Echogenicity and ultrasound visibility of peripheral nerves of the upper extremity

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Abstract

Aim: Regional anesthesia with ultrasound-guidance is an excellent option for pain control if nerves are adequately visualized. Gender, body mass index (BMI), history of diabetes, neck and forearm circumference may affect echotexture and visualization. This study evaluates patient characteristics for their ability to predict the echogenicity or visibility of upper extremity peripheral nerves. **Material and methods:** This is a prospective observational study. A convenience sample of adult emergency department patients were enrolled. Gender, BMI, history of diabetes, neck circumference and arm circumference were recorded. Sonographic images of the brachial plexus at interscalene and supraclavicular levels, the median, the radial and ulnar nerves were recorded. Three reviewers independently graded the echogenicity and visibility using subjective scales. **Results:** 395 peripheral nerves were included. Nerves of the forearm (median, ulnar, radial nerves) were found to be more echogenic (OR=9.3; 95% CI: 5.7, 15.3) and visible (OR=10.0; 6.3, 16.0) than more proximal nerves (brachial plexus at interscalene and supraclavicular levels). Gender, BMI, and history of diabetes mellitus were not significantly related to nerve visibility ($p=0.9$, 0.2 , 0.2 , respectively) or echogenicity ($p=0.3$, 0.8 , 0.3). Neck circumference was not related to visibility or echogenicity of proximal nerves. Increased forearm circumference improved echogenicity (OR=1.25; 1.09, 1.43) but not visibility of forearm nerves. **Conclusions:** Gender, BMI and presence of diabetes were not related to echogenicity or visibility of upper extremity nerves. Increasing forearm circumference was associated with increased echogenicity of the adjacent nerves, but not visibility. Neck circumference was not associated with either nerve visibility or echogenicity of brachial plexus nerve bundles.

Keywords: Ultrasonography; nerve block; peripheral nerve injection; regional anesthesia

Introduction

Ultrasound-guided peripheral nerve blocks are used with increasing frequency to manage pain in a variety of hospital settings. A successful ultrasound-guided peripheral nerve block hinges on adequate visualization

of the targeted nerve. Physicians performing regional anesthesia could save time and resources if they could identify *a priori* patient characteristics that would predict a more difficult ultrasound depiction of peripheral nerves. Nerves that are difficult to visualize makes the procedure more challenging to perform and could potentially lead to complications, failure to perform the procedure, or decreased success. Prior research documents the common anatomical appearance of the target nerves by ultrasound in healthy subjects and in states of pathology such as neuropathy, nerve damage or disease [1-4]. These studies have identified that the echogenicity of nerves changes based on ratio of total fascicular area to whole nerve area and fascicle pattern [5]. Since myelin sheaths are lipid-based, it is possible that increased body

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mass index (BMI) could confer increased echogenicity of a nerve, leading to improved visibility. Traditionally, however, increased BMI and increased depth to target structures leads to poor sonographic visualization. In addition to BMI, another factor known to affect the sonographic visualization of nerves is the presence of diabetes. Watanabe et al [6] found a significant increase in the cross-sectional area and in the hypoechoic aspect of the nerves in diabetic patients when compared with controls. This is due to increased water content related to increased aldose reductase conversion of glucose to sorbitol, local ischemia from microvascular injury, and interference with the innate metabolism of the peripheral nerves in diabetic patients [7-8]. Similarly, several small studies exist that have addressed the varying sonographic appearance of nerves with respect to gender. Multiple studies have noted a difference in the cross-sectional area of peripheral nerves, with those in females being significantly smaller [9-10]. While it is known that various patient characteristics have an effect on the sonographic appearance of nerves, there appears to be a gap in the current literature in regards to which of these have a significant effect on the nerve visualization necessary for providing ultrasound-guided regional anesthesia.

This study aims to identify patient characteristics that could predict difficult peripheral nerve visualization. Our hypothesis is that certain patient physical characteristics (neck and forearm circumference, gender) as well clinical history (diabetes, obesity) can predict the echogenicity and visibility of peripheral nerves of the upper extremity.

Material and methods

This is a prospective observational study. The University of Arizona Institutional Review Board approved this study. Written informed consent was obtained from all subjects. A convenience sample of adults (>18 years old) presenting to an academic emergency department

were enrolled after consent process. Subjects with altered mental status, acute anxiety state or hemodynamic or respiratory instability were excluded. Also, subjects were excluded if they were unable to sit in a semi-reclined position for ultrasound examination.

