Impact of an extrafascial versus intrafascial injection for supraclavicular brachial plexus block on respiratory function: a randomized, controlled, double-blind trial

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ABSTRACT

Introduction Hemidiaphragmatic paresis after ultrasound-guided supraclavicular brachial plexus block is reported to occur in up to 67% of patients. We tested the hypothesis that an injection outside the brachial plexus sheath reduces the incidence of hemidiaphragmatic paresis compared with an intrafascial injection while providing similar analgesia.

Methods Fifty American Society of Anesthesiologists I–III patients scheduled for elective upper limb surgery received a supraclavicular brachial plexus block using 30 mL of 1:1 mixture of mepivacaine 1% and ropivacaine 0.5%. The block procedures were randomized to position the needle tip either within the brachial plexus after piercing the sheath (intrafascial injection) or outside the brachial plexus sheath (extrafascial injection). The primary outcome was the incidence of hemidiaphragmatic paresis 30 min after the injection, measured by M-mode ultrasonography. Additional outcomes included time to surgery readiness, and resting and dynamic pain scores at 24 hours postoperatively (Numeric Rating Scale, 0–10).

Results The incidence of hemidiaphragmatic paresis 30 min after the injection was 9% (95% CI 1% to 29%) and 0% (95% CI 0% to 15%) in the intrafascial and extrafascial groups respectively (p=0.14). Extrafascial injection was associated with a longer time to surgery readiness (intrafascial: 18 min (95% CI: 16 to 21 min); extrafascial: 37 min (95% CI: 31 to 42 min); p<0.001). At 24 hours, resting and dynamic pain scores were similar between groups.

Discussion Ultrasound-guided supraclavicular brachial plexus block with an extrafascial injection does not reduce the incidence of hemidiaphragmatic paresis although it provides similar analgesia, when compared with an intrafascial injection. The longer time to surgery readiness is less compatible with contemporary operating theater efficiency requirements.

Trial registration number NCT03957772.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ An extrafascial injection for supraclavicular brachial plexus block provides effective anesthesia, but the impact on hemidiaphragmatic paresis is unknown.

WHAT THIS STUDY ADDS

⇒ An extrafascial injection for supraclavicular brachial plexus block does not reduce the incidence of hemidiaphragmatic paresis although it provides similar analgesia, when compared with an intrafascial injection.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND POLICY

⇒ The longer time to surgery readiness associated with an extrafascial injection is less compatible with contemporary operating theater efficiency requirements.

INTRODUCTION

Supraclavicular brachial plexus block is widely used to provide anesthesia and postoperative analgesia for surgery on the upper limb. However, this block is associated with an incidence of hemidiaphragmatic paresis that is as high as 67%,[1] possibly resulting from retrograde diffusion of the local anesthetic to the C3–C5 nerve roots when injected below the brachial plexus sheath,[2] also recently called the circumneurium.[3 4] Several authors have demonstrated that local anesthetic injected subfascially or subcirumneurally might spread longitudinally over many centimeters at the level of the costoclavicular brachial plexus,[5] or the sciatic nerve at the popliteal crease.[6] The high risk of hemidiaphragmatic paresis means that patients with moderate to severe respiratory disease are frequently precluded from receiving the benefits of this technique.

Previously, Sivashanmugam et al reported that an injection outside the sheath surrounding the brachial plexus block at the supraclavicular level provides effective anesthesia, although at the expense of an increased time to surgery readiness, and a decrease in duration of analgesia.[7] Notably, respiratory outcomes were not assessed in this trial, nor were pain scores or opioid consumption. At the level of the interscalene brachial plexus block, we have previously demonstrated that an extrafascial injection reduces the rate of hemidiaphragmatic paresis from 90% to 21%, when compared with an intrafascial injection, while better preserving other respiratory outcomes, and providing similar postoperative analgesia.[8] Similarly, an extrafascial injection for the supraclavicular block would have the theoretical advantage of preserving the

hemidiaphragm due to absence of retrograde spread, as it is the case with intrafascial injections.[5 6]

In this randomized controlled double-blind trial, we tested the hypothesis that injection outside the brachial plexus sheath during supraclavicular brachial plexus block reduces the incidence of hemidiaphragmatic paresis compared with an intrafascial injection, while providing similar analgesia.

