

Importance of Volume and Concentration for Ropivacaine Interscalene Block in Preventing Recovery Room Pain and Minimizing Motor Block after Shoulder Surgery

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ABSTRACT

Background: This three-staged study estimated the volume and concentration of interscalene ropivacaine that would prevent recovery room pain after shoulder surgery under general anesthesia.

Methods: Stages 1/2: Interscalene catheter administration of ropivacaine was by a 10% incremental up–down sequential manner depending on the presence of recovery room pain in the previous patient. Stage 1: Ropivacaine (0.5% volume) was varied from 30 ml. Stage 2: Ropivacaine (20 ml, the ED(volume)₉₅ estimate from stage 1) concentration was varied from 0.45%. Stage 3: Subjects were randomly assigned to receive 30 ml of ropivacaine, 0.5% (“conventional dose”), or 20 ml of ropivacaine, 0.375% (the estimated ED(volume+concentration)₉₅ from stages 1/2). A postoperative elastomeric infusion of 0.2% ropivacaine (2 ml/h) was administered. Grip strength was measured in the recovery room and time to first pain at 24 h.

Results: Stage 1 (n = 34): Ropivacaine 0.5% ED(volume)₅₀/ED(volume)₉₅ (95% CI) estimates were 2.7/20.5 ml (2.4–9.5/17.3–25.8). Stage 2 (n = 29): Ropivacaine 20 ml ED(concen-

tration)₅₀/ED(concentration)₉₅ (95% CI) estimates were 0.15/0.34% (0.13–0.30/0.29–0.43). The ED(dose)₅₀ was similar for stages 1/2 (13.5 *vs.* 30 mg), but the ED(dose)₉₅ was higher for stage 1 (102.5 *vs.* 68 mg). Stage 3 (n = 40): Satisfaction (0–10) was modestly higher for the new/lower dose (median [interquartile range] = 10 [10–10] *versus* 9 [8–10], *P* = 0.007). Pooled data regression analysis showed that increasing ropivacaine concentration increased grip weakness but not block duration.

Conclusions: Ropivacaine interscalene block requires a threshold volume and concentration, with concentration primarily determining motor block. When combined with continuous blockade, suprathreshold ropivacaine doses do not significantly prolong primary block duration but may compromise patient satisfaction.

What We Already Know about This Topic

- ❖ The relative contributions of concentration and volume of local anesthetic for peripheral nerve block for surgery are unclear

What This Article Tells Us That Is New

- ❖ In the first stage, the optimum concentration and volume of ropivacaine for interscalene shoulder surgery were determined
- ❖ In the second stage, these optima (20 ml of 0.375%) resulted in equivalent analgesia but better patient satisfaction than a traditional dose (30 ml of 0.5%)

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LITTLE is known about the relative importance of local anesthetic volume *versus* concentration for clinical peripheral nerve blockade.^{1–4} Previous dose-finding studies in humans have simply compared two different combinations of volume and concentration at a fixed total dose,^{3,4} or fixed a single variable and then adjusted the other variable to estimate the corresponding local anesthetic volume (EDvol) or concentration (EDconc) for a specific quantal response; the relative role of each variable, as assessed by up–down dose-finding methodology, in determining clinical peripheral nerve blockade has not been investigated previously. Second,

little is known regarding the optimal primary bolus dose of interscalene local anesthetic required to prevent recovery room pain, minimize motor block, and prolong block duration after shoulder surgery.^{3,5–11}

With the commonly used combined interscalene block/general anesthesia approach to anesthesia/analgesia for shoulder surgery, the relative role of nerve blockade for postoperative analgesia assumes greater importance over the requirement for surgical anesthesia and so does the duration of effect of the block. However, adding a continuous interscalene infusion to a single injection block renders the duration of action of the preoperative local anesthetic bolus less important and, therefore, allows the administration of a lower primary local anesthetic bolus dose, which might theoretically reduce block-related side effects: mild dyspnea, hoarseness, ptosis, and motor block.¹² Many patients experience dissatisfaction with a densely blocked hand. Furthermore, dense motor block can be problematic when early active (as opposed to passive) physiotherapy is planned, such as following procedures for “frozen shoulder” and some shoulder replacement surgeries.¹³ However, reducing the preoperative local anesthetic dose could potentially shorten the duration of potent post shoulder surgery analgesia and, therefore, result in an earlier time to first demand for analgesic rescue. This is relevant not only for single injection techniques but also for ambulatory patient-controlled interscalene analgesia where a well-accepted limitation is early ambulatory pump exhaustion.¹⁴

