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# Comparison of minimum effective volume of local anesthetic for ultrasound guided supraclavicular block ($MEAV_{95}$) in elderly and middle aged patients

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**Abbreviations:**
US – SCB, supraclavicular brachial plexus block
LA – local anesthetic
BP – brachial plexus
MEAV – minimum effective local anesthetics volume
$MEAV_{95}$ – minimum effective local anesthetic volume in 95% of patients
$ED_{50}$ – effective dose in 50% of patients
CSA – cross sectional ar

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## Abstract

***Backgrund and Purpose:*** *The aim of this study was to determine the minimum effective volume of local anesthetic (LA) required to produce an efficient supraclavicular block in 95% of patients ($MEAV_{95}$) using an ultrasound (US)-guided technique in an elderly (>65 y) and a middle aged group (<45 y) of patients. Furthermore, we aimed to calculate potency ratio of LA between the groups. We assumed a reduced $MEAV_{95}$ in elderly group.*

***Matherials and Methods:*** *Fourty-four patients (N=22 per group) undergoing upper limb surgery received a US-guided supraclavicular block. The study method is a previously validated step-up/step-down sequential model where the volume of LA for each following patient is determined according to the outcome of the previous block. The starting volume was 30 mL; in the case of block failure, the volume was increased by 5 ml. After successful block, the volume was reduced by 5 mL. $MEAV_{95}$ was calculated using probit transformation and logistic regression. Potency ratio of LA is calculated using Fieller's method.*

***Results and Conclusions:*** *The calculated minimum effective anesthetic volume in 95% of patients was 16.49 mL (95% CI, 12.23–20.75 mL) in elderly and 44.52 mL (95% CI, 19.05–69.99 mL) in middle aged group (95% CI, 0.7–55.3 mL, P=0.044). A potency ratio of LA between middle aged and elderly is 2.69 (95% CI 2.13 to 3.44). The minimum volume requirement for effective US-guided supraclavicular block in 95% of elderly patients was significantly reduced. A potency ratio of 2.69 indicates almost three times stronger LA potency in the elderly.*

## INTRODUCTION

Ultrasound-guided supraclavicular brachial plexus block (US-SCB) is widely used for upper extremity surgery because of its ability to anesthetize all four distal upper extremity nerve territories (the median, radial, ulnar and musculocutaneous) at the level of the clavicle. Elderly patients (>65 years) are particularly sensitive to local anesthetics (LA) in peripheral blocks and several mechanisms may account for the increased sensitivity. Conduction velocities, number of large diameter fibers and peripheral nerve (Na+, K+) ATP-ase all decrease with aging and smaller doses of LA are required for regional blocks in elderly patients *(1, 2)*. Up to date, Duggan *et al. (3)* reported the minimum volume required for an effective US-SCB in 95% of patients ($MEAV_{95}$). They performed a study on a population with an average of 48 years of age and found $MEAV_{95}$ to be 42 ml. Recently we conducted a study where we described structural changes of brachial plexus in the elderly population *(4)*. We observed a significantly smaller surface area in comparison to the younger patients. Also, we determined the minimum volume of LA required for an effective US-SCB in 50% of patients ($MEAV_{50}$) using the Dixon and Massey study protocol. However, in clinical practice, the $MEAV_{50}$ carries little probative value, the $MEAV_{90}$ or $MEAV_{95}$ provide a more accurate measure of the volumes needed to ensure a successful block. The aforementioned structural changes to the brachial plexus in addition to the increased sensitivity that the elderly patients exhibit to LA render the data referring to the minimum anesthetic volume required for an effective US-SCB in 95% of middle aged patients not applicable to the elderly population. Therefore, the aim of this study is to calculate the minimum effective volume of LA (50:50 mixture of 0.5% levobupivacaine and 2% lidocaine) required to produce an effective US-SCB for surgical anesthesia in 95% of patients in elderly patients (>65 years) and in middle aged patients (<45 years) by using logistic regression. We hypothesize reduced LA requirements for the elderly as compared to the middle-aged patients. Since the present study is a dose-response model, the secondary outcome is a potency ratio of LA between the two groups.

