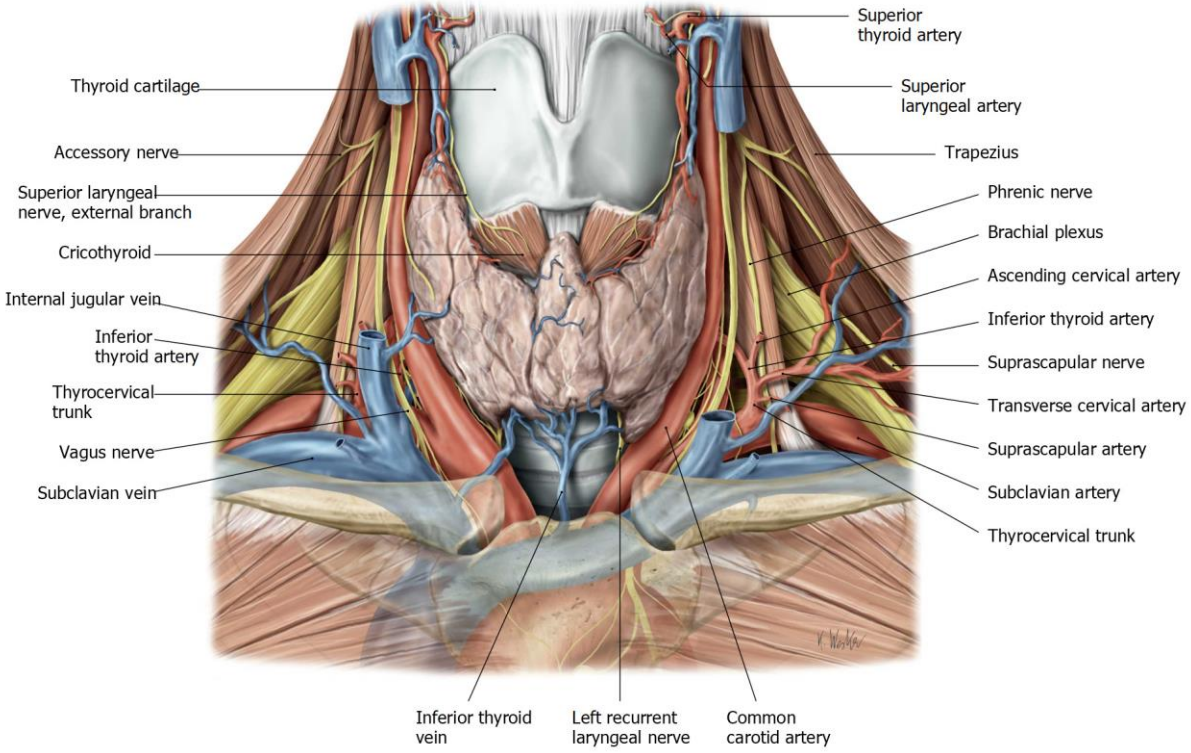

Figure 12 - The brachial plexus at the level of the interscalene cleft and surrounding structures.
Source: Gilroy et al., Atlas of Anatomy. All rights reserved. © Thieme 2018, www.thieme.com

In the pre-ultrasound era hemidiaphragmatic paralysis was a known, and inevitable, consequence of the interscalene block[44]. The introduction of ultrasound techniques has allowed a reduction of the minimal effective volume to achieve a successful ISB and thus the effect on the phrenic nerve. Nevertheless, no single intervention such as digital compression of the interscalene cleft, reduced volume and/or concentration of LA, or modified injection site, has shown an incidence of hemidiaphragmatic impairment below 27%[41]. Hemidiaphragmatic

paralysis is usually well tolerated by most patients and not seldom totally asymptomatic, but it has shown to be able to cause significant respiratory impairment, when tested with spirometry. This may lead to severe consequences in patients suffering from serious lung pathology, which paradoxically is the population who would benefit most from peripheral nerve blocks, as opioids can further compromise ventilation.

Furthermore, several cases of long lasting/permanent diaphragm paralysis have been reported. Kaufman *et al.* reported 14 patients suffering from this complication after shoulder surgery, involving an interscalene block, at a tertiary referral centre for peripheral nerve injury centre covering the entire United States[40]. The incidence of this event is unclear, being that diaphragmatic paralysis is often subclinical and therefore probably underreported, but it is presumed to be relatively low. Nevertheless, this risk should not be ignored. Albeit a minor respiratory impairment may not lead to significant morbidity, it may lead to tangible consequences on the quality of life, even among otherwise healthy individuals. The etiopathogenesis is a matter of debate and several mechanisms, including mechanical, traumatic, toxic and ischemic origin have been proposed[38,40,45-50].

Several alternatives to the ISB have been suggested to avoid hemidiaphragmatic impairment, yet many of them require further confirmatory trials. These include: C7-root blocks[51], supraclavicular blocks[52-58], costoclavicular block[59], anterior suprascapular nerve blocks[52,56,60], superior trunk block[61], axillary-suprascapular block[62] and combinations of infraclavicular and suprascapular blocks[63,64].

5.8 Further complications related to shoulder surgery and the interscalene block

As previously mentioned, the ISB has shown to be related to long-term nerve effects. However, the phrenic nerve does not seem to be the only nerve suffering from this kind of adverse event. Two nerves run together in the middle scalene muscle and may be subject to complications during the classic posterior approach.

The dorsal scapular nerve (DSN) is derived from C5, with a possible contribution from C6, and supplies the motor innervation of levator scapulae and the two rhomboid muscles. The long thoracic nerve (LTN) is derived from C5-C7 (though the contribution from C7 may be absent) and innervates the serratus anterior muscle. Both nerves run within or are superficial to the middle scalene muscle, with the LTN usually being located deeper than the DSN. The identification of these nerves has proven to be routinely possible[65] and is recommended[66], since the posterior ISB may be an underreported cause of nerve injury[67,68].

Even though nerve injuries as a complication of nerve blocks appear to be rare, their incidence seems to be higher for ISB than for other peripheral nerve blocks[69,70].

The beach chair position is widely used for shoulder surgery because of several advantages, including ease of setup and conversion to open surgery, easier arthroscopic visualisation and orientation, decrease of brachial plexus traction and anaesthesia flexibility. Although uncommon, ischemic brain damage has been reported, with symptoms spreading from cognitive impairment[71] to visual loss, deafness and stroke[72]. A further factor calling for caution is that hypotensive and bradycardic events (HBE) are reported to be very common during surgery in beach chair position (13-61%)[11,73]. Possible aetiologies of HBE includes β_1-agonist effects of exogenous adrenaline and the activation of the Bezold-Jarisch reflex[74]. This reflex is

initiated by the combination of decreased venous return and increased sympathetic tone, leading to enhanced contraction of a near-empty left ventricle and resulting in parasympathetic-mediated vasodilation and bradycardia. Though the mechanism is unknown, the ISB seems to be an independent three-fold risk factor[73].

6 Aims

6.1 Study I

We hypothesised that a combination of superficial cervical plexus block, suprascapular nerve block, and lateral sagittal infraclavicular brachial plexus block would provide intraoperative anaesthesia and post-operative analgesia for patients undergoing arthroscopic shoulder surgery. The primary aim was to find the proportion of patients who could be operated with this triple block, eventually supplemented by light propofol sedation, but without the need for opioids or artificial airway. Secondary aims were patients' satisfaction and surgeons' judgment of the operating conditions.

6.2 Study II

The axillary, subscapular, and lateral pectoral nerves are the shoulder relevant nerves at the cord level, arising from the posterior and lateral cord. Consequently, we assumed that blocking the medial cord may be unnecessary for shoulder surgery. Therefore, we hypothesised that those nerves may be blocked by a single injection at the infraclavicular level, targeting the posterior and lateral cords. The aim for this study was to determine MEV_{50} and estimate MEV_{95} for a single-deposit infraclavicular block of the posterior and lateral cords using ropivacaine 7.5 mg/ml.

6.3 Study III

We hypothesised that a combination of anterior suprascapular nerve block and lateral sagittal infraclavicular block of the posterior and lateral cords would provide effective postoperative analgesia for patients undergoing shoulder arthroplasty. Primary aims for this study were to NRS and use of OMEq during the first 24 hours after surgery. A secondary aim was to determine the incidence of ipsilateral hemidiaphragmatic paralysis 30 minutes after the blocks.

7 Methods

7.1 Study design

All three studies were conducted on patients scheduled for elective surgery. In study I and III the surgical treatment was given with performed nerve blocks, whereas in study II the surgery was first performed after a supplementary nerve block.

The studies were preceded by pilot cases, not included in the data analysis, and a conspicuous time spent for the training of the block operator. Part of this training was a natural part of the clinical work at the hospital, as regional anaesthetic techniques of the upper extremity are a daily practice for an anaesthetist working with orthopaedic surgery. In the specific, the lateral sagittal infraclavicular block is standard of care in our department for surgery distal to the shoulder. Concerning the superficial cervical plexus block (SCPB), this technique was not used as a routine in our facility at the time the studies were planned. To overcome this problem, we performed first an extensive ultrasonographic training of this anatomic area on patients, medical students and colleagues who volunteered. The suprascapular nerve block was studied with the same ultrasonographic approach on volunteers and the final practical refinements were achieved thanks to Dr. Flohr-Madsen's kind supervision at Sørlandet Hospital in Kristiansand, in June 2015. The blocks were then introduced to practice in selected cases when indicated. Examples of these are surgery in the region of the throat (SCPB) or dorsal surgery of the hand (SSNB) on the ulnar side, where a pronation of the anaesthetised hand was required[75].

The three trials are differently designed and all of them are single armed. This is both because the specific needs of the actual study and to overcome logistic and ethical issues.

Study I was an observational prospective case series in 20 patients, where we explored the feasibility of a novel block combination to perform arthroscopic shoulder surgery with only

light sedation. Since the patients were awake and the use of other analgesics was not allowed by protocol, surgery would not have been possible without a successful anaesthetic block. A control group was not included as the single arm design was sufficient to answer our research question.

Study II was a dose-finding investigation performed with the staircase up-and-down method. A predefined volume of LA was administered to the first patient. Subsequent volume was determined by assessment of the block in the previous patient. In case of block success, the following patient would be injected with a volume of LA decrease by 1 ml. On the contrary, in case of block failure, the subsequent patient would receive a volume of LA increased by 1 ml. The method was used to determinate the MEV_{50}, whereas the MEV_{95} was estimated using logistic regression and probit transformation.

Study III was an observational prospective case series. A control group would have unarguably provided a stronger study design and we considered to perform a randomised controlled trial by using ISB as a control group. This plan was discarded due to limited access to patients for recruitment and other logistic issues. However, considering the limited knowledge about the actual block combination, we strongly felt that an observational study design could be justified and serve as a valuable data source for design of future randomised controlled trials.

7.2 Setting and demography

All three studies were mainly conducted in Northern Norway, which is a region characterized by vast areas and scarce population. The total amount of eligible patients was therefore limited, compelling us to restrict the number of participants and to recruit patients in several centres. Study I was performed at the University Hospital of North Norway (Tromsø and Narvik) from April to November 2016. Study II was conducted at the University Hospital of North Norway

(Tromsø) from November 2017 to March 2018. Finally, in study III the patients were recruited at the University Hospital of North Norway in Tromsø, Nordland Hospital in Bodø, and Sørlandet Hospital in Kristiansand, from March 2019 to August 2020. For the latter study, the COVID-19 pandemic caused a total stop in the research activity for over half a year.

Patients in all the three studies were healthy or with only minor systemic disease (ASA 1-2 and stable ASA 3). In study III we allowed the recruitment of older patients (18-80 years old, as opposed to 18-70 in study I and II). This was both in order to recruit more broadly, but was also motivated by the fact that total arthroplasty is frequently performed in the elderly population. The exclusion criteria between the different studies were similar, but showed some slightly variations. The complete list of exclusion criteria included: pregnancy, coagulation disorders, severe respiratory disease, use of anticoagulation drugs other than acetylsalicylic acid or dipyridamole, allergy to local anaesthetics, patients on regular opioids, atrioventricular block, pacemaker, diabetes and peripheral neuropathy. The specific exclusion criteria for each study can be singularly appreciated in the method section of the attached papers, at the end of this thesis.

7.3 Technical aspects

All peripheral blocks were performed by the same operator (Dr. Musso). The blocks were ultrasound-guided and different units were used: SonoSite M-Turbo (study I), SonoSite Edge (study I) and SonoSite S-II (study II and III). The use of probes showed an evolution as well, reflecting both the availability of different equipment and the changing preferences of the operator. Whereas in study I the LSIB was performed with a C11x 5-8 MHz broadband curved array, this was later substituted in study II by a 50 mm 6-15 MHz linear array probe, in favour of a higher picture resolution, and in study III by a 38 mm 6-13 MHz linear array probe, in order to achieve a balance between resolution and handiness. A similar choice was made for

the SSNB between study I and III. We used block needles from Pajunk in all three studies (Pajunk SonoPlex STIM 22G). The SCPB and SSNB in study I were performed with a 50 mm needle, whereas all the other blocks were performed with an 80 mm needle. Even though the first one was long enough for these superficial nerve blocks, the latter was chosen in the last two studies to reduce the variety of the equipment and ultimately simplify the procedure. No premedication was provided before the nerve blocks, but a skin wheal was raised with 1-2 ml lidocaine before the block needle was inserted. The initial needle insertion was counted as the first pass. An additional needle pass was defined as needle retraction of at least 10 mm prior to further needle insertion. In all the three studies a nerve stimulator was used. A nerve stimulator response set at a current ≤ 0.3 mA, 0.1 ms and 2 Hz defined the need for a small retraction of the needle. In study I even a syringe manometer was adopted, in order to prevent an injection pressure ≥ 103 kPa (15 psi). The manometer was later discarded in study II and III. The reason of this was that in the latter studies the block performer operated alone, making the visual marker on the manometer challenging to be seen, while at the same time observing the images on the ultrasound machine. In study I, the nerve stimulator was used also to confirm the right position of the needle, by eliciting a sensory (superficial cervical plexus) and a motor (suprascapular nerve) response, that were mandatory before starting the injection.

Since the studies have taken place between April 2016 to August 2020, it is not unexpected that some minor technical adjustments occurred. This included, as mentioned, different kind of probes and needles. Furthermore, even the patient position was slightly adapted between the studies with the intention to simplify the block procedure and make the process easier for both operator and patients. These refinements developed in parallel with the increasing experience of the operator and can be looked at as part of a maturing process.

7.4 The nerve blocks

The shoulder innervation is provided by several nerves. Most of them emerge from the distal part of the brachial plexus and can be reached with an infraclavicular approach. However, in order to achieve anaesthesia, it is mandatory to block even the suprascapular nerve, which originates from the superior trunk, and the supraclavicular nerves, which originate from the cervical plexus. As a result, in study I, we performed a combination of superficial cervical plexus block, anterior suprascapular block and lateral sagittal infraclavicular block.

As previously described in section 5.2.2, the shoulder relevant nerves at the infraclavicular level are the subscapular, axillary and lateral pectoral nerves, originating from the posterior and lateral cords, respectively. Hence, we hypothesised that blocking the medial cord may be unnecessary and we therefore wanted to determine MEV_{50} and estimate MEV_{95} for a single-deposit infraclavicular posterior and lateral cord block using ropivacaine 7.5 mg/ml.

In study I, we observed that the combination of SCPB, SSNB and LSIB provided surgical anaesthesia for arthroscopic shoulder surgery. Its most important limitations were that it was technically challenging, time consuming and the total dose of local anaesthetic was fairly high. In study III, we therefore wanted to apply the results from study I and II and explore a simpler sequence of nerve blocks, in combination with general anaesthesia. By doing this we hoped to both overcome the limitations from study I and enhance patient comfort. Hence, we decided to perform SSNB and the LSIB of the posterior and lateral cords prior to total arthroplasty surgery. In this last trial, the SCPB was discarded and substituted by local anaesthetic infiltration of the wound provided by the surgeon at the end of surgery. This decision was made in order to ease the burden of the procedure for both the operator and the patients.

7.4.1 Superficial cervical plexus block

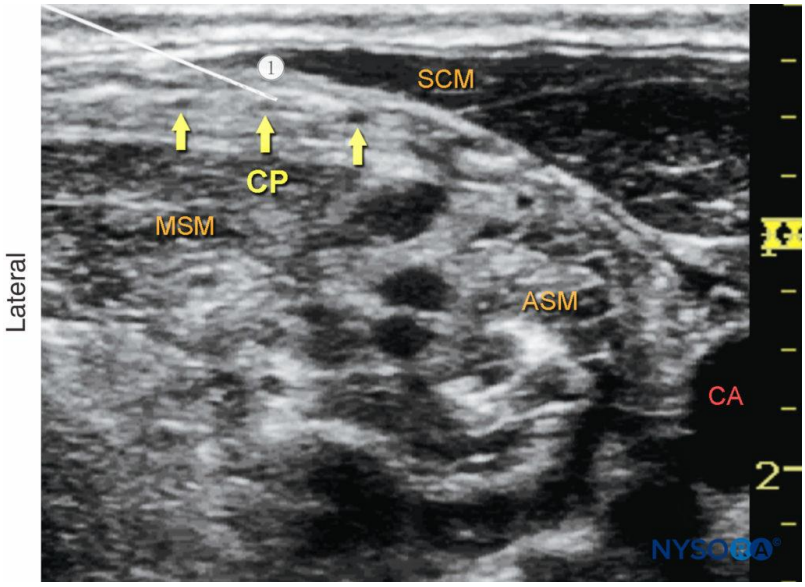

Figure 13 - Superficial cervical plexus block.

Source: NYSORA.com

CP: Cervical plexus. SCM: Sternocleidomastoideus muscle. MSM: Middle scalene muscle. ASM: Anterior scalene muscle. CA: Carotid artery.

We used a slight modification of the method first described by Tran *et al.*[76] The probe was placed axially, just below the midpoint of the sternocleidomastoid muscle, to visualize the intermuscular plane between the sternocleidomastoid and the scalene muscles (between the deep part of the superficial cervical fascia and the prevertebral fascia). The needle was slowly advanced from posterolateral to anteromedial in this potential space, using the in-plane technique. The patient was instructed to signal paraesthesia toward the clavicle or shoulder, while receiving a current of 0.3-0.8 mA, 0.1 ms, 2 Hz. Five ml ropivacaine 5 mg/ml was injected in the described interfascial space with the aim to avoid distribution medial to the interscalene groove. Although the supraclavicular nerves often can be visualized, a systematic search was not performed, because the technique relied on injection of local anaesthetic agents in the intermuscular space and not towards individual nerves.

7.4.2 Suprascapular nerve block

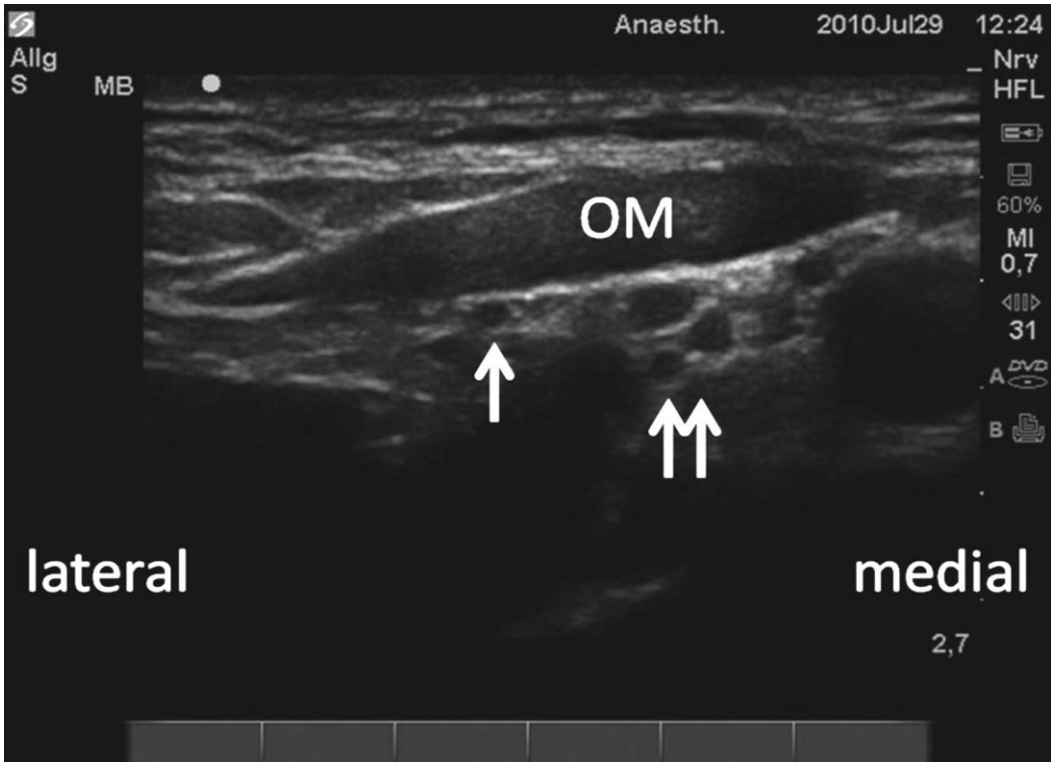

Figure 14 - Ultrasound image of the supraclavicular region.

Source: Siegenthaler et al. 2012, RAPM[77]

Single arrow: Suprascapular nerve. Double arrow: Brachial plexus. OM: Omohyoid muscle.

The supraclavicular approach to the suprascapular block was first described by Siegenthaler *et al.*[77] and has since then undergone some modifications[75,78]. The suprascapular nerve is usually the most craniolateral nerve emerging from the supraclavicular brachial plexus. Sonographically, the nerve can be traced laterally in the posterior cervical triangle, deep to the omohyoid muscle, by tilting the probe incrementally steeper in the caudal direction. This ultrasonographic observation is consistent with anatomical studies by Leung *et al.*[79] The ultrasound probe was placed on the supraclavicular fossa to identify the brachial plexus. Subsequently, the plexus was followed proximally until the suprascapular nerve was observed branching from the superior trunk. The nerve was then followed back distally, until it was visualised deep to the omohyoid muscle. The local anaesthetic was injected at the most lateral short axis view of the nerve that we could obtain with the in-plane technique, while advancing

the needle from posterolateral to anteromedial. In study I, an electric nerve stimulation (0.3-0.8 mA, 0.1 ms, 2 Hz) served to confirm the sonographic identification of the nerve, by palpable contractions of the infra- and supraspinatus muscles. The local anaesthetic dose was 4 ml ropivacaine 5 mg/ml, as described by Flohr-Madsen *et al.*[75]

7.4.3 Lateral sagittal infraclavicular block

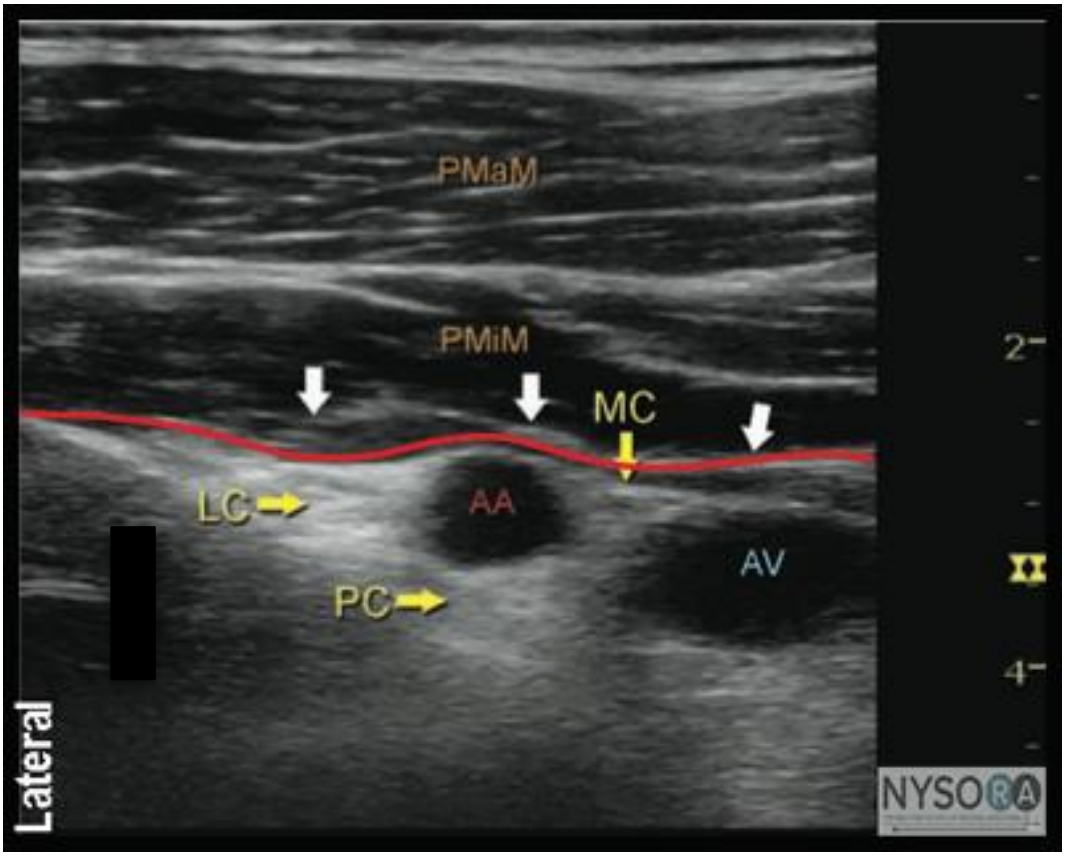

Figure 15 - Ultrasound image of the infraclavicular region.