The primary aim of this study was to estimate, at a predetermined ropivacaine concentration and then volume, the ED(vol)₅₀/ED(vol)₉₅ and ED(conc)₅₀/ED(conc)₉₅, that is, the volume and concentration respectively, of interscalene ropivacaine that in 50 or 95% of patients would prevent recovery room pain in those who had undergone shoulder surgery under general anesthesia. Secondary aims were to evaluate the relative influence of local anesthetic volume and concentration on recovery room hand strength and time to the first onset of operative site pain.

Materials and Methods

Following institutional review board (Northern Y Regional Ethics Committee, Hamilton, New Zealand) approval and trial registration (ANZCTR—12609000347268), American Society of Anesthesiologists physical status 1 to 2 patients scheduled for elective shoulder surgery in two of the authors' practices (M.F. and A.W.) were recruited. Exclusion criteria included patient refusal of interscalene block, severe respiratory disease, known allergy to amide local anesthetic drugs, and preoperative opioid therapy administered for more than 1 month before surgery. Written informed consent was obtained from all patients.

Oral acetaminophen (1 g) with or without diclofenac slow release (75 mg) and omeprazole (20 mg) were administered 1 h before surgery. Intravenous sedation up to 2 mg of midazolam and 0.5 mg of alfentanil was administered 5 min

before catheter placement. A superficial cervical plexus block was administered to all patients to facilitate catheter placement and ensure blockade of the supraclavicular nerves.

Perineural Catheter¹⁴

A perineural catheter was placed by one of two investigators (M.F. and A.W.), both of whom were experienced in ultrasound and nerve stimulation–assisted interscalene catheter insertion. The scalene muscles and interscalene brachial plexus were imaged in the short axis at approximately the level of the 6th or 7th cervical vertebrae with a 38-mm 13–6 MHz linear ultrasound probe (SonoSite HFL/MicroMaxx, Bothell, WA). A 3.8-cm 18G insulated Tuohy needle (Contiplex Tuohy, BBraun, Bethlehem, PA) was inserted at the posterior border of the sternocleidomastoid muscle approximately 3 cm cephalad of the level of the 6th or 7th cervical vertebrae. The needle was advanced using out-of-plane needle-probe orientation superficially in a peripheral direction into the middle scalene muscle until tissue displacement was observed just lateral to the two most superficial elements of the brachial plexus. At the 6th or 7th cervical vertebral level, these correspond to the 5th or 6th cervical roots/superior-middle trunks. The tip of the needle was then angled medially toward the two most superficial brachial plexus roots/trunks until a resultant medial movement was observed. The position of the needle tip was ultimately determined by the injection of 10 ml dextrose, 5%, and observation of injectate spread immediately lateral to the target roots/trunks, or alternatively by elicitation of a sustained deltoid or biceps motor response at less than 0.5 mA (0.1 ms, 2 Hz) (Pajunk Vario, Tucker, GA). The choice of endpoint was left to operator experience or preference based on the results of a recent study.¹⁵ In both groups, a non-stimulating multiorificed catheter was advanced blindly and then withdrawn such that 2 cm of catheter remained past the original needle tip position.

The study was conducted in three stages, each stage having a different protocol for allocating the dose of ropivacaine to be administered preoperatively *via* the catheter as follows.

Stages 1 and 2. By using up–down sequential dose allocation (in increments of 10% of the starting volume/concentration) depending on the presence or absence of pain in the recovery room in the previous patient, that is, if the previous patient had a successful block, the dose of ropivacaine for the subsequent patient was reduced by 10%. If the block was unsuccessful, the dose was increased by 10%. Block success was defined as the worst numerical rating pain score (NRPS) (0–10) in the shoulder, upper arm, or elbow on emergence of 2 or less without the requirement for any additional rescue local anesthetic bolus.

Stage 1. The ropivacaine concentration was set at 0.5%, and the volume was sequentially allocated in increments of 3 ml with a starting volume of 30 ml.

Stage 2. The ropivacaine volume was set at 20 ml, and the concentration was sequentially allocated in increments of 0.05%, with a starting concentration of 0.45%. The volume of 20 ml was based on the *a priori* plan of using the ED(vol)₉₅

(the volume estimate of ropivacaine 0.5% that would prevent recovery room pain in 95% of patients) determined in stage 1 of the study.

