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Peripheral Nerve

Mega Nerves: Factors Associated with Large Median Nerves on Ultrasound of the Carpal Tunnel

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Background: Although increased cross-sectional area of the median nerve on ultrasound has been associated with carpal tunnel syndrome, there has been little research examining outlier cases with exceedingly large nerves. The purpose of this study was to identify factors associated with these "mega" nerves, and to determine whether these nerves carry with them increased severity of disease.

Methods: Patients who presented to clinic with upper extremity paresthesias over a 4-year period were included in this study. Two groups were created: mega nerves (cross-sectional area >2 SD above average), and nonmega nerves. Statistical analysis was performed to compare demographics, symptom scores, and nerve conduction studies (NCS). Significant variables were then compared between patients with mega nerves and those with ultrasound positive nerves (≥10 mm^2), which did not reach mega size (normal nerves were excluded).

Results: The cohort included 425 median nerves with 25 mega nerves. The groups differed significantly in diabetes status, body mass index (BMI), Boston Carpal Tunnel Questionnaire (BCTQ) Symptom Severity Scale scores, and NCS results. When compared only with ultrasound positive but nonmega nerves, mega nerves were still associated with diabetes, higher BMI, and worse NCS results.

Conclusions: Diabetes, BMI, NCS results, and BCTQ Symptom Severity Scale scores are associated with mega nerves. However, BCTQ scores do not differ between mega nerves and other ultrasound positive nerves. In patients with obesity or diabetes, outlier ultrasound measurements may not correlate with worsened clinical symptoms, even in the setting of more significantly altered NCS results. *(Plast Reconstr Surg Glob Open 2022;10:e4597; doi: 10.1097/GOX.0000000000004597; Published online 24 October 2022.)*

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most prevalent compressive neuropathy, present in at least 1.5% of adults.[1-3] History and physical examination are essential for making the diagnosis, with the carpal compression test found to be most sensitive and specific.[4] With frequent atypical presentations and confounding conditions such as ulnar neuropathy and cervical radiculopathy, additional diagnostic tests have been sought. The CTS-6[5–7] serves as a well-studied clinical diagnostic tool, and nerve conduction studies (NCS) have also long been used as a supplement to clinical diagnosis.[8,9]

In recent years, ultrasound examination has been increasingly utilized to aid in the diagnosis of carpal tunnel syndrome. Studies have shown that ultrasound may offer similar diagnostic accuracy when compared with NCS without added cost or patient discomfort.[10,11] Median nerves in patients with clinical and electrodiagnostic evidence of CTS have a larger cross-sectional area (CSA) at the carpal tunnel than those without.[12,13] A few studies have additionally shown that body mass index (BMI) and diabetes are associated with larger median nerves at the carpal tunnel.[13-15]

A recent study determined that an optimal cutoff value for CSA in the diagnosis of CTS is 10 mm^2.[16] However, the range of CSA values in our clinical experience extends far beyond this cutoff value. While previous studies have examined differences in patients on either side of this or a similar cutoff value, or have correlated risk factors (such as BMI and diabetes) with increasing CSA as continuous variables, none have singled out those nerves that far exceed the norm in size. This study sought to examine factors associated with a median nerve CSA greater than two SDs above the mean, a phenomenon we

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have termed "mega nerve," and to determine whether these nerves behave similarly to nerves of smaller caliber which are still considered diseased. Our hypothesis is that larger BMI and the presence of diabetes are associated with mega nerves.

MATERIALS AND METHODS

Patient Selection

All patients presenting to the hand clinic at a single institution with numbness and or paresthesias in the upper extremity were entered into a database between October 2014 and September 2020. Data entered into the database included basic demographics, height/weight, diabetes status, laterality, NCS results, CTS-6[5] and BCTQ[17] scores, and the ultrasound-measured CSA of the median nerve. Many patients had both left and right median nerves measured; these were entered into the database twice, once for each hand.