Source: NYSORA.com

PMaM: Pectoral major muscle. PMiM: Pectoral minor muscle. LC: Lateral cord. PC: Posterior cord. MC: Medial cord. AA: Axillary artery. AV: axillary vein

A periarterial injection technique was used, slightly modified from the method described by Flohr-Madsen *et al.*[80] Usually, the dose was administered by three local anaesthetic deposits. Considering the artery as a clock face with 12 o'clock ventral, the aim was to cover the artery with fluid from 3 to 11 o'clock. The needle insertion point was 0.5-1.0 cm caudal to the lower edge of the clavicle, just medial to the coracoid process. The needle was carefully advanced in

the sagittal plane with the in-plane technique, between the artery and the lateral cord, tangential to the cranial aspect of the artery. The first deposit was at 6 o'clock, the second on withdrawal of the needle between 9 and 11 o'clock and the third at 3 o'clock. The latter deposit required a needle pass ventral to the artery. Total local anaesthetic dose was 31 ml ropivacaine 7.5 mg/ml.

7.4.4 Lateral sagittal infraclavicular block of the posterior and lateral cords

The block was ultrasound-guided, using the in-plane technique. The needle insertion point was 0.5-1.0 cm caudal to the lower edge of the clavicle, just medial to the coracoid process. Needle advancement was in the parasagittal plane, with continuous observation of the needle tip. Considering the artery as a clock face with 12 o'clock ventral, the cords are normally found inside a periarterial sector from 3 to 11 o'clock and within 2 cm from the midaxis of the axillary artery[81]. More specifically, with reference to the centre of the artery, the lateral cord is usually at an angle of 276° and the posterior cord at 236°. This means that the lateral cord is commonly at 9 o'clock and the posterior cord at 8 o'clock in this imaginary clock face. On the basis of this observation we decided to inject the local anaesthetic as a single deposit between 8 and 9 o'clock. In study II, the very aim of the study was to find the MEV for this block. Therefore, the injected volume was variable, ranging from 15 to 6 ml. Despite being the MEV_{95} estimated to be 9 ml, we decided to increase the injected volume to 15 ml in study III, representing a 50% increase from estimated MEV_{99}.

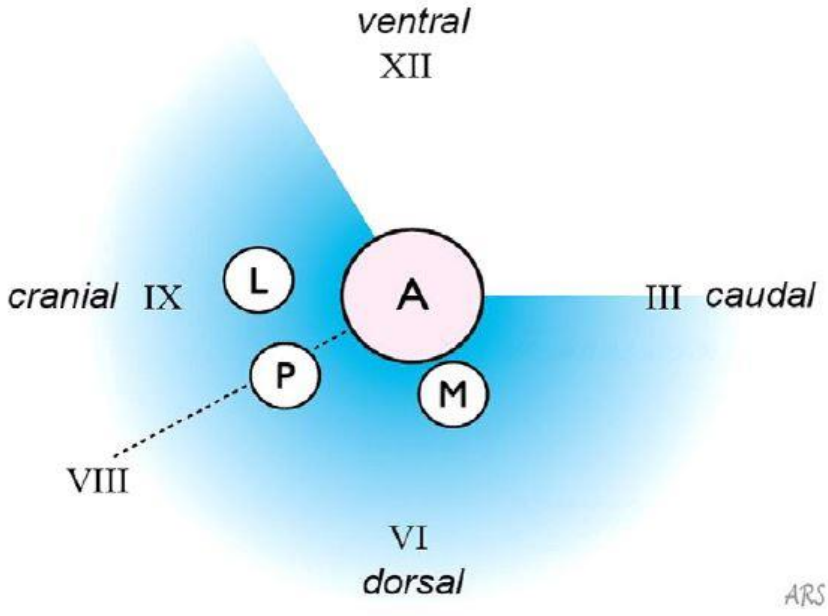

Figure 16 - Schematic drawing in the parasagittal plane of the lateral sagittal infraclavicular block.

Source: Musso et al. 2019, Acta Anaesthesiol Scand[82]. Drawing made by Axel R. Sauter, permission from John Wiley & Sons

The picture shows the axillary artery (A) with clock face orientation (XII o'clock ventral), the cords and position of the deposit at VIII o'clock.

7.5 Block assessment

Neurologic status of the upper limb and the cervical area (study I) was assessed before (baseline) and 30 minutes after completion of the blocks. We performed sensory testing by applying an ice cube on pre-marked points in the areas of cutaneous innervation of several nerves (Figure 17).

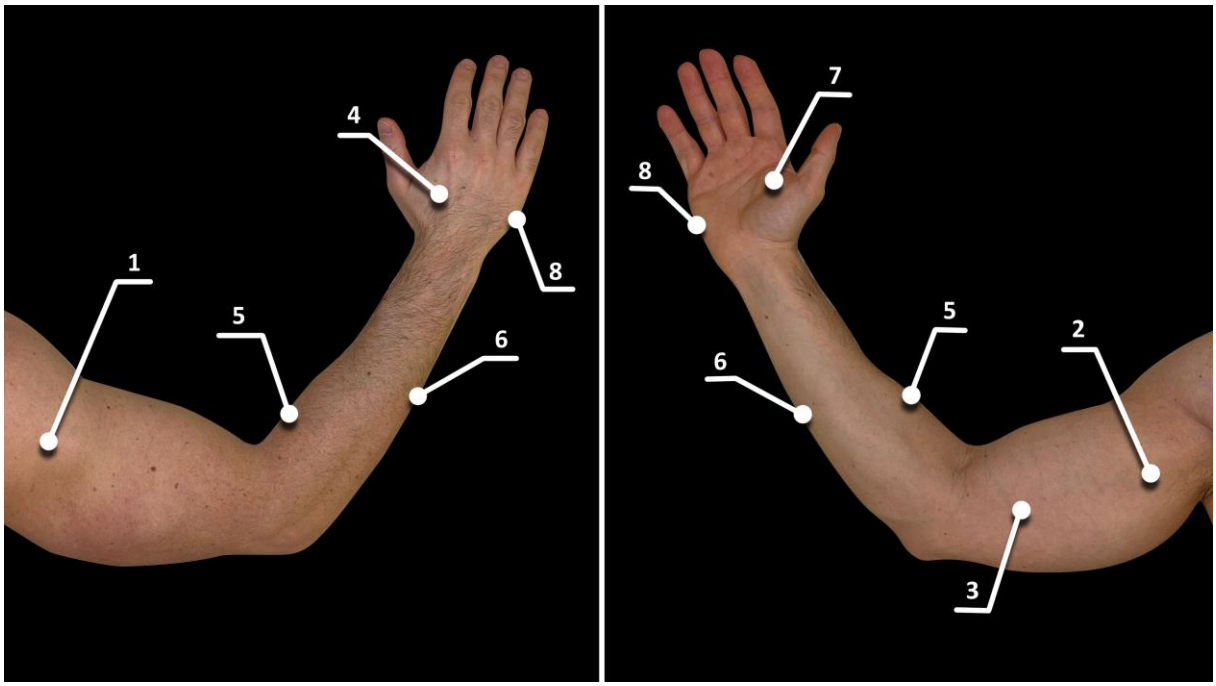

Figure 17 – Sensory testing points. Photo of the author's upper limb.

Dorsal and volar side of the upper extremity. 1: N. axillaris, 2: N. intercostobrachialis, 3: N. cutaneus brachii medialis, 4: N. radialis, 5: N. musculocutaneus, 6: N. cutaneus antebrachii medialis, 7: N. medianus, 8: N. ulnaris

Supraclavicular test points were at the soft spot (the area of the posterior portal used for shoulder arthroscopy, between infraspinatus and teres minor muscles, approximately 2-3 cm inferior and 1-2 cm medial to the posterolateral corner of the acromion) and at the upper border of the clavicle in the midclavicular line. Further sensory testing points included the areas of cutaneous innervation of the axillary, intercostobrachial, medial brachial cutaneous, musculocutaneous, medial antebrachial cutaneous, radial, median and ulnar nerves. These points were in the middle of the proximal half of the humerus laterally, in the middle of the proximal half of the humerus medially, in the middle of the distal half of the humerus medially, on the most prominent part of the brachioradial muscle belly, in the middle of the forearm on the ulnar side, between the first and second metacarpal bone dorsally, between the first and second metacarpal bone volarly and on the ulnar side of the fifth metacarpal bone, respectively.

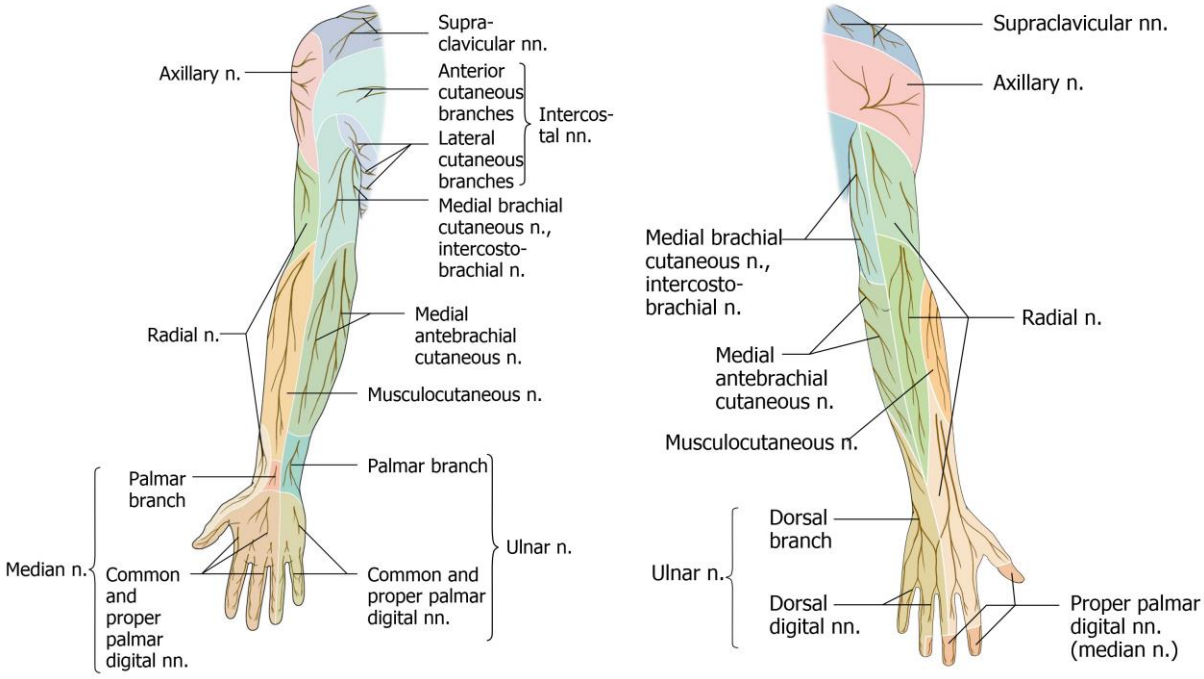

Figure 18 - Cutaneous innervation of the upper limb.

Source: Gilroy et al., Atlas of Anatomy. All rights reserved. © Thieme 2018, www.thieme.com

Individual motor testing was performed according to the following. Axillary nerve block was tested by elevation of the extended upper limb in the sagittal plane. Suprascapular nerve block was tested by the force for lateral rotation of the humerus against manual resistance, while the arm was adducted and the elbow flexed at 90°. Subscapular nerve block was tested by the force for medial rotation of the humerus against manual resistance, while the arm was adducted and the elbow flexed at 90°. Musculocutaneous nerve was tested by flexion of the elbow with supinated forearm. Radial nerve was tested by extension of the elbow and extension of the wrist. Median nerve was tested by flexion of the distal phalanx of the second finger. Ulnar nerve was tested by abduction of the fingers[83]. A synopsis of the tests is presented in Table 2.

Table 2 - Sensory and motor test		
Nerve	*Sensory test*	*Motor test*
Suprascapular	-	External rotation of the arm
Subscapular	-	Internal rotation of the arm
Supraclavicular	Soft spot and upper border of the clavicle (midclavicular line)	-
Axillar	Middle of the proximal half of the humerus, laterally	Elevation of the extended upper limb, in the sagittal plane
Intercostobrachial	Middle of the proximal half of the humerus, medially	-
Medial brachial cutaneous	Internal side of the arm, caudally	-
Radial	Between I and II metacarpal, dorsally	Extension of the elbow and of the wrist
Musculocutaneous	Over the most prominent part of the brachioradial muscle	Flexion of the elbow
Medial antebrachial cutaneous	Middle of the forearm, ulnar side	-
Median	Between I and II metacarpal bones, volarly	Flexion of the distal phalanx of the 2nd finger
Ulnar	Medial side of the 5th metacarpal bone	Abduction of the fingers

For the sensory test, a four-point scale was applied:

Table 3 - Sensory assessment scale	
3	Normal cold feeling
2	Reduced cold feeling (hypoalgesia)
1	No cold feeling, but feels touch (analgesia)
0	No cold or touch feeling (anaesthesia)

On the contrary, the muscle power was assessed using a modified seven-point scale[84]:

Table 4 - Motor assessment scale	
5	Normal power
4+	Active movement against gravity and resistance (> 50% of normal power)
4-	Active movement against gravity and resistance (< 50% of normal power)
3	Active movement against gravity
2	Active movement with gravity eliminated
1	Flicker or trace contraction
0	No contraction

The final block success was assessed 30 min after withdrawal of the needle upon the last block.

7.5.1 Success criteria

The scoring systems presented in Table 3 and 4 were applied in the different studies. How this was applied to assess the blocks is presented in the following section.

7.5.1.1 Study I

The initial success criteria in study I are shown in Table 5.

Table 5 *- Success criteria for study I, patients # 1-7*	
1	Superficial cervical plexus block ≤ 1
2	Suprascapular nerve block ≤ 2
3	Lateral sagittal infraclavicular block (axillary sensory point) ≤ 1

Patients who failed the success criteria were followed up with repeated assessments until admittance to the operation theatre. The criteria for acceptance to surgery were changed during the study, as shown in Table 6. This change was due to increasing clinical experience, which made use quite confident that the first set of criteria was too conservative. Furthermore, the observation of the use of more permissive success criteria by other research groups (Rothe et al.[78]) corroborated our decision.

	Table 6 *- Success criteria for study I, patients # 8-20*
1	Superficial cervical plexus block ≤ 1
2	Suprascapular nerve block ≤ 4-
3	Lateral sagittal infraclavicular block (axillary sensory point) ≤ 1

7.5.1.2 Study II

Only the nerves arising from the posterior and lateral cords were considered in the assessment of block success, as shown in Table 7.

	Table 7 *- Success criteria for the infraclavicular block of the posterior and lateral cords*
1	Posterior cord: axillary nerve sensory score ≤ 1
2	Lateral cord: musculocutaneous nerve sensory score ≤ 1 OR musculocutaneous nerve motor score ≤ 4-

The rationale for the mixed sensomotoric success criteria for the musculocutaneous nerve was due to an anatomic consideration, namely the possible anastomoses between the median and musculocutaneous nerves[85], which may have interfered with sensory testing of the lateral cord.

7.5.1.3 Study III

Block success was assessed by applying the following criteria:

Table 8 - Success criteria for the combination of suprascapular block and infraclavicular block of the posterior and lateral cords

1	The suprascapular nerve block motor score ≤ 4-
2	The axillary nerve sensory score ≤ 1 (posterior cord)
3	The musculocutaneous nerve sensory score ≤ 1 OR musculocutaneous nerve motor score was ≤ 4- (lateral cord)

7.6 Assessment of diaphragmatic motion

As opposed to the first two studies, in study III we implemented the assessment of diaphragmatic motion. This was performed by a blinded investigator using ultrasound before and 30 minutes after the blocks. The liver and spleen served as acoustic windows on the right and left side, respectively. Hemidiaphragmatic paralysis was defined as the absence of diaphragmatic motion during normal respiration coupled with absent or (paradoxical) cranial diaphragmatic movement when the patient forcefully sniffed. Patients with a positive ultrasound scan underwent a chest x-ray to confirm the diagnosis.

7.7 Registrations of adverse events

The list of adverse events recorded included paraesthesia, vessel puncture, systemic local anaesthetic toxicity, Horner's syndrome, dyspnoea, hoarseness, and dysphagia. Lung ultrasound was used to excluded pneumothorax within 15 min after completed block procedure.

7.8 Intraoperative treatment

7.8.1 Study I

All patients were offered propofol sedation to maintain a sedation score between -2 and 0 on the Richmond Agitation and Sedation Scale[86]. The protocol required that no other sedatives or analgesics were administered.

7.8.2 Study II

Study protocol was terminated after the clinical assessment at 30 minutes. All patients received subsequently a complementary LSIB to ensure anaesthesia for hand surgery. No intraoperative data collection was performed.

7.8.3 Study III

All patients underwent general anaesthesia with endotracheal intubation using target-controlled infusion (TCI) anaesthesia with propofol and remifentanil. Perioperative adjuvants included 4 mg dexamethasone administrated intravenously, and the infiltration of the surgical incision with 20 ml bupivacaine 2.5 mg/ml with adrenaline 5 µg/ml at the end of surgery.

7.9 Postoperative assessment

7.9.1 Study I

All patients were interviewed in the recovery room and by phone on the first postoperative day. In the recovery room, postoperative nausea and vomiting (PONV), pain at rest (numerical rating scale, 1-10), medication, signs of Horner's syndrome, hoarseness, dyspnea, or dysphagia were recorded. The same questions were repeated on day one. Additionally, we asked about time to pain debut, average and maximum pain scores at rest (numerical rating scale, 1-10) and

patients' total intake of analgesics. Analgesics were converted to oral morphine equivalents (OMEq). Patients' overall satisfaction score was assessed by asking them, both in the recovery room and during the follow-up telephone call, if they would prefer the same type of anesthetic technique for a similar operation in the future. The surgeons' judgement of the operative conditions was given by the operator in the recovery room immediately after surgery.

7.9.2 Study II

Study protocol did not include intra- or postoperative follow up. However, we ensured that all patients received a successful complementary LSIB and that this block provided anaesthesia without any adverse effects on the study day.

7.9.3 Study III

All patients received 1 g paracetamol four times daily and 10 mg prolonged-release oxycodone tablets twice a day. First dose was given postoperative at 6:00 pm. In the post-anaesthesia care unit (PACU), rescue pain medication was given as intravenous morphine. In the hospital ward, rescue pain medication was given as oxycodone, either orally or intravenously.

NRS (0-10) pain score was recorded at 1 hr, 3 hrs, 6 hrs, 8 hrs, and 24 hrs after arrival to the PACU. Occurrence of postoperative nausea and vomiting (PONV) in the PACU was registered. All patients were interviewed by DM after the first postoperative day and opioid consumption was converted to OMEq[87]. Static median NRS pain score and maximum NRS pain score during the first 24 postoperative hours were recorded. Conversion factors are presented in Table 9.

Table 9 – OMEq conversion factors	
Morphine p.o.	1
Morphine i.v.	3
Oxycodone p.o.	1.5
Oxycodone i.v.	3
Tramadol p.o.	0.2
Codeine p.o.	0.13

7.10 Statistics

In study I, we calculated the sample size with the presupposition of a block success rate of 90% with a confidence of interval of ±13%. This would require a total number of 20 patients included. In study II, we used the staircase up-and-down method to determine MEV_{50} and its 95% CI[88]. To estimate MEV_{95}, logistic regression and probit transformation were used. The first patient received 15 ml, which we clinically considered, *a priori*, to be an appropriate volume of local anaesthetic. In case of failure, the next patient received a higher volume, defined as the previous volume with an increment of 1 ml. If the previous patient had a successful block, the next subject received the previous volume with a decrement of 1 ml. As study III was an exploratory case series, no formal power calculation was performed. *A priori*, we decided to include 20 patients as we believed that data would provide enough information about the efficacy of this block combination as well as serving as a data source for power calculation and sample size estimation in future studies.

7.11 Ethical considerations and approvals

Study I was approved by the Institutional Board at the University Hospital of North Norway (registration number 0472) and registered at www.clinicaltrials.gov (NCT02809144). Study protocol was reviewed by the Regional Committee for Medical and Health Research Ethics (REK nord, TANN-bygget, UiT-The Arctic University of Norway, 9037 Tromsø, Norway). The Committee classified the study as a quality improvement project, which does not require an ethical approval. However, their assessment was recorded with the approval number 2015/2229 on 13th November 2015. In the final published manuscript, only the Institutional Board assessment registration number and Clinical Trials registration number were included.

Study II was approved by the Institutional Board at the University Hospital of North Norway (registration number 0676) and the Regional Committee for Medical and Health Research Ethics (REK nord, TANN-bygget, UiT-The Arctic University of Norway, 9037 Tromsø, Norway). It received approval number 2017/464 on 26th October 2017 and was registered at www.clinicaltrials.gov (NCT03329456).

Study III was approved by the Institutional Board at the University Hospital of North Norway (registration number 02232) and the Regional Committee for Medical and Health Research Ethics (REK nord, TANN-bygget, UiT-The Arctic University of Norway, 9037 Tromsø, Norway). It received registration number 2018-2081 REK Nord, 2nd November 2018), Nordland Hospital in Bodø (registration number 02-19, 28th January 2019), and Sørlandet Hospital in Kristiansand (registration number 01-20, 15th January 2020). It was also registered at www.clinicaltrials.gov (registration number NCT 03877835, 18th March 2019). All the trials were performed in accordance with the Helsinki Declaration.

All study participants received oral and written information about the actual study. Signed consent was obtained before patients were formally included. They also received information about the possibility to withdraw their consent at any time, before, during and after the trial. The research group was not involved in the indication for surgery

In study I, we applied regional anaesthesia with only light sedation. This protocol was not controversial as our anaesthetist colleagues in Narvik had practiced this combination for years. In Tromsø, light sedation was not common practise for this type of surgery, but accepted as a good alternative for arthroscopic shoulder surgery. The anaesthesiologic risks in this setting are mainly related to the combination of beach chair position and general anaesthesia, rather than to regional anaesthesia itself. Accordingly, we could not identify major any extra risk in the procedure. On the contrary, awake surgery may have been protective.

In study II we performed LSIB on patients scheduled for hand surgery, which is the standard anaesthetic procedure for this type of surgery in our hospital. The supplementary LSIB block was performed on a partly anaesthetised brachial plexus. This procedure may carry a higher risk for nerve injury due to lack of patient response and the fact that nerve stimulator in this setting is unreliable. Nevertheless, it is acceptable practice to perform peripheral nerve blocks on patients receiving general anaesthesia or complementary blocks in case of block failure. We therefore considered the benefits for future patients to outweigh the risk for the actual patient.

In study III we tested an alternative to the interscalene block (ISB) for major shoulder surgery. Challenging the gold standard always raises ethical questions, especially around the principle of non-maleficence. On the other hand, the pursue of alternatives to the ISB is well renown and object of study in the scientific community. Given both our practical (study I and II) and theoretical knowledge (anatomic observations), we expected the block combination applied in study III to be a plausible alternative.

8 Results

8.1 Study I

Nineteen out of twenty patients (95% CI: 85-100) underwent arthroscopic shoulder surgery with this triple block and light propofol sedation, but without the need for opioids or artificial airway. Total block performance time was 21.8 (20.4-26.7 [15.9-34.5]), median (IQR [range]) minutes. Propofol dose given was 1.4 (0.4-2.6 [0.0-3.4]), median (IQR [range]) mg/kg/t.

One patient (#5) had successful blocks, but felt uneasy in the beach chair position. After starting light propofol sedation, she became restless and therefore received general anaesthesia. Two patients reported slight discomfort intraoperatively (numerical rating scale 1-2 on a 0-10 scale) located at the posterior portal (soft spot). Both were offered analgesics, but refused. None of the patients required additional local anaesthetic.

Four patients did not fulfil the block success criteria at 30 min, which resulted in a block success rate of 80%. One patient (#7) failed the midclavicular superficial cervical plexus block test at 30 min, but met the success criteria 10 min later. Three patients (#8, #9, and #20) failed the SSN test. Patient #20 and patient #9 met the success criteria 45 and 90 min after the last block, respectively. Patient #8 retained suprascapular nerve mediated muscle power score 4- up to the time of surgery. In spite of this suboptimal score, we decided to proceed to surgery. The precondition was to convert to general anaesthesia if the slightest intraoperative pain occurred. The patient did not experience any pain during surgery and received only propofol according to the protocol.

No signs of LAST were observed. One vascular puncture was registered (LSIB) and four patients reported paraesthesia (SCPB: 1, SSNB: 2, LSIB: 1). None of the patients showed sonographic signs of pneumothorax. In the PACU none of the patients suffered from

nausea/vomiting, dyspnoea, hoarseness, or dysphagia. One patient demonstrated temporary Horner's syndrome and one patient reported a pain score of 2 (numeric rating scale 0-10), while the others were pain free. No drugs were required. Accordingly, in the PACU all the patients were very satisfied with the regional anaesthesia. Furthermore, all of them wished to receive the same regional anaesthesia, should they require the same type of surgery in the future.

Patient #3 was excluded from post-operative day one data analyses because of protocol violation by receiving 16 mg dexamethasone i.v. intraoperatively. During the telephone interview on the first post-operative day, no patient reported PONV, dysphagia, dyspnoea, or hoarseness. Time to pain onset was 12.5 (11.7-14.8 [7.6-15.6]), median (IQR [range]) hours. Average pain score at rest was 0 (0-2.3 [0-6]), median (IQR [range]). Maximum pain score was 5 (3.5-8.5 [0-10]), median (IQR [range]). Analgesic opioid consumption was 40 (30-60 [0-100]), median (IQR [range]) mg OMEq during the first 24 h after surgery. Surgeons were satisfied with the working conditions in 19 of 20 patients (all except patient #5) and would recommend this novel block combination to all new patients scheduled for arthroscopic shoulder surgery.

8.2 Study II

Block performance time was 3.7 (2.9-7.7) median (range) minutes. Only one patient required premedication and received 50 μg fentanyl for the block procedure. Transient paraesthesia with a duration of 1-2 seconds was recorded in two patients. Vascular puncture of a small vein was recorded in one patient, but without any signs of local haematoma. There were no signs of LAST and pneumothorax was not detected by lung ultrasound in any patient.

Ropivacaine 7.5 mg/ml was injected in a volume range from 6 to 15 ml. The up-and-down sequence is shown in Figure 18. The MEV_{50} was calculated to 7.8 ml (95% CI, 7.3-8.4) and MEV_{95} was estimated to 9.0 ml (95% CI, 7.8-10.3).