Stage 3. Patients were randomly assigned to receive a “conventional” dose of 30 ml of ropivacaine (0.5%)^{3,5–7,16} or a new dose (as determined during stages 1 and 2) that was estimated to prevent recovery room pain in 95% of patients. Randomization was performed using a computer random number generator and implemented using a sealed opaque envelope system, with group allocation being revealed immediately after catheter placement. The purpose of stage 3 was to allow a randomized comparison between two clinically relevant doses.

Intraoperative Management

For the reasons stated previously, all patients were given a standardized light general anesthetic (end-tidal minimum alveolar concentration 0.8–1.0) using a laryngeal mask airway, desflurane anesthesia, and spontaneous respiration. Sensory and motor testing before surgery was not performed. No long-acting opioid was administered; however, 0.25 mg of alfentanil was administered as required for a respiratory rate more than 25.

PACU Protocol

In the postanesthesia care unit (PACU), patients reporting an NRPS of more than 2 were first given a bolus of 10 ml of lidocaine (1%). If the NRPS subsequently remained more than 2, the catheter was withdrawn 1 cm and an additional 10 ml lidocaine, 1%, was administered. If the NRPS still remained more than 2, the catheter was replaced (table 1). In stages 1 and 2, the patients who received a replacement catheter were excluded from subsequent analysis; in stage 3, the patient was retained on an “intention-to-treat” basis with the randomly allocated ropivacaine dose repeated *via* the replacement catheter. In stages 1 and 2, patients who received a replacement catheter did not influence the management of subsequent patients in the up–down sequential dose allocation stages of the study, that is, the next patient received the same dose as the patient having just received the replacement catheter. Patients who achieved an NRPS of 2 or less after a local anesthetic bolus with or without a catheter withdrawal intervention were regarded as having satisfactory catheter placement but an unsuccessful block, that is, during stages 1 and 2, subsequent patients had their ropivacaine dose increased by 10%.

Table 1. Protocol for Sequential Ropivacaine Dose Allocation (Stages 1 and 2)

NRPS in the PACU	Dose for Next Patient
NRPS \leq 2	Decrease by 10%
NRPS \leq 2 with lidocaine bolus \pm catheter withdrawal	Increase by 10%
NRPS $>$ 2 despite lidocaine bolus and catheter withdrawal	Same

NRPS = numerical rating pain score; PACU = postanesthesia care unit.

Postoperative Management

Postoperative management of the catheter was as described previously.¹² Specifically, the infusion was administered *via* an elastomeric pump (PainBuster, Surgical Synergies, Auckland, New Zealand) delivering 2 ml/h with patient-controlled boluses of an additional 5 ml every hour. Patients were instructed to depress the ropivacaine bolus button if the NRPS increased to more than 2. Acetaminophen (1 g every 6 h) and diclofenac slow release (75 mg every 12 h) were continued postoperatively if any postoperative pain occurred. If the NRPS was more than 3 despite regular acetaminophen, diclofenac, and ropivacaine boluses, 100 mg of tramadol slow release was added every 12 h. Discharge home occurred either on the day of surgery or on the morning of postoperative day 1.

Data Collection

The operating investigator recorded grip strength in the operative limb using a dynamometer (Jamar, Sammons Preston, Nottinghamshire, United Kingdom), immediately before the administration of intravenous sedation. The needle endpoint used for catheter placement (ultrasound or neurostimulation) and the number of alfentanil (0.25 mg boluses) administered during surgery were also recorded. The patient’s primary PACU nurse recorded the worst NRPS in the PACU and details of catheter interventions. The PACU nurse measured operative limb grip strength just before PACU discharge using the same dynamometer. A research assistant phoned all subjects on the afternoon of postoperative day 1 and questioned for time to first shoulder pain. She also questioned for NRPS, arm numbness or weakness, and satisfaction (0–10, 0 = no pain, numbness/weakness, very unsatisfied; 10 = worst imaginable pain, numbness/weakness, very satisfied) during the first 24 postoperative hours.

