Cross-sectional area in median and ulnar nerve ultrasound correlates with hand volume

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Abstract
Background: The influence of demographic and anthropometric factors on nerve cross-sectional area (CSA) reference values in high-resolution ultrasound was evaluated in a prospective observational study.

Methods: We measured CSA of median, ulnar, radial, and sural nerves in 80 healthy adults from 18 to 98 years of age. Pearson's correlation and multiple linear regression with age, gender, body mass index, and hand volume were calculated.

Results: Ulnar and median nerve CSA showed a significant positive correlation with ipsilateral hand volume. Median nerve CSA in the left forearm (mean, 6.2 mm²; SD, 1.2) increased by 0.006 mm² (SE = 0.002; \( P < .001 \)) per cm³ of hand volume, resulting in a difference of 1.9 mm² predictable by hand volume (mean, 326 cm³; SD, 81; range, 180–500).

Conclusions: The observed correlation of CSA and hand volume may influence the interpretation of CSA values in patients with very large or small hands.

KEYWORDS
anthropometric factors, cross-sectional area, demographic factors, hand volume, high resolution nerve ultrasound, reference values

1 | INTRODUCTION

Cross-sectional area (CSA) measurements in high-resolution nerve ultrasound (HRUS) are influenced by demographic and anthropometric factors, such as gender, age, and body mass.\(^1\)–\(^4\)

Some studies addressed a possible correlation of nerve CSA and morphometric values of the extremities. Kessler et al.\(^5\) analyzed the volar digital nerves of 10 healthy adults using HRUS with respect to glove size. There was no correlation between nerve thickness and glove size. Ortiz et al.\(^6\) analyzed nerve diameters in 18 cadaveric hands. There was a positive correlation between hand span, hand width, and nerve diameter in the hand and at the wrist. Marcinia et al. reported that median nerve CSA in 25 healthy adults\(^6\) correlated with the abductor pollicis brevis muscle action potential and weight, concluding that anthropometric measurements might affect sonographic CSA measurements and recommending further studies of these relationships.

In the present prospective observational study, the volume of each hand was recorded as morphometric data to evaluate the influence of hand volume on CSA measurements in nerve ultrasound.

2 | METHODS

The local ethics committee of the Ruhr University of Bochum, Germany, approved the study protocol. All participants signed informed consent.
2.1 | Participants

Medical students and hospital employees, their relatives, and independent inpatients admitted to hospital because of diseases not related to the peripheral nervous system were eligible for this study. Ten participants were recruited per age decade to provide an even age distribution.

2.2 | Exclusion criteria

Pre-existing conditions with a potential impact on nerve CSA (eg, diabetes, history of entrapment syndromes, peripheral nerve lesions, radiculopathies, peripheral neurosurgical procedures) led to exclusion from the study. Strength, coordination, sensory symptoms, and reflexes were examined by J.P. or M.T. Any positive item in the clinical part of the total neuropathy score (TNS) led to exclusion, as well as edema of the extremities. Nerve conduction studies (NCSs) of the sural (sensory) and ulnar and median nerves (motor, sensory, and F-wave) were performed by a board-certified neurophysiologist (J.P.) on all participants, and those with abnormal NCS were excluded. Reference values of the local laboratory were used.

2.3 | Sonography examination

All ultrasound examinations were performed by MT with an Affiniti 50 (Philips, Amsterdam, Netherlands) device using a 5 to 18 MHz linear array transducer. Measurements were supervised and validated by J.P. (neurologist with more than 8 years of experience in neuromuscular ultrasound).

The transducer was held at a perpendicular angle to the nerve measured to avoid anisotropic effects caused by nerve structures and to obtain the correct CSA. For CSA measurements in mm², the nerves were visualized in a transverse plane and measured within the inner border of the hyperechoic epineurium using the free-hand tracer-tool.

2.4 | Selection of nerve sites

The nerve sites studied were selected to permit the use of reference values from the local laboratory at sites frequently used in routine clinical studies. Concerning the correlation with hand volume, the sural nerve served as a negative control.