METHODS

We followed the Consolidated Standards of Reporting Trials statement's recommended process.[9]

Recruitment and randomization

All patients aged 18–85 years, identified as American Society of Anesthesiologists physical status I–III, and scheduled to undergo elective elbow, forearm, wrist or hand surgery between December 2019 and February 2021 at the Valais Hospital were eligible to participate in this study. Exclusion criteria included contraindications to peripheral nerve block (allergy to local anesthetics, coagulopathy, infection in the area), pre-existing neurological deficit in the upper limb, history of clavicle surgery, severe pulmonary disease, chest deformity, and pregnancy. After providing written informed consent at least 24 hours prior to surgery, a computer-generated randomization table in aggregates of 10 was used to randomize participating patients to a supraclavicular brachial plexus block with either an intrafascial or an extrafascial injection. A sealed opaque envelope was used to conceal treatment assignments.

Ultrasound-guided procedures

Ultrasound-guided blocks were performed in a dedicated block procedure room prior to surgery. All blocks were performed by one of the authors who is an experienced provider of regional anesthesia (SG) and did not have any further involvement with the study protocol. Patients were placed a semi-sitting position with their head turned to the non-operative side by 45°, and with the ipsilateral arm placed by the patient's side. ECG, pulse oximetry, and blood pressure monitoring were performed routinely, and supplemental oxygen was provided. Peripheral intravenous access was established, and intravenous midazolam 1–4 mg was given for anxiolysis and sedation as needed. Needle insertion site preparation was performed using chlorhexidine 2% in isopropyl alcohol 70% solution. A high-frequency linear array transducer (13–6 MHz, SonoSite S-Nerve, SonoSite, Bothell, Washington; 18–6 MHz, HF Linear Array 8870, BK Ultrasound, Pea-body, Massachusetts) was placed over the supraclavicular fossa under sterile conditions. Positioning was parallel to the clavicle to allow a short-axis view of the divisions of the brachial plexus and the subclavian artery, lying superficial to the first rib. The brachial plexus sheath was identified as the hyperechoic layer surrounding the divisions of the brachial plexus. After skin infiltration with 1–3 mL of lidocaine 1%, a 23 gage 70 mm insulated block needle (Temena UPC, Felsberg-Gensungen, Germany) was inserted from the lateral side of the transducer in-plane with the ultrasound beam.

In the intrafascial injection group, the needle tip was positioned at the junction of the first rib and subclavian artery, in the location traditionally called the 'corner pocket'.[10] After injection of 15 mL of local anesthetics, the needle was withdrawn and the tip positioned in the upper part of the brachial plexus, just underneath the sheath, close to the artery, where another volume of 15 mL was deposited (figure 1A).
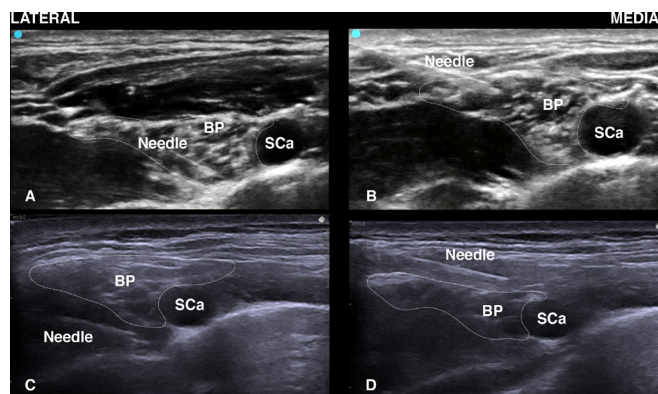
Figure 1 Ultrasound-guided supraclavicular brachial plexus block. Intrafascial injection with the needle positioned first in the lower part (A) and then upper part (B); Extrafascial injection with the needle positioned first in the lower part (C) and then upper part (D). BP, brachial plexus; SCa, subclavian artery.