Data collection and ultrasound examinations were performed by study personnel consisting of emergency medicine residents and attending physicians. Two senior-level resident physicians and four attending physicians performed the ultrasound examinations and captured images. Resident physicians had previously taken a standardized 8 hour course on emergency ultrasonography that included a 4 hour lecture and 4 hours of hands-on training. They also completed a 2 week emergency ultrasound elective and performed approximately 400 point-of-care ultrasound examinations. The attending physicians had emergency ultrasound fellowship training experience and performed approximately 900 point-of-care ultrasound examinations. The attending physicians routinely used bedside ultrasound in the emergency department for patient care. Patient characteristics including gender, BMI, and past medical history of diabetes were recorded from the electronic medical record and clarified with subjects. Neck circumference was measured with a standard tape measure at the level of the cricoid cartilage. Forearm circumference was measured at the widest portion of the forearm.

Prior to data collection, study physicians reviewed sonographic anatomy of the nerves of the upper extremity. The study protocol for image acquisition utilized a high-frequency linear transducer (12-4 MHz) and a Philips Sparq ultrasound machines (Andover, MA). Study personnel were instructed to optimize images to obtain the best possible image as if they would be performing a peripheral nerve block. Cross-sectional (transverse plane) images of the brachial plexus at interscalene level and supraclavicular level, as well as the radial, median and ulnar nerves at the level of the mid-forearm, were obtained and recorded (fig 1).

Fig 1. Sonographic images of the peripheral nerves of the upper extremity and neck evaluated in this study (a) Interscalene brachial plexus, b) supraclavicular brachial plexus, c) median nerve at the level of the mid-forearm, d) radial nerve at the level of the mid-forearm, e) ulnar nerve at the level of the mid-forearm).

Three reviewers blinded to patient data independently graded the echogenicity and visibility of each nerve from recorded images. These reviewers were emergency physicians with advanced training in emergency ultrasound. They graded the echogenicity of each nerve using a four-point subjective echogenicity index (SEI) (Table I). This previously published index performed well against gray-scale image measurements [5]. Visibility was assessed using a five-point Likert scale adapted from a previous study assessing sonographic visibility of structures for procedures (Table II) [11]. Prior to image review, reviewers studied a collection of sample images representing the range of possible grades for each scale. All three reviewers graded a 20% overlapping sample so that interrater reliability could be assessed.

Data Analysis

Statistics were calculated using Stata (version 14, Stata Corp, College Station, TX). Means (95% confidence intervals [CIs]), medians (interquartile range), and percentages (95% CIs) are used for descriptive data.

Our power and sample size calculation assumed the analysis would use linear regression; however, our outcome variables (echogenicity and visibility) were not normally distributed. Thus, we used random-effects ordered logistic regression (ideal for continuous ordinal outcomes) to assess the relative odds of each unit increase in the outcome variables (echogenicity and visibility) for the following independent variables: Nerve location, neck circumference for neck nerves, forearm circumference for forearm nerves, BMI, and presence of diabetes mellitus, and sex. Each subject was considered a cluster. We used the final regression models for echogenicity and visibility to estimate the predicted (marginal) probability of each outcome stratified by nerve location and used goodness of fit tests for ordered logistic

regression to assess the final fit of all models [12]. We used fractional polynomial regression to determine if continuous independent variables were linearly related to the outcome variables in the log odds (logit) scale. We calculated inter-rater reliability (kappa) for the three reviewers. We used a weighted kappa with weights for the difference between reviewer scores as the square of the difference. In other words, a difference of 1 had a lower weight than a difference of 2. For the main analysis, we only used one randomly chosen reviewer's ratings for the subset of samples utilized for interrater reliability analysis.

Sample size

Our study was powered (power=0.8) to detect an R^2 value of 0.1 for one key predictor variable with a total R^2 of 0.25 for all variables in a linear regression model with 4 other independent variables. The following 5 independent variables were chosen a priori: BMI, neck circumference, forearm circumference, nerve location, and sex) with an $\alpha = 0.05$. We had sufficient power to include 5 independent variables in a linear regression model and detect an R^2 of 0.1 for one predictor variable and an R^2 of .25 overall (i.e., one independent variable would explain 10% of the variance in the dependent variable and the other 4 variables would explain an additional 15% of the variance). A sample size of 73 was required to achieve the power stated above and we chose 80 subjects to account for missing data. An R^2 value of 0.25 for up to five variables is a modest effect size and thus is reasonable given our study goals to identify potentially significant predictors of nerve visualization using ultrasound. This effect size is a clinically relevant number since accounting for 25% of the variance overall (and 10% of the variance with one predictor) in nerve echogenicity would be a clinically significant finding.