Each nerve was measured at predefined sites. The ulnar nerve was measured at Guyon’s canal, 15 cm proximal to Guyon’s canal, at the ulnar sulcus, and in the upper arm 10 cm proximal to the elbow. The median nerve was measured at the carpal tunnel, in the forearm 15 cm proximal to the carpal tunnel, and in the upper arm 10 cm proximal to the elbow. The ulnar and median nerve were visualized over their whole course to detect the maximum and the minimum CSA. The radial nerve was measured in the spiral groove. The sural nerve was measured 15 cm proximal to the medial malleolus.

For intra-rater reliability testing, MT performed the measurements following the study protocol twice on one volunteer 14 days apart at the beginning of the study. For inter-rater reliability testing, J.P. and M.T. performed CSA measurements of 18 nerve sites on one volunteer 1 mo apart. The measurements were not included in the study data set. For blinding, each measurement was performed after a delay of 14 days and saved separately.

2.5 | Measurement of hand volume

Hand volume was measured separately for each hand by submerging the hand into an overflow vessel filled with water up to the second skin fold at the wrist. The displaced water corresponding to the hand volume was collected in a measuring cylinder and measured in cubic centimeters (cm³).

2.6 | Calculations

The intra-nerve CSA variability, defined as the ratio of the largest to the smallest CSA of one nerve, was calculated for the median and ulnar nerves. As a nerve-specific side-to-side comparison value, we calculated the side-to-side difference ratio of the intra-nerve CSA variability (SSDIVA) for the median and ulnar nerves, defined as the ratio of the intra-nerve CSA variability on the side with the larger intra-nerve CSA variability to that on the side with the smaller intra-nerve CSA variability. The body mass index (BMI) was calculated as weight (kg) / height (m)².

2.7 | Statistical analyses

Intra-class correlation coefficients (ICC) for repeated single measurements with fixed observers and absolute agreement were

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**Table 1** Demographic and anthropometric characteristics of the participants

| Characteristic     | Value   | SD  | Range          |
|--------------------|---------|-----|----------------|
| Female             | 46 (57%)| n.a.| n.a.           |
| Male               | 34 (43%)| n.a.| n.a.           |
| Dominance left hand| 5 (6%)  | n.a.| n.a.           |
| BMI                | 24.6 kg/m²| 4.0 | 17.8–37.4      |
| Age                | 56.71 y | 22.8| 18–98          |
| Hand volume left   | 320.6 cm³| 81.1| 180–500        |
| Hand volume right  | 331.0 cm³| 80.7| 180–500        |

Note: Means are displayed for BMI, age, and hand volume. Abbreviation: n.a.: not applicable.
calculated to assess inter- and intra-rater reliabilities. Means, SDs, and 95% confidence intervals of nerve CSA were calculated for the left side only to avoid artificial reduction of variance. Independent samples t-tests were used to compare CSA means and SDs with previously published reference values. Normal distribution of the data was tested using the modified Kolmogorov-Smirnov test. Pearson’s product-moment correlation coefficient for CSA, intra-nerve CSA variability, SSDIVA, age, BMI, gender, and hand volume was calculated at each nerve site for both sides separately. Multiple linear regression analysis with automated backward exclusion was calculated to acquire the best-fitting model to predict CSA. Model selection was based on the Akaike information criterion (AIC), selecting the model with the lowest value for AIC.

IBM SPSS for Windows version 25 (IBM, Armonk, NY) was used for statistical analysis.

## 3 | RESULTS

### 3.1 | Study population

Complete data were obtained from all 80 participants. The characteristics of the study population are shown in Table 1.

### 3.2 | Inter- and intra-rater reliabilities

The intra-rater reliability was 0.63. The inter-rater reliability was 0.67.