In the extrafascial injection group, the needle was inserted along the lower part of the brachial plexus sheath without crossing it up to the junction of the first rib and subclavian artery. The 15 mL were injected outside the brachial plexus; then, the needle was withdrawn, and the tip was placed above the brachial plexus sheath, where 15 mL were injected (figure 1B). The extrafascial deposit of local anesthetic was ensured by following three ultrasound criteria[7]: (1) indentation of the brachial plexus sheath; (2) diffusion of the local anesthetic around the brachial plexus without separating the different neural structures; and (3) movement of the brachial plexus away from the needle tip during injection.

All patients received 30 mL of a 1:1 mixture of mepivacaine 1% and ropivacaine 0.5%. This was injected slowly using 5 mL increments, with intermittent aspiration. Ultrasound visualization was maintained throughout the procedure and the needle tip was not repositioned unless the patient complained of paresthesia. The 30 mL volume was chosen because this is the most common volume injected according to a meta-analysis that investigated various ultrasound-guided brachial plexus blocks.[11] Patients remained fully monitored after completion of the block, up until their transfer to the operating room.

Block assessment and definition of successful block

Assessment of both motor and sensory blockade was performed by one of the authors (NZ) who was unaware of the group allocation and who evaluated the block 5 min after local anesthetic injection and then every 5 min thereafter, up to a total duration of 60 min. The assessment followed a previously published method.[12] Briefly, sensory block was evaluated in the following dermatomes using a blunt tip needle pinprick test (0, normal sensation; 1, decreased sensation; 2, no sensation): lateral side of the forearm (musculocutaneous), first interdigital space of the dorsum of the hand (radial), ventral side of the second finger (median), and ventral side of the fifth finger (ulnar nerves). Motor block was assessed by evaluating elbow flexion, thumb abduction, thumb opposition, and thumb adduction (musculocutaneous, radial, median and ulnar nerves, respectively) on a 3-point scale from 0 (no loss of force) to 2 (inability to overcome gravity). A composite score of ≥14 within 30 min of completing the regional procedure was defined as successful block. If the composite score was <14 after 30 min, assessment was continued every 5 min until 60 min. If the composite score remained <14

after 60 min the block was considered a failure, and surgery was performed under general anesthesia.

Hemidiaphragmatic excursion and respiratory function assessment

Hemidiaphragmatic excursion was assessed before, and at 30 and 120 min after the block using a subcostal approach and a low-frequency curvilinear transducer (2-5 MHz, SonoSite S-Nerve; SonoSite, Bothell, Washington), as previously described.[13] For this assessment, patients were in a half-sitting position and the hemidiaphragm was identified as an hyperechoic line using the liver or spleen as an acoustic window. Hemidiaphragmatic excursion from the resting expiratory position to a deep and normal inspiration was measured using real-time M-mode ultrasonography.

Respiratory function was assessed using a bedside spirometer (EasyOne Spirometer; ndd Medical Technologies, Andover, UK) at the same timepoints after the block. As per routine practice, while sitting in an upright position the patient was asked to inspire maximally then blow into the device as fast and strong as possible. The best value from three tests was recorded.

Intraoperative and postoperative procedures

After the application of routine physiological monitors and administration of supplemental oxygen, conscious sedation was provided on request using a target-controlled infusion of propofol 0–2 μg/mL. After surgery, patients were transferred to phase I recovery. Standardized oral postoperative analgesia consisted of acetaminophen 1000 mg every 4 hours and ibuprofen 400 mg every 8 hours. Oxycodone 5 mg every 4 hour as needed could also be given as per routine practice at our center. As-needed antiemetic treatment with oral granisetron 1 mg was available, and an antihistamine could be used to treat pruritus.