## MATHERIALS AND METHODS

After we obtained a Hospital Ethics Committee approval for the study as well as a written informed consent from every participant, we recruited 22 elderly (>65 years) and 22 middle aged (<45 years) patients undergoing upper limb surgery to this observer-blinded, up–down sequential allocation study. The study was registered in ClinicalTrials.gov and identifier number NCT01467596 has been issued on the November 4th, 2011. The inclusion criteria were age (>65 years in elderly group and 18–45 years in middle aged group) and a pressumed upper limb surgery in nerve territories of the brachial plexus. Exclusion criteria were the patient's refusal of regional anesthesia, neurologic or neuromuscular diseases, diabetes mellitus and clinical signs of cutaneous infection at the site of needle insertion. We examined all patients with the same ultrasound (Nemio Toshiba Medical System Inc 2001, Japan) with a linear 12 MHz probe. The patients were placed in a supine position with their heads turned opposite to the upper extremity being anesthetized. Brachial plexus is found lateral to the round pulsating hypoechoic subclavian artery that lies on top of the hyperechoic first rib. Prior to performing the block we administered 25 mcg of fentanyl to all patients. We placed a 25G spinal needle (90 mm, Quincke type, Vygon, France) on the outer (lateral) end of the probe and advanced it along the long axis of the probe in the same plane as the ultrasound beam (in plane techniqe). Once the needle tip almost reached the cluster on the ultrasound image, half of the LA volume was injected in proximity to the plexus. We then repositioned the needle cranially in order to distribute the remaining anesthetic volume around the entire brachial plexus cluster. For the purpose of block assessment, we defined time zero as the time of needle removal from the skin. Every 5 min for up to 30 min, a blinded observer checked for pinprick anesthesia with a 23G needle as well as for the loss of cold sensation by applying an alcohol swab in the central sensory region of each nerve location (the median, ulnar, radial and musculocutaneous nerve). The response was compared to the same stimuli delivered to the contralateral arm. We defined a successful block as a total loss of pinprick sensation and total loss of cold sensation in all four regions innervated by the distal nerves assessed within 30 min of LA injection.

The starting volume of the LA mixture was 30 mL. If a successful block was achieved, volume of LA administered to the following patient was reduced for 5 ml. Otherwise, if a complete sensory block in any of distal nerve distributions did not occur, we declared it as failed block and increased the volume administered to the following patient for 5 mL of LA. We first estimated the minimum effective volume required in 50% of patients ($MEAV_{50}$) and then applied logistic regression to calculate the $MEAV_{95.}$ We only used the data of unsuccessful blocks to estimate $MEAV_{50}$ and its 95% confidence interval (CI), applying it to the empirical formula of Dixon and Massey for large sample ($x = (\sum f_i x_i / n) + d/2$; x is $MEAV_{50}$; $x_i$ is volume of LA; $f_i$ is frequency of successful or unsuccessful sensory blocks associated with used LA volume; n is the total number of patients with successful or unsuccessful blocks, and d is volume interval-5 ml) *(5)*. We based the sample size calculation on the anticipated mean LA volume from previous studies that analysed US-SCB *(3, 6–8)*. Since our recent study showed structural changes of the brachial plexus in elderly associated with an almost 50% reduction in $MEAV_{50}$ of LA, we presumed a minimum of a 40% reduction of $MEAV_{95}$ in elderly patients. Based on that assumption, we expected a $MEAV_{95}$ of 25

**TABLE 1**

Demographic Characteristics of Patients.

| | Elderly group (N=22) | Middle aged group (N=22) |
|---|---|---|
| Age, (years) | 74.7 ± 7.1 | 41.6 ± 5.9 |
| BMI, (kg/m²) * | 26.5 ± 3.5 | 25.9 ± 2.9 |
| Male/Female, (n) | 8/14 | 13/9 |
| ASA status I/II/III/IV, (n)** | 0/5/14/3 | 7/14/1/0 |
| Surgical time, (min) | 76.1 ± 33.9 | 89.6 ± 33.8 |

Data are expressed as mean ± SD or n (Number of patients)

* BMI – body mass index

** ASA status – American Society of Anestesiology classification system for assessing the fitness of patients before surgery ml (i.e. 40% of 42 ml from Duggan' study) with an estimated SD of 10 ml. Such volume difference is also clinically significant (effect size, d=0.6). A probability level of 0.001 and power of 0.90 yielded a sample size of at least 21 patients for each tested group. We performed all calculations using the Minitab 15 statistical software.

## RESULTS

Twenty-two patients in each group completed the study protocol. We achieved an appropriate ultrasound visualization of the brachial plexus at the first rib for all patients. The study group baseline characteristics are shown in Table 1. The sequence of successful and unsuccessful US-SCB in elderly group is presented in Figure 1. The same data for the middle-aged group are shown in Figure 2. We calculated effective volumes of 16.49 mL (95% CI, 12.23 – 20.75 mL) and 44.52 mL (95% CI, 19.05 – 69.99 mL) for US-SCB in 95% of patients in the study group and in the middle aged group, resepctively. A potency ratio of local anesthetics between the middle aged and the elderly is 2.69 (95% CI 2.13 to 3.44). The administered volumes ranged from 30 to 5 mLfor the elderly group, while the administered volumes ranged from 35 to 10 mL in the middle-aged group. Nine patients in the elderly group had a failed block. Ten patients in the middle-aged group had a failed block.