## TABLE 2 | Results for cross-sectional area, intranerve cross-sectional area variability and side-to-side difference ratio of the intranerve cross-sectional area variability

| Nerve                          | Mean (Standard deviation) | 95%-confidence interval |
|-------------------------------|---------------------------|-------------------------|
| Median nerve at the carpal tunnel CSA | 8.8 (1.7)               | 5.4 – 12.2              |
| Median nerve in the forearm CSA | 6.2 (1.2)               | 3.8 – 8.6               |
| Median nerve in the upper arm CSA | 7.7 (1.4)               | 4.9 – 10.5              |
| Ulnar nerve at Guyon’s canal CSA | 5.0 (1.0)               | 3.0 – 7.0               |
| Ulnar nerve in the forearm CSA | 5.4 (1.0)               | 3.4 – 7.4               |
| Ulnar nerve at the ulnar sulcus CSA | 7.2 (1.8)               | 3.6 – 10.8              |
| Ulnar nerve in the upper arm CSA | 6.5 (1.4)               | 3.7 – 9.3               |
| Radial nerve CSA              | 5.1 (1.2)               | 2.7 – 7.5               |
| Sural nerve CSA               | 3.4 (1.2)               | 1.0 – 5.8               |
| Intraneve CSA variability median nerve | 1.84 (0.30)             | 1.24 – 2.44             |
| SSDIVA median nerve           | 1.16 (0.14)             | 0.88 – 1.44             |
| Intraneve CSA variability ulnar nerve | 2.0 (0.41)             | 1.18 – 2.82             |
| SSDIVA ulnar nerve            | 1.17 (0.15)             | 0.87 – 1.47             |

SSDIVA: Side-to-side difference ratio of the intranerve CSA variability
CSA: Cross-sectional area

## TABLE 3 | Regression coefficients of hand volume and cross-sectional area for the median and ulnar nerve

| Nerve                          | b     | SE    | r     | P    |
|-------------------------------|-------|-------|-------|------|
| Median nerve in the forearm   |       |       |       |      |
| Right                         | 0.007 | 0.002 | 0.401 | < .001 |
| Left                          | 0.006 | 0.002 | 0.431 | < .001 |
| Median nerve in the upper arm |       |       |       |      |
| Right                         | 0.004 | 0.002 | 0.245 | .028 |
| Left                          | 0.006 | 0.002 | 0.327 | .003 |
| Ulnar nerve at Guyon’s canal  |       |       |       |      |
| Right                         | 0.004 | 0.001 | 0.275 | .013 |
| Left                          | 0.004 | 0.001 | 0.341 | .002 |
| Ulnar nerve in the forearm    |       |       |       |      |
| Right                         | 0.006 | 0.001 | 0.400 | < .001 |
| Left                          | 0.004 | 0.001 | 0.342 | .002 |
| Ulnar nerve at the ulnar sulcus |       |       |       |      |
| Right                         | 0.009 | 0.002 | 0.404 | < .001 |
| Left                          | 0.008 | 0.002 | 0.339 | .002 |
| Ulnar nerve in the upper arm  |       |       |       |      |
| Right                         | 0.004 | 0.002 | 0.276 | .013 |
| Left                          | 0.006 | 0.002 | 0.356 | .001 |

Abbreviations: b, beta coefficient; r, Pearson’s product-moment correlation coefficient.
3.3 | CSA reference values

The CSA reference values for the left median, ulnar, radial and sural nerve at different sites, the intra-nerve CSA variability and SSDIVA are listed in Table 2.

3.4 | Regression analysis

Pearson’s product–moment correlation yielded 12 nerve sites in the median and ulnar nerve with significant positive correlations between CSA and hand volume. Regression coefficients are shown in Table 3. To estimate the effect size, the regression equation yields a CSA difference of 1.9 mm² predictable by the ipsilateral hand volume in our sample (range, 320 cm³; regression factor, 0.006 mm²/cm³) for the left median nerve. Thus, the maximum CSA deviation from an average hand is approximately 1 mm² in both directions.