Statistical Analysis

Stages 1 and 2. For each of the stages 1 and 2, the effective 50th and 95th percentiles for volume and concentration were estimated using the $\hat{\mu}_3$ estimator following application of the pooled-adjacent violators’ algorithm (also known as isotonic regression).¹⁷ Ninety-five percentage CIs were obtained by bootstrapping using the bias-corrected method,¹⁸ with 2,000 bootstrap replicates of the original data set generated for each percentile. As a sensitivity analysis, percentiles were also estimated following probit regression, with the delta method used to estimate the appropriate nonlinear combinations of regression coefficients.¹⁹

A sample size of 30 was chosen for each up–down sequential stage, with a view to recruiting further patients into a stage if the 95% CI around the percentile estimate was judged unacceptably wide (approximately 7 ml for volume and 0.15% for concentration). In this event, we planned to recruit a further five subjects before recalculating the isotonic estimators. This procedure does not involve multiple testing, as it involves establishing precision rather than performing a statistical comparison.

As the SD for the effective 50th percentiles were unknown, the optimum incremental size (generally accepted as 0.5–2 times the expected SD)²⁰ could not be calculated; therefore, the incremental size was arbitrarily set at 10% of the starting volume and concentration, an incremental size consistent with similar previous studies.^{21,22}

Stage 3. The sample size was based on the time to the first onset of operative site pain. The “new” dose represented a 50% reduction in drug dose, and the primary interest was whether this 50% reduction in dose would negatively impact on the time to first pain. Given that all patients had the benefit of patient-controlled local anesthetic boluses, it was considered that anything less than a 4-h reduction in time to first pain would be clinically unimportant. A previous study reported that time to first pain after shoulder surgery under interscalene block had a mean (SD) of 10 (5) h.⁷ Therefore, using this distributional assumption, 40 patients would be required to detect a 4-h reduction in time to first pain (one-sided unpaired *t* test, type 1 error = 0.05, power 80%). However, the analysis of the stage 3 data revealed that approximately 50% of patients had not experienced pain at the time of the 24-h phone consultation. A revised calculation indicated that 40 patients would provide 89% power to detect a 35% reduction (50–15%) in the proportion of patients still pain free at 24 h using a type 1 error rate of 5%. A difference of less than 35% was still considered clinically acceptable in the context of patient-controlled interscalene analgesia.

The proportion of patients in each group pain-free at 24 h was compared using Pearson’s chi-square test. Kaplan–Meier (product–limit) survival curves were also constructed and compared with the log-rank test. The change in grip strength was compared between groups using linear regression (adjusted for baseline grip strength) with robust standard errors. Ordinal outcomes (numerically rated pain, numbness, weakness, and satisfaction) were compared using the Mann–Whitney *U* test. *P* less than 0.05 was considered statistically significant. Two-sided tests were used for all experimental outcomes.

The associations among ropivacaine volume, concentration, and change in grip strength were investigated using linear regression adjusting for baseline grip strength, whereas the associations of volume and concentration with pain at 24 h were investigated using logistic regression. These analyses used data from all stages of the study. Subjects who had received a rescue local anesthetic bolus in the PACU were included in this analysis.

Other data were summarized using appropriate descriptive statistics (mean and SD for normally distributed or symmetric variables; median and interquartile ranges for skewed variables; number and proportion for categorical variables). All statistical analyses were performed using Stata version 10.0 statistical software (StataCorp LP, College Station, TX).

Post Hoc Protocol Deviation

During stage 1, the minimum incremental volume (3 ml) was reached, and there were several successive “successful” blocks at this volume. Consequently (after recruitment of the first 30 patients), the isotonic regression estimate of success at this volume was 58%. To approach ED(vol)₅₀ more closely, it was necessary to reduce the minimum volume, which we arbitrarily set at 1.5 ml, in the event of 3 ml being associated with successful block.

Results

One hundred seven patients were recruited. Four patients (two patients each from stages 1 and 2) were excluded after enrollment, one as a result of a protocol deviation during catheter placement, and three as a result of unsuccessful catheter placements. Therefore, 103 subjects completed the study according to protocol and were, thus, retained for analysis. Patient characteristics of all patients and those patients in each group of stage 3 are presented in table 2.

Stages 1 and 2

Stage 1 (n = 34). The ED(vol)₅₀/ED(vol)₉₅ (95% CI) of ropivacaine (0.5%) estimated by isotonic regression was 2.7/20.5 ml (2.4–9.5/17.3–25.8) and by probit regression 1.6/34.5 ml (–12.1 to 16.9/1.5 to 67.6) (fig. 1).