Outcomes

The primary outcome was the incidence of hemidiaphragmatic paresis 30 min after the procedure or when the composite score was 14. Hemidiaphragmatic paresis was defined as either the reduction of hemidiaphragmatic excursion by more than 75% compared with the preprocedure value, absence of excursion or paradoxical excursion.[14 15] Secondary outcomes were divided into respiratory-related outcomes, block-related outcomes, and pain-related outcomes. Respiratory-related outcomes included the incidence of hemidiaphragmatic paresis measured at 120 min after the procedure and the rates of forced vital capacity, and forced expiratory volume in 1 s, measured 30 and 120 min after the injection. Block-related outcomes included the onset times for sensory and motor blocks (defined as time from removal of the needle until complete loss of sensory and motor function); rate of paresthesia during block performance; rates of dyspnea 30 and 120 min after the injection; duration of sensory block (defined as time from the injection of local anesthetic to the time the patient recovered sensation over the arm and hand); and duration of motor block (defined as time from injection of local anesthetic to the time the patient could bend their elbow and wrist). Pain-related outcomes included the pain score during the block procedure (Numeric Rating Scale (NRS) out of 10); time to first analgesic request (defined as time from block completion to the time to first dose of analgesic intake); resting and dynamic pain scores at 24 postoperative hours (NRS out of 10), and cumulative oxycodone consumption during the first 24 postoperative hours (converted to equivalent doses of intravenous

morphine).[16] Patient satisfaction with overall anesthetic management (NRS out of 10) was also collected.

After completing the phase II recovery process, patients were discharged home and required to write down the time to recovery of full arm sensation, full arm mobilization, pain scores at rest and during movement, and time to first oxycodone consumption. At 24 postoperative hours and on the seventh postoperative day, all patients received a phone call by one of the investigators (NZ) to collect data on the above parameters, and obtain answers to questions about the presence of hematoma, infection, persistent paresthesia, or weakness.

Patients remained blinded to treatment group allocation because the puncture site was identical whether an extrafascial or intrafascial injection was used. Anesthetists caring for the patient in the operating theater, phase I and II recovery nurses, the investigator performing the respiratory and ultrasound assessments and follow-up visits, and the person performing the statistical analysis were also all unaware of group allocation.

Sample size calculation

A previous study reported that the rate of hemidiaphragmatic paresis after an intrafascial injection was 67%.[1] Assuming a reduction in this rate of 20% with an extrafascial injection, an alpha error of 0.05 and a power of 80%, it was calculated that 17 patients per group would be required to detect a statistically significant between-group difference. The plan was to enroll a total of 50 patients to allow for a 20% rate of drop-out or protocol violation.

Statistical analysis

All analyses were performed on an intention-to-treat basis. Frequencies were used to describe categorical variables, while continuous variables are reported as mean values with 95% CIs. Continuous parametric data were compared using the Student's t-test, and non-parametric data were compared using Mann-Whitney U test. The Fisher's exact test or Pearson test was used to compare categorical and dichotomous data, as appropriate. A two-tailed $p<0.05$ was defined as statistically significant. Statistical analyses was performed using the JMP V.15.1.0 statistical package (SAS Institute).

RESULTS

Fifty patients were recruited, and all completed the protocol and the 7-day follow-up visit, excepting 5 patients who underwent left upper limb surgery in whom the diaphragm could not be visualized. Figure 2 describes the flow of patients during the trial and table 1 presents the patient characteristics, which were similar between groups.

All blocks were successful, and all patients allocated to the extrafascial injection had visually confirmed deposit of local anesthetic outside the plexus. Three patients in the extrafascial group and two in the intrafascial group reported paresthesia during the procedure.