Table I. Subjective echogenicity index for grading peripheral nerve echogenicity [5]

Grade	Definition
0	Cannot visualize nerve
1	Hypoechoic (echogenicity of a muscle belly)
2	Mixed echogenicity (typical honeycomb appearance)
3	Hyperechoic (echogenicity of an intermuscular septum)

Table II. Subjective visibility scale 5-point Likert scale for grading peripheral nerve visibility [11]

Grade	Definition
1	Cannot visualize the nerve
2	The nerve can be located, but visualization is poor and using this image for performing a nerve block would be very difficult.
3	An adequate view was obtained but a better image of the nerve might be desired for a nerve block.
4	A good view was obtained and the reviewer would feel comfortable performing a nerve block.
5	An excellent view was obtained and this is an optimal image for using for performing a nerve block.

Fig 2. This bar graph depicts the probability of each possible echogenicity score (0 to 3) for each nerve of the neck and forearm evaluated in this study based on the final logistic regression model.

Results

A total of 80 subjects were enrolled. One subject's data was not analyzed due to missing data. Nerves at five sites were analyzed for each subject for a total of 395 nerves. The median BMI was 26 (IQR: 23-31). Of the subjects whose data was analyzed, 13.9% (95% CI: 7.2, 23.5) had a history of diabetes and 44.2% (29.1, 60.1) of subjects were male. The mean neck circumference was 38.3 cm (37.0, 39.6) and the mean forearm circumference was 24.9 cm (24.0, 25.8).

Neither BMI, gender, nor presence of diabetes mellitus was significantly related to nerve visibility ($p=0.9$, 0.2 , 0.2 , respectively) or echogenicity ($p=0.3$, 0.8 , 0.3 , respectively), after controlling for differences among nerves.

Forearm nerves (radial, median, ulnar) as a group had significantly higher echogenicity and visibility compared to brachial plexus nerves (at interscalene and supraclavicular level) with $p<0.001$. The predicted (i.e. marginal) probability of each individual echogenicity (0, 1, 2, or 3) and visibility (1, 2, 3, 4, or 5) score for each nerve site, calculated from the final logistic regression models, can be seen in figures 2 and 3, which show that the forearm nerves as a group have higher echogenicity and visibility on average compared to the nerves of the neck. Forearm nerves had 9.3 times higher odds of a higher echogenicity score (95%CI: 5.7, 15.3) and 10.0 times higher odds of a higher visibility score (95%CI: 6.3, 16.0) compared to the nerves of the neck. Forearm circumference was significantly related to echogenicity for the 3 forearm nerves, with each 1 cm increase in forearm circumference being associated with an increase in the

Fig 3. This bar graph depicts the probability of each possible visibility score (1 to 5) for each nerve of the neck and forearm evaluated in this study based on the final logistic regression model.

odds of a higher echogenicity (OR=1.25; 95%CI: 1.09, 1.43). The radial nerve had a higher echogenicity compared to both the median (OR=2.7; 95% CI: 1.3, 6.0) and ulnar (OR=2.3; 95%CI: 1.1, 4.9) nerves, which did not differ significantly from each other ($p=0.64$). Forearm circumference was not significantly related to visibility for the 3 forearm nerves [OR per 1 cm = 1.16 (95%CI: 0.96, 1.40)]. For the forearm nerves, both ulnar (OR=2.5; 95%CI: 1.2, 5.0) and median (OR=2.2; 95%CI: 1.1, 4.4) nerves had higher odds of improved visibility compared to the radial nerve, but the ulnar and median nerves did not differ significantly from each other ($p=0.72$).

Neck circumference was not related significantly to echogenicity (OR per 1 cm increase in circumference = 0.9; 95%CI: 0.8, 1.0) or visibility (OR=1.0; 95%CI: 0.9, 1.1) for the nerves of the neck. In addition, the brachial plexus at supraclavicular level did not differ significantly from the brachial plexus at interscalene level for either echogenicity (OR=0.8; 95%CI: 0.4, 1.6) or for visibility (OR=0.7; 95%CI: 0.4, 1.2).