Stage 2 (n = 29). The ED(conc)₅₀/ED(conc)₉₅ (95% CI) of 20 ml ropivacaine estimated by isotonic regression was 0.15/0.34% (0.13–0.30/0.29–0.43) and by probit analysis 0.17/0.37% (0.11–0.24/0.21–0.53) (fig. 2).

The ED(dose)₅₀ (95% CI) was similar for stages 1 and 2 (13.5 [12–47.5] vs. 30 [26–60] mg), but the ED(dose)₉₅ (95% CI) was higher for stage 1 (102.5 [86.5–129] vs. 68 [58–86] mg).

Table 2. Patient, Anesthesia, and Surgical Characteristics (Stages 1–3)

	Stages 1 and 2 (n = 63)	Stage 3	
		20 ml 0.375% (n = 21)	30 ml 0.5% (n = 19)
Male sex	45 (71)	16 (76)	14 (74)
Age, yr	40 (16)	44 (16)	41 (15)
Weight, kg	78 (14)	85 (14)	81 (13)
Needle endpoint US (vs. NS)	62 (98)	21 (100)	18 (95)
Surgery (n)			
Acromioplasty/ excision lateral clavicle	19 (30)	3 (14)	5 (26)
Stabilization	28 (44)	8 (38)	6 (32)
Rotator cuff repair	15 (23)	8 (38)	5 (26)
Other	1 (11)	2 (10)	3 (16)

Data are expressed as n (%) or mean (SD).
NS = neurostimulation; US = ultrasound.

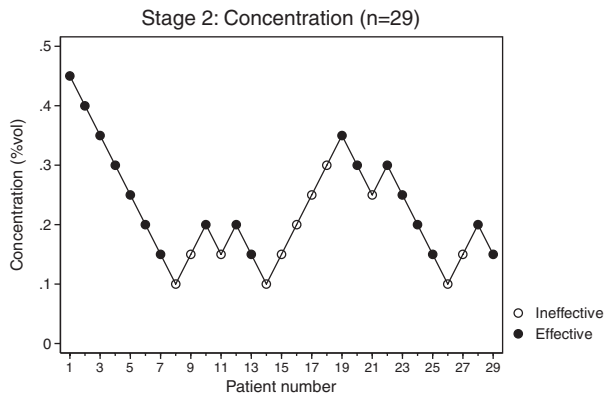


Fig. 2. Up-down sequential concentration allocation of 20 ml of ropivacaine.

Stage 3 (n = 40)

There was no evidence for an association between dose and pain at 24 h ($P = 0.34$): 8/19 (42%) of patients at the conventional dose were pain-free at 24 h, compared with 12/21 (57%) of patients at the lower dose (table 3; fig. 3).

There was no evidence that grip strength differed between the two groups ($P = 0.81$). There was also no evidence to indicate that pain on movement, numbness, and weakness during the first 24 postoperative hours differed between groups ($P > 0.73$). Satisfaction was modestly higher for the new and lower dose (median satisfaction 10 compared with 9 for the conventional dose, $P = 0.007$). This result should be interpreted with caution, given the small difference and the lack of corresponding differences in other patient-rated outcomes.

Linear regression of all study data found moderate evidence for an association between ropivacaine concentration and grip strength in the PACU after adjusting for baseline grip strength ($P = 0.02$), with PACU grip strength decreasing by 0.7 units for every 0.05% increase in concentration (95% CI 0.1 decrease to 1.3 decrease; fig. 4). However, the aggregated data do not indicate that PACU grip strength differs between the two doses used in stage 3 ($P = 0.90$). No such association was found for ropivacaine volume ($P = 0.91$, 0.01 decrease per 1-ml increase, 95% CI 0.2 decrease to

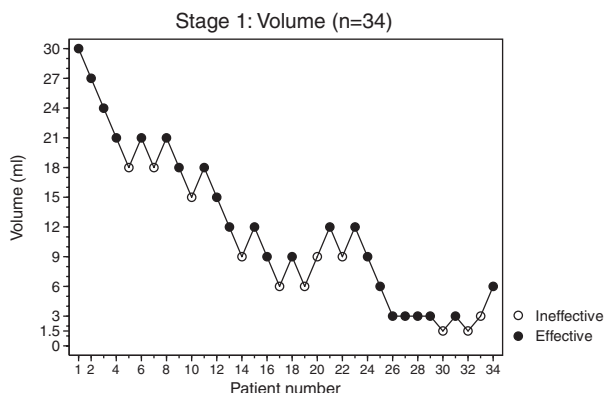


Fig. 1. Up-down sequential volume allocation of 0.5% ropivacaine.