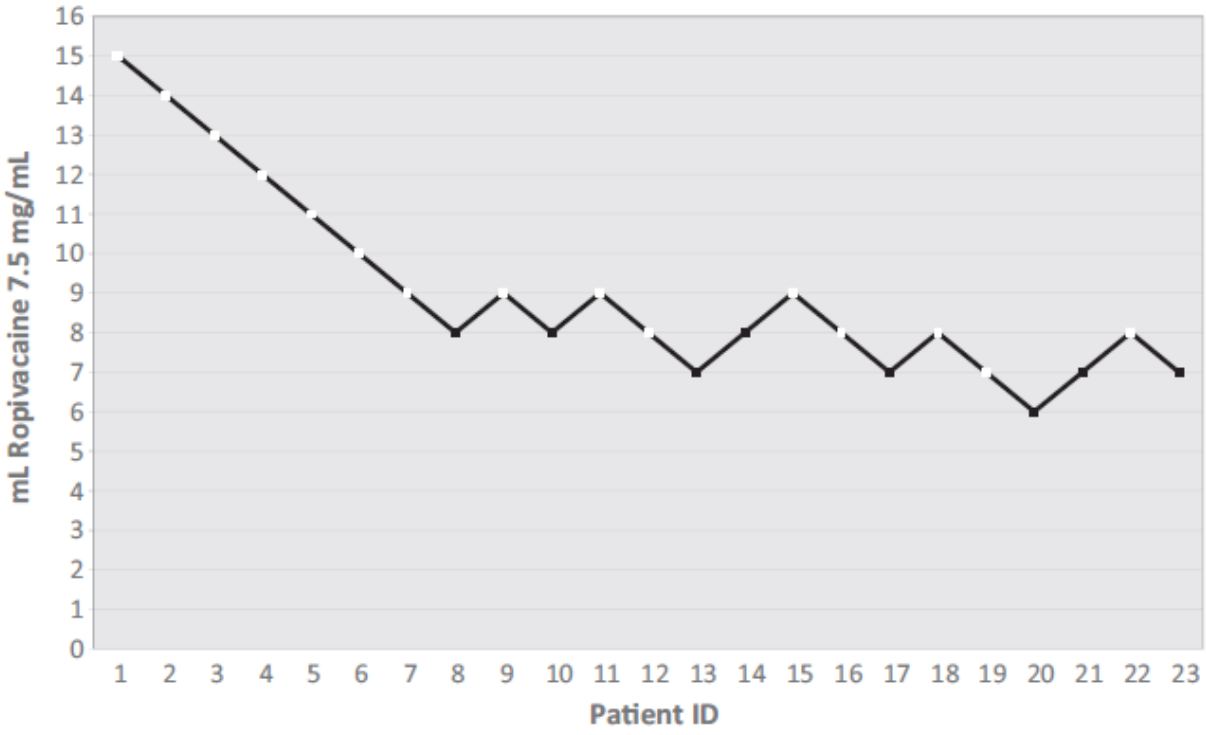

Figure 19 - Up-and-down sequence of the ultrasound-guided block of the posterior and lateral cords of the infraclavicular brachial plexus using ropivacaine 7.5 mg/ml.

Source: Musso et al. 2019, Acta Anaesthesiol Scand[82]

8.3 Study III

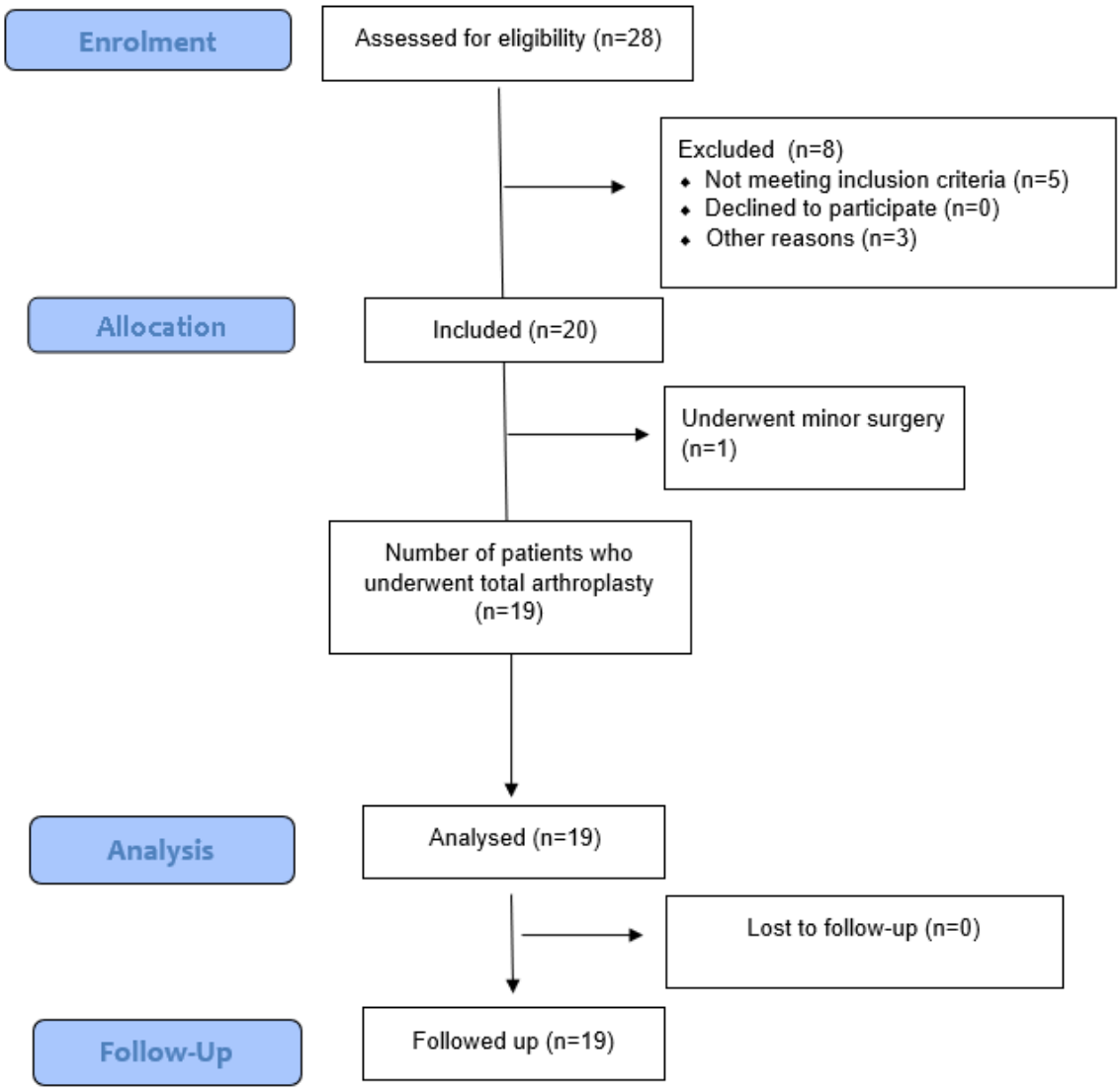

Figure 20 - Patient flow diagram in study III.

Source: Musso et al. 2021, Acta Anaesthesiol Scand[89]

Twenty-eight consecutive patients scheduled for shoulder arthroplasty were screened. Of these, 20 patients fulfilled the inclusion criteria (Tromsø: 9, Bodø: 9, Kristiansand: 2). One patient did not receive total arthroplasty and was therefore excluded from the data analyses.

The block combination was successful in 18 out of 19 patients (95%) after 30 minutes. The failed block was due to late onset of the SSNB in patient #6, but met the success criteria after 35 minutes. We applied the intention-to-treat principle and therefore included all 19 patients in the subsequent analyses.

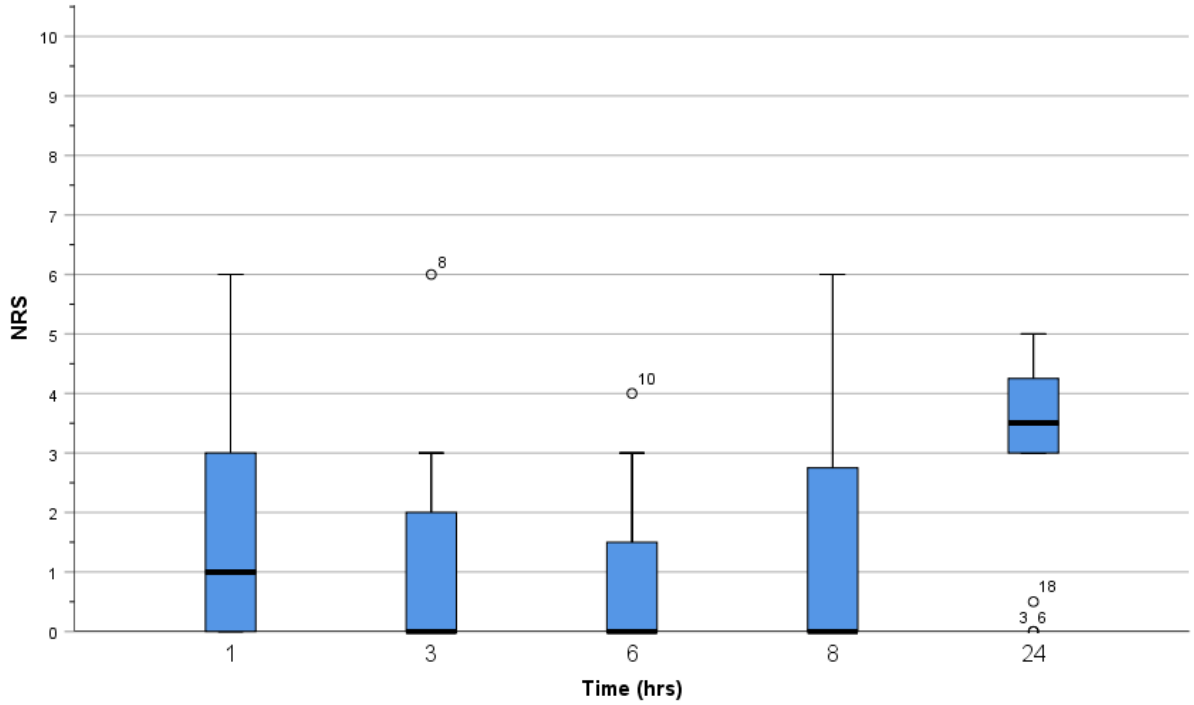

Figure 21 - Boxplot with NRS values 1, 3, 6, 8 and 24 hours after arrival to the PACU (study III)
Source: Musso et al. 2021, Acta Anaesthesiol Scand[89]

Time to pain onset was 12.7 (0-19.5 [0-21.7]) median (IQR [range]) hours. During the first 24 hours, average pain score at rest was 4 (2.5-4.5 [0-5]), median (IQR [range]). Maximum pain score was 6.5 (5-8 [0-10]) median (IQR [range]). Median NRS values 1, 3, 6, 8 and 24 hours after arrival to the PACU are shown in Figure 20. Cumulative OMEq over time, with and without the scheduled prolonged-release oxycodone, are shown in Table 9. Median consumption of OMEq during the first 24 postoperative hours was 52.5 (30-60 [26.4-121.5]) (IQR [range]) mg.

	PACU	0-8 hrs	0-24 hrs
Rescue OMEq	0 (0-0 [0-24])	0 (0-0 [0-31.5])	22.5 (7.5-30 [0-91.5])
Total OMEq	0 (0-0 [0-24])	15 (15-15 [15-46.5])	52.5 (30-60 [26.4-121.5])

Table 10 - Cumulative doses of rescue OMEq and total OMEq over time.

Values are median (IQR [range]).

No signs of LAST were observed. No vascular punctures were registered and two patients reported paraesthesia (LSIB: 2). None of the patients reported dysphagia, dyspnoea or hoarseness. No cases of Horner's syndrome were observed and none of the patients showed ultrasonographic signs of pneumothorax. One patient (5%) was diagnosed with hemidiaphragmatic paralysis, which was confirmed by chest x-ray.

Total block performance time was 7.2 (6.8-7.8 [6.3-10.5]), median (IQR [range]) minutes.

In the PACU, no patients suffered from PONV. Three patients required intravenous morphine and mean NRS in this group of patients was 3.5. The mean morphine dose administered to these three patients was 5.1 mg.

9 Discussion

In recent years, we have witnessed an increasing interest in alternative peripheral nerve blocks to provide analgesia for shoulder surgery[41,42]. This has resulted in a plethora of studies investigating nerve blocks from nerve root to terminal nerve level. Our focus has been at the cord level and, therefore, on the infraclavicular block. The rationale for this is simple. One of the most distal approaches described for shoulder analgesia is by injection close to terminal nerves, namely the combination of suprascapular and axillary nerve blocks. These distal blocks may provide good postoperative analgesia after shoulder arthroscopy, but their use in more extensive surgery has not been recommended[90-92]. This is allegedly due to the contributions of proximal branches from the axillary nerve, the subscapular and lateral pectoral nerves, all arising from the posterior and the lateral cord of the brachial plexus. Hence, the infraclavicular block is theoretically expected to result in a better analgesic profile, by blocking all these branches. At the same time, this may and can be achieved with a single deposit technique performed further away from the phrenic nerve, when compared to alternative supraclavicular approaches. The triple block combination described in study I showed some practical limitations, mostly related to the infraclavicular block. In order to solve some of these issues, in study II, we designed a nerve block targeting the posterior and the lateral cords. The results suggested the possibility to explore a combination of anterior suprascapular nerve block and lateral sagittal infraclavicular block of the posterior and lateral cords and its effect om postoperative analgesia, which was the main object of study in our third trial. Study limitations of our three studies are presented throughout the discussion and divided in the topics highlighted by the section title.

9.1 Study design

Observational studies (study I and III) carry some intrinsic limitations that would otherwise be addressed in a randomised control trial. On the other hand, exploratory studies have a role in strengthening new knowledge and in developing new methods. From this point of view, our case series may be considered as preliminary works preceding future randomised controlled trials. Furthermore, because of the demographics in Northern Scandinavia, a randomisation in two groups would have taken a very long time to complete, raising ethical questions concerning the optimal use of research funds.

Concerning study II, we decided to apply the staircase up-and-down method for this study. To assess the 50^{th} interquartile in a MEV-study, an initial volume must be chosen. This value can be selected as the lowest value expected to result in a successful block. Alternatively, it can be picked out in an arbitrary fashion with the volume administered to each patient dependent on the response of the previous one. In case of failure, the next patient received a higher volume, whereas in case of success the next subject received a lower volume. This allowed us to determinate MEV_{50} and to estimate MEV_{95} by using logistic regression and probit transformation. Saranteas *et al.*[93] have pointed out that selection of the initial dose may bias the outcome. Another main weakness was that by targeting the MEV_{50}, the estimation of higher quartiles far away from the mean value would lead to a misjudgement. The biased coin design and the continual reassessment method are two other methods discussed by this group[93]. Both methods have a close mean square error and bestow a better precision of the confidence interval. We are aware that the staircase up-and-down method should primarily be applied for investigation of the 50^{th} quartile and that extrapolations to find MEV_{95} may cause wide confidence intervals. However, in this study 95% CI was quite narrow due to the fact that all block failures appeared in the interval between 6 and 8 ml. The main reason why we chose the

staircase up-and-down method was because it required a lower number of subjects compared to other methods. Pilot data indicated that we could expect a substantial reduction in the volume needed to obtain a block of the posterior and lateral cords compared to the volume needed to block all three cords[80]. The results of our study showed that the actual effective local anaesthetic volumes were much lower than 15 ml, which was the starting volume. However, this did not affect the calculations of the MEV_{50} and MEV_{95} since all block failures appeared in the interval between 6 and 8 ml.

9.2 Technical and anatomical considerations

The block combination proposed in study I consisted in a superficial cervical plexus block, a suprascapular block and a lateral sagittal infraclavicular block. The anatomic rationale for this has been explained in section 5.2. The cutaneous innervation of the shoulder is mainly provided by the supraclavicular nerves and the axillary nerve[8]. The first of these are not derived from the brachial plexus, but arise from the superficial cervical plexus. The shoulder joint is mainly innervated by the suprascapular and the axillary nerve, but receives contributions from the subscapular and the lateral pectoral nerves[9,10]. The suprascapular nerve derives from the upper trunk. The axillary and the subscapular nerves are derived from the posterior cord of the brachial plexus, whereas the lateral pectoral nerve originates from the lateral cord. Thus, the latter four nerves can be blocked with a single injection by the infraclavicular block.

In study I, we described an anaesthetic triple nerve block alternative to the interscalene block for arthroscopic shoulder surgery[94]. A triple block is obviously more technically demanding and time consuming when compared to the interscalene block[62]. However, in order to provide surgical anaesthesia, the alternative of low volume interscalene block, requires an additional anaesthesiologic technique (sedation/general anaesthesia, local skin infiltration or a supraclavicular nerve block), which is time consuming as well. On the other hand, a high

volume interscalene block consistently blocks the supraclavicular nerves[11], but carries such a high incidence of phrenic block that this complication should be taken as granted.

The relatively large LA dose of the infraclavicular component had been a concern to us due to the possible risk of toxicity and potential for spread of LA to the phrenic nerve[95]. To potentially reduce LA volume for this block, we decided in study II to explore the possibility of targeting only two of the three cords. As previously mentioned, this appeared reasonable since the shoulder relevant nerves of infraclavicular origin are the axillary nerve, the subscapular nerves and lateral pectoral nerve, of which the first ones are derived from the posterior cord and the latter from the lateral cord. The position of the three cords has previously been examined by MRI in 20 volunteers[81,96]. Based on our extrapolation of the authors' description, we decided to target the posterior and lateral cords with a single deposit injection between 8 o'clock and 9 o'clock. We believed that this method, built on simple sonographic reference points, would decrease ultrasound apparatus requirements and operator-dependent variations in performance. However, we were aware that this approach does not take into account the anatomical variations of the positions of the cords and, as a result, it may have had an effect on the volume needed to block the cords.

When the study was completed, we found the estimated MEV_{95} to be 9.0 ml (95% CI, 7.8-10.3 ml), which is considerably lower than the volume used in our previous study[94]. We indeed had some effect on the medial cord as well. However, this was not unexpected, since this LSIB-variant was meant to effectively block the lateral and the posterior cords, with little regard for the medial cord. It is certainly possible to inject selectively towards the individual cords[97], but it should be noted that identifying all cords by ultrasound may be challenging[98] and the ability relies on both the operator and the resolution of the ultrasound unit.

Technically, the block was easy and quick to perform. Only one needle pass was required for 87% of the patients and the mean block time was 3.7 minutes.

One more issue related to study I was that a triple block implied a technical complex procedure with a relatively long performance time. To solve these matters, we decided in study III to explore the postoperative analgesic profile of a combination two blocks, namely anterior suprascapular nerve block and lateral sagittal infraclavicular block of the posterior and lateral cords. As opposed to the block combination in study I, the block combination in study III did not aim to provide surgical anaesthesia, but rather provide effective postoperative analgesia, since the supraclavicular nerves were not anaesthetised. It was therefore required that the surgeon supplied the cutaneous area with local infiltration anaesthesia. Although the MEV_{95} of the infraclavicular block of the posterior and lateral cords described in study II was estimated to be 9 ml, we opted for a higher volume (15 ml), to prevent the risk of inadequate post-operative analgesia.

To our knowledge, the minimum effective dose for a successful SSNB is currently unknown. A lower volume for a successful block has been described[78], but the clinical analgesic effect of this approach remains unexplored. Nonetheless, our previous experience with the triple block of SCPB, SSNB and LSIB in study I[94] encouraged us to apply the same SSNB dose (4 ml ropivacaine 5 mg/ml) in study III, yet further clinical studies are required to define the optimal SSNB dose.

9.3 Success criteria

The suprascapular nerve seldom has sensory branches to the skin[99,100]. We therefore used a muscle power test as a surrogate test for the sensory assessment of the suprascapular nerve block, even though this may imply imprecisions in both density and onset time of the block[17].

After study I was initiated, we started to speculate whether our success criterion for the motor test was too strict (motor score ≤ 2, or "active movement with gravity eliminated"). Consequently, we allowed patients with a weaker motor block to proceed to surgery in accordance to the intraoperative study protocol. These patients did not experience any pain and received propofol as per protocol. This is the reason why, after the study was started, we changed to a more liberal motor success criterion for acceptance to surgery (motor score ≤ 4-). Although we can only speculate about their reasoning, other authors have come to similar conclusions regarding success criterion after a suprascapular block[78].

In study II, our success criteria were based on the assessment of the posterior and the lateral cords. The posterior cord block was considered successful if the sensory score for the axillary nerve was ≤ 1. In that case, also the subscapular nerve was assumed to be blocked, since both nerves derive from the posterior cord. The success criteria for the lateral cord block were slightly more complex. Our nerve of interest was the lateral pectoral nerve, which lacks a cutaneous innervation[101]. As a surrogate, we tested another nerve of the lateral cord, the musculocutaneous nerve. This raised another issue. It is clinically acknowledged that anastomoses between the lateral and medial cords are common[85] and may interfere with sensory testing after an infraclavicular block. These anatomical variations may be the reason why we, in the pilot phase, observed patients with paralysis of the biceps muscle (musculocutaneous nerve), in spite of intact sensory function in the cutaneous area of this nerve. The normal sensibility may then have been provided by anastomoses between the musculocutaneous and median nerve, with the median nerve not affected by local anaesthetic. Accordingly, the success criterion for the lateral cord (which assumed the effect on the lateral pectoral nerve) was therefore defined as either a sensory test of ≤ 1 in the cutaneous area of the musculocutaneous nerve or a biceps motor score of ≤ 4-.

In study III we applied the same success criteria as in the first two studies.

9.4 Preoperative analgesic regime

In study I and III, no preoperative analgesics were administered. In study I, we aimed to achieve an anaesthetic block, where systemic medication during surgery would have either been unnecessary or a confusing factor for the evaluation of the block combination. In study II, our data collection was limited to the block assessment and did not affect planned treatment. In study III, we feared that systemic medication would interfere with our data collection without offering any clear advantage. This decision was ethically justified, since pilot patients experienced very low, if any pain in the PACU.

9.5 The pursuit of a diaphragm-sparing block

In study I, the block combination consisted of a superficial cervical plexus block, a suprascapular block and a lateral sagittal infraclavicular block, all of which may potentially have an impact on diaphragmatic function.

Since injection site for the superficial cervical plexus block is anatomically close to the phrenic nerve and the brachial plexus, both structures may potentially become affected[102] if the local anaesthetic penetrates the prevertebral fascia and diffuses into the interscalene groove and to the superficial aspect of the anterior scalene muscle. However, to our knowledge there are no reports of phrenic nerve block associated with ultrasound-guided superficial cervical plexus block[76,103] and the incidence of this event is historically very low[104]. Nevertheless, to further reduce the risk of phrenic nerve block, we used a lower volume of local anaesthetic than in the studies by Tran *et al.* and Gürkan *et al.*[76,103]

The suprascapular nerve block has traditionally been performed via a posterior approach, targeting the nerve close to the scapular notch, between the scapula and the supraspinatus muscle. The ultrasound-guided supraclavicular suprascapular nerve block was first described

by Siegenthaler *et al.* in 2012[77]. Since then, it has undergone various modifications and become a common used technique, due to the ease of visualisation by ultrasound[77] and better analgesic profile[105] compared to the traditional posterior approach.

In a former study on supination of the hand after ultrasound-guided infraclavicular block, 15 patients received infraclavicular block alone and 15 combined infraclavicular and suprascapular nerve block[75]. Chest radiographs were taken approximately 75 min after the blocks and there were no signs of diaphragmatic paresis or paralysis. This may suggest that neither infraclavicular nor suprascapular block, or the combination of them, challenges the phrenic nerve. However, in another recent study of 32 patients receiving ultrasound-guided infraclavicular block, one patient developed hemidiaphragmatic paralysis and three patients developed hemidiaphragmatic paresis, as diagnosed by M-mode ultrasonography[95]. The authors emphasize that though this risk appears to be low, it is not zero. Suggested possible explanations include distribution of local anaesthetic proximally along the course of the brachial plexus and further to the phrenic nerve or anatomic variations, such as aberrant phrenic nerve anatomy or an accessory phrenic nerve[15,16]. In study III, we reported one case of hemidiaphragmatic paralysis, which accounts for a 5% incidence. Unfortunately, the mechanisms for how the phrenic nerve became anaesthetised can only be speculated on. In this patient (#8), the ultrasonographical visualisation of the SSN proved to be challenging and the nerve was eventually blocked in a more craniomedial position, closer to the cervical structures, with possible cranial spread to the phrenic nerve. This risk has been underlined both in cadaver[106] and clinical studies[64]. The same anatomic variations mentioned by Petrar *et al.*[95] in their study on supraclavicular and infraclavicular blocks may offer an alternative aetiology.

Based on the data from these studies, it is reasonable to assume a lower incidence of hemidiaphragmatic paresis with these techniques compared to the interscalene block, which, despite several modifications, shows an incidence not lower than 27%[41]. Accordingly,

clinicians should be aware of the potential risks associated in patients with impaired respiratory function, no matter the chosen block technique.

Our research group had former experience with assessment of the diaphragm using chest radiographs[75]. The process proved to be challenging, requiring demanding logistics to coordinate with the needs of a busy surgery program. This discouraged us from performing this examination in study I, especially since the trial took place in several hospitals. At first, we felt no need for a specific assessment of the diaphragmatic motion, based on data from previous observations[75,76,103,104]. However, we soon regretted the need to only rely on our assumptions instead of actual observations. This is why we decided to perform an assessment of the diaphragmatic motion by ultrasound in study III. In this study we applied a binary scale, because we feared that a more fine-tuned one would be clinically challenging. This is particularly true on the left side where the spleen can be used as an acoustic window.