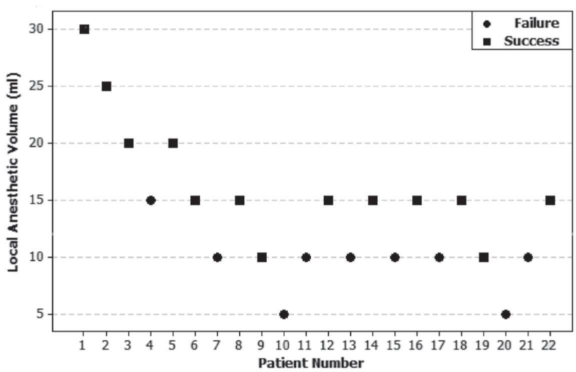


**Figure 1.** *Up-and-down sequences of US-SCB in elderly group*

*Figure 1 presents step-up/step-down sequence model where the local anesthetic volume for the following patient is determined by the outcome of previous block. The starting volume was 30 ml. In the case of block failure, the volume was increased by 5 mL whereas after successful block, the volume was reduced by 5 mL. The calculated effective volume for US-SCB in 95% of patients (MEAV$_{95}$) is 16.49 mL.*

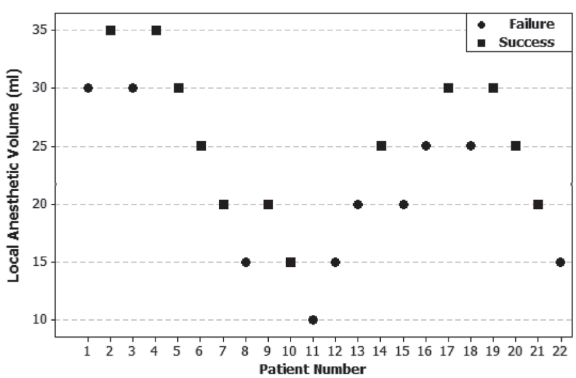


**Figure 2.** *Up-and-down sequences of US-SCB in middle aged group*

*Figure 2 presents step-up/step-down sequence model where the local anesthetic volume for the following patient is determined by the outcome of previous block. The starting volume was 30 ml. In the case of block failure, the volume was increased by 5 mL whereas after successful block, the volume was reduced by 5 mL. The calculated effective volume for US-SCB in 95% of patients (MEAV$_{95}$) is 44.52 mL.*

## DISCUSSION

In the present study we demonstrated that the calculated minimum effective LA volume required to produce an effective US-SCB in 95% of patients is 16 mL for the elderly and 44 mL for the middle-aged patients thus supporting our hypothesis of a reduced LA volume required for US-SCB in the elderly. We found that the elderly required an approximately two and half times smaller volume of LA mixture for an effective US-SCB in 95% patients in comparison to the MEAV$_{95}$ determined for the middle aged population. On one hand, these results might be explained by the morphological changes of peripheral nerves due to aging, and on the other hand by increased sensitivity of the elderly to LA agents. Aging related structural changes of brachial plexus in supraclavicular region were assessed by measuring the cross sectional surface area as high-resolution sonography appears to be accurate and previously validated tool for the assessment and mapping of the brachial plexus *(6, 9–12)*. The brachial plexus surface area of the elderly patients, as measured at the first rib, is approximately two times smaller than the brachial plexus surface area of the middle aged patients, measured at the same site. We attribute the difference to global involutive changes of the peripheral nervous system that affect brachial plexus as well. Since the area to be blocked was two times smaller in comparison to the middle aged population, we assume that the LA requirements are reduced for elderly patients. Furthermore, the present study explored the dose-response relationship of LA according to different age of patients and we report a potency ratio of 2.69 indicating that LA requirements in middle age are greater by a factor of 2.69. Therefore, a dramatically stronger effect of LA is observed in elderly patients as LA requirements for effective sensory blockade are two and half times lower.

The present study might have some limitations. To date, the majority of published dose-finding studies have focused exclusively on MEAV$_{50}$ and relied on the Dixon and Massey up-down method *(3, 13–16)*. Historically, the up and down methods were employed to investigate the concentration of inhaled anesthetic agents required to prevent movement upon surgical incision in 50% of patients, the $ED_{50}$ which is also known as minimal alveolar concentration *(17)*. As the concentration-response relation for inhaled anesthetics is steep, the $ED_{95}$ can be estimated using the $ED_{50}$ *(18)*. Furthermore, the sample sizes required by up and down methods are usually small *(17)*. These two factors have contributed to their great popularity. Unfortunately, the dose –response curve of other anesthetic agents differs (for example, LA) and may not be as steep as for inhaled anesthetics. Therefore, the particular Dixon and Massey up and down methodology has recently been criticized as insufficient for accurate determination of LA doses, particularly the extrapolation of the $MEAV_{95}$ number. Tran *et al.* recently published two studies in which the biased coin design was used to approximate minimum effective LA volume for ultrasound guided peripheral nerve blocks *(19, 20)*. However, the present study reports a $MEAV_{95}$ of 16 mL in the elderly and 44 mL in the middle aged patients that strongly correlates with our clinical practice and provides an accurate measure of the volume needed to ensure successful blocks. Therefore, as far as we are concerned, the Dixon and Massey method is still methodologically acceptable, even though it is now becoming a little outdated.

In conclusion, the present study demonstrates reduced requirements ($MEAV_{95}$) as well as a stronger effect of LA in elderly patients.

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