Correlations were also found for the variable age in 10 sites. For the left radial (P = .01) and the left sural nerve (P < .01) a significant negative correlation with age was found. Figure 1 shows the mean CSA of the left radial and sural nerve for each age decade. Hand dominance showed no correlation with CSA. For the intraneuron variability and SSDIVA of the median and ulnar nerve, no correlation with age, BMI, gender, and hand volume was detected.

Regression models in multiple linear regression analysis with automated backward exclusion were significant (P < .05) in 17 nerve sites. Hand volume was confirmed as a predictor of nerve CSA in nine nerve sites in the median and ulnar nerve, BMI in four, age in five, gender in three sites. In the radial and sural nerves, hand volume was not predictive; BMI and age were found to be the main predictors. The results including F-values, P-values, and R² of the regression models are shown in Supporting Information Table S1, which is available online.

4 | DISCUSSION

The main finding of the current study is a correlation between hand volume and CSA found in the median and ulnar nerves but not in the radial nerve. CSA appears to be inversely correlated with age.

To discuss our data in the context of previously published data, we selected a study conducted in the same region with a comparable study population and age distribution. There is no significant difference between the two studies in the CSA of the median nerve at both sites and of the ulnar nerve at Guyon’s canal and in the forearm. Results for the ulnar nerve at the sulcus and the radial and sural nerves differ from our results (Table 4). The SSDIVA shows no significant difference between the two studies for the ulnar nerve, but a significant difference for the median nerve. The intra-nerve CSA variability is different. The comparison is limited as Kerasnoudis et al. seem to have calculated CSA means using data from both sides, whereas in our study only one side is reported. The different degrees of agreement can be compared with the structured analysis of HRUS results of different laboratories in one region reported by Telleman.

**FIGURE 1** Mean CSA values and 95% confidence interval of the left radial and sural nerves for each age decade, n = 80

**TABLE 4** Title: Comparison of cross-sectional area values, intraneuron cross-sectional area variability and side-to-side difference ratio of the intraneuron cross-sectional area variability to previous data

| Nerve | Current study | Kerasnoudis et al.² |
|-------|--------------|-------------------|
|       | n = 80       | n = 75            |
| Median nerve at the carpal tunnel CSA | 8.8 (1.7) | 8.4 (2.07) | p = 0.74 |
| Median nerve in the forearm CSA | 6.2 (1.2) | 6.6 (1.6) | p = 0.08 |
| Ulnar nerve at Guyon’s canal CSA | 5.0 (1.0) | 5.16 (1.03) | p = 0.33 |
| Ulnar nerve in the forearm CSA | 5.4 (1.0) | 5.46 (1.26) | p = 0.74 |
| Ulnar nerve at the ulnar sulcus CSA | 7.2 (1.8) | 5.33 (1.4) | p < 0.01 |
| Radial nerve CSA | 5.1 (1.2) | 3.26 (1.52) | p < 0.01 |
| Sural nerve CSA | 3.4 (1.2) | 1.82 (0.64) | p < 0.01 |
| Intraneuron CSA variability median nerve | 1.84 (0.30) | 1.05 (0.13) | p < 0.01 |
| SSDIVA median nerve | 1.16 (0.14) | 1.21 (0.04) | p = 0.03 |
| Intraneuron CSA variability ulnar nerve | 2.0 (0.41) | 1.53 (0.51) | p < 0.01 |
| SSDIVA ulnar nerve | 1.17 (0.15) | 1.2 (0.25) | p = 0.37 |

p values for difference in independent samples t-tests, significant values (p < 0.05) in bold
SSDIVA: Side-to-side difference ratio of the intraneuron CSA variability
CSA: Cross-sectional area
Age is a significant predictor of nerve CSA at several sites in our study. Particularly in the radial and sural nerves, CSA appears to be inversely correlated with age. This supports the results reported by Kerasnoudis et al., who described a significant decrease in CSA of the radial nerve in the spiral groove with increasing age. Cartwright et al. reported a significant increase in CSA with increasing age in all nerves. This might be explained by differences in participant selection in the geriatric study population as no NCSs were performed in the study of Cartwright et al.