9.6 Pain measurements methods

The NRS scale is a validated pain scoring tool, but relies on an accurate patient response. At times, it was challenging to assess the average pain score during the day. Some patients struggled to recall pain levels while others struggled to understand the meaning of this score. To overcome this limitation, OMEq consumption was chosen as an additional primary aim. The option of patient-controlled analgesia (PCA) was considered, but dismissed due to logistical reasons. A clear advantage of this approach would have been to receive data directly from the patient, independent of the interaction with the nurses or other potential bias related to administration of analgesics. Furthermore, PCA would also provide a tailor-made analgesic therapy. We considered NRS assessments at 1, 3, 6, 8 and 24 hours after the arrival to the PACU as clinically relevant time points.

9.7 Perioperative considerations

In study I, no premedication was administered for two reasons. First of all, because the superficial cervical plexus anesthetises the supraclavicular nerves and thus the injection sites of the subsequent blocks. Secondly, the study required an accurate and timely performed neurological assessment before and after the blocks. Therefore, we did not want any sedative or opioid to confound the interpretation of the data. Further positive experiences with this method with only injections of local anaesthetic corroborated our trust in this approach, which was applied in the following studies as well.

As previously discussed in the introduction, the beach chair position during shoulder surgery is encumbered with a high incidence of arterial hypotension, especially when combined with the ISB, which may lead to different neurological symptoms. Studies using near-infrared spectroscopy (NIRS) has shown a causal relation between arterial hypotension and regional cerebral oxygenation ($rScO_2$)[107]. This may be counteracted by higher mean artery pressure and controlled hypoventilation, resulting in increased p_aCO_2 and thus intracranial vasodilation[108]. However, awake surgery is likely to result in a higher hemodynamic stability, with no effect on the $rScO_2$ and may reduce the risk of neurologic damage[109]. A major advantage of the block combination in study I was that general anaesthesia could be omitted in 19 out of 20 patients. By using only light propofol sedation, we could easily communicate with the patient and thereby directly monitor cerebral function intraoperatively. However, in study III all patients were given general anaesthesia. We made that decision because total shoulder arthroplasty is more invasive and time demanding compared to arthroscopic surgery and we also believe general anaesthesia provides better patient comfort for this type of surgery

9.8 Postoperative considerations

9.8.1 Postoperative analgesic regime

In study I, only one patient reported pain in the PACU. He was offered analgesics, but refused to take any. Since the postoperative pain scores were not among the aims of this study, the postoperative analgesic regime was not part of the protocol either and analgesics were provided according the local standard of care. In study III, we prescribed a postoperative medication protocol consisting of regular administrated peroral paracetamol and prolonged-release oxycodone. Intravenous morphine and peroral oxycodone served as rescue pain medications. Our results are encouraging, since OMEq consumption during the first postoperative day was comparable with other shoulder arthroplasty studies where ISB has been applied[52,110-112]. However, prescription of a more extensive multimodal pain medication strategy could potentially have reduced OMEq consumption. Administration of adjuvants are known to prolong block duration of peripheral nerve blocks[113] and in this study we opted for 4 mg dexamethasone administered intravenously, regardless of patients' body weight. It is possible to speculate that a higher dose[114] or a combination of adjuvants[115,116] could have resulted in longer lasting blocks and thus lower total consumption of OMEq.

Rotator cuff repair is associated with significant postoperative pain. PROSPECT (procedure-specific post-operative pain management) published recommendations for optimal pain management after this type of surgery[117]. These guidelines, though supported by varying degrees of evidence, give the following advices:

Overall recommendations for pain management in patients undergoing rotator cuff repair surgery
Pre-operative and intra-operative
Paracetamol (Grade D)
COX-2-specific inhibitor (Grade D)
Dexamethasone i.v. (Grade B)
Regional analgesia
Interscalene brachial plexus block, continuous (Grade A)
Interscalene brachial plexus block, single-shot (Grade A)
Suprascapular nerve block with or without axillary nerve block (but not as first choice, Grade B)
Postoperative
Paracetamol (Grade D)
COX-2-specific inhibitor (Grade D)
Opioid for rescue (Grade D)
Surgical technique
Arthroscopic technique (Grade B)

Table 11 - PROSPECT guideline for pain management for rotator cuff repair surgery

Table adapted from: Toma et al. 2019, Anaesthesia[117]

The very aim of our research has been to explore possible alternatives to the ISB and in our studies we had several different kinds of surgeries, so these guidelines may not fully apply. Nevertheless, PROSPECT aims to give recommendations for painful shoulder surgery and its guidance is valuable. The most important discrepancy from these guidelines is related to the choice of systemic supplementary analgesia. In study I, pre- and intra-operatively analgesia was not an issue, since the combination of nerve blocks provided surgical anaesthesia. However, the implementation of a single dose of intravenous corticosteroid could have further improved

the quality of the post-operative analgesia. In study III, we did administer dexamethasone intravenously prior to surgery, but the administration of other systemic analgesics (paracetamol and opioids) was delayed until after surgery, which is in contrast with the guidelines from PROSPECT. *A posteriori*, considering the non-anaesthetic effect of the block and some cases of opioid-related nausea and vomiting, a different choice of analgesics, their time of administration and dose could have provided a better outcome. In addition, multimodal analgesia has a proven opioid-sparing effect[118] that our trial did not take advantage of. Paracetamol and NSAIDs[119] are relatively safe choices, whereas codeine and tramadol are encumbered with both more severe side effects and, occasionally, unpredictable analgesic effect[17,120], making their use for treatment of acute pain a matter of debate.

9.8.2 Block duration

Both in study I and III, block duration could not be accurately determined, since block effects wore off during the night and most patients struggled to exactly recall the time when sensory function was restored. However, they could easily place the pain onset on a timeline. Therefore, the time from the retraction of the block needle to first report of pain was used as a surrogate for block duration. It is worth mentioning that in several cases a broad discrepancy between time to first reported pain and time to reported restored sensory status was reported.

Nevertheless, considered the level of pain experienced after the block wore off, the duration of the analgesic effect was shorter than desired. The insufficient duration of single-shot nerve blocks after shoulder surgery is not an unknown issue. Besides the use of dexamethasone as a block adjuvant, discussed in the next paragraph, there are several possible options. Continuous nerve blocks are potentially a good choice, as recommended by PROSPECT. However, this approach demands higher technical skills and resources to follow up, which may be especially challenging to establish in ambulatory surgery settings. Liposomal bupivacaine is currently not

recommended, but may show its value in the coming years or lead the path for new pharmacological developments. Interestingly, a recent trial showed a significant prolonged time to first rescue analgesic after an ISB with intravenously administrated dexamethasone and dexmedetomidine as adjuvants, suggesting a possible synergic effect of these drugs[115].

9.8.3 Dexamethasone as a block adjuvant

The choice of intravenous dexamethasone in study III was not controversial. In a recent study, dexamethasone was administered perineurally or intravenously to prolong the effect of a low-volume ISB. The two approaches were not equivalent, but there were no clinically significant differences in the outcomes[121]. However, the choice of the dose in our study was not as simple. There is reasonable evidence suggesting that 4 mg dexamethasone administrated perineurally may represent an optimal dose[122], while the intravenous route may require a higher dose. According to a meta-analysis, intravenous dexamethasone may provide direct analgesia with doses between 0.1-0.2 mg/kg[114], whereas several studies comparing intravenous and perineural dexamethasone have been designed to answer a specific question concerning equivalence. Whether the intravenous dose should be higher is still an unanswered question, but a recent trial comparing different doses of intravenous dexamethasone combined with ISB for shoulder surgery seems to point in that direction[123].

10 Conclusions

10.1 Study I

The combination of superficial cervical plexus, anterior suprascapular block and lateral sagittal infraclavicular plexus block is feasible and provides surgical anaesthesia and satisfactory post-operative analgesia for patients scheduled for arthroscopic shoulder surgery, offering an alternative anaesthetic modality for this kind of surgery.

10.2 Study II

This single-deposit method to block the lateral and posterior cord of the infraclavicular plexus with ropivacaine 7.5 mg/ ml revealed a MEV_{50} and MEV_{95} of 7.8 mL (95% CI, 7.3-8.4) and 9.0 mL (95% CI, 7.8-10.3), respectively.

10.3 Study III

The combination of suprascapular and infraclavicular nerve blocks shows an encouraging postoperative analgesic profile after total shoulder arthroplasty. Success rate and performance time, together with a reduced risk of hemidiaphragmatic paralysis, suggest that this block combination could be an effective alternative to the interscalene block.

10.4 Overall conclusions

The gold standard for intraoperative and postoperative pain management in patients undergoing shoulder surgery is the interscalene brachial plexus block. However, several alternatives are being explored. Our trials propose different alternatives for major and minor shoulder surgery, with and without general anaesthesia, respectively. The block combinations appear to be feasible and probably with a lower incidence of diaphragmatic paralysis. Further direct comparisons with other nerve blocks are needed to plot out the differences, especially concerning postoperative analgesia and incidence of phrenic palsy.

11 Future perspectives

Data from study I-III open for new areas of interest and further research.

In our trials we explored both an analgesic block combination for minor shoulder surgery and an anaesthetic one for major shoulder surgery, combined with general anaesthesia. These different approaches do not need to be mutually exclusive, but may rather coexist with different indications and in different settings. The triple block combination in study I may be a viable alternative to ISB for shoulder arthroplasty, possibly without general anaesthesia. In our facility, this kind of surgery is not routinely performed with only regional techniques, but this approach is described[124]. Furthermore, it is reasonable to expect that the modified LSIB variant targeting posterior and lateral cords may be applicable. Similarly, the block combination shown in study III should be feasible for shoulder arthroscopy, whenever general anaesthesia would be preferable.

In all these cases our proposed alternatives would profit from a direct comparison with other shoulder blocks (and especially with the ISB) in randomised control trials, in order to provide data rather than conjectures. An improvement to our previous studies would be to implement a wider multimodal analgesic regime, as suggested by PROSPECT guidelines. Studies of the use of peripheral nerve catheters should also be considered as rebound pain is a frequent clinical issue. Outcome measures of particular interest in this context would be the use of opioids, postoperative NRS pain score and incidence of hemidiaphragmatic paralysis.

Another exciting research field would be to explore the effects of various nerve block adjuvants, especially trying out different doses of intravenous dexamethasone and relate them to postoperative outcome. The combination of intravenous dexamethasone and dexmedetomidine should be further explored.

In study II we elaborated data to refine the LSIB for study III. Accordingly, we could reduce the volume of ropivacaine 7.5 mg/ml from 31 ml in study I to 15 ml in study III, with a conspicuous decrease of the dose for total block combination dose from 277,5 mg to 132,5 mg. This was expected to make the technique safer concerning the possible risk of toxicity and, at the same time, allow us to perform rescue blocks in case of block failure, or provide local infiltration anaesthesia in areas with suboptimal anaesthetic coverage. Further MEV studies may be of interest also for the SCPB and SSNB. Even though the volume of the latter two is considerably lower and the advantage regarding toxicity less important, a lower injected volume may further reduce the incidence of diaphragm paralysis with this block combination.

In study II, we decided to design a technique built on simple sonographic reference points, aiming to decrease the requirements of the ultrasound machine and to reduce operator dependency. However, the average skills of anaesthetists in regional anaesthesia are increasing and ultrasound machines are becoming more readily available. A technique based on actual sonoanatomic findings and selective injections towards the individual cords may therefore become a further refinement of this block technique.

12 References

1. Balboni GC, Bastianini A, Brizzi E, et al. Anatomia umana: Edi. Ermes; 1990.
2. Brizzi E, Casini M, Castorina S. Anatomia topografica: Edi. Ermes; 1978.
3. Tran DQ, Tiyaprasertkul W, Gonzalez AP. Analgesia for clavicular fracture and surgery: a call for evidence. Reg Anesth Pain Med 2013;38:539-43.
4. Emamhadi M, Chabok SY, Samini F, et al. Anatomical Variations of Brachial Plexus in Adult Cadavers; A Descriptive Study. Arch Bone Jt Surg 2016;4:253-8.
5. Matejcik V. Variations of nerve roots of the brachial plexus. Bratisl Lek Listy 2005;106:34-6.
6. Singh R. Variations of Cords of Brachial Plexus and Branching Pattern of Nerves Emanating From Them. J Craniofac Surg 2017;28:543-7.
7. El-Boghdadly K, Chin KJ, Chan VWS. Phrenic Nerve Palsy and Regional Anesthesia for Shoulder Surgery: Anatomical, Physiologic, and Clinical Considerations. Anesthesiology 2017;127:173-91.
8. Borgeat A, Ekatodramis G. Anaesthesia for shoulder surgery. Best Pract Res Clin Anaesthesiol 2002;16:211-25.
9. Aszmann OC, Dellon AL, Birely BT, McFarland EG. Innervation of the human shoulder joint and its implications for surgery. Clin Orthop Relat Res 1996:202-7.
10. Tran J, Peng PWH, Agur AMR. Anatomical study of the innervation of glenohumeral and acromioclavicular joint capsules: implications for image-guided intervention. Reg Anesth Pain Med 2019;44:452-8.
11. Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. Reg Anesth Pain Med 2009;34:134-70.
12. Verin E, Marie JP, Similowski T. Cartography of human diaphragmatic innervation: preliminary data. Respir Physiol Neurobiol 2011;176:68-71.
13. Kessler J, Schafhalter-Zoppoth I, Gray AT. An ultrasound study of the phrenic nerve in the posterior cervical triangle: implications for the interscalene brachial plexus block. Reg Anesth Pain Med 2008;33:545-50.
14. Loukas M, Kinsella CR, Jr., Louis RG, Jr., Gandhi S, Curry B. Surgical anatomy of the accessory phrenic nerve. Ann Thorac Surg 2006;82:1870-5.
15. Mendelsohn AH, Deconde A, Lambert HW, et al. Cervical variations of the phrenic nerve. Laryngoscope 2011;121:1920-3.
16. Rajanna MJ. Anatomical and surgical considerations of the phrenic and accessory phrenic nerves. J Int Coll Surg 1947;10:42-52.
17. Hugh C. Hemmings B, Egan TD. Pharmacology and Physiology for Anesthesia: Foundations and Clinical Application: Elsevier Health Sciences; 2013.
18. Becker DE, Reed KL. Essentials of local anesthetic pharmacology. Anesth Prog 2006;53:98-108.
19. Aitkenhead AR, Thompson J, Rowbotham DJ, Moppett I. Smith and Aitkenhead's Textbook of Anaesthesia E-Book: Elsevier Health Sciences; 2013.
20. Culp WC, Jr., Culp WC. Practical application of local anesthetics. J Vasc Interv Radiol 2011;22:111-8.
21. Local anesthetic systemic toxicity. UpToDate, 2019. at https://www.uptodate.com/contents/local-anesthetic-systemic-toxicity.)
22. Chan EY, Fransen M, Parker DA, Assam PN, Chua N. Femoral nerve blocks for acute postoperative pain after knee replacement surgery. Cochrane Database Syst Rev 2014:CD009941.

23. Hadzic A, Arliss J, Kerimoglu B, et al. A comparison of infraclavicular nerve block versus general anesthesia for hand and wrist day-case surgeries. Anesthesiology 2004;101:127-32.
24. O'Donnell BD, Ryan H, O'Sullivan O, Iohom G. Ultrasound-guided axillary brachial plexus block with 20 milliliters local anesthetic mixture versus general anesthesia for upper limb trauma surgery: an observer-blinded, prospective, randomized, controlled trial. Anesth Analg 2009;109:279-83.
25. Ullah H, Samad K, Khan FA. Continuous interscalene brachial plexus block versus parenteral analgesia for postoperative pain relief after major shoulder surgery. Cochrane Database Syst Rev 2014:CD007080.
26. Grauman S, Boethius J, Johansson J. Regional Anaesthesia Is Associated with Shorter Postanaesthetic Care and Less Pain Than General Anaesthesia after Upper Extremity Surgery. Anesthesiol Res Pract 2016;2016:6308371.
27. Kapral S, Krafft P, Eibenberger K, Fitzgerald R, Gosch M, Weinstabl C. Ultrasound-guided supraclavicular approach for regional anesthesia of the brachial plexus. Anesth Analg 1994;78:507-13.
28. Ting PL, Sivagnanaratnam V. Ultrasonographic study of the spread of local anaesthetic during axillary brachial plexus block. Br J Anaesth 1989;63:326-9.
29. Wu TJ, Lin SY, Liu CC, Chang HC, Lin CC. Ultrasound imaging aids infraclavicular brachial plexus block. Ma Zui Xue Za Zhi 1993;31:83-6.
30. Winnie AP. Interscalene brachial plexus block. Anesth Analg 1970;49:455-66.
31. la Grange P, Foster PA, Pretorius LK. Application of the Doppler ultrasound bloodflow detector in supraclavicular brachial plexus block. Br J Anaesth 1978;50:965-7.
32. Lanz E, Theiss D, Jankovic D. The extent of blockade following various techniques of brachial plexus block. Anesth Analg 1983;62:55-8.
33. Liu SS, Gordon MA, Shaw PM, Wilfred S, Shetty T, Yadeau JT. A prospective clinical registry of ultrasound-guided regional anesthesia for ambulatory shoulder surgery. Anesth Analg 2010;111:617-23.
34. Conroy PH, Awad IT. Ultrasound-guided blocks for shoulder surgery. Curr Opin Anaesthesiol 2011;24:638-43.
35. Lee JH, Cho SH, Kim SH, et al. Ropivacaine for ultrasound-guided interscalene block: 5 mL provides similar analgesia but less phrenic nerve paralysis than 10 mL. Can J Anaesth 2011;58:1001-6.
36. Riazi S, Carmichael N, Awad I, Holtby RM, McCartney CJ. Effect of local anaesthetic volume (20 vs 5 ml) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. Br J Anaesth 2008;101:549-56.
37. Sites BD, Taenzer AH, Herrick MD, et al. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. Reg Anesth Pain Med 2012;37:478-82.
38. Hogan QH. Phrenic nerve function after interscalene block revisited: now, the long view. Anesthesiology 2013;119:250-2.
39. Jules-Elysee K, Reid SC, Kahn RL, Edmonds CR, Urban MK. Prolonged diaphragm dysfunction after interscalene brachial plexus block and shoulder surgery: a prospective observational pilot study. Br J Anaesth 2014;112:950-1.
40. Kaufman MR, Elkwood AI, Rose MI, et al. Surgical treatment of permanent diaphragm paralysis after interscalene nerve block for shoulder surgery. Anesthesiology 2013;119:484-7.
41. Tran DQ, Elgueta MF, Aliste J, Finlayson RJ. Diaphragm-Sparing Nerve Blocks for Shoulder Surgery. Reg Anesth Pain Med 2017;42:32-8.

42. Tran DQ, Layera S, Bravo D, Cristi-Sanchez I, Bermudez L, Aliste J. Diaphragm-sparing nerve blocks for shoulder surgery, revisited. Reg Anesth Pain Med 2019:73-8.
43. Fredrickson MJ, Krishnan S, Chen CY. Postoperative analgesia for shoulder surgery: a critical appraisal and review of current techniques. Anaesthesia 2010;65:608-24.
44. Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. Anesth Analg 1991;72:498-503.
45. Bashein G, Robertson HT, Kennedy WF, Jr. Persistent phrenic nerve paresis following interscalene brachial plexus block. Anesthesiology 1985;63:102-4.
46. De A, Hayes JE. Persistent phrenic nerve paresis after interscalene block: a "triple crush" hypothesis of nerve injury. Reg Anesth Pain Med 2013;38:553.
47. Deruddre S, Vidal D, Benhamou D. A case of persistent hemidiaphragmatic paralysis following interscalene brachial plexus block. J Clin Anesth 2006;18:238-9.
48. Ediale KR, Myung CR, Neuman GG. Prolonged hemidiaphragmatic paralysis following interscalene brachial plexus block. J Clin Anesth 2004;16:573-5.
49. Robaux S, Bouaziz H, Boisseau N, Raucoules-Aime M, Laxenaire MC, Service SOSRHL. Persistent phrenic nerve paralysis following interscalene brachial plexus block. Anesthesiology 2001;95:1519-21.
50. Upton AR, McComas AJ. The double crush in nerve entrapment syndromes. Lancet 1973;2:359-62.
51. Renes SH, van Geffen GJ, Rettig HC, Gielen MJ, Scheffer GJ. Minimum effective volume of local anesthetic for shoulder analgesia by ultrasound-guided block at root C7 with assessment of pulmonary function. Reg Anesth Pain Med 2010;35:529-34.
52. Auyong DB, Yuan SC, Choi DS, Pahang JA, Slee AE, Hanson NA. A Double-Blind Randomized Comparison of Continuous Interscalene, Supraclavicular, and Suprascapular Blocks for Total Shoulder Arthroplasty. Reg Anesth Pain Med 2017;42:302-9.
53. Kim BG, Han JU, Song JH, Yang C, Lee BW, Baek JS. A comparison of ultrasound-guided interscalene and supraclavicular blocks for post-operative analgesia after shoulder surgery. Acta Anaesthesiol Scand 2017;61:427-35.
54. Trabelsi W, Ben Gabsia A, Lebbi A, Sammoud W, Labbene I, Ferjani M. Suprascapular block associated with supraclavicular block: An alternative to isolated interscalene block for analgesia in shoulder instability surgery? Orthop Traumatol Surg Res 2017;103:77-83.
55. Koltka AK, Buget M, Bingul ES, et al. Postoperative analgesia after arthroscopic shoulder surgery: A comparison between single-shot interscalene block and single-shot supraclavicular block. Agri 2017;29:127-31.
56. Auyong DB, Hanson NA, Joseph RS, Schmidt BE, Slee AE, Yuan SC. Comparison of Anterior Suprascapular, Supraclavicular, and Interscalene Nerve Block Approaches for Major Outpatient Arthroscopic Shoulder Surgery: A Randomized, Double-blind, Noninferiority Trial. Anesthesiology 2018;129:47-57.
57. Karaman T, Karaman S, Asci M, et al. Comparison of Ultrasound-Guided Supraclavicular and Interscalene Brachial Plexus Blocks in Postoperative Pain Management After Arthroscopic Shoulder Surgery. Pain Pract 2019;19:196-203.
58. Aliste J, Bravo D, Fernandez D, Layera S, Finlayson RJ, Tran DQ. A Randomized Comparison Between Interscalene and Small-Volume Supraclavicular Blocks for Arthroscopic Shoulder Surgery. Reg Anesth Pain Med 2018;43:590-5.
59. Aliste J, Bravo D, Layera S, et al. Randomized comparison between interscalene and costoclavicular blocks for arthroscopic shoulder surgery. Reg Anesth Pain Med 2019;44:472-7.

60. Wiegel M, Moriggl B, Schwarzkopf P, Petroff D, Reske AW. Anterior Suprascapular Nerve Block Versus Interscalene Brachial Plexus Block for Shoulder Surgery in the Outpatient Setting: A Randomized Controlled Patient- and Assessor-Blinded Trial. Reg Anesth Pain Med 2017;42:310-8.
61. Kim DH, Lin Y, Beathe JC, et al. Superior Trunk Block: A Phrenic-sparing Alternative to the Interscalene Block: A Randomized Controlled Trial. Anesthesiology 2019;131:521-33.
62. Dhir S, Sondekoppam RV, Sharma R, Ganapathy S, Athwal GS. A Comparison of Combined Suprascapular and Axillary Nerve Blocks to Interscalene Nerve Block for Analgesia in Arthroscopic Shoulder Surgery: An Equivalence Study. Reg Anesth Pain Med 2016;41:564-71.
63. Aliste J, Bravo D, Finlayson RJ, Tran DQ. A randomized comparison between interscalene and combined infraclavicular-suprascapular blocks for arthroscopic shoulder surgery. Can J Anaesth 2018;65:280-7.
64. Taha AM, Yurdi NA, Elahl MI, Abd-Elmaksoud AM. Diaphragm-sparing effect of the infraclavicular subomohyoid block vs low volume interscalene block. A randomized blinded study. Acta Anaesthesiol Scand 2019;63:653-8.
65. Hanson NA, Auyong DB. Systematic ultrasound identification of the dorsal scapular and long thoracic nerves during interscalene block. Reg Anesth Pain Med 2013;38:54-7.
66. Kim H. Dorsal scapular and long thoracic nerves during ultrasound-guided interscalene brachial plexus block. Asian J Anesthesiol 2017;55:26-7.
67. Saporito A. Dorsal scapular nerve injury: a complication of ultrasound-guided interscalene block. Br J Anaesth 2013;111:840-1.
68. Thomas SE, Winchester JB, Hickman G, DeBusk E. A confirmed case of injury to the long thoracic nerve following a posterior approach to an interscalene nerve block. Reg Anesth Pain Med 2013;38:370.
69. Brull R, McCartney CJ, Chan VW, El-Beheiry H. Neurological complications after regional anesthesia: contemporary estimates of risk. Anesth Analg 2007;104:965-74.
70. Saba R, Brovman EY, Kang D, Greenberg P, Kaye AD, Urman RD. A Contemporary Medicolegal Analysis of Injury Related to Peripheral Nerve Blocks. Pain Physician 2019;22:389-400.
71. Aguirre JA, Marzendorfer O, Brada M, Saporito A, Borgeat A, Buhler P. Cerebral oxygenation in the beach chair position for shoulder surgery in regional anesthesia: impact on cerebral blood flow and neurobehavioral outcome. J Clin Anesth 2016;35:456-64.
72. Murphy GS, Greenberg SB, Szokol JW. Safety of Beach Chair Position Shoulder Surgery: A Review of the Current Literature. Anesth Analg 2019;129:101-18.
73. Choi JW, Kim DK, Jeong HJ, Kim YR, Chung YJ, Son YH. Risk factors associated with hypotensive bradycardic events during open shoulder surgery in the beach chair position. Korean J Anesthesiol 2020;74:38-44.
74. Liguori GA, Kahn RL, Gordon J, Gordon MA, Urban MK. The use of metoprolol and glycopyrrolate to prevent hypotensive/bradycardic events during shoulder arthroscopy in the sitting position under interscalene block. Anesth Analg 1998;87:1320-5.
75. Flohr-Madsen S, Ytrebo LM, Valen K, Wilsgaard T, Klaastad O. A randomised placebo-controlled trial examining the effect on hand supination after the addition of a suprascapular nerve block to infraclavicular brachial plexus blockade. Anaesthesia 2016;71:938-47.
76. Tran DQ, Dugani S, Finlayson RJ. A randomized comparison between ultrasound-guided and landmark-based superficial cervical plexus block. Reg Anesth Pain Med 2010;35:539-43.