All subjects in the database with ultrasound-measured median nerve CSA were included in this study. No other exclusion criteria were applied; subjects both with and without clinical or electrodiagnostic evidence of CTS were included. This broad inclusion created a cohort with both diseased and healthy median nerves. The goal of this cohort design was to create results, which are generalizable to the appropriate population—patients who present to clinic with possible CTS (based on chief complaint of numbness and/or paresthesias).

Study Groups

Subjects were initially divided into two groups: those with "mega nerves," and those without. The CSA which qualified a nerve as "mega" was set at roughly two SDs above the mean of the cohort (Fig. 1). Mean CSA was 11.28 mm^2 and SD was 3.97. Two SDs above mean was calculated to be 19.22 mm^2. For simplicity, nerves were considered to be mega nerves if they had a CSA greater than or equal to 19 mm^2. For additional comparison as described below, another subgroup was made from the nonmega group—ultrasound positive, nonmega nerves (10 mm^2 ≤ CSA < 19 mm^2) (Fig. 2).

Takeaways

Question: What factors are associated with "mega" median nerves [cross sectional area (CSA) outliers] at the carpal tunnel, and do these nerves carry with them increased severity of disease?

Findings: Mega and nonmega nerve groups differ in diabetes status, BMI, Boston Carpal Tunnel Questionnaire Symptom Severity Scale scores, and NCS results. When compared only with other ultrasound positive (CSA ≥ 10 mm^2) nerves, mega nerves no longer portend significantly different BCTQ scores.

Meaning: In patients with obesity or diabetes, grossly enlarged median nerves at the carpal tunnel may not correlate with worse clinical symptoms, even in the setting of more significantly altered NCS results.

Statistical Analysis

Student *t* tests and chi square tests were performed using Microsoft Excel (2016) for continuous and categorical variables, respectively, to determine if patients with mega nerves and those without mega nerves differed significantly in the following variables: age, height, weight, BMI, sex, race, laterality, diabetes status, CTS-6 score, BCTQ scores, and NCS results (specifically distal motor latency (DML) and compound muscle action potential (CMAP)). DML and CMAP were used because they were the most consistently recorded measures in the NCS results. Sensory latencies and amplitudes were far more often missing from the data set and were therefore not used.

RESULTS

The study sample included 288 patients for a total of 425 measured nerves. The entire sample's average CSA

Figure 1. Borderline positive median nerve (10 mm^2).

Figure 2. Mega nerve (24 mm²).

Table 1. Mega versus Nonmega Nerves: Demographics, Symptoms Scores, and NCS Data

Variable	Entire Cohort N = 425	Mega Nerve (CSA ≥ 19 mm²) N = 25	Nonmega Nerve N = 400	*P* [CI = 95%]
	Avg (SD)	Avg	Avg	
CSA	11.3 (4.0)	21.7	10.6	
Age	52.3 (14)	56.0	52.0	0.18
Height (in)	65.5 (4.0)	65.6	65.1	0.59
Weight (lbs)	197 (51)	223	196	**0.029**
BMI	32.2 (7.3)	36.9	31.9	**0.0063**
CTS-6	13.4 (6.6)	15.2	13.3	0.19
Severity Scale score	2.9 (0.86)	3.3	2.9	**0.036**
Functional severity scale	N = 419	N = 25	N = 394	0.081
	2.3 (0.87)	2.6	2.3	
DML	N = 404	N = 20	N = 384	**0.00064**
	5.0 (2.0)	7.9	4.8	
CMAP	N = 399	N = 20	N = 379	**0.010**
	9.7 (4.0)	7.1	9.8	
	n (%)	n (%)	n (%)	
Gender				0.42
Women	303 (71.3)	19 (76.0)	284 (71.0)	
Men	122 (28.7)	6 (24.0)	116 (29.0)	
Race				0.91
White	324 (75.5)	19 (76.0)	305 (75.5)	
Black	99 23.2)	6 (24.0)	93 (23.3)	
Other	2 (1.18)	0 (0)	2 (1.25)	
Hand				0.20
Right	240 (56.5)	17 (68.0)	223 (55.8)	
Left	185 (43.5)	8 (32.0)	177 (44.3)	
Diabetes				**<0.0001**
No	324 (76.2)	11 (44.0)	313 (78.3)	
Yes	101 (23.8)	14 (56.0)	87 (21.8)	

Significant *P* values are indicated in bold.

was 11.28 ± 3. Cohort averages for all variables can be found in Table 1.