Gender and BMI are correlated with CSA in multiple nerve sites, confirming the observations of Cartwright et al., Won et al., and Kerasnoudis et al.

As a further morphometric factor, we assessed the influence of hand volume on CSA measurements. Pearson's correlation reveals that in 12 sites of the ulnar and median nerves the ipsilateral hand volume correlates with nerve CSA. As hand volume, gender, and BMI interact, it should be emphasized that hand volume is a predictor of nerve CSA in nine nerve sites in multiple linear regression analysis. The backward elimination process and model selection using the AIC confirms that hand volume is not a surrogate parameter for BMI and gender, but has an independent predictive value on CSA in the median and ulnar nerve. The sural nerve as a negative control shows no correlation with hand volume. The correlation between hand volume and CSA found in the median and ulnar nerves but not in the radial nerve might be due to the predominant innervation of the hand by the median and ulnar nerve. However, the influence on clinical decision making is limited, because correlation coefficients are not consistently high enough to create reference values or to introduce a correction factor based on hand volume.

Marciniak et al. reported that median nerve CSA correlated with the abductor pollicis brevis muscle action potential in healthy adults. This might represent the effect of more muscle tissue innervated by the median nerve. Our findings are in line with these observations and the positive correlation between hand span, hand width, and nerve diameter found by Ortiz et al. in 18 fresh frozen cadaveric hands from adult donors. Kessler et al. analyzed the volar digital nerves of 10 healthy adults using HRUS. They introduced the morphometric value of glove size into analysis. There was no correlation between nerve thickness and glove size. Glove size is measured on an ordinal scale and usually determined by the length and circumference of the hand. It is not validated for the assessment of hand volume. Therefore, a possible influence of hand volume on measurements of the digital nerves might have been undetectable. Further studies on the influence of anthropometric factors on nerve CSA are needed.

The correlation between the volume of innervated tissue, mostly muscle mass, and nerve CSA does not suggest a causal relationship in one or the other direction. The emerging concept of a strong somatotopic organization of peripheral nerves in the lower extremity found in nerve MRI studies is a possible explanation of our findings. The inverse relation of age and nerve CSA in some nerves observed in our study points in the same direction. A decrease in CSA in older subjects may be explained by the loss and degeneration of larger myelinated fibers and a loss of motor neurons in the physiological ageing process or in sarcopenia.

In amyotrophic lateral sclerosis as an example of severe progressive loss of motor neurons, the decrease of nerve CSA can be used to monitor disease progression. On the other hand, Molin et al. reported that high-resistance strength training did not increase the CSA of the median and the musculocutaneous nerve, although the size of the biceps muscle was larger in trained subjects. These observations favor an influence of nerve size on muscle mass and not an influence of muscle mass on nerve size. Probably nerve size is an indicator of motor unit number in the absence of demyelination or inflammation, whereas muscle mass represents both motor unit size and number.

Our study is limited by its relatively small sample size and the inclusion of healthy participants and patients with diseases not related to the peripheral nervous system. Even though maximum care was taken to exclude neuropathies by history, clinical examination, and NCS, we cannot exclude a bias by including individuals who had been admitted to hospital. The lack of NCSs of the radial nerve is another limitation of the present study. Radial nerve lesions were excluded based on history and clinical examination.

In conclusion, the finding of a correlation between median and ulnar nerve CSA and hand volume should be kept in mind when examining patients with very small or large hands. The intra-nerve CSA variability and SSDIVA showed no correlation with hand volume, so the use of these and other commonly used nerve CSA ratios could be recommended in patients with extremely small or large hands.

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CONFLICT OF INTEREST
None of the authors has any conflict of interest related to the content of the submitted manuscript and research.

ETHICAL PUBLICATION STATEMENT
We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.
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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.

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