Table 3. Outcomes for the “New” vs. “Conventional” Doses (Stage 3)

	20 ml 0.375% (n = 21)	30 ml 0.5% (n = 19)	P Value
Intraoperative alfentanil bolus ≥ 1	4 (19)	3 (16)	
PACU			
PACU catheter bolus only	1 (5)	0 (0)	
PACU catheter withdrawal + bolus	0 (0)	0 (0)	
PACU catheter replacement	0 (0)	1 (5)	
PACU grip strength, kgf	30.2 (12.1)	28.6 (8.2)	0.81
Ward/home			
Pain free at 24 h	12 (57)	8 (42)	0.34
Worst NRPS with movement	1 (0–3)	2 (0–3)	0.73
Numbness NRS	8 (6–10)	10 (7–10)	0.74
Weakness NRS	9 (7–10)	9 (7–10)	0.78
Satisfaction NRS	10 (10–10)	9 (8–10)	0.007

Data expressed as n (%), mean (SD), or median (interquartile range).

kgf = kilogram-force (1 kgf \sim 10 N); NRPS = numerical rating pain score (0–10; 0 = no pain, 10 = worst imaginable pain); NRS = numerical rating score (0–10; 0 = no numbness/weakness or very unsatisfied, 10 = very numb/weak or very satisfied); PACU = postanesthesia care unit.

0.2 increase; fig. 5). There was no evidence that ropivacaine volume ($P = 0.49$) or concentration ($P = 0.93$) was associated with remaining pain-free at 24 h.

Discussion

To our knowledge, this is the first study in humans to investigate, with up-down methodology, the relative importance of both local anesthetic volume and concentration for peripheral nerve blockade, in this instance, as assessed by the prevention of pain after surgery. The current results es-

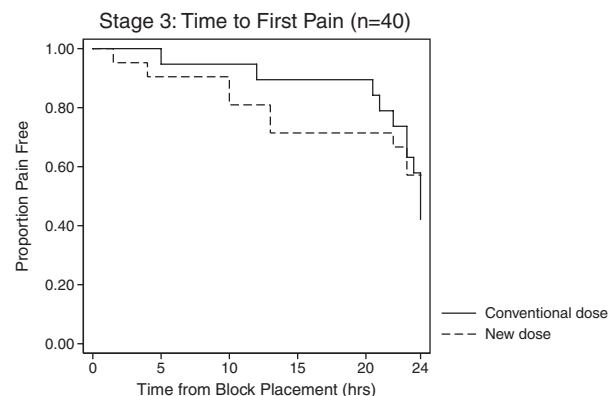


Fig. 3. Kaplan-Meier curves for time to first onset of surgical site pain for 0.375% ropivacaine, 20 ml (“new dose”), versus 30 ml of 0.5% ropivacaine (“conventional dose”). Difference between curves was not significant (chi-square test = 0.24; $P = 0.62$).

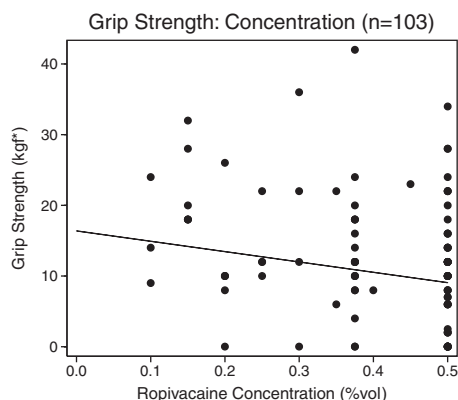


Fig. 4. Scattergram of recovery room grip strength by ropivacaine concentration for all patients. Predicted values are shown for a patient with mean preoperative grip strength (41 kgf). After adjusting for baseline grip strength, there was evidence for an association ($P = 0.02$). * kgf = kilogram-force (1 kgf \sim 10 N).

essentially reproduce the results from a tightly controlled laboratory study in animals, in which the intensity of nerve blockade was primarily determined by local anesthetic concentration.²