77. Siegenthaler A, Moriggl B, Mlekusch S, et al. Ultrasound-guided suprascapular nerve block, description of a novel supraclavicular approach. Reg Anesth Pain Med 2012;37:325-8.
78. Rothe C, Steen-Hansen C, Lund J, Jenstrup MT, Lange KH. Ultrasound-guided block of the suprascapular nerve - a volunteer study of a new proximal approach. Acta Anaesthesiol Scand 2014;58:1228-32.
79. Leung S, Zlotolow DA, Kozin SH, Abzug JM. Surgical Anatomy of the Supraclavicular Brachial Plexus. J Bone Joint Surg Am 2015;97:1067-73.
80. Flohr-Madsen S, Ytrebo LM, Kregnes S, Wilsgaard T, Klaastad O. Minimum effective volume of ropivacaine 7.5 mg/ml for an ultrasound-guided infraclavicular brachial plexus block. Acta Anaesthesiol Scand 2013;57:495-501.
81. Sauter AR, Smith HJ, Stubhaug A, Dodgson MS, Klaastad O. Use of magnetic resonance imaging to define the anatomical location closest to all three cords of the infraclavicular brachial plexus. Anesth Analg 2006;103:1574-6.
82. Musso D, Klaastad O, Wilsgaard T, Ytrebo LM. Brachial plexus block of the posterior and the lateral cord using ropivacaine 7.5 mg/mL. Acta Anaesthesiol Scand 2019;63:389-95.
83. Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: Nerve Injuries Research Committee. His Majesty's Stationery Office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 Figures. Brain 2010;133:2838-44.
84. Paternostro-Sluga T, Grim-Stieger M, Posch M, et al. Reliability and validity of the Medical Research Council (MRC) scale and a modified scale for testing muscle strength in patients with radial palsy. J Rehabil Med 2008;40:665-71.
85. Caetano EB, Vieira LA, Cavalheiro CS, Razuk MF, Almargo MA, Caetano MF. Anatomic Study of the Nervous Communication between the Median and Musculoucutaneous Nerve. Acta Ortop Bras 2016;24:200-3.
86. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med 2002;166:1338-44.
87. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. Pharmacoepidemiol Drug Saf 2016;25:733-7.
88. Dixon WJ. Staircase bioassay: the up-and-down method. Neurosci Biobehav Rev 1991;15:47-50.
89. Musso D, Klaastad O, Ytrebo LM. A combination of infraclavicular and suprascapular nerve blocks for total shoulder arthroplasty: A case series. Acta Anaesthesiol Scand 2021;65:674-80.
90. Checcucci G, Allegra A, Bigazzi P, Gianesello L, Ceruso M, Gritti G. A new technique for regional anesthesia for arthroscopic shoulder surgery based on a suprascapular nerve block and an axillary nerve block: an evaluation of the first results. Arthroscopy 2008;24:689-96.
91. Price DJ. The shoulder block: a new alternative to interscalene brachial plexus blockade for the control of postoperative shoulder pain. Anaesth Intensive Care 2007;35:575-81.
92. Price DJ. Combined suprascapular and axillary nerve blockade. Arthroscopy 2008;24:1316-7.
93. Saranteas T, Finlayson RJ, Tran DQ. Dose-finding methodology for peripheral nerve blocks. Reg Anesth Pain Med 2014;39:550-5.
94. Musso D, Flohr-Madsen S, Meknas K, Wilsgaard T, Ytrebo LM, Klaastad O. A novel combination of peripheral nerve blocks for arthroscopic shoulder surgery. Acta Anaesthesiol Scand 2017;61:1192-202.

95. Petrar SD, Seltenrich ME, Head SJ, Schwarz SK. Hemidiaphragmatic paralysis following ultrasound-guided supraclavicular versus infraclavicular brachial plexus blockade: a randomized clinical trial. Reg Anesth Pain Med 2015;40:133-8.
96. Klaastad O, Smith HJ, Smedby O, et al. A novel infraclavicular brachial plexus block: the lateral and sagittal technique, developed by magnetic resonance imaging studies. Anesth Analg 2004;98:252-6.
97. Cinquegrana D, Chu T, McFarland EG, Hanna MN, Lin JD. Combined suprascapular nerve block and selective lateral and posterior cord infraclavicular block for reverse total shoulder arthroplasty: A case report. J Clin Anesth 2018;51:38-9.
98. Perlas A, Chan VW, Simons M. Brachial plexus examination and localization using ultrasound and electrical stimulation: a volunteer study. Anesthesiology 2003;99:429-35.
99. Ajmani ML. The cutaneous branch of the human suprascapular nerve. J Anat 1994;185 (Pt 2):439-42.
100. Horiguchi M. The cutaneous branch of some human suprascapular nerves. J Anat 1980;130:191-5.
101. Last RJ. Anatomy, regional and applied / R.J. Last. Edinburgh ; New York : New York: Churchill Livingstone ; distributed by Longman; 1978.
102. Shih ML, Duh QY, Hsieh CB, et al. Bilateral superficial cervical plexus block combined with general anesthesia administered in thyroid operations. World J Surg 2010;34:2338-43.
103. Gurkan Y, Tas Z, Toker K, Solak M. Ultrasound guided bilateral cervical plexus block reduces postoperative opioid consumption following thyroid surgery. J Clin Monit Comput 2015;29:579-84.
104. Pandit JJ, Satya-Krishna R, Gration P. Superficial or deep cervical plexus block for carotid endarterectomy: a systematic review of complications. Br J Anaesth 2007;99:159-69.
105. Lim YC, Koo ZK, Ho VW, Chang SS, Manohara S, Tong QJ. Randomized, controlled trial comparing respiratory and analgesic effects of interscalene, anterior suprascapular, and posterior suprascapular nerve blocks for arthroscopic shoulder surgery. Korean J Anesthesiol 2020;73:408-16.
106. Sehmbi H, Johnson M, Dhir S. Ultrasound-guided subomohyoid suprascapular nerve block and phrenic nerve involvement: a cadaveric dye study. Reg Anesth Pain Med 2019;44:561-4.
107. Nielsen HB. Systematic review of near-infrared spectroscopy determined cerebral oxygenation during non-cardiac surgery. Front Physiol 2014;5:93.
108. Murphy GS, Szokol JW, Avram MJ, et al. Effect of ventilation on cerebral oxygenation in patients undergoing surgery in the beach chair position: a randomized controlled trial. Br J Anaesth 2014;113:618-27.
109. Koh JL, Levin SD, Chehab EL, Murphy GS. Neer Award 2012: cerebral oxygenation in the beach chair position: a prospective study on the effect of general anesthesia compared with regional anesthesia and sedation. J Shoulder Elbow Surg 2013;22:1325-31.
110. Hasan SS, Rolf RH, Sympson AN, Eten K, Elsass TR. Single-Shot Versus Continuous Interscalene Block for Postoperative Pain Control After Shoulder Arthroplasty: A Prospective Randomized Clinical Trial. J Am Acad Orthop Surg Glob Res Rev 2019;3:e014.
111. Namdari S, Nicholson T, Abboud J, Lazarus M, Steinberg D, Williams G. Interscalene Block with and without Intraoperative Local Infiltration with Liposomal Bupivacaine in Shoulder Arthroplasty: A Randomized Controlled Trial. J Bone Joint Surg Am 2018;100:1373-8.
112. Okoroha KR, Lynch JR, Keller RA, et al. Liposomal bupivacaine versus interscalene nerve block for pain control after shoulder arthroplasty: a prospective randomized trial. J Shoulder Elbow Surg 2016;25:1742-8.

113. Kirksey MA, Haskins SC, Cheng J, Liu SS. Local Anesthetic Peripheral Nerve Block Adjuvants for Prolongation of Analgesia: A Systematic Qualitative Review. PLoS One 2015;10:e0137312.
114. De Oliveira GS, Jr., Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology 2011;115:575-88.
115. Kang RA, Jeong JS, Yoo JC, et al. Improvement in postoperative pain control by combined use of intravenous dexamethasone with intravenous dexmedetomidine after interscalene brachial plexus block for arthroscopic shoulder surgery: A randomised controlled trial. Eur J Anaesthesiol 2019;36:360-8.
116. Noor NA, Urits I, Viswanath O, Kaye A, Eskander J. Synergistic Effect of Perineural Dexamethasone and Dexmedetomidine (Dex-Dex) Prolong Analgesic Effect of a Preoperative Interscalene Block. Cureus 2020;12:e9473.
117. Toma O, Persoons B, Pogatzki-Zahn E, Van de Velde M, Joshi GP, collaborators PWG. PROSPECT guideline for rotator cuff repair surgery: systematic review and procedure-specific postoperative pain management recommendations. Anaesthesia 2019;74:1320-31.
118. Martinez V, Beloeil H, Marret E, Fletcher D, Ravaud P, Trinquart L. Non-opioid analgesics in adults after major surgery: systematic review with network meta-analysis of randomized trials. Br J Anaesth 2017;118:22-31.
119. Borgeat A, Ofner C, Saporito A, Farshad M, Aguirre J. The effect of nonsteroidal anti-inflammatory drugs on bone healing in humans: A qualitative, systematic review. J Clin Anesth 2018;49:92-100.
120. Sachs CJ. Oral analgesics for acute nonspecific pain. Am Fam Physician 2005;71:913-8.
121. McHardy PG, Singer O, Awad IT, et al. Comparison of the effects of perineural or intravenous dexamethasone on low volume interscalene brachial plexus block: a randomised equivalence trial. Br J Anaesth 2020;124:84-91.
122. Kirkham KR, Albrecht E. Perineural or intravenous dexamethasone in interscalene brachial plexus block. Br J Anaesth 2020;124:15-7.
123. Desmet M, Vanneste B, Reynvoet M, et al. A randomised controlled trial of intravenous dexamethasone combined with interscalene brachial plexus blockade for shoulder surgery. Anaesthesia 2015;70:1180-5.
124. Ding DY, Mahure SA, Mollon B, Shamah SD, Zuckerman JD, Kwon YW. Comparison of general versus isolated regional anesthesia in total shoulder arthroplasty: A retrospective propensity-matched cohort analysis. J Orthop 2017;14:417-24.

Paper 1

A novel combination of peripheral nerve blocks for arthroscopic shoulder surgery

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Conflict of interest
Concert Medical LLC provided the B-smart pressure manometers.

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Background: Interscalene brachial plexus block is currently the gold standard for intra- and post-operative pain management for patients undergoing arthroscopic shoulder surgery. However, it is associated with block related complications, of which effect on the phrenic nerve have been of most interest. Side effects caused by general anesthesia, when this is required, are also a concern. We hypothesized that the combination of superficial cervical plexus block, suprascapular nerve block, and infraclavicular brachial plexus block would provide a good alternative to interscalene block and general anesthesia.

Methods: Twenty adult patients scheduled for arthroscopic shoulder surgery received a combination of superficial cervical plexus block (5 ml ropivacaine 0.5%), suprascapular nerve block (4 ml ropivacaine 0.5%), and lateral sagittal infraclavicular block (31 ml ropivacaine 0.75%). The primary aim was to find the proportion of patients who could be operated under light propofol sedation, without the need for opioids or artificial airway. Secondary aims were patients' satisfaction and surgeons' judgment of the operating conditions.

Results: Nineteen of twenty patients (95% CI: 85–100) underwent arthroscopic shoulder surgery with light propofol sedation, but without opioids or artificial airway. The excluded patient was not comfortable in the beach chair position and therefore received general anesthesia. All patients were satisfied with the treatment on follow-up interviews. The surgeons rated the operating conditions as good for all patients.

Conclusion: The novel combination of a superficial cervical plexus block, a suprascapular nerve block, and an infraclavicular nerve block provides an alternative anesthetic modality for arthroscopic shoulder surgery.

Editorial comment
In this feasibility study including 20 patients, the authors present a novel combination of a superficial cervical plexus block, suprascapular nerve block, and infraclavicular nerve block for arthroscopic shoulder surgery. Results are encouraging, but need confirmation in large scale studies.

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SSAI The Scandinavian Society of Anaesthesiology and Intensive Care Medicine

Interscalene brachial plexus block remains the gold standard for intraoperative and post-operative pain management in patients undergoing arthroscopic shoulder surgery. In expert hands, it has a very high success rate,[1] but may cause a wide spectrum of complications and undesired side effects.[2–6] The risk of neurological complications, particularly concerning the phrenic nerve,[7,8] has encouraged the development of alternative peripheral block methods for arthroscopic shoulder surgery.[9]

The shoulder joint is innervated by a few nerves: subscapular, axillary, lateral pectoral, and suprascapular nerve. The subscapular, axillary, and lateral pectoral nerve can be blocked with the infraclavicular block, while the suprascapular nerve must be blocked separately. Two nerves provide the cutaneous innervation of the shoulder: the supraclavicular and the axillary nerves. The supraclavicular nerves are not derived from the brachial plexus, but arise from the superficial cervical plexus.[9–11] Novel block methods should block all these nerves in order to provide effective intraoperative anesthesia and post-operative analgesia.

Several alternatives to the interscalene block have been proposed in order to avoid the effect on the diaphragmatic function, yet many of them require further confirmatory trials. In the last years some authors have proposed a C7 root block,[12,13] an alternative supraclavicular block limited to the distal upper extremity,[14] and an axillary-suprascapular block.[15]

We hypothesized that a combination of superficial cervical plexus block, suprascapular nerve block, and lateral sagittal infraclavicular brachial plexus block would provide intraoperative anesthesia and post-operative analgesia for patients undergoing arthroscopic shoulder surgery. To test this hypothesis we performed a feasibility study in 20 patients scheduled for arthroscopic shoulder surgery. The primary aim was the proportion of patients who could be operated under light propofol sedation, but without the need for opioids or artificial airway. Secondary aims were patients' satisfaction and surgeons' judgment of the operating conditions.

Methods

The study was approved by the Institutional Board at the University Hospital of North Norway (registration number 0472) and registered at www.clinicaltrials.gov (NCT02809144). The trial was performed at the University Hospital of North Norway (Tromsø and Narvik) from April to November 2016, in accordance with the Helsinki Declaration. Written informed consent was obtained from patients scheduled for arthroscopic shoulder surgery using the following inclusion criteria: age 18–70 years, BMI 20–35 kg/m^2 and ASA physical status 1–3. Exclusion criteria included: pregnancy, coagulation disorders, allergy to local anesthetics, atrioventricular block, peripheral neuropathy and use of anticoagulation drugs other than acetylsalicylic acid or dipyridamol.

All blocks were performed by DM with assistance from LMY. For the two-first blocks (the superficial cervical and suprascapular nerve blocks) the patients were in semilateral position with slightly elevated upper body. Subsequently the patients were supine for the infraclavicular block. All blocks were ultrasound-guided, using either a SonoSite Edge unit or a SonoSite M-Turbo (SonoSite, Inc., Bothell, WA, USA). A 50 mm linear array probe 6–15 MHz was applied for the superficial cervical and the suprascapular nerve blocks, while a C11x broadband curved array probe 5–8 MHz was used for the lateral sagittal infraclavicular block. For the two-first blocks, correct nerve identification by ultrasound was confirmed by nerve stimulator response (Stimuplex HNS 12, B. Braun AG, Melsungen, Germany). To reduce the risk of intraneural needle tip position, for all blocks, the relationship between needle and nerve was carefully observed by ultrasound. Moreover, a nerve stimulator response by a current ≤ 0.3 mA, 0.1 ms and 2 Hz or an injection pressure (measured by B-Smart™; Concert Medical LLC, Norwell, MA, USA) ≥ 103 kPa (15 psi) defined the need for a small retraction of the needle. The initial needle insertion was counted as the first pass. An additional needle pass was defined as needle retraction of at least 10 mm prior to further needle insertion.

Standard monitoring included pulse oximetry, electrocardiogram and non-invasive blood pressure. All patients received oxygen supplementation by a nasal cannula.

Superficial cervical plexus block

We used a slight modification of the method first described by Tran et al.[16] Before the insertion of the block needle, the skin was infiltrated with 1–2 ml lidocaine 10 mg/ml. The probe was placed axially, just below the midpoint of the sternocleidomastoid muscle, to visualize the intermuscular plane between the sternocleidomastoid and the scalene muscles (between the deep part of the superficial cervical fascia and the prevertebral fascia). The needle was slowly advanced from posterolateral to anteromedial in this potential space, using the in-plane technique. The patient was instructed to signal paresthesia toward the clavicle or shoulder, while receiving a current of 0.3–0.8 mA, 0.1 ms, 2 Hz. Five ml ropivacaine 0.5% was injected in the described interfascial space while trying to avoid distribution medial to the interscalene groove. Although the supraclavicular nerves can often be visualized, a systematical search for them was not done because the technique relied on injection of local anesthetic agents in the intermuscular space.

Suprascapular nerve block

The anterior suprascapular block was first described by Siegenthaler et al.[17] and has since then undergone some modifications.[18,19] The suprascapular nerve is usually the most craniolateral nerve emerging from the supraclavicular plexus. Sonographically the nerve can be traced laterally in the posterior cervical triangle, deep to the omohyoid muscle, by tilting the probe incrementally steeper in the caudal direction. This ultrasonographic observation agrees with anatomical studies by Leung et al.[20] The local anesthetic was injected at the most lateral short-axis view of the nerve that we could obtain, with an in-plane technique, while advancing the needle from posterolateral to anteromedial. During injection we tried to avoid fluid distribution to the supraclavicular brachial plexus cluster and (more medially) to the phrenic nerve. Electric nerve stimulation (0.3–0.8 mA, 0.1 ms, 2 Hz) served to confirm the sonographic identification of the nerve, by palpable contractions of the infra- and supraspinatus muscles. The local anesthetic dose was 4 ml ropivacaine 0.5%, as recently described by Flohr-Madsen et al.[19]

Lateral sagittal infraclavicular block

A periarterial injection technique was used, slightly modified from the method described by Flohr-Madsen et al.[21] Usually, the dose was administered by three local anesthetic deposits. Considering the artery as a clock face with 12 o'clock ventral, the aim was to cover the artery by fluid from 3 to 11 o'clock. The needle insertion point was 0.5–1.0 cm caudal to the lower edge of the clavicle, just medial to the coracoid process. The needle was carefully advanced in the sagittal plane with the in-plane technique, between the artery and the lateral cord, tangential to the cranial aspect of the artery. The first deposit was at 6 o'clock, the second on withdrawal of the needle between 9 and 11 o'clock and the third at 3 o'clock. The latter deposit required a needle pass ventral to the artery. Total local anesthetic dose was 31 ml ropivacaine 0.75%. The volume of each injection varied depending on observed fluid distribution, but the largest volume (15–18 ml) regularly at 6 o'clock.

Total block performance time was the time from the probe was placed on the neck for the superficial cervical plexus block to final withdrawal of the block needle after the lateral sagittal infraclavicular block.

Block assessment

Neurologic status of the upper limb and the cervical area was assessed before the blocks (baseline) and 15 and 30 min after completion of the blocks. We performed sensory testing by applying an ice cube on pre-marked points in the areas of the supraclavicular nerves, intercostobrachial, axillary, medial brachial cutaneous, musculocutaneous, medial antebrachial cutaneous, radial, median and ulnar nerves. Supraclavicular test points were at the soft spot and at the upper border of the clavicle in

the midclavicular line. The soft spot is the posterior portal used for shoulder arthroscopy. It is formed by the interval between the infraspinatus and teres minor muscles, approximately 2 cm caudal and 1 cm medial to the posterolateral tip of the acromion. The following scale was used: 3 = normal cold feeling; 2 = reduced cold feeling (hypoalgesia); 1 = no cold feeling, but feels touch (analgesia); and 0 = no cold or touch feeling (anesthesia). Muscle power was assessed using a modified seven-point scale (Table 1).[22] Axillary nerve block was tested by elevation of the extended upper limb in the sagittal plane. Suprascapular nerve block was tested by the force for lateral rotation of the humerus against manual resistance, while the arm was adducted and the elbow flexed at 90°. Subscapular nerve block was tested by the force for medial rotation of the humerus against manual resistance, while the arm was adducted and the elbow flexed at 90°. The other motor nerve tests were for the musculocutaneous, radial, median, and ulnar nerves.[23]

Block success was assessed 30 min after withdrawal of the needle upon the last of the three blocks. The superficial cervical plexus block was judged successful if the sensory score at both of its test points was 0 or 1. The suprascapular nerve block was successful if the motor score was ≤ 2. The lateral sagittal infraclavicular block was successful if the axillary sensory score was 0 or 1. Patients who failed the success criteria were followed up with repeated assessments until admittance to the operation theatre. Patients # 1–7 were accepted for surgery if the sensory score was ≤ 1 (the supraclavicular and axillary nerves) and the motor test score was ≤ 2 (the suprascapular nerve). Patients # 8–20 were accepted for surgery if the sensory score was ≤ 1 (the supraclavicular and axillary nerves) and the motor test score was $\leq 4-$ (the suprascapular nerve).

Table 1 Modified Medical Research Council scale of muscle power.

5	Normal power
4+	Active movement against gravity and resistance (> 50% of normal power)
4−	Active movement against gravity and resistance (< 50% of normal power)
3	Active movement against gravity
2	Active movement with gravity eliminated
1	Flicker or trace contraction
0	No contraction

We recorded the incidence of adverse events including paresthesia, vessel puncture, systemic local anesthesia toxicity, Horner's syndrome, dyspnea, hoarseness, and dysphagia. To detect pneumothorax, ultrasound was used within 15 min after completed procedure.

Intraoperative treatment

All patients were offered propofol sedation to maintain a score between −2 and 0 on the Richmond Agitation and Sedation Scale. The protocol required that other sedatives or analgesics were not administered.

Post-operative assessment

All patients were interviewed in the recovery room and by phone approximately 24 h after the surgery was completed. In the recovery room, post-operative nausea and vomiting (PONV), pain at rest (numerical rating scale, 1–10), medication, signs of Horner's syndrome, hoarseness, dyspnea, or dysphagia were recorded. The same questions were repeated on day one. Additionally, we asked about time to pain debut, average and maximum pain scores at rest (numerical rating scale, 1–10) and patients' total intake of analgesics. Analgesics were converted to oral morphine equivalents.

Patients' overall satisfaction score was assessed by asking them, both in the recovery room and during the follow-up telephone call, if they would like to receive the same type of anesthetic technique for a similar operation in the future. Surgeons' judgement of the operative conditions was given by the operator in the recovery room, immediately after surgery.

A priori, we assumed a block success rate of 90% with a confidence of interval of $\pm$ 13%. This would require a total number of 20 patients included. Descriptive characteristics are presented as mean (standard deviation), median (interquartile range and range), or number, as appropriate. The primary aim is presented as

proportion with 95% confidence interval. Analyses were performed using the Statistical Package for Social Sciences (SPSS) program version 23.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Twenty-six consecutive patients scheduled for arthroscopic shoulder surgery were screened and 20 patients fulfilled the inclusion criteria. Patient characteristics are presented in Table 2.

Patient flow chart is presented in Fig. 1. One patient (#5) had successful blocks, but felt uneasy in the beach chair position. After starting light propofol sedation, she became restless and therefore received general anesthesia. The other 19 out of 20 patients (95% CI: 85–100) underwent arthroscopic shoulder surgery with light propofol sedation, but without any need for opioids or artificial airway. Propofol dose given was 1.4 (0.4–2.6 [0.0–3.4]), median (IQR [range]) mg/kg/t. Two patients reported slight discomfort intraoperatively (numerical rating scale 1–2) located at the posterior portal (soft spot). Both were offered analgesics, but refused. None of the patients required additional local anesthetic.

Four patients did not fulfill the block success criteria at 30 min, which resulted in a block success rate of 80%. One patient (#7) failed the midclavicular superficial cervical plexus block test at 30 min, but met the success criteria 10 min later. Three patients (#8, #9, and #20) failed the SSN test. Patient #20 and patient #9 met the success criteria 45 and 90 min after the last block, respectively.

Patient #8 retained suprascapular nerve mediated muscle power score 4− up to the time of surgery. In spite of this suboptimal score, we decided to proceed to surgery. The precondition was, by the slightest intraoperative pain, to convert to general anesthesia. The patient did not experience pain during surgery and received only propofol according to the protocol.

Summary data of block performance of the three blocks are presented in Table 3. None of the patients showed sonographic signs of pneumothorax. Total block performance time was 21.8 (20.4–26.7 [15.9–34.5]), median (IQR [range]) minutes. Time from end of local anesthetic injection until start of surgery was 118 (92–150 [71–200]), median (IQR [range]) minutes. Tables 4 and 5 show the individual sensory-motor status of all patients 15 and 30 min after the blocks.

The duration of surgery was 49 (24–63 [18–85]), median (IQR [range]) minutes. Surgeons were satisfied with the working conditions in 19 of 20 patients (all except patient #5) and would recommend this novel block combination to all new patients scheduled for arthroscopic shoulder surgery.

In the post-anesthesia care unit (PACU) none of the patients suffered from nausea/vomiting, dyspnea, hoarseness, or dysphagia. One patient demonstrated temporary Horner's syndrome and another patient reported a pain score of 2 (numeric rating scale 0–10), while the others were pain free. No drugs were required. Accordingly, in the PACU all the patients were very satisfied with the regional anesthesia. Furthermore, all of them wished to receive the same regional anesthesia, should they require the same type of surgery in the future.

Patient #3 was excluded from post-operative day one data analyses because of protocol violation. This patient was given 16 mg dexamethasone i.v. intraoperatively. During the telephone interview on the first post-operative day, no patient reported PONV, dysphagia, dyspnea, or hoarseness. Time to pain debut was 12.5 (11.7–14.8 [7.6–15.6]), median (IQR [range]) hours. Average pain score at rest was 0 (0–2.3 [0–6]), median (IQR [range]). Maximum pain score was 5 (3.5–8.5 [0–10]), median (IQR [range]).

Table 2 Characteristics of study patients scheduled for arthroscopic shoulder surgery (n = 19).