Once divided, there were 25 subjects in the mega nerve group (CSA ≥ 19 mm²) and 400 subjects in the nonmega nerve group (CSA < 19 mm²), with an average CSA of 21.7 mm² and 10.6 mm², respectively. Comparisons between these groups are detailed in Table 1. The groups differed significantly in three of the demographic variables analyzed: diabetes status, BMI, and weight. Of the functional and symptom score variables, Boston Carpal Tunnel Questionnaire Symptom Severity Scale score was significantly higher (worse) in patients with mega nerves. Both NCS measures were also worse in patients with mega nerves. Variables which were not significantly different between the groups were age, height, sex, race, laterality, CTS-6 score, and BCTQ functional severity scale score.

When the 136 ultrasound negative nerves (CSA <10 mm²) were removed from the nonmega nerve group, 264 ultrasound positive, nonmega nerve subjects remained. These subjects were then compared with the mega nerve subjects in regard to all variables that were previously found to be significant. These comparisons can be found in Table 2. The significant differences between the groups remained for BMI, diabetes status, and NCS results.

Table 2. Mega versus Ultrasound Positive, Nonmega Nerves

Variable	Mega Nerve (CSA ≥ 19 mm²) N = 25	Ultrasound + (CSA 10–18 mm²) N = 264	*P*
	Avg	Avg	
CSA	22.0	12.2	
Weight (lbs)	223.5	202.3	0.10
BMI	36.9	32.9	**0.031**
Severity Scale scores	3.3	3.1	0.21
DML	N = 20	N = 252	**0.0023**
	7.9	5.2	
CMAP	N = 20	2 = 247	**0.045**
	9.2	7.1	
	n (%)	n (%)	
Diabetes			**0.00041**
No	11 (44.0)	202 (77)	
Yes	14 (56.0)	62 (23)	

Significant *P* values are indicated in bold.

However, the significance was lost for weight and Boston Carpal Tunnel Questionnaire Symptom Severity Scale.

DISCUSSION

While it has been well established that increasing median nerve CSA at the carpal tunnel is associated with carpal tunnel syndrome,[10] there is no existing literature that examines extremely large median nerves as a distinct group. Studies have looked for correlations between several patient-specific factors and median nerve CSA, but this study sought to identify only those factors associated with nerves of a size far exceeding the norm (>2 SD above average), termed mega nerves.

This study demonstrates that higher BMI and weight are associated with mega nerves, and that higher BMI is associated with mega nerves even among other enlarged, ultrasound positive nerves. Tahmaz et al performed regression analysis on 80 patients, comparing the CSA of multiple nerves at multiple sites with age, gender, BMI, and hand volume, and found that BMI was positively correlated with median nerve CSA at the carpal tunnel.[13] Variables such as age, gender, and hand volume did affect some nerves at some locations, but no relationship between those variables and the median nerve at the carpal tunnel was found. Similarly, our study found no association between mega nerves and age, gender, or height. These findings in conjunction suggest that although larger body size/higher ideal body weight (as predicted by height in our study and hand volume in Tahmaz et al) may naturally carry with it a larger peripheral nerve size, obesity as a pathologic state is a more significant contributor to increased median nerve CSA at the carpal tunnel.