The current study was designed to determine the volume of local anesthetic required (at a concentration above the presumed minimum effective blocking concentration) to satisfy the anatomic requirements of plexus blockade in the interscalene area and then to determine the minimum effective blocking concentration at that volume. The marked difference between the 95th dose percentiles, yet relative similarity between the 50th dose percentiles between stages 1 and 2, are in keeping with the aforementioned theoretical requirements: the administration of 0.5% ropivacaine during stage 1 was a concentration higher than the estimated 95th percentile for concentration during stage 2, as reflected by the marked difference between 95th dose percentiles of

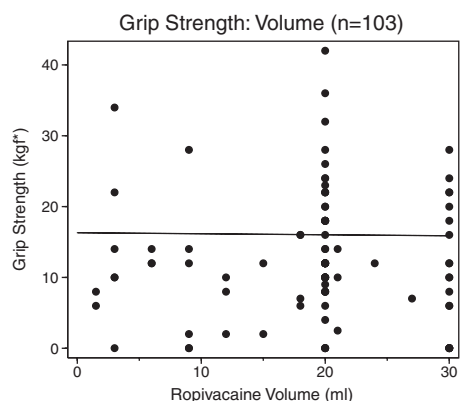


Fig. 5. Scattergram of recovery room grip strength by ropivacaine volume for all patients. Predicted values are shown for a patient with mean preoperative grip strength (41 kgf). After adjusting for baseline grip strength, there was no evidence for association ($P = 0.91$). One patient at 12 ml volume/grip strength = 65 not plotted. * kgf = kilogram-force (1 kgf \sim 10 N).

stages 1 and 2. Moreover, we surmise that just as individual patients may have different responses to the same dose of the same drug delivered in exactly the same location (in relation to the target nerves), the accuracy with which the local anesthetic drug can be deposited, in reality, differs between patients. In other words, in 50% of patients in stage 1, the sonographic images and/or needle-to-nerve proximity was probably such that local anesthetic deposition was achieved with an accuracy such that only 3 ml of 0.5% ropivacaine was required for satisfactory blockade: the 50th dose percentiles were consequently relatively similar between stages 1 and 2. In the other 50% of patients during stage 1, the sonographic images and/or needle-to-nerve proximity was probably less than ideal, such that local anesthetic deposition was less accurate, and, therefore, required a larger volume of ropivacaine. This was also reflected during stage 1 in the very large disparity between the 50th and 95th percentiles for volume. In stage 2, with the administration of a larger volume of ropivacaine (20 ml), the placement accuracy was less critical, as reflected by the less marked difference between the 50th and 95th percentiles for concentration.

The second clinically important finding from this study was the determination of the minimum primary bolus dose of interscalene ropivacaine required to prevent recovery room pain after shoulder surgery. The estimated ED(vol)₅₀/ED(vol)₉₅ of ropivacaine, 0.5%, was 2.7/20.5 ml, and the ED(conc)₅₀/ED(conc)₉₅ of ropivacaine 20 ml was 0.15/0.34%. In the context of a low-dose postoperative continuous ropivacaine infusion, when compared with a commonly administered interscalene ropivacaine dose (30 ml 0.5%), the administration of the derived ED₉₅ for volume and concentration (20 ml 0.375%) did not compromise primary block duration, but it was associated with a modest increase in patient satisfaction. Strictly, on the basis of our data, we cannot conclude for certain the reason for the observed modest increase in patient satisfaction with the new and lower dose of ropivacaine. Previous studies have suggested that an increase in postoperative motor block (as defined by the frequency of episodes of an insensate or densely blocked upper extremity) is associated with a reduction in patient satisfaction.¹⁴ The current findings are consistent with these previous data, in that an association was demonstrated, from the aggregated data, between ropivacaine concentration (but not volume) and motor block. However, the stage 3 protocol did not allow us to differentiate between the relative role of ropivacaine concentration and the volume, and therefore, any real association between satisfaction and motor block (and by extrapolation, ropivacaine concentration) remains speculative. This potential association should, therefore, be subject to further study.

We were unable to demonstrate an association between ropivacaine concentration and block duration;^{2,4} however, this was almost certainly influenced by the utilization of a continuous ropivacaine infusion (albeit at a low dose) after the administration of the primary ropivacaine bolus. This

lack of association may have also been influenced by the absence of outcome data for blocks lasting more than 24 h.