Age (yrs)	55.7 (11.9)
Gender (male/female)	12/7
BMI; kg/m^2	26.0 (3.4)
ASA physical status (I/II/III)	6/12/1
Types of surgery (acromioplasty/supraspinatus suture/intraarticular surgery)	9/6/4
Side (right/left)	9/10

Mean (SD) or number (n). Continuous variables are presented as mean (standard deviation); categorical variables are presented as counts. ASA, American Society of Anesthesiologists; BMI, mass body index.

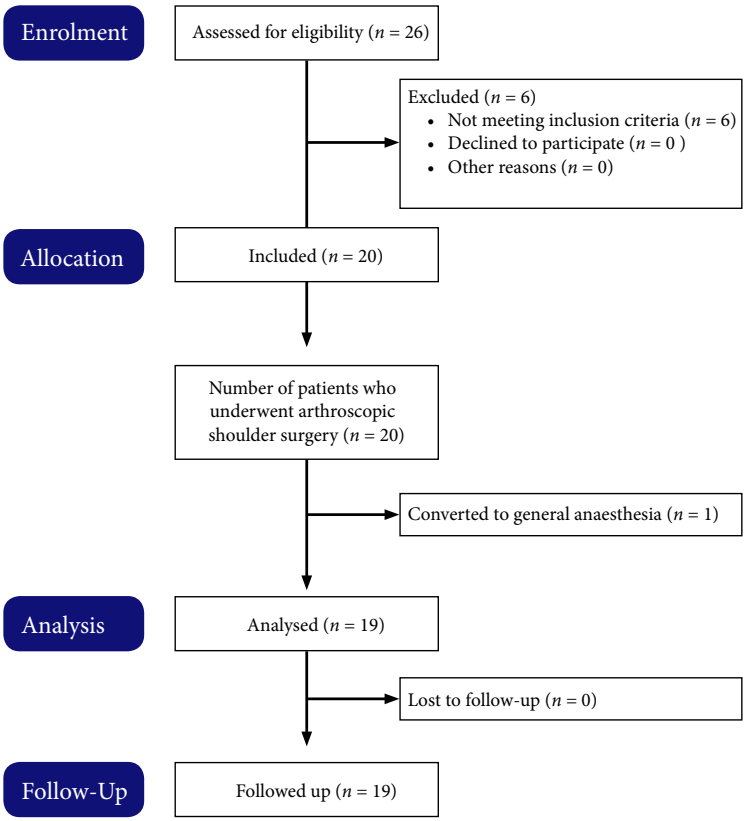

Fig. 1. CONSORT flow diagram.

Table 3 Summary data of block performance of the three blocks (*n* = 19).

	SCPB	SSNB	LSIB
Performance time (min)	6.0 (5.4–8.0 [3.6–11.2])	5.0 (3.9–7.9 [2.8–14.8])	6.5 (5.5–7.1 [4.7–12.0])
Number of needle passes (*n*)	1 (1–1 [1–2])	1 (1–1 [1–3])	2 (2–3 [2–3])
Paresthesia (*n*)	1	2	1
Vascular puncture (*n*)	0	0	1
Local anesthetic systemic toxicity (*n*)	0	0	0

Values are median (IQR [range]) or number (*n*). SCPB, Superficial cervical plexus block; SSNB, Suprascapular nerve block; LSIB, Lateral sagittal infraclavicular block.

Analgesic consumption was 40 (30–60 [0–100]), median (IQR [range]) mg oral morphine equivalents during the first 24 h after surgery.

Discussion

The study shows that this novel combination of peripheral nerve blocks is feasible and provides surgical anesthesia and satisfactory post-operative analgesia in patients scheduled for arthroscopic shoulder surgery.

The superficial cervical plexus block can potentially affect the brachial plexus and the phrenic nerve[24] if local anesthesia penetrates the prevertebral fascia and diffuses into the inter-scalene groove and to the superficial aspect of the anterior scalene muscle. Nevertheless, to our knowledge there are no reports of phrenic nerve

Table 4 Individual sensory test data 15 and 30 min after the blocks (N = 20).

	Supraclavicular nerve (soft spot)		Supraclavicular nerve (midclavicular)		Axillary nerve		Intercostobrachial nerve		Medial brachial cutaneous nerve		Musculocutaneous nerve		Medial antebrachial cutaneous nerve		Radial nerve		Median nerve		Ulnar nerve	
Patient id	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min
1	0	0	0	0	1	0	3	1	1	0	0	0	0	0	1	0	0	0	1	1
2	0	0	0	1	1	1	3	3	3	2	1	0	1	0	1	1	1	0	1	1
3	1	0	0	0	0	0	2	2	1	1	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	0
5	1	1	0	0	1	1	3	3	2	2	1	0	0	0	0	0	0	0	1	0
6	0	0	0	0	0	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0
7	0	0	2	2	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	1	0	3	3	2	1	1	1	1	0	1	1	1	1	1	0
9	0	0	1	1	0	0	2	2	0	0	0	0	1	0	1	1	1	0	2	1
10	0	0	0	0	1	0	3	2	0	0	1	1	0	0	1	0	0	0	1	0
11	1	1	0	0	0	0	3	2	2	1	0	0	1	0	0	0	0	0	0	0
12	0	0	0	0	1	0	1	2	0	0	1	1	1	1	1	1	2	2	2	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
14	0	0	1	1	1	0	1	2	1	1	1	1	1	0	1	0	1	0	2	1
15	1	0	1	1	1	0	1	0	1	0	2	0	0	0	1	0	1	0	0	0
16	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0	0	0
17	0	0	0	0	1	0	3	2	0	0	2	1	0	0	1	0	1	0	1	0
18	0	0	0	0	0	0	3	3	2	1	1	0	0	0	0	0	0	0	1	0
19	1	0	0	0	1	0	2	2	0	0	1	0	0	0	1	1	1	0	1	0
20	0	0	0	0	1	0	0	0	1	0	0	0	0	0	1	1	1	0	0	0

Supraclavicular test points were at the soft spot and at the upper border of the clavicle in the midclavicular line. The soft spot is the posterior portal used for shoulder arthroscopy. It is formed by the interval between the infraspinatus and teres minor muscles, approximately 2 cm caudal and 1 cm medial to the posterolateral tip of the acromion. The following scale was used: 3 = normal cold feeling; 2 = reduced cold feeling (hypoalgesia); 1 = no cold feeling, but feels touch (analgesia); and 0 = no cold or touch feeling (anesthesia).

Table 5 Individual motor power data 15 and 30 min after the blocks ($N = 20$).

Patient id	Axillary nerve		Suprascapular nerve		Subscapular/lateral pectoral nerve		Musculocutaneous nerve		Radial nerve (elbow)		Radial nerve (wrist)		Median nerve		Ulnar nerve	
	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min	15 min	30 min
1	0	0	0	0	3	3	1	0	0	0	4−	3	4−	4−	4−	4−
2	2	0	2	1	3	0	4−	0	4−	2	4−	4−	1	0	4−	4−
3	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	2	0	0	0	0	0	1	0	4−	4−	1	0
5	0	0	1	0	0	0	0	0	1	0	1	0	0	0	0	0
6	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
7	0	0	1	0	0	0	2	0	1	0	1	0	0	0	0	0
8	2	1	4−	4−	0	0	4−	4−	1	0	4−	1	4−	4−	4−	1
9	2	1	4+	4−	4−	0	1	0	1	0	4−	1	1	0	4−	1
10	1	0	2	1	0	0	1	0	4−	1	4−	3	4−	0	4−	1
11	1	0	4−	1	0	0	0	0	0	0	0	0	0	0	1	0
12	4−	1	4−	1	4−	4−	4−	4−	4−	1	4−	4−	4−	4−	4−	1
13	0	0	1	0	0	0	3	0	1	0	1	0	0	0	1	0
14	1	0	2	0	4−	0	4−	2	1	1	4−	1	5	4−	4−	1
15	2	1	2	1	3	0	4−	4−	4−	4−	4−	4−	3	0	4−	1
16	1	0	1	0	0	0	1	0	1	0	1	0	0	0	1	0
17	1	0	2	1	4−	0	4−	2	4−	2	4−	1	0	0	4−	0
18	1	0	0	0	0	0	2	1	1	0	0	0	0	0	0	0
19	4−	1	4−	1	4−	0	4−	1	4−	1	4−	4−	1	0	4−	0
20	1	0	4+	4−	4−	4−	4−	4−	2	1	4−	4−	4−	0	4−	0

The nerve motor power was tested using the Modified Medical Research Council scale (Table 1). Axillary nerve: elevation of the extended upper limb in the sagittal plane. Suprascapular nerve: lateral rotation of the humerus. Subscapular/lateral pectoral nerve: medial rotation of the humerus. Musculocutaneous nerve: elbow flexion. Radial nerve: elbow and wrist extension. Median nerve: flexion of the second finger's distal interphalangeal joint. Ulnar nerve: finger abduction.

block associated with ultrasound-guided superficial cervical plexus block[16,25] and the incidence of this event is historically very low.[26] To reduce the risk of phrenic nerve block, we used a lower volume of local anesthetic than in the studies by Tran et al. and Gürkan et al.[16,25]

In our former study on supination of the hand after ultrasound-guided infraclavicular block, 15 patients received infraclavicular block alone and 15 combined infraclavicular and suprascapular nerve block.[19] Chest radiographs were taken approximately 75 min after the blocks. There were no signs of diaphragmatic paresis or paralysis. This may suggest that neither infraclavicular nor suprascapular block, or the combination of them, challenges the phrenic nerve. However, in a recent study of 32 patients receiving ultrasound-guided infraclavicular block, one patient developed hemidiaphragmatic paralysis and three patients hemidiaphragmatic paresis, as diagnosed by M-mode ultrasonography.[27] Based on data from these two studies, clinicians should be aware of the potential risk of infraclavicular block in patients with impaired respiratory function.

The suprascapular nerve seldom has sensory branches to the skin.[28,29] We therefore used a muscle power test to evaluate the suprascapular nerve block. Interestingly, surgery could be performed successfully even in patients with suprascapular nerve block failure after 30 min. Most remarkable was patient #8 who failed the suprascapular nerve test until start of surgery. We allowed this patient to be operated in accordance to protocol because of two considerations. First, there may be a significant disparity between motor power and sensory function after a peripheral nerve block.[30] Second, our success criterion may be too strict.[18] The patient did not experience any pain and received propofol only according to the protocol. In future studies we will consider using a more liberal success criterion (motor score $\leq 4-$) for the suprascapular nerve block.

Premedication was not administrated for two reasons. First of all, because the superficial cervical plexus block anesthetizes the supraclavicular nerves and thus the injection sites of the subsequent blocks. Secondly, our study required an accurate and timely performed neurological assessment before and after the blocks. Therefore, we did not want any sedative or opioid to confound the interpretation of the data.

The need for three injections, change of patient's body position, and change of needle type during the procedure, make our triple block method more time consuming compared to the interscalene block.[15] However, in order to provide surgical anesthesia, the alternative of low volume interscalene block, requires an additional anesthesiological technique (general anesthesia, local skin infiltration or a supraclavicular nerve block), which is time consuming as well. This novel block combination might reduce costs spent on personnel and supplies, but such benefit over the interscalene block must be tested in a randomized controlled study.

The incidence of intraoperative cerebral desaturation in patients receiving general anesthesia in the beach-chair position is of great concern.[6] A major advantage of this novel block combination is that general anesthesia could be omitted in 19 out of 20 patients. By using only light propofol sedation, we could easily communicate with the patient and thereby directly monitor cerebral function intraoperatively.

In conclusion, this novel combination of peripheral nerve blocks provides surgical anesthesia and satisfactory post-operative analgesia for patients scheduled for arthroscopic shoulder surgery. A randomized controlled trial should be undertaken to compare this shoulder block with the interscalene block.

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References

1. Liu SS, Gordon MA, Shaw PM, Wilfred S, Shetty T, Yadeau JT. A prospective clinical registry of ultrasound-guided regional anesthesia for ambulatory shoulder surgery. Anesth Analg 2010; 111: 617–23.
2. Lee JH, Cho SH, Kim SH, Chae WS, Jin HC, Lee JS, Kim YI. Ropivacaine for ultrasound-guided interscalene block: 5 mL provides similar analgesia but less phrenic nerve paralysis than 10 mL. Can J Anaesth 2011; 58: 1001–6.
3. Riazi S, Carmichael N, Awad I, Holtby RM, McCartney CJ. Effect of local anaesthetic volume

(20 vs 5 ml) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. Br J Anaesth 2008; 101: 549–56.
4. Conroy PH, Awad IT. Ultrasound-guided blocks for shoulder surgery. Curr Opin Anaesthesiol 2011; 24: 638–43.
5. Sites BD, Taenzer AH, Herrick MD, Gilloon C, Antonakakis J, Richins J, Beach ML. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. Reg Anesth Pain Med 2012; 37: 478–82.
6. Nielsen HB. Systematic review of near-infrared spectroscopy determined cerebral oxygenation during non-cardiac surgery. Front Physiol 2014; 5: 93.
7. Hogan QH. Phrenic nerve function after interscalene block revisited: now, the long view. Anesthesiology 2013; 119: 250–2.
8. Jules-Elysee K, Reid SC, Kahn RL, Edmonds CR, Urban MK. Prolonged diaphragm dysfunction after interscalene brachial plexus block and shoulder surgery: a prospective observational pilot study. Br J Anaesth 2014; 112: 950–1.
9. Tran DQ, Elgueta MF, Aliste J, Finlayson RJ. Diaphragm-sparing nerve blocks for shoulder surgery. Reg Anesth Pain Med 2017; 42: 32–8.
10. Borgeat A, Ekatodramis G. Anaesthesia for shoulder surgery. Best Pract Res Clin Anaesthesiol 2002; 16: 211–25.
11. Aszmann OC, Dellon AL, Birely BT, McFarland EG. Innervation of the human shoulder joint and its implications for surgery. Clin Orthop Relat Res 1996; 330: 202–7.
12. Renes SH, Rettig HC, Gielen MJ, Wilder-Smith OH, van Geffen GJ. Ultrasound-guided low-dose interscalene brachial plexus block reduces the incidence of hemidiaphragmatic paresis. Reg Anesth Pain Med 2009; 34: 498–502.
13. Renes SH, van Geffen GJ, Rettig HC, Gielen MJ, Scheffer GJ. Minimum effective volume of local anesthetic for shoulder analgesia by ultrasound-guided block at root C7 with assessment of pulmonary function. Reg Anesth Pain Med 2010; 35: 529–34.
14. Renes SH, Spoormans HH, Gielen MJ, Rettig HC, van Geffen GJ. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. Reg Anesth Pain Med 2009; 34: 595–9.
15. Dhir S, Sondekoppam RV, Sharma R, Ganapathy S, Athwal GS. A comparison of combined suprascapular and axillary nerve blocks to interscalene nerve block for analgesia in arthroscopic shoulder surgery: an equivalence study. Reg Anesth Pain Med 2016; 41: 564–71.
16. Tran DQ, Dugani S, Finlayson RJ. A randomized comparison between ultrasound-guided and landmark-based superficial cervical plexus block. Reg Anesth Pain Med 2010; 35: 539–43.
17. Siegenthaler A, Moriggl B, Mlekusch S, Schliessbach J, Haug M, Curatolo M, Eichenberger U. Ultrasound-guided suprascapular nerve block, description of a novel supraclavicular approach. Reg Anesth Pain Med 2012; 37: 325–8.
18. Rothe C, Steen-Hansen C, Lund J, Jenstrup MT, Lange KH. Ultrasound-guided block of the suprascapular nerve - a volunteer study of a new proximal approach. Acta Anaesthesiol Scand 2014; 58: 1228–32.
19. Flohr-Madsen S, Ytrebo LM, Valen K, Wilsgaard T, Klaastad O. A randomised placebo-controlled trial examining the effect on hand supination after the addition of a suprascapular nerve block to infraclavicular brachial plexus blockade. Anaesthesia 2016; 71: 938–47.
20. Leung S, Zlotolow DA, Kozin SH, Abzug JM. Surgical anatomy of the supraclavicular brachial plexus. J Bone Joint Surg Am 2015; 97: 1067–73.
21. Flohr-Madsen S, Ytrebo LM, Kregnes S, Wilsgaard T, Klaastad O. Minimum effective volume of ropivacaine 7.5 mg/ml for an ultrasound-guided infraclavicular brachial plexus block. Acta Anaesthesiol Scand 2013; 57: 495–501.
22. Paternostro-Sluga T, Grim-Stieger M, Posch M, Schuhfried O, Vacariu G, Mittermaier C, Bittner C, Fialka-Moser V. Reliability and validity of the Medical Research Council (MRC) scale and a modified scale for testing muscle strength in patients with radial palsy. J Rehabil Med 2008; 40: 665–71.
23. Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: Nerve Injuries Research Committee. His Majesty's Stationery Office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 Figures. Brain 2010; 133: 2838–44.
24. Shih ML, Duh QY, Hsieh CB, Liu YC, Lu CH, Wong CS, Yu JC, Yeh CC. Bilateral superficial cervical plexus block combined with general anesthesia administered in thyroid operations. World J Surg 2010; 34: 2338–43.

25. Gurkan Y, Tas Z, Toker K, Solak M. Ultrasound guided bilateral cervical plexus block reduces postoperative opioid consumption following thyroid surgery. J Clin Monit Comput 2015; 29: 579–84.
26. Pandit JJ, Satya-Krishna R, Gration P. Superficial or deep cervical plexus block for carotid endarterectomy: a systematic review of complications. Br J Anaesth 2007; 99: 159–69.
27. Petrar SD, Seltenrich ME, Head SJ, Schwarz SK. Hemidiaphragmatic paralysis following ultrasound-guided supraclavicular versus infraclavicular brachial plexus blockade: a randomized clinical trial. Reg Anesth Pain Med 2015; 40: 133–8.
28. Horiguchi M. The cutaneous branch of some human suprascapular nerves. J Anat 1980; 130: 191–5.
29. Ajmani ML. The cutaneous branch of the human suprascapular nerve. J Anat 1994; 185(Pt 2): 439–42.
30. Hemmings HC, Egan TD. Pharmacology and physiology for anesthesia: foundations and clinical application. Philadelphia, PA: Elsevier/Saunders, 2013.

Paper 2

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ORIGINAL ARTICLE

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Brachial plexus block of the posterior and the lateral cord using ropivacaine 7.5 mg/mL

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Background: We recently showed that the novel combination of a superficial cervical plexus block, a suprascapular nerve block, and the lateral sagittal infraclavicular brachial plexus block (LSIB) provides an alternative anaesthetic method for arthroscopic shoulder surgery. In this study, we hypothesised that the LSIB dose for this shoulder block could be significantly reduced by injecting only towards the shoulder relevant posterior and lateral cords. Our aim was to determine the minimum effective volume in 50% of the patients (MEV_{50}) and to estimate the MEV_{95}, when using ropivacaine 7.5 mg/mL to block these cords.

Methods: Twenty-three adult patients scheduled for hand surgery participated in the study. Considering the artery as a clock face with 12 o'clock ventral, the designated volume was injected immediately outside the arterial wall and between 8 and 9 o´clock. The in-plane technique was used. Block success was assessed 30 minutes after withdrawal of the needle. Successful posterior cord block was defined as anaesthesia or analgesia of the axillary nerve. Successful lateral cord block was defined as either anaesthesia or analgesia, or >50% motor block of the musculocutaneous nerve. MEV_{50} was determined by the staircase up-and-down method. Logistic regression and probit transformation were applied to estimate MEV_{95}.

Results: MEV_{50} and MEV_{95} were 7.8 mL [95% confidence interval (CI), 7.3-8.4] and 9.0 mL (95% CI, 7.8-10.3), respectively.

Conclusion: For single-deposit infraclavicular posterior and lateral cord block, the MEV_{95} of ropivacaine 7.5 mg/mL was estimated to 9.0 mL.

1 | INTRODUCTION

Ultrasound guidance for peripheral nerve blocks allows real-time observation of the needle, nerves and local anaesthetic (LA) distribution. This has reduced the volume requirement of LA compared to methods guided by nerve stimulation and is of particular interest in patients requiring more than one block.

We have previously shown that the novel combination of a superficial cervical plexus block, a suprascapular nerve block, and the lateral sagittal infraclavicular brachial plexus block (LSIB) provides an alternative anaesthetic method for arthroscopic shoulder surgery.[1] In that study, a total of 277.5 mg ropivacaine was used, of which 31 mL of ropivacaine 7.5 mg/mL (ie 232.5 mg) was given for the LSIB. This dose was based on data from our previous MEV study.[2]

The shoulder joint is innervated by the suprascapular, axillary, subscapular and lateral pectoral nerves. The musculocutaneous nerve may provide branches to the anterosuperior and posterior portions of the glenohumeral joint, but these branches are described as inconsistent or "completely absent".[3] The axillary, subscapular, and lateral pectoral nerves can be blocked by the infraclavicular block, while the suprascapular nerve must then be blocked separately. Two nerves provide the cutaneous innervation of the shoulder: the supraclavicular and the axillary nerves. The supraclavicular nerves are not derived from the brachial plexus, but arise from the superficial

ClinicalTrials.gov (NCT03329456).

cervical plexus. The suprascapular and the cutaneous nerves are not object of this study. The remaining nerves (the axillary, subscapular, and lateral pectoral) originate from the lateral and posterior cords.[4] Hence, we assumed that blocking the medial cord may be unnecessary for shoulder surgery. Accordingly, we hypothesised that the volume of ropivacaine 7.5 mg/mL for a new block designed to target the posterior and lateral cords would be significantly less than the 31 mL required to block all three cords. Aim for our study was to determine MEV_{50} and estimate MEV_{95} for a novel single-deposit infraclavicular posterior and lateral cord block using ropivacaine 7.5 mg/mL.

Editorial Comment

Ultrasound guidance for regional anaesthesia of the shoulder region can facilitate better injection precision. The volume of local anaesthesia needed to block components of the infraclavicular brachial plexus block was determined. Potentially, this block can be combined with the suprascapular nerve block for shoulder surgery.

2 | METHODS

The study was approved by the Regional Committee for Medical and Health Research Ethics (REK nord, TANN-bygget, UiT-The Arctic University of Norway, 9037 Tromsø, Norway). It received approval number 2017/464 on 26 October 2017 and was registered at www.clinicaltrials.gov (NCT03329456). The trial was performed in accordance with the Helsinki Declaration, at the University Hospital of North Norway from November 2017 to March 2018. Written informed consent was obtained from patients scheduled for hand surgery, who met the following inclusion criteria: age 18-70 years, BMI 20-35 kg/m^2 and ASA physical status 1-3. Exclusion criteria were: pregnancy, coagulation disorders, allergy to LA, atrioventricular block, pacemaker, diabetes and use of anticoagulation drugs other than acetylsalicylic acid or dipyridamol.

All blocks were performed by DM. Before the block all patients received oxygen supplementation by nasal cannula. Standard monitoring included electrocardiogram, non-invasive arterial pressure and pulse oximetry. On demand, intravenous midazolam or fentanyl was administered to ensure patient comfort. The patients were supine with the arm to be blocked adducted, while the hand rested comfortably on the abdomen. We used a SonoSite S-II unit (SonoSite, Inc, Bothell, WA, USA) with a 50 mm, 6-15 MHz linear array probe. A pre-scan was carried out to optimise the settings of the ultrasound apparatus. Sterile preparations included scrubbing the skin with chlorhexidine 5 mg/mL, use of sterile transducer covers (CIVCO, Kalona, Iowa, USA) and sterile ultrasound gel (Parker laboratories inc, Fairfield, USA). A skin wheal was raised with 1-2 mL lidocaine 10 mg/mL before insertion of an ultrasound echogenic 22G × 80 mm needle (PAJUNK® GmbH Medizintechnologie, Geisingen, Germany). The needle insertion point was 0.5-1.0 cm caudal to the lower edge of the clavicle, just medial to the coracoid process. Needle advancement was in the parasagittal plane, with continuous observation of the needle tip, using the in-plane technique. Considering the artery as a clock face with 12 o´clock ventral, the cords are normally found inside a periarterial sector from 3 to 11 o´clock and within 2 cm from the midaxis of the axillary artery[5] (Figure 1). More specifically, with reference to the centre of the artery, the lateral cord is usually at an angle of 276° and the posterior cord at 236°. This means that the lateral cord is commonly at 9 o'clock and the posterior cord at 8 o'clock in this imaginary clock face. On the basis of this observation, we injected the LA as a single deposit between 8 and 9 o'clock. We call this novel block the lateral sagittal infraclavicular block of the posterior and lateral cords. Injection rate was approximately 1 mL per second and we aimed to deliver LA in the immediate proximity of the arterial wall.

An electrical nerve stimulator (Stimuplex ® HNS11, B.Braun, Melsungen, Germany) with a current of 0.3 mA and 0.1 ms duration at 2 Hz was used to help reducing the risk of intraneural needle tip position. If a motor response was obtained, the needle was withdrawn in steps of 1 mm until the response disappeared.