The inter-rater reliability (kappa statistics) for echogenicity and visibility was calculated among three independent reviewers for a 20% random sample of all observations ($N=80$) and showed that reviewers had moderate agreement [13]. For echogenicity, paired kappas were 0.491 (95%CI: 0.292 - 0.653), 0.597 (0.425 - 0.758), and 0.414 (0.309 - 0.526), while for visibility, paired kappas were 0.483 (0.363 - 0.611), 0.595 (0.441 - 0.748), and 0.447 (0.266 - 0.591).

All final ordinal logistic regression models met the assumption of proportional odds across outcome categories as well as having adequate fit, with all p -values for goodness of fit tests >0.05 .

Discussions

Echogenicity and visibility vary by nerve with the peripheral nerves of the forearm, median, ulnar, and radial nerves being significantly more echogenic and more visible than the brachial plexus nerves. The differences in echogenicity between peripheral and proximal nerves have been well-documented in prior literature [14]. Nerves located more peripherally are both easier to visualize and farther from other structures to be avoided. This is predominantly due to the differences in the area of connective tissue to the area of fascicle in the nerve bundle. This study adds to the prior literature by attempting to identify patient characteristics that could predict difficult nerve visualization.

Neither patient gender nor BMI had any effect on visibility or echogenicity for any of the nerves. While clinicians may use the patient's body habitus to determine whether a nerve block should be attempted, BMI was not significantly predictive of nerve visibility or echogenicity in this study's population. Notably, the study population was, on average, overweight with a median BMI of 26. Forearm circumference was significantly related to echogenicity of the forearm nerves, with higher echogenicity associated with increasing circumference. This could be related to the increased proportion of myelin sheath to the nerve volume in more peripheral nerves and increased myelin (fat) associated with greater circumference. This aspect of our findings requires further study. Notably, visibility of the nerves was not related to neck or forearm circumference, therefore a clinicians' assessment of a patient's size may not predict success in visualizing nerves.

Diabetes can cause several nerve disorders that can change the sonographic appearance of peripheral nerves. The most common of these is diabetes-related polyneuropathy which is visualized sonographically as increased circumference and loss of the fascicular pattern of the affected nerves [15]. Our study detected no change in echogenicity or visualization based on a past medical history of diabetes, indicating that this factor was not clinically relevant in our study population. The underlying prevalence of diabetic-related neuropathy in our study population is unknown. It is possible that with a larger sample size and with a study population that encompasses the full spectrum patients with and without a diabetes-related neuropathy, it would be possible to detect a change in visibility or echogenicity of the nerves.

To our knowledge, this was the first study to explore patient characteristics that could predict peripheral nerve visualization in the emergency department patient population. Peripheral nerve images were obtained by clini-

cians with varied ultrasound experience reflecting real-world clinical practice setting. To make this study robust, we trained study physicians in sonographic anatomy of the peripheral nerves of the upper extremity and also used previously published echogenicity index to avoid any discrepancies in grading the peripheral nerve images. In addition, we studied peripheral nerves most commonly used to provide ultrasound guided regional anesthesia by clinicians practicing in the acute care settings.

Our study is limited by convenience sampling and the subjective nature of the grading scales used. Whereas some research has found that subjective grading of echogenicity leads to similar results as quantitative analysis, other research has found it inferior to quantitative grayscale, computer-driven analysis [5,16]. Another limitation of this study is in regards to the level of training and scanning experience of the physicians that performed the scout scans. The scout scans were performed by both residents and attending physicians who had varied levels of experience in ultrasound. This heterogeneity constitutes a limitation of the study as it had significant influence on the quality of the acquired images. We did not obtain information on whether the patients had neuropathy or prior procedures or injuries affecting the examined region. Nor did we record whether the patients with diabetes had experienced any neurological symptoms. In addition, the study was powered to detect the threshold effect size that we had set and any changes with diabetes were not sufficient to detect a correlation. We also did not perform neurological examination on our subjects. Had such patient information been obtained, our results may have been more robust.

In conclusion, we have found peripheral nerves of the forearm to be more echogenic and more visible than those of the neck. While BMI and diabetes do not affect visualization or echogenicity of nerves, increasing forearm circumference was associated with increased nerve echogenicity.

Conflict of interest: None

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