Our study design incorporated up–down methodology to accurately determine the 50th percentiles, and then by derivation, the 95th percentiles. This may be seen as a study weakness. It could be argued that a “k-in-a-row” or “biased coin” design focusing on the 95th percentile would be more appropriate. However, utilization of an indwelling catheter readily enables the administration of supplemental local anesthetic in the event of inadequate blockade or recovery room pain. Therefore, primary determination of the 95th percentile (as opposed to the 50th percentile) is not as important when using this analgesic technique. Nevertheless, the use of isotonic regression combined with a relatively large number of subjects enabled the estimation of the 95th percentiles with acceptable precision.

A potential limitation was our method that was used to assess patient satisfaction: a simple one-dimensional numerical rating scale at 24 postoperative hours. However, patient satisfaction is a complex multidimensional concept and best quantified using an instrument that has undergone appropriate psychometric validation.²³ Use of such an instrument would have increased the validity of our results. A well-recognized limitation of simple one-dimensional scales is that most patients tend to report high scores, and further, their ability to detect subtle changes is limited.^{24,25} Nevertheless, in the current study, a difference in satisfaction was demonstrated using a scale similar to an instrument previously shown to demonstrate convergent validity with a psychometrically constructed expanded 40-item questionnaire.²⁶ Another limitation was the protocol for the management of patients reporting pain in the PACU, which included a catheter withdrawal intervention (6 of 63 patients in stages 1 and 2). This may not reflect typical practice in other settings. Furthermore, including these “suboptimal” catheters in the up–down sequential dose allocation might seem inappropriate; however, a comprehensive review of this study methodology suggested that these patients should be included in up–down sequencing as removing them would misleadingly underestimate the respective percentiles.¹⁷

One of the goals of reducing the preoperative ropivacaine dose was to reduce motor block. Our previous experience had revealed that some patients experience dissatisfaction with a paralyzed hand, despite reassurance that this usually resolves with resolution of the primary block. Motor blockade can also be problematic when early active physiotherapy is planned or in some arthroplasty procedures (e.g., “reverse” shoulder joint replacement), where there is a risk of joint dislocation from relaxation of the rotator cuff muscles.²⁷ However, it should be recognized that dense motor block of the entire upper extremity can be advantageous during emergence from general anesthesia, to protect some surgical repairs, for example, rotator cuff repair. In these patients, it may be preferable to use a short-acting local anesthetic (e.g., lidocaine, mepivacaine) at a concentration likely to result in

motor block, with or without a long-acting agent (e.g., 10 ml ropivacaine, 0.75%, diluted with 10 ml lidocaine, 1–2%).

Although an association between ropivacaine concentration and motor block was demonstrated, patients were not assessed for other interscalene block–related side effects such as dyspnea, hoarseness, and ptosis. Previous investigators have already demonstrated a clear association between local anesthetic volume and phrenic nerve blockade as assessed by objective measures of diaphragmatic function.^{10,28} It would be tempting to speculate that hoarseness and Horner’s syndrome are also volume- and dose-dependent given that these side effects require local anesthetic to have to spread to the adjacent recurrent laryngeal nerve and sympathetic chain. If the goal is the prevention of recovery room pain and extended postoperative analgesia, the results of this study show that in the context of a low-dose postoperative ropivacaine infusion, there is little advantage in administering a primary bolus dose of more than approximately 20 ml of 0.34% ropivacaine.

Finally, we caution against the extrapolation of our results to other nerve block locations. Intuitively, the demonstrated critical importance of both local anesthetic volume and concentration could be expected to apply to other peripheral nerve block locations; however, quantitatively, the current results can only really be applied to the interscalene area.

In summary, on the basis of the estimates for the ED(vol)₉₅ and ED(conc)₉₅, in the context of patient-controlled interscalene analgesia, we recommend 20 ml of 0.375% ropivacaine as a convenient dose (0.75% 10 ml + 10 ml diluent) that will prevent recovery room pain in approximately 95% of patients. Using a higher primary ropivacaine bolus dose will not increase primary block duration but may compromise patient satisfaction. Finally, on the basis of the observed disparity between the ED(dose)₉₅ estimates when varying either drug volume or concentration, which is in keeping with previous laboratory studies in animals,² this study provides a compelling argument for future peripheral nerve block dose-finding studies incorporating methodology to estimate the required threshold for both drug volume and concentration.

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