Sensory-motor status of the upper limb was assessed by LMY before (baseline) and 30 minutes after completion of the blocks. Sensory testing was performed at pre-marked skin points in the areas of the axillary, intercostobrachial, medial brachial cutaneous, musculocutaneous, medial antebrachial cutaneous, radial, median and ulnar nerves. These points were in the middle of the proximal half part of the humerus laterally, in the middle of the proximal half of the humerus medially, in the middle of the distal half of the humerus

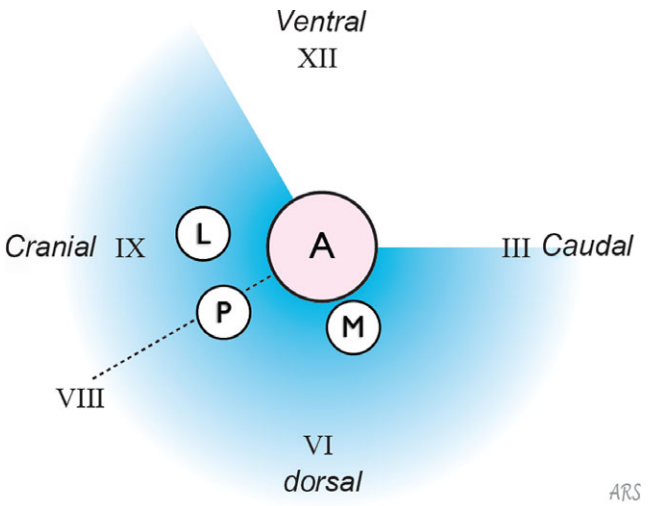

FIGURE 1 Schematic drawing of the cord positions with reference to the axillary artery. The infraclavicular drawing is parasagittal and shows the axillary artery (A) with clock face orientation (12 o´clock ventral) and the position of cords.[5] The point of injection was between 8 and 9 o´clock, immediately outside the arterial wall. The drawing is made by Axel R. Sauter. Reprint with permission from John Wiley & Sons[2]

medially, on the most prominent part of the brachioradial muscle belly, in the middle of the forearm on the ulnar side, between the first and second metacarpal bone dorsally, between the first and second metacarpal bone volarly and on the ulnar side of the fifth metacarpal bone, respectively.

The following scale was used: 3 = normal cold feeling; 2 = reduced cold feeling (hypoalgesia); 1 = no cold feeling, but feels touch (analgesia); and 0 = no cold or touch feeling (anaesthesia). Muscle power was assessed using a modified seven-point scale (Table 1).[6]

Block success was assessed 30 minutes after withdrawal of the needle. Posterior cord block was considered successful if the sensory score for the axillary nerve was 0 or 1. The musculocutaneous nerve test was used as test for block success of the lateral cord. However, anastomoses between the median and musculocutaneous nerves[7] may interfere with sensory testing of the lateral cord. Accordingly, the lateral cord block was judged successful if the sensory score of the musculocutaneous nerve was 0 or 1 or if the muscle power of the biceps was ≤4–.

Block performance time was the time from placing the probe on the skin to withdrawal of the block needle. The number of needle passes was counted and the initial needle insertion was defined as the first pass. An additional needle pass was defined as needle retraction of at least 10 mm prior to further needle insertion.

We recorded the incidence of adverse events including paresthesia, vessel puncture, LA systemic toxicity, Horner's syndrome, dyspnoea, hoarseness and dysphagia. Ultrasound was used within 15 minutes after completed procedure to exclude ipsilateral pneumothorax.

After the 30 minutes assessment, all patients received a complementary LSIB dose to ensure anaesthesia for hand surgery. Data collection was terminated after administration of the supplemental dose of LA.

2.1 | Statistics and power analysis

The staircase up-and-down method was used to determine MEV_{50} and its 95% CI.[8] To estimate MEV_{95}, logistic regression and probit transformation were used. For sample size calculation we applied the formula by Dixon and Massey, n = 2(SD/SEM),[2] where SD is standard deviation and SEM the standard error of the mean. Assuming a 2.5 mL SD and 0.75 mL SEM, the formula then suggested a need for 23 patients to determine MEV_{50}. The binary response in the logistic regression model was failed block (yes/no) with LA volume as the independent variable. We used the SAS statistical software package (SAS®, V9.2, SAS Institute Inc, Cary, NC, USA) for this work.

Volume assignment was carried out using an up-and-down sequential method, where the volume administered to each patient depended on the response of the previous one. The first patient received 15 mL, which we clinically a priori considered to be an appropriate volume of LA. In case of failure, the next patient received a higher volume, defined as the previous volume with an increment of 1 mL. If the previous patient had a successful block, the next subject received the previous volume with a decrement of 1 mL.

Continuous data are presented as mean (SD) or median (range) as appropriate. Categorical data are presented as n (%).

TABLE 1 Modified Medical Research Council scale of muscle power

5	Normal power
4+	Active movement against gravity and resistance (>50% of normal power)
4–	Active movement against gravity and resistance (<50% of normal power)
3	Active movement against gravity
2	Active movement with gravity eliminated
1	Flicker or trace contraction
0	No contraction

3 | RESULTS

All patients completed the study and were included in the statistical analyses. Their characteristics are shown in Table 2. Block performance data are summarised in Table 3. LA was injected in a volume range from 6 to 15 mL. The up-and-down sequence is presented in

TABLE 2 Patient characteristics (n = 23)

Age, mean (SD), y	48.1 (14.1)
Gender (male/female), n	9/14
BMI, mean (SD), kg/m^2	24.6 (3.3)
ASA physical status (I/II/III), n	13/10/0

Continuous variables are presented as mean (SD). Categorical variables are presented as counts.
BMI, body mass index; ASA, American Society of Anaesthesiologists.

TABLE 3 Block data (n = 23)

Performance time, median (range), min	3.7 (2.9-7.7)
No. needle passes, n (%)	
1	20 (87)
2	2 (8)
3	1 (5)
Paresthesia, n (%)	2 (8)
Vascular puncture, n (%)	1 (5)
Horner's syndrome, n (%)	0 (0)
Dyspnoea, n (%)	0 (0)
Hoarseness, n (%)	0 (0)
Dysphagia, n (%)	0 (0)
LA systemic toxicity, n (%)	0 (0)
Pneumothorax, n (%)	0 (0)

Continuous variables are presented as median (range). Categorical variables are presented as count (percentage).
LA, local anaesthetic.

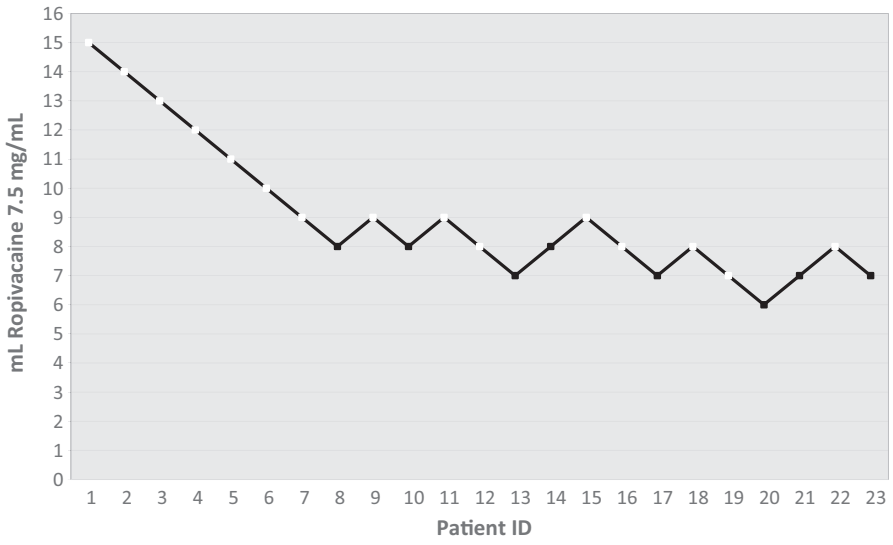

FIGURE 2 Up-and-down sequence of the ultrasound-guided block of the posterior and lateral cords of the infraclavicular brachial plexus using ropivacaine 7.5 mg/mL. □ Successful block; ■ Failed block

TABLE 4 Individual sensory test data 30 minutes after the blocks (n = 23)

Patient id	Volume injected (mL)	Axillary nerve	Intercostobrachial nerve	Medial brachial cutaneous nerve	Musculocutaneous nerve	Medial antebrachial cutaneous nerve	Radial nerve	Median nerve	Ulnar nerve
1	15	1	1	0	1	0	2	1	3
2	14	1	3	3	2	2	1	1	3
3	13	1	3	1	0	0	0	0	0
4	12	1	1	2	1	3	2	1	3
5	11	1	2	2	2	0	1	2	1
6	10	0	2	1	2	2	2	2	2
7	9	1	2	0	1	1	1	0	2
8	8	3	3	3	1	2	1	1	3
9	9	1	3	0	2	-	1	1	2
10	8	3	3	3	3	0	3	3	3
11	9	1	2	1	1	0	0	2	1
12	8	1	3	2	1	1	0	1	-
13	7	3	2	2	2	-	2	2	3
14	8	2	1	0	2	0	1	0	1
15	9	0	3	0	1	0	1	1	1
16	8	1	3	3	3	-	2	2	2
17	7	1	3	3	3	3	3	1	3
18	8	1	3	3	3	3	3	3	3
19	7	1	1	2	1	-	0	0	3
20	6	2	3	3	1	1	1	1	1
21	7	2	2	3	0	3	3	3	3
22	8	0	3	1	1	1	2	3	1
23	7	2	3	3	2	-	1	2	3

3 = normal feeling. 2 = reduced cold sensation (hypoalgesia). 1 = no cold feeling (analgesia). 0 = no cold or touch feeling (anaesthesia). Failed blocks are presented in grey.

Figure 2. Using ropivacaine 7.5 mg/mL, the MEV_{50} was calculated to 7.8 mL (95% CI, 7.3-8.4) and MEV_{95} was estimated to 9.0 mL (95% CI, 7.8- 10.3).

Only one patient required premedication and received 50 µg fentanyl for the block procedure. Transient paresthesia with a duration of 1-2 seconds was recorded in two patients. Vascular puncture

of a small vein was recorded in one patient, but without any signs of local haematoma. There were no signs of LA systemic toxicity and pneumothorax was not detected by ultrasound in any patient.

4 | DISCUSSION

Recently, we published a distal triple-block alternative to interscalene block for arthroscopic shoulder surgery.[1] The relatively large LA dose of its infraclavicular component has been a concern. To potentially reduce LA volume for this block, we decided to explore the possibility of blocking only two of the three cords, instead of earlier all three cords.[1,2] This appeared reasonable since the shoulder relevant nerves of infraclavicular origin are the axillary, subscapular and lateral pectoral nerves, of which the two first are derived from the posterior cord and the latter from the lateral cord. Aim for this study was therefore to determine MEV_{50} and estimate MEV_{95} for a single-deposit infraclavicular posterior and lateral cord block using ropivacaine 7.5 mg/mL. We then found an estimated MEV in 95% of the patients to be 9.0 mL (95% CI, 7.8-10.3 mL), which is considerably less compared to the volume used in our previous study.[1]

Our definition of successful blocks deserves some comments. We considered the posterior cord block successful if the sensory score for the axillary nerve was 0 or 1. In that case, also the subscapular nerve was assumed to be blocked, since both nerves belong to the posterior cord. Success criteria for the lateral cord block were slightly more complex. A successful block of this cord was assumed to include a block of the lateral pectoral nerve, originating from this cord. However, this nerve does not have cutaneous representation.[9] As a substitute, we tested another nerve of the lateral cord, the musculocutaneous nerve. This raised another issue. It is clinically acknowledged that anastomoses between the lateral and medial cords are common[7] and may interfere with sensory testing after an infraclavicular block. These anatomical variations may be the reason why we, in the pilot fase, observed patients with paralysis of the biceps muscle (musculocutaneous nerve), in spite of intact sensory function in the cutaneous area of this nerve. The normal sensibility may then have been provided by anastomosis between the musculocutaneous and median nerve, with the median nerve not affected by local anaesthetic. The success criterion for the lateral cord was therefore either a sensory test of 0 or 1 in the cutaneous area of

TABLE 5 Individual motor power data 30 minutes after the blocks (n = 23)

Patient id	Volume injected (mL)	Axillary nerve	Suprascapular nerve	Subscapular/lateral pectoral nerve	Musculocutaneous nerve	Radial nerve (elbow)	Radial nerve (wrist)	Median nerve	Ulnar nerve
1	15	4–	4+	4–	2	4–	4+	3	4–
2	14	4–	5	4–	2	4–	-	5	4–
3	13	2	5	4–	0	0	0	0	0
4	12	2	5	4+	4–	5	4+	4–	5
5	11	2	5	4–	4–	4–	4–	4–	4–
6	10	4–	5	4+	4–	4–	3	4–	4+
7	9	1	5	4+	1	4+	4–	4–	4–
8	8	4–	5	4+	4–	4+	4–	4–	4–
9	9	1	5	4–	4–	4–	-	4–	4–
10	8	4+	5	5	4+	5	5	1	4+
11	9	3	5	4–	4–	1	4–	4–	4–
12	8	4–	5	4–	4–	1	-	4–	1
13	7	3	5	4+	4–	4–	-	4–	4–
14	8	2	4+	4–	1	4–	4–	4–	1
15	9	1	5	3	1	4–	4–	4–	4–
16	8	4–	5	4–	4–	4+	-	4+	4–
17	7	4–	5	4+	4+	5	5	4–	4+
18	8	4–	5	4–	4–	4+	4+	5	5
19	7	1	5	4–	1	4–	-	1	4–
20	6	4–	5	4–	3	4+	4–	4–	3
21	7	4–	5	4–	4+	4+	-	-	5
22	8	2	5	4–	4–	1	0	4–	1
23	7	3	5	4+	1	4–	-	4–	4–

5 = Normal power. 4+ = Active movement against gravity and resistance (>50% of normal power). 4– = Active movement against gravity and resistance (<50% of normal power). 3 = Active movement against gravity. 2 = Active movement with gravity eliminated. 1 = Flicker or trace contraction. 0 = No contraction. Failed blocks are presented in grey.

the musculocutaneous nerve, or a biceps motor score of ≤4−. This motor power criterion was chosen based on previous assessments of patients who had received our novel combination of blocks for arthroscopic shoulder surgery[1] and our clinical experience. We indeed had some effect on the medial cord as well, as shown in Tables 4 and 5. This was not unexpected, since this LSIB variant is meant to effectively block the lateral and the posterior cords, but it does not have the ambition to spare the medial cord.

It is possible to inject selectively towards the individual cords. However, it should be noted that identifying all cords by ultrasound may be difficult[10] and the ability relies on both the experience of the anaesthesiologist and the resolution of the ultrasound unit. The position of the three cords has been examined by MRI of 20 volunteers.[5,11] On the basis of the authors' description, to block the posterior and lateral cords, we chose to perform a single deposit between 8 o'clock and 9 o'clock. We believe this method, built on simple sonographical reference points, may decrease ultrasound apparatus requirements and operator dependent variations in performance.

Technically, the block was easy and quick to perform. Only one needle pass was required for 20 (87%) of the patients and the mean block time was 3.7 minutes. Two patients required two needle passes and one patient three passes to achieve correct needle position before injection. The latter patient was technically challenging because of small vessels along the trajectory of the needle.

Pilot data indicated that we could expect a substantial reduction in the volume needed to obtain a block of the posterior and lateral cords compared to the volume needed to block all three cords.[2] The results of our study showed that the actual effective LA volumes were much lower than our starting volume of 15 mL. However, this did not affect the calculations of the MEV_{50} and MEV_{95}. Several dose-finding methods can be used to investigate the pharmacodynamic properties of LA for peripheral nerve blocks.[12] Sigmoidal dose-response curve analysis and the continual reassessment method are alternative methods that have been applied in MEV studies. We chose the staircase up-and-down method primarily because it requires a limited number of subjects. We were aware that the staircase up-and-down method should primarily be applied for investigation of the 50th quantile and that extrapolations to find MEV_{95} may cause wide confidence intervals. However, in this study 95% CI was quite narrow due to the fact that all block failures appeared in the interval between 6 and 8 mL.

Some limitations should be addressed. First, the position for injection was a priori decided to be between 8 and 9 o' clock, considering the axillary artery as the centre of a clock face. This was based on a statistical extrapolation from a MRI study.[5,11] Although it simplifies the technique, it does not take into account the anatomical variations of the cords' positions. As a result, it may have had an effect of the volume needed to block the cords. Furthermore, all the blocks were performed by an expert operator, which raises the question if the results are applicable to apprentices. The assessor was not blinded and this could theoretically have played a role.

We could certainly have used a lower concentration of ropivacaine, but this study evolved from the need to reduce the doses of our three-component shoulder block. This study suggests that the total LA dose for our novel shoulder block can possibly be reduced from 277.5 to 112.5 mg. However, this hypothesis needs to be confirmed in a future clinical study. Moreover, further dose-finding studies are required for other concentrations and other LA agents.

In summary, this single-deposit method to block the lateral and posterior cord of the infraclavicular plexus with ropivacaine 7.5 mg/mL revealed a MEV_{50} and MEV_{95} of 7.8 mL (95% CI, 7.3-8.4) and 9.0 mL (95% CI, 7.8-10.3), respectively.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

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REFERENCES

1. Musso D, Flohr-Madsen S, Meknas K, Wilsgaard T, Ytrebo LM, Klaastad O. A novel combination of peripheral nerve blocks for arthroscopic shoulder surgery. *Acta Anaesthesiol Scand*. 2017;61:1192-1202.
2. Flohr-Madsen S, Ytrebo LM, Kregnes S, Wilsgaard T, Klaastad O. Minimum effective volume of ropivacaine 7.5 mg/ml for an ultrasound-guided infraclavicular brachial plexus block. *Acta Anaesthesiol Scand*. 2013;57:495-501.
3. Borgeat A, Ekatodramis G. Anaesthesia for shoulder surgery. *Best Pract Res Clin Anaesthesiol*. 2002;16:211-225.
4. Aszmann OC, Dellon AL, Birely BT, McFarland EG. Innervation of the human shoulder joint and its implications for surgery. *Clin Orthop Relat Res*. 1996;202-207.
5. Sauter AR, Smith HJ, Stubhaug A, Dodgson MS, Klaastad O. Use of magnetic resonance imaging to define the anatomical location closest to all three cords of the infraclavicular brachial plexus. *Anesth Analg*. 2006;103:1574-1576.
6. Paternostro-Sluga T, Grim-Stieger M, Posch M, et al. Reliability and validity of the Medical Research Council (MRC) scale and a modified scale for testing muscle strength in patients with radial palsy. *J Rehabil Med*. 2008;40:665-671.
7. Caetano EB, Vieira LA, Cavalheiro CS, Razuk MF, Almargo MA, Caetano MF. Anatomic study of the nervous communication between the median and musculoucutaneous nerve. *Acta Ortop Bras*. 2016;24:200-203.
8. Dixon WJ. Staircase bioassay: the up-and-down method. *Neurosci Biobehav Rev*. 1991;15:47-50.
9. Last RJ. *Anatomy. Regional and applied*. New York: Churchill Livingstone; 1978.

10. Perlas A, Chan VW, Simons M. Brachial plexus examination and localization using ultrasound and electrical stimulation: a volunteer study. *Anesthesiology*. 2003;99:429-435.
11. Klaastad O, Smith HJ, Smedby O, et al. A novel infraclavicular brachial plexus block: the lateral and sagittal technique, developed by magnetic resonance imaging studies. *Anesth Analg*. 2004;98:252-256.
12. Saranteas T, Finlayson RJ, Tran DQ. Dose-finding methodology for peripheral nerve blocks. *Reg Anesth Pain Med*. 2014;39:550-555.

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Paper 3

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CLINICAL INVESTIGATION

acta Anaesthesiologica Scandinavica

A combination of infraclavicular and suprascapular nerve blocks for total shoulder arthroplasty: A case series

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Abstract

Background: Shoulder arthroplasty is associated with significant post-operative pain. Interscalene plexus block is the gold standard for pain management in patients undergoing this surgery, however, alternatives are currently being developed. We hypothesized that a combination of anterior suprascapular nerve block and lateral sagittal infraclavicular block would provide effective post-operative analgesia. Primary aims for this study were to document numeric rating scale (NRS) pain score and use of oral morphine equivalents (OMEq) during the first 24 hours after surgery. Secondary aim was to determine the incidence of hemidiaphragmatic paralysis.

Methods: Twenty patients (ASA physical status I-III) scheduled for shoulder arthroplasty were studied. Four mL ropivacaine 0.5% was administered for the suprascapular nerve block and 15 mL ropivacaine 0.75% for the infraclavicular block. Surgery was performed under general anaesthesia. Paracetamol and prolonged-release oxycodone were prescribed as post-operative analgesics. Morphine and oxycodone were prescribed as rescue pain medication. Diaphragm status was assessed by ultrasound.

Results: Median NRS (0-10) at 1, 3, 6, 8 and 24 hours post-operatively were 1, 0, 0, 0 and 3, respectively. NRS at rest during the first 24 post-operative hours was 4 (2.5-4.5 [0-5]), median (IQR [range]). Maximum NRS was 6.5 (5-8 [0-10]) median (IQR [range]). Total OMEq during the first 24 post-operative hours was 52.5 mg (30-60 [26.4-121.5]) median (IQR [range]). Hemidiaphragmatic paralysis was diagnosed in one patient (5%).

Conclusions: The combination of suprascapular and infraclavicular nerve block shows an encouraging post-operative analgesic profile and a low risk for hemidiaphragmatic paralysis after total shoulder arthroplasty.

Institutional review board contact information: The present study received ethical approval on 2nd November 2018 from the Regional Ethics Committee, REK nord, TANN-bygget, UiT- The Arctic University of Norway, 9037 Tromsø, Norway (reference 2018-2081). Institutional Board approval number 02-19 was issued by Nordland Hospital in Bodø, Parkveien 95, 8005 Bodø, Norway on 28th January 2019. Institutional Board approval number 01-20 was issued by Sørlandet Hospital in Kristiansand, Lundsiden, 4604 Kristiansand S, Norway on 15th January 2020.

1 | INTRODUCTION

Shoulder surgery is frequently associated with high levels of post-operative pain, which may require analgesia with opioids for several days.[1] The use of regional anaesthetic techniques is therefore recommended. Interscalene brachial plexus block is currently the gold standard for intraoperative and post-operative pain management in patients undergoing shoulder surgery. However, in recent years there has been increasing research into alternatives to the classic interscalene block due to a wide spectrum of complications, with the risk of hemidiaphragmatic paresis of prominent interest.[2-5] The innervation of the shoulder joint is provided by several nerves[6,7]: subscapular, axillary, lateral pectoral and suprascapular nerve. The subscapular, axillary and lateral pectoral nerve can be blocked with a single injection as distal as at the cord level with the infraclavicular block, while the suprascapular nerve must be blocked separately. In a previous randomized placebo-controlled study,[8] we explored the effects of an anterior suprascapular block (SSNB) in patients undergoing hand surgery under regional anaesthesia, provided by a lateral sagittal infraclavicular block (LSIB). The diaphragmatic function was assessed by chest x-ray and none of the 15 patients showed any sign of ipsilateral phrenic palsy. We have also showed that a combination of peripheral nerve blocks allowed patients to undergo arthroscopic shoulder surgery without the need for opioids or an artificial airway.[9] The patients received a combination of superficial cervical plexus block, SSNB and LSIB. More recently, we have determined the minimum effective local anaesthetic volume needed to block shoulder relevant nerves with the LSIB-method.[10] Data indicated a significantly reduced total volume of local anaesthetics needed to anesthetize the shoulder. Accordingly, we hypothesized that a combination of anterior suprascapular nerve block and lateral sagittal infraclavicular block of the posterior and lateral cords would provide effective post-operative analgesia for patients undergoing shoulder arthroplasty. Primary aims for the current study were to document numeric rating scale (NRS) and use of oral morphine equivalents (OMEq) during the first 24 hours after surgery. Secondary aim was to determine the incidence of ipsilateral hemidiaphragmatic paralysis 30 minutes after the blocks.

2 | METHODS

In this prospective case series, 20 patients scheduled for shoulder arthroplasty were included. The study was approved by the Institutional Boards at the University Hospital of North Norway (registration number 2018-2081 REK Nord, 2nd November 2018), Nordland Hospital in Bodø (registration number 02-19, 28th January 2019), and Sørlandet Hospital in Kristiansand (registration number 01-20, 15th January 2020). It was also registered at www.clinicaltrials.gov (registration number NCT 03877835, 18th March 2019). The study was performed at the University Hospital of North Norway in Tromsø, Nordland Hospital in Bodø, and Sørlandet hospital in Kristiansand, from March 2019 to August 2020, in accordance with the Helsinki Declaration. Written informed consent was obtained and the following inclusion criteria were applied: 18-80 years old, BMI 20-35 kg m^{-2} and ASA physical status 1-3. Exclusion criteria included: pregnancy, severe respiratory disease, use of anticoagulation drugs other than acetylsalicylic acid or dipyridamole, allergy to local anaesthetics, patients on regular opioids, atrioventricular block, pacemaker and peripheral neuropathy.

Editorial Comment

There is no generally agreed upon single approach to regional anaesthesia for shoulder arthroplasty. In this prospective series, a combination of two blocks is examined, and found to be promising.

All patients received oxygen supplementation by a nasal cannula. No premedication was given. Standard monitoring included pulse oximetry, electrocardiogram and non-invasive blood pressure.

All blocks were performed by DM. LMY assessed neurological status in all patients, before and 30 minutes after the block, but was not present during the procedure. The patients were placed supine with slightly elevated upper body. All blocks were ultrasound-guided, using a SonoSite S-II unit (SonoSite, Inc). A 38 mm linear array probe 6-13 MHz was applied. The initial needle insertion counted as the first pass. Moreover, a nerve stimulator response by a current ≤0.3 mA, 0.1 ms and 2 Hz defined the need for a small retraction of the needle. Additional passes were defined as needle advancement upon a retraction of at least 10 mm. A pre-scan was carried out to optimize the settings of the ultrasound apparatus. Skin preparation was performed using chlorhexidine 0.5%. The probe was covered with a sterile transducer cover and sterile ultrasound gel was used. A skin wheal was raised with 1-2 mL lidocaine 1% before insertion of an ultrasound echogenic 22G × 80 mm needle (PAJUNK® GmbH Medizintechnologie, Geisingen, Germany).

The supraclavicular approach to the suprascapular block was first described by Siegenthaler et al.[11] The suprascapular nerve is usually the most craniolateral nerve emerging from the supraclavicular brachial plexus. The ultrasound probe was placed on the supraclavicular fossa to identify the brachial plexus. Subsequently, the plexus was followed proximally until the suprascapular nerve was observed branching from the superior trunk. The nerve was then followed back distally, until it was visualized deep to the omohyoid muscle. The local anaesthetic was injected at the most lateral transverse view of the nerve that could be obtained with the in-plane technique, while advancing the needle from posterolateral to anteromedial. The local anaesthetic dose was 4 mL ropivacaine 0.5%.