The rates of hemidiaphragmatic paresis 30 min after the supraclavicular brachial plexus block were 9% (95% CI 1% to 29%) and 0% (95% CI 0% to 15%) in the intrafascial and extrafascial groups, respectively, with no significant difference between groups (p=0.14). While the two patients who experienced hemidiaphragmatic paresis described dyspnea, neither required any treatment, and both had recovered 120 min after the regional procedure. The other respiratory outcomes were maintained in the extrafascial group while they were significantly reduced in
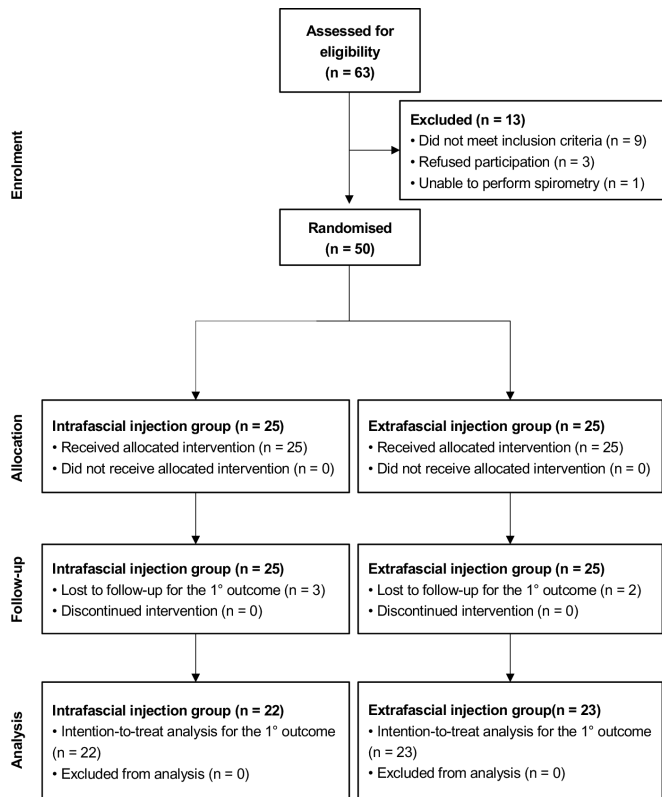
Figure 2 Flow of patients through trial.

the intrafascial group at 30 min, with a slight improvement at 120 min (table 2).

An extrafascial injection was associated with a slower onset of sensory and motor block. Indeed, the mean times to composite score of 14 were 37 min (95% CI 31 to 42) in the extrafascial group, and 18 min (95% CI 16 to 21 min) in the intrafascial group (p<0.001). Time to first analgesic request, and durations

of sensory and motor blocks were slightly longer in the extrafascial group, while pain-related outcomes were similar between groups (table 3).

No patients developed hematoma, infection, persistent paresthesia or weakness in the upper limb within the 7 days after the regional procedure.

DISCUSSION

The results of this double-blinded randomized controlled trial do not support our hypothesis that an extrafascial injection for supraclavicular brachial plexus block would reduce the incidence of hemidiaphragmatic paresis when compared with an intrafascial injection. The impact of the injection location on the respiratory function was measurably less in the extrafascial group, however, without clinical impact and this finding is probably not relevant.

The lack of difference in the rates of hemidiaphragmatic paresis may be a consequence of the very low incidence found in the intrafascial group. Given the 9% rate observed, a post hoc analysis revealed that 116 patients per group would have been needed to identify a significant difference. Other authors investigated the incidence of hemidiaphragmatic paresis after intrafascial injection with different volumes of local anesthetic agents; they reported rates ranging from 0%[14] to 67%.[1] These differences stem from the non-standardized definition of hemidiaphragmatic paresis. While Kang et al included in their definition patients with reduced excursion of 25% or more,[1] Renes et al only included patients with an excursion reduced more than 75%.[14] Other authors have reported an incidence of 45% when the outcome is defined as a reduction of the excursion of more than 50%.[17] A post hoc analysis of our data set, applying a definition of excursion reduction of >25%, suggested rates of 86% and 17% in the intrafascial and extrafascial groups, respectively (p<0.0001). While this finding suggests some functional difference between groups, we believe that only complete paresis, defined by a >75% reduction in diaphragmatic excursion, is