Additionally, diabetes is associated with mega nerves, even when compared with other enlarged, ultrasound positive nerves. Other studies have demonstrated a relationship between diabetes and increased median nerve CSA. Elnady et al found, in a group of 60 subjects with CTS (diagnosed clinically or with electrodiagnostic testing), that those with diabetes had a significantly greater median nerve CSA.[12] Kotb et al found the same. Interestingly, Kotb et al also found that patients with CTS, diabetes, and peripheral neuropathy (DPN) had significantly smaller median nerves than those with CTS and diabetes, but no DPN (similar in size to patients with idiopathic CTS).[14]

Mega nerves are also associated with more significantly altered NCS results (specifically motor latency and amplitude), even when compared with other enlarged, ultrasound positive nerves. The correlation between NCS results and increased median nerve CSA is well documented. Pulikkottil et al performed a prospective study on patients with clinical signs and symptoms of CTS and found a significant positive correlation between median nerve CSA and distal motor and sensory latencies on NCS.[17] Similarly, Torres-Cuenca et al found in a prospective study that the ultrasound-measured diameter of the median nerve correlates with NCS severity (mild, moderate, or severe).[18] Our study suggests that this trend remains even into CSA two SDs above the mean.

Mega nerves were also found to be associated with worse Boston Carpal Tunnel Questionnaire Symptom Severity Scale scores when compared with all nerves in the cohort, but did not have significantly different scores when compared to other enlarged, ultrasound positive nerves. This finding suggests that, though their ultrasound results (and, as discussed above, NCS results) may be impressive, patients with mega nerves have a symptom severity profile that does not differ greatly from other ultrasound positive patients, or other patients with carpal tunnel syndrome. Several studies have identified a correlation between BCTQ scores and increasing median nerve CSA. Akturk et al performed a cross sectional analysis on 41 clinically assigned CTS wrists and 20 controls and found a correlation between CSA and BCTQ scores (as well as BMI).[19] Padua et al also found a significant correlation between CSA and BCTQ in their study of 54 wrists referred for EDX with clinical evidence of CTS.[20] Our study demonstrates that this correlation likely has a limit, where increase in CSA past a significant outlier margin no longer produces worsening in patients' symptom severity scores.

This information helps the clinician to expect to see larger median nerves, oftentimes much larger than the norm, in patients with obesity and diabetes. Clinicians should use this study to understand that outlier ultrasound measurements do not correlate with outlier symptom severity in the setting of these mega nerves. Therefore, decision to proceed with surgery and with what urgency should be determined based on other factors such as symptom burden and patient preferences, and trials of nonoperative management need not necessarily be foregone.

There are a few limitations to this study. By the nature of examining an outlier group such as mega nerves, the size of the affected group is small. Though there were 425 total subjects, only 25 had mega nerves. This sample size is too small to perform a regression or correlation analysis, which is why *t* tests and chi square tests were used. Additionally, our study is clearly examining neither CTS patients nor a random sample of the general population. Since the cohort is made up of patients who presented to hand clinic with paresthesias, with or without the inclusion of their contralateral hand, the sample includes hands both with and without CTS, but is heavily skewed towards the presence of the disease. Therefore, our findings cannot necessarily be generalized to either CTS patients or the general population. However, they can be generalized to patients presenting to hand clinic with paresthesias, which is where they will likely be most used. Lastly, since obesity and diabetes are correlated in the general population, one may be confounding the other in our study. We cannot say that either is independently associated with mega nerves.

CONCLUSIONS

Median nerves that are found to be extremely large in size on ultrasound examination of the carpal tunnel (mega nerves) are associated with increased weight and BMI, diabetes, NCS results, and BCTQ symptom scores. When compared with other enlarged median nerves which don't quite reach "mega" size, mega nerves are no different in their BCTQ scores, but do have an association with greater BMI, diabetes, and NCS results. The pathologic states of diabetes and morbid obesity seem to contribute to the presence of these mega nerves and, though these patients may have large CSA measurements and more altered NCS results, they may not be anymore symptomatic than their nonmega counterparts. In short, clinicians should not be surprised by the presence of mega nerves in patients with obesity and diabetes, and their usual treatment course need not necessarily be swayed by the alarming size of the nerve on ultrasound examination.

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