For the infraclavicular block of the posterior and lateral cord, the needle insertion point was 0.5-1.0 cm caudal to the lower edge of the clavicle, just medial to the coracoid process. Needle advancement was in the parasagittal plane, with continuous observation of the needle tip, using the in-plane technique. Considering the artery as a clock face with 12 o´clock ventral, the local anaesthetic was

injected as a single deposit of 15 mL ropivacaine 0.75% between 8 and 9 o'clock.[10]

Total block performance time was defined as the time interval between contact of the ultrasound probe with the patient for the suprascapular block and the withdrawal of the needle for the infraclavicular block. Dexamethasone (4 mg) was administrated intravenously, as a block adjuvant, after the completed block procedure.

Subsequently, all patients underwent general anaesthesia with endotracheal intubation using target-controlled infusion (TCI) anaesthesia with propofol and remifentanil. During the surgery all subjects were placed in the beach chair position and no other opioids were administrated. The surgical incision was infiltrated with 20 mL bupivacaine 0.25% with adrenaline 5 μg mL^{-1} at the end of surgery.

All patients received 1 g paracetamol four times daily and 10 mg prolonged-release oxycodone tablets twice a day. First dose was given post-operative at 6:00 PM In the post-anaesthesia care unit (PACU), rescue pain medication was given as intravenous morphine. In the hospital ward, rescue pain medication was given as oxycodone, either orally or intravenously.

2.1 | Block assessment

Sensory-motor status of the upper limb was assessed by LMY before the blocks and 30 minutes after block completion. Sensory testing was performed by applying an ice cube to the cutaneous innervation areas of the axillary and musculocutaneous nerves. The following scale was used: 3 = normal cold feeling; 2 = reduced cold feeling (hypoalgesia); 1 = no cold feeling, but feels touch (analgesia); and 0 = no cold or touch feeling (anaesthesia).

Muscle power was assessed using a modified seven-point scale (Table 1).[12] The suprascapular nerve block was tested by the force for lateral rotation of the humerus against manual resistance, while the arm was adducted and the elbow flexed at 90°.

Block success was assessed 30 minutes after withdrawal of the needle from the last of the two blocks. The block combination was considered successful if it met the following three criteria: (a) the suprascapular nerve block had a motor score ≤4−; (b) the axillary nerve sensory score was 0 or 1; (c) the musculocutaneous nerve sensory score was 0 or 1, or if the motor score was ≤4−. As previously mentioned, the suprascapular and the axillary nerves are of direct interest for the anaesthesia of the shoulder. The musculocutaneous nerve test was used as a surrogate test for the lateral cord, where the lateral pectoral nerve is of most interest. Since anastomoses between the median and musculocutaneous nerves[13] may interfere with sensory testing of the lateral cord, the lateral cord block was judged with both a sensory and a muscle power score.

The incidence of adverse events was recorded, including paraesthesia, vessel puncture, systemic local anaesthetic toxicity, Horner's syndrome, dyspnoea, hoarseness and dysphagia. A lung ultrasound scan was performed within 15 minutes after completed procedure to look for signs of pneumothorax.

Diaphragm status was assessed by a blinded investigator (LMY) with the use of ultrasound before and 30 minutes after the blocks were performed. A 2-5 MHz curvilinear US transducer (SonoSite, Inc) were used in all subjects; the liver and spleen served as acoustic windows on the right and left side, respectively. Hemidiaphragmatic paralysis was defined as the absence of diaphragmatic motion during normal respiration, coupled with absent or (paradoxical) cranial diaphragmatic movement when the patient forcefully sniffed. Patients with a positive ultrasound scan underwent a chest x-ray to confirm the diagnosis.

2.2 | Post-operative assessment

NRS (0-10) pain score was recorded at 1, 3, 6, 8 and 24 hours after arrival to the PACU. Occurrence of post-operative nausea and vomiting (PONV) in the PACU was registered. All patients were interviewed by DM after the first post-operative day and opioid consumption was converted to OMEq.[14] Static median NRS pain score and maximum NRS pain score during the first 24 post-operative hours were recorded. Conversion factors are presented in Table 2.

As this study was an exploratory case series, no formal power calculation was performed. A priori, it was decided that the inclusion of 20 patients would provide sufficient information to serve as a hypothesis-generating data source. Descriptive characteristics are presented as mean (standard deviation), median (interquartile range and range) or number, as appropriate. Analyses were performed using the Statistical Package for Social Sciences (SPSS) program version 26.0 for Windows (SPSS Inc).

3 | RESULTS

Twenty-eight consecutive patients scheduled for shoulder arthroplasty were screened. Of these, 20 patients fulfilled the inclusion

TABLE 1 Modified Medical Research Council scale of muscle power[1]

5	Normal power
4+	Active movement against gravity and resistance (>50% of normal power)
4−	Active movement against gravity and resistance (<50% of normal power)
3	Active movement against gravity
2	Active movement with gravity eliminated
1	Flicker or trace contraction
0	No contraction

criteria (Tromsø: 9, Bodø: 9, Kristiansand: 2). One patient did not receive total arthroplasty and was therefore excluded from the data analyses. Consort flow diagram is presented in Figure 1. Patient characteristics are presented in Table 3.

The block combination was successful in 18 of 19 patients (95%) after 30 minutes. The failed block was due to late onset of the SSNB in patient #6, but met the success criteria after 35 minutes. We applied the intention-to-treat principle and therefore included all 19 patients in the subsequent analyses.

Time to pain onset was 12.7 (0-19.5 [0-21.7]) median (IQR [range]) hours. During the first 24 hours, pain score at rest was 4 (2.5-4.5 [0-5]), median (IQR [range]). Maximum pain score was 6.5 (5-8 [0-10]) median (IQR [range]). Median NRS values 1, 3, 6, 8 and 24 hours after arrival to the PACU are shown in Figure 2. Cumulative OMEq over time, with and without the scheduled prolonged-release oxycodone, are shown in Table 4. Median consumption of OMEq during the first 24 postoperative hours was 52.5 (30-60 [26.4-121.5]) (IQR [range]) mg.

None of the patients reported dysphagia, dyspnoea and hoarseness. No cases of Horner's syndrome were observed and none of the patients showed ultrasonographic signs of pneumothorax. One patient (5%) was diagnosed with hemidiaphragmatic paralysis, which was confirmed by chest x-ray. Hemidiaphragmatic function resumed when the local anaesthetic effect had worn off, and this was documented by a new chest x-ray on the first post-operative day.

Individual block data are presented in Table 5. Total block performance time was 7.2 (6.8-7.8 [6.3-10.5]), median (IQR [range]) minutes. Time from end of local anaesthetic injection until the first NRS measurement was 6.7 (5.3-7.4 [4.6-9.3]), median (IQR [range])

TABLE 2 OMEq conversion factors applied for 1 mg of different opioids

	OMEq
Morphine p.o.	1
Morphine iv	3
Oxycodone p.o.	1.5
Oxycodone iv	3
Tramadol p.o.	0.2
Codeine p.o.	0.13

Note: Adapted from Nielsen et al[2]

TABLE 3 Characteristics of study patients scheduled for total shoulder arthroplasty (n = 19)

Age (yr)	69.9 (5.2)
gender (male/female)	10/9
Body mass index; kg m^{-2}	29.2 (2.6)
ASA physical status (I/II/III)	1/15/3
Types of prothesis (anatomic/reverse)	9/10
Side (right/left)	7/12

Note: Continuous variables are presented as mean (standard deviation); categorical variables are presented as counts.
Abbreviation: ASA, American Society of Anaesthesiologists.

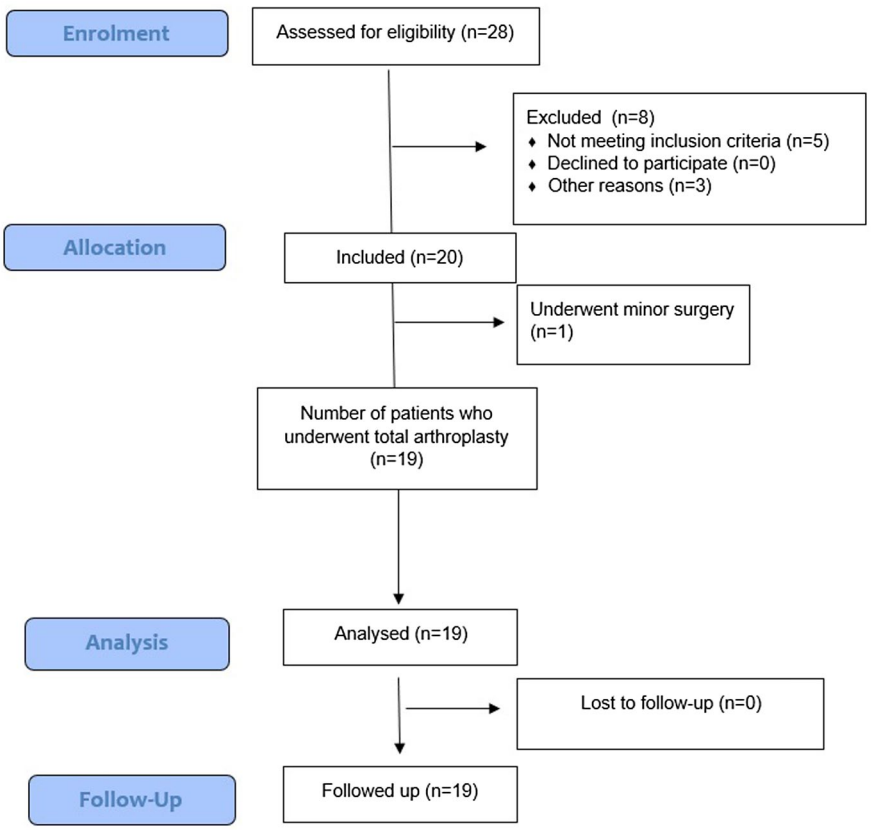

FIGURE 1 Consort flow diagram

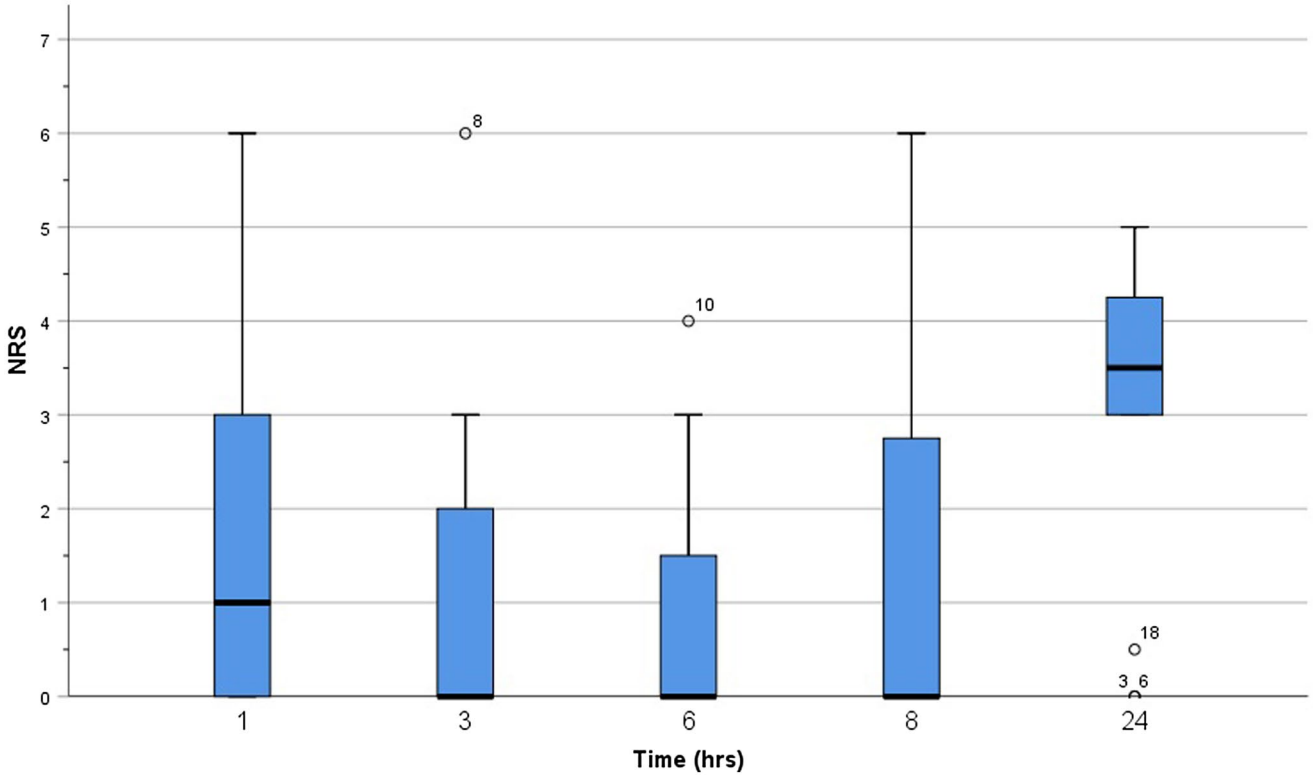

FIGURE 2 NRS at different timepoints. Boxplot showing median, quartiles, range and outliers

TABLE 4 Cumulative doses of rescue OMEq and total OMEq over time. Values are median (IQR [range])

	PACU	0-8 hrs	0-24 hrs
Rescue OMEq	0 (0-0 [0-24])	0 (0-0 [0-31.5])	22.5 (7.5-30 [0-91.5])
Total OMEq	0 (0-0 [0-24])	15 (15-15 [15-46.5])	52.5 (30-60 [26.4-121.5])

Note: Total OMEq = Rescue OMEq + regular OMEq prescribed.
Abbreviation: PACU, Post Anaesthesia Care Unit.

TABLE 5 Individual block performance data (n = 19). Values are median (IQR [range])

	SSNB	LSIB	Total
Performance time (min)	3.2 (2.8-3.6 [2.3-6.4])	3.0 (2.7-3.3 [2.3-4.2])	7.2 (6.8-7.8 [6.3-10.5])
Number of passes (n)	1 (1-1 [1-2])	1 (1-1 [1-2])	2 (2-3 [2-3])
Paraesthesia (n)	0	2	2
Vascular puncture (n)	0	0	0
Local anaesthetic systemic toxicity (n)	0	0	0

Abbreviations: SSNB, suprascapular nerve block; LSIB, lateral sagittal infraclavicular block.

hours. The median duration of surgery was 1.8 (1.7-2.5 [1.5-3.2]) (IQR [range]) hours.

In the PACU, no patient suffered from PONV. Three patients required intravenous morphine and mean NRS in this group of patients was 3.5. The mean morphine dose administered to these three patients was 5.1 mg.

4 | DISCUSSION

In this case series, we explored a combination of an infraclavicular brachial plexus block and anterior suprascapular nerve block in 20 patients receiving total shoulder arthroplasty surgery under general anaesthesia. A successful block was achieved in 95% of patients, with short performance time and a good safety profile. We reported one case of hemidiaphragmatic paralysis (5%). The median NRS pain score at 1, 3, 6 and 8 hours post-operatively were low, though a noticeable increase in score was observed after the nerve blocks wore off. Median use of OMEq during the first 24 post-operative hours was 52.5 mg.

In recent years, we have witnessed an increasing interest in alternative peripheral nerve blocks to provide analgesia for shoulder

References

1. Paternostro-Sluga T, Grim-Stieger M, Posch M, et al Reliability and validity of the Medical Research Council (MRC) scale and a modified scale for testing muscle strength in patients with radial palsy. J Rehabil Med 2008;40:665-71.
2. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. Pharmacoepidemiol Drug Saf 2016;25:733-7.

surgery.[4,5] This has resulted in a plethora of studies investigating nerve blocks from nerve root to terminal nerve level. Our focus has been at the cord level and, therefore, on the infraclavicular block. The rationale for this is simple. One of the most distal approaches described for shoulder analgesia is by injection close to terminal nerves, namely the combination of suprascapular and axillary nerve blocks. These distal blocks may provide good post-operative analgesia after shoulder arthroscopy, but their use in more extensive surgery is not recommended.[15-17] This is allegedly due to the contributions of proximal branches from the axillary nerve, the subscapular and lateral pectoral nerves, all arising from the posterior and the lateral cord of the brachial plexus. Hence, the infraclavicular block allows blocking of all these nerves with a single injection and is theoretically expected to result in a denser block. The infraclavicular block dose was extrapolated by data from a recent minimum effective volume (MEV) publication,[10] where we calculated a MEV_{50} of 7.8 mL and estimated a MEV_{95} of 9.0 mL. However, in the current study, we opted for a higher volume (15 mL), to prevent the risk of inadequate post-operative pain coverage.

To our knowledge, the minimum effective dose for a successful SSNB is currently unknown. A lower volume for a successful block has been described,[18] but the clinical analgesic effect of this approach remains unexplored. Nonetheless, we have previously shown that 4 mL ropivacaine 0.5% provided satisfying post-operative analgesia after shoulder arthroscopy.[9]

Paracetamol and oxycodone were prescribed as regular medication, with morphine and oxycodone as rescue pain medications. However, prescription of a wider multimodal pain medication strategy could potentially have reduced OMEq consumption. Administration of adjuvants are known to prolong block duration of peripheral nerve blocks[19] and in this study we opted for 4 mg dexamethasone administered intravenously. It is possible to speculate that a higher dose[20] or a combination of adjuvants[21,22] could have resulted in longer lasting blocks and thus lower total consumption of OMEq.

Our block combination does not aim to provide surgical anaesthesia, but rather provide effective post-operative analgesia. It is therefore not unexpected that a few patients experienced some level of pain in the PACU. Nevertheless, the median NRS in the immediate post-operative setting was 1 and rescue medication was only required in three patients with mean NRS of 3.5. Block duration could not be accurately determined since block effects wore off during the night and most patients struggled to exactly recall the time that sensory function was restored. However, they could place with ease the pain onset on a timeline. Therefore, the time from the retraction of the block needle to first report of pain was used as a surrogate for block duration. It is worth acknowledging that this could be a conspicuous underestimation of the real block duration, considering the broad discrepancy between time to first reported pain and time to reported restored sensory status (12.7 hours vs 19.8 hours). The consumption of extra OMEq, beyond the pre-scheduled analgesic regime, is clearly concentrated between 8 and 24 hours after the arrival to the PACU and therefore after the effect of the blocks has worn off. As a result, even if no patients suffered from PONV in the PACU, five experienced opioid-induced nausea or vomiting. Further modifications including dose adjustments, type and dose of adjuvants applied, catheter-based techniques, as well as design of a more complex multimodal analgesic regime may prolong pain relief and thus improve NRS results and OMEq consumption.

Despite several modifications, no single intervention on the interscalene technique seems to decrease the incidence of phrenic palsy below 27%.[4] In the present study, we report one case of hemidiaphragmatic paralysis, which accounts for a 5% incidence. Unfortunately, the mechanisms for how the phrenic nerve became anaesthetised can only be speculated. In this patient (#8) the ultrasonographical visualisation of the SSN proved to be challenging and the nerve was eventually blocked in a more cranial position, closer to the cervical structures, with possible cranial spread to the phrenic nerve. Clinicians should be aware of this possibility and be vigilant during the ultrasonographic phase, in order to optimize the subsequent injection of local anaesthetic.

Our study presents some further limitations. The NRS scale is a validated pain scoring tool but relies on an accurate patient response. At times, it was challenging to assess average pain score during the day, as some patients struggled to recall pain levels and others struggled to understand the meaning of this score. To overcome this limitation, OMEq consumption was chosen as an additional primary aim. The option of patient-controlled analgesia (PCA) was considered but dismissed due to logistical issues. NRS assessments at 1, 3, 6, 8 and 24 hours after the arrival to the PACU although arbitrary, are considered to be clinically relevant time points.

As an observational case series, this study carries some intrinsic limitations that would otherwise be addressed in a randomized control trial and therefore warrants further investigation. However, as both the NRS pain scores and the OMEq consumption during the first post-operative day were promising, this block combination appears comparable with other shoulder arthroplasty studies where interscalene blockade has been applied.[23-26]

In summary, the combination of infraclavicular and suprascapular nerve blocks shows an encouraging post-operative analgesic profile after total shoulder arthroplasty. However, randomized controlled trials should be performed to compare this block combination with other shoulder blocks.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

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REFERENCES

1. Fredrickson MJ, Krishnan S, Chen CY. Postoperative analgesia for shoulder surgery: a critical appraisal and review of current techniques. *Anaesthesia*. 2010;65:608-624.
2. Hogan QH. Phrenic nerve function after interscalene block revisited: now, the long view. *Anesthesiology*. 2013;119:250-252.
3. Jules-Elysee K, Reid SC, Kahn RL, Edmonds CR, Urban MK. Prolonged diaphragm dysfunction after interscalene brachial plexus block and shoulder surgery: a prospective observational pilot study. *Br J Anaesth*. 2014;112:950-951.
4. Tran DQ, Elgueta MF, Aliste J, Finlayson RJ. Diaphragm-sparing nerve blocks for shoulder surgery. *Reg Anesth Pain Med*. 2017;42:32-38.
5. Tran DQ, Layera S, Bravo D, Cristi-Sanchez I, Bermudez L, Aliste J. Diaphragm-sparing nerve blocks for shoulder surgery, revisited. *Reg Anesth Pain Med*. 2020;45(1):73-78.
6. Aszmann OC, Dellon AL, Birely BT, McFarland EG. Innervation of the human shoulder joint and its implications for surgery. *Clin Orthop Relat Res*. 1996;330:202-207.
7. Borgeat A, Ekatodramis G. Anaesthesia for shoulder surgery. *Best Pract Res Clin Anaesthesiol*. 2002;16:211-225.
8. Flohr-Madsen S, Ytrebo LM, Valen K, Wilsgaard T, Klaastad O. A randomised placebo-controlled trial examining the effect on hand supination after the addition of a suprascapular nerve block to infraclavicular brachial plexus blockade. *Anaesthesia*. 2016;71:938-947.
9. Musso D, Flohr-Madsen S, Meknas K, Wilsgaard T, Ytrebo LM, Klaastad O. A novel combination of peripheral nerve blocks for arthroscopic shoulder surgery. *Acta Anaesthesiol Scand*. 2017;61:1192-1202.
10. Musso D, Klaastad O, Wilsgaard T, Ytrebo LM. Brachial plexus block of the posterior and the lateral cord using ropivacaine 7.5 mg/mL. *Acta Anaesthesiol Scand*. 2019;63:389-395.
11. Siegenthaler A, Moriggl B, Mlekusch S, et al. Ultrasound-guided suprascapular nerve block, description of a novel supraclavicular approach. *Reg Anesth Pain Med*. 2012;37:325-328.
12. Paternostro-Sluga T, Grim-Stieger M, Posch M, et al. Reliability and validity of the Medical Research Council (MRC) scale and a modified scale for testing muscle strength in patients with radial palsy. *J Rehabil Med*. 2008;40:665-671.
13. Caetano EB, Vieira LA, Cavalheiro CS, Razuk MF, Almargo MA, Caetano MF. Anatomic study of the nervous communication between the median and musculoucutaneous nerve. *Acta Ortop Bras*. 2016;24:200-203.
14. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. *Pharmacoepidemiol Drug Saf*. 2016;25:733-737.
15. Checcucci G, Allegra A, Bigazzi P, Gianesello L, Ceruso M, Gritti G. A new technique for regional anesthesia for arthroscopic shoulder surgery based on a suprascapular nerve block and an axillary nerve block: an evaluation of the first results. *Arthroscopy*. 2008;24:689-696.
16. Price DJ. The shoulder block: a new alternative to interscalene brachial plexus blockade for the control of postoperative shoulder pain. *Anaesth Intensive Care*. 2007;35:575-581.
17. Price DJ. Combined suprascapular and axillary nerve blockade. *Arthroscopy*. 2008;24(11):1316-1317; author reply 7.
18. Rothe C, Steen-Hansen C, Lund J, Jenstrup MT, Lange KH. Ultrasound-guided block of the suprascapular nerve - a volunteer study of a new proximal approach. *Acta Anaesthesiol Scand*. 2014;58:1228-1232.
19. Kirksey MA, Haskins SC, Cheng J, Liu SS. Local anesthetic peripheral nerve block adjuvants for prolongation of analgesia: a systematic qualitative review. *PLoS One*. 2015;10:e0137312.
20. De Oliveira GS, Almeida M, Benzon H, McCarthy R. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. *Anesthesiology*. 2011;115:575-588.
21. Noor NA, Urits I, Viswanath O, Kaye A, Eskander J. Synergistic effect of perineural dexamethasone and dexmedetomidine (DexDex) prolong analgesic effect of a preoperative interscalene block. *Cureus*. 2020;12:e9473.
22. Kang RA, Jeong JS, Yoo JC, et al. Improvement in postoperative pain control by combined use of intravenous dexamethasone with intravenous dexmedetomidine after interscalene brachial plexus block for arthroscopic shoulder surgery: a randomised controlled trial. *Eur J Anaesthesiol*. 2019;36:360-368.
23. Auyong DB, Yuan SC, Choi DS, Pahang JA, Slee AE, Hanson NA. A double-blind randomized comparison of continuous interscalene, supraclavicular, and suprascapular blocks for total shoulder arthroplasty. *Reg Anesth Pain Med*. 2017;42:302-309.
24. Hasan SS, Rolf RH, Sympson AN, Eten K, Elsass TR. Single-shot versus continuous interscalene block for postoperative pain control after shoulder arthroplasty: a prospective randomized clinical trial. *J Am Acad Orthop Surg Glob Res Rev*. 2019;3:e014.
25. Namdari S, Nicholson T, Abboud J, Lazarus M, Steinberg D, Williams G. Interscalene block with and without intraoperative local infiltration with liposomal bupivacaine in shoulder arthroplasty: a randomized controlled trial. *J Bone Joint Surg Am*. 2018;100:1373-1378.
26. Okoroha KR, Lynch JR, Keller RA, et al. Liposomal bupivacaine versus interscalene nerve block for pain control after shoulder arthroplasty: a prospective randomized trial. *J Shoulder Elbow Surg*. 2016;25:1742-1748.

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