Table 1 Patient characteristics

	Intrafascial injection group	Extrafascial injection group	P value*†
Sample size, n	25	25	
Sex, n (%)			0.09
Male	11 (44)	17 (68)	
Female	14 (56)	8 (32)	
Mean age (95% CI) in years	54 (49 to 60)	48 (41 to 55)	0.16
Mean height (95% CI) in cm	169 (166 to 173)	171 (167 to 175)	0.59
Mean weight (95% CI) in kg	74 (68 to 81)	74 (68 to 80)	0.89
Mean body mass index (95% CI) in kg/m²	26.0 (23.9 to 28.1)	25.2 (23.7 to 26.7)	0.55
ASA, n (%)			0.56
I	11 (44)	11 (44)	
II	11 (44)	13 (52)	
III	3 (12)	1 (4)	
Mean duration of surgery (95% CI) in minutes	59 (45 to 73)	59 (44 to 74)	0.98
Surgical location, n (%)			0.35
Elbow	1 (4)	0 (0)	
Forearm	9 (36)	5 (20)	
Wrist	12 (48)	14 (56)	
Hand	3 (25)	6 (24)	

*P value compares intrafascial versus extrafascial injection.
†Student's t-test used to compare means and Fisher's exact test used to compare proportions.
ASA, American Society of Anesthesiologists.

Table 2 Respiratory-related outcomes

	Intrafascial injection group	Extrafascial injection group	P value*
Preprocedure			
Mean hemidiaphragmatic excursion (95% CI) in cm	5.5 (4.9 to 6.0)	5.9 (5.4 to 6.5)	0.26
Mean forced vital capacity (95% CI) in L	3.1 (2.8 to 3.5)	3.8 (3.3 to 4.3)	0.03
Mean forced expiratory volume in 1 s (95% CI) in L	2.6 (2.3 to 2.9)	3.1 (2.6 to 3.5)	0.08
30 min postprocedure			
Mean hemidiaphragmatic excursion (95% CI) in cm	3.0 (2.5 to 3.5)	5.5 (4.9 to 6.2)	<0.001
Mean forced vital capacity (95% CI) in L	2.5 (2.1 to 2.8)	3.5 (3.0 to 4.1)	<0.01
Mean forced expiratory volume in 1 s (95% CI) in L	2.0 (1.7 to 2.3)	2.8 (2.4 to 3.2)	<0.01
Percentage reduction between 30 min and preprocedure			
Mean hemidiaphragmatic excursion (95% CI) in %	45% (36% to 54%)	6% (0% to 13%)	<0.001
Mean forced vital capacity (95% CI) in %	21% (15% to 27%)	8% (3% to 12%)	<0.001
Mean forced expiratory volume in 1 s in %	24% (17% to 30%)	8% (2% to 13%)	<0.001
120 min postprocedure			
Mean hemidiaphragmatic excursion (95% CI) in cm	3.8 (3.3 to 4.4)	5.6 (5.0 to 6.2)	<0.001
Mean forced vital capacity (95% CI) in L	2.7 (2.3 to 3.0)	3.7 (3.2 to 4.2)	<0.01
Mean forced expiratory volume in 1 s (95% CI) in L	2.2 (1.9 to 2.6)	3.0 (2.5 to 3.4)	<0.01
Percentage reduction between 120 min and preprocedure			
Mean hemidiaphragmatic excursion (95% CI) in %	29% (19% to 38%)	6% (2% to 10%)	<0.001
Mean forced vital capacity (95% CI) in %	14% (9% to 19%)	3% (0% to 7%)	<0.01
Mean forced expiratory volume in 1 s in %	14% (7% to 20%)	1% (0% 7%)	<0.01

*P value compares intrafascial versus extrafascial injection with Student's t-test.

likely to result in clinical symptoms and be of consequence in routine practice.[14]

While the absence of differences in resting and dynamic pain scores or morphine consumption at 24 hours postoperatively is not surprising given the mixture of long-acting and intermediate-acting local anesthetics, the longer time to first analgesic request, together with the extended duration of sensory and motor blocks in patients receiving extrafascial injection is unexpected. While the differences do not appear clinically relevant, these outcomes raise questions regarding the pharmacodynamics of this process. Indeed, one might arguably anticipate that the intrafascial injection of local anesthetic would result in longer block characteristics, since the medication is contained within the fascia. This pattern has been previously demonstrated with the supraclavicular brachial plexus blocks,[7] and with the sciatic nerve block at the popliteal crease.[18 19] Potential explanations for the conflicting observations found in our study might be type I errors or imprecision in self-reported outcomes as patients were asked to independently complete a diary at home.

An extrafascial injection has the theoretical advantage of reducing the needle-to-nerve contact, and the potential risk of nerve injury, although this outcome has not been investigated in this study. It is doubtful that such a study would be ever realized as a sample of 16,000 patients is required to determine a difference between groups, with a 0.04% average rate of nerve injury.[20] The very low risk of nerve injury should be balanced against the increased time to surgery readiness. Indeed, in this study, the extrafascial injection was associated with twice the time required for the block to be effective. In many busy contemporary operating theaters, this outcome might not be suitable although the existence of a block room, and the local environment (specialized hospital with experienced physicians vs university hospital with an education mission), may permit increased flexibility.[21 22]

In our study, a single experienced operator performed all the blocks and, therefore, generalizability of the results may be limited and may not be equally applicable to an educational environment. Furthermore, some outcomes relied on a self-reporting process and while accuracy may inherently be affected, this only concerns a small number of secondary outcomes and we do not believe that it undermines our overall findings. Finally, while we were confident that our extrafascial and intrafascial injections were in the appropriate locations based on the above mentioned

Table 3 Pain-related outcomes

	Intrafascial injection group	Extrafascial injection group	P value*
Mean pain related to the procedure (95% CI) in NRS	2.1 (1.7 to 2.5)	1.8 (1.4 to 2.2)	0.24
Mean time to first analgesic request (95% CI) in minutes	312 (255 to 370)	411 (343 to 478)	0.03
Mean duration of sensory block (95% CI) in minutes	313 (264 to 363)	400 (344 to 456)	0.02
Mean duration of motor block (95% CI) in minutes	347 (291 to 403)	432 (377 to 486)	0.03
Mean iv morphine equivalent consumption at 24 postoperative hours (95% CI) in mg	5.0 (2.3 to 7.7)	6.9 (4.3 to 9.5)	0.30
Mean rest pain score at 24 hours postoperatively (95% CI) in NRS	2.8 (1.9 to 3.6)	2.9 (2.2 to 3.6)	0.75
Mean dynamic pain score at 24 hours postoperatively (95% CI) in NRS	4.8 (3.9 to 5.6)	4.4 (3.6 to 5.3)	0.59
Mean satisfaction score (95% CI) in NRS	8.6 (8.1 to 9.1)	8.4 (8.0 to 8.9)	0.64

*P value compares intrafascial versus extrafascial injection.
. NRS, Numeric Rating Scale.

ultrasound criteria, our ultrasound machines did not allow us to make a distinction between extrafascial extraepimyseal or extrafascial subepimyseal injections. This is an area that requires further exploration because it might result in different block characteristics.[23]

CONCLUSIONS

An ultrasound-guided supraclavicular brachial plexus block with an extrafascial injection does not reduce the incidence of hemidiaphragmatic paresis but provides similar analgesia, when compared with an intrafascial injection. The longer time to surgical readiness is likely to be incompatible with an efficient contemporary operating theater.

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