*Research Article*

# Normative anatomical cutoff values of median nerve dimensions in Egyptian population. Sonographic comparison with those of carpal tunnel syndrome.

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## Abstract
**Objective:** To assess the usefulness of ultrasonography of the median nerve in accurate differentiation between normal and neuropathic nerve measurement in Egyptian population.
**Material and Methods:** The study was conducted on thirty normal subjects; fifteen males and fifteen females, with their mean age was ٣٦.٧±٤.٨٦ (range ٢٩-٤٥y). Another thirty patients with carpal tunnel syndrome CTS; twelve males and eighteen females with mean age was ٤٣.٩٣±٤.٥١ (range ٣٥-٥٢y). The cross sectional area CSA and flattening ratio (FR) at the level of pronator quadrates and pisiform were measured. Data from the CTS patient group and normal control group were compared to determine the statistical significance. The accuracy of the ultrasonographic diagnostic criteria for CTS was evaluated using receiver operating characteristic (ROC) analysis. **Results:** All measurements showed significant differences between normal and CTS groups except CSA at pronator quadratus. Increased CSA of the median nerve was the most predictive measurement of CTS. Using the ROC curve, a cut-off value of >١٠ at the level of pisiform bone provided a diagnostic sensitivity of ١٠٠٪ and specificity of ١٠٠%. **Conclusion:** The ultrasonographic measurement of the median nerve can yield an accurate cutoff values with high sensitivity and specificity between normal and neuropathic median nerve and can be used as useful non-invasive method for the diagnosis of CTS.
**Key Words**: median nerve, ultrasonography, cutoff value, carpal tunnel syndrome.

## Introduction
Median nerve (MN) is one of the important nerves that originate from the brachial plexus; it travels down through the arm and enters the forearm between the two heads of the pronator teres. When it reaches the wrist, it lies deep to the Palmaris long us muscle, slightly to its ulnar side. It passes through the flexor retinaculum tunnel, lying closer to the transverse carpal ligament than the flexor tendons of the hand. Median nerve divides into its terminal motor and sensory branches when leaving the flexor retinaculum. Carpal tunnel syndrome (CTS) is the most common nerve entrapment encountered in the clinical practice. It affects about ١٪ of the general population, and mostly seen in persons whose work requires repetitive wrist motion[١].

The carpal tunnel (CT) is a narrow unyielding space that entraps the MN between the transverse carpal ligament (TCL) ventrally and carpal bones dorsally.

Inflammatory swelling of the flexor tendon sheaths increases the compartment pressure within the CT[٢&٣]. Compression of the median nerve leads to an enlargement of the median nerve cross-sectional area (CSA)[٤]. Many studies reported that an increase in the cross-sectional area (CSA) measurement of the median nerve is a significant criterion in the diagnosis of CTS[٥-٧].

Many studies documented that intra-carpal pressure elevated in patients with CTS as compared to non-CTS subjects[٢&٣].

Ultrasonography is generally considered as a convenient diagnostic method, because of its wide availability, mobility, rapid performance, noninvasiveness, and relatively low

price as compared to magnetic resonance and other radiologic procedures[٨].
Ultrasonography evaluation of the musculo-skeletal system is used for the diagnosis of many cases, median nerve enlargement just proximal to the carpal tunnel and bowing of the flexor retinaculum was described as sonographic findings in patients with CTS[٩&١٠]. Normally, the median nerve was largest at the most distal region, the size of the nerve dose not vary greatly throughout its entire length (٧.٥ to ٩.٨mm$^{٢}$). No consensus about the cutoff value between normal and neuropathic nerves, most studies conclude a cutoff of ٩ to ١٢mm$^{٢}$[١١-١٢].

## Subjects and methods

The number of patients required in the study was determined after a power calculation according to data obtained from pilot study. Pilot study reported area PS mean of ٩.٨ with SD of ٠.٤٤ in normal persons, and reported area PS mean of ١١.٣٥ with SD of ١.٨٩ in cases with CTS. A sample size of ٣٠ persons in each group was determined to provide ٩٩٪ power for two-tail 't' test at the level of ٠.٠٥ significance using G Power ٣.١ ٩.٢ software.

The study was conducted in Radiology Department, Faculty of Medicine, Minia University during the period from January ٢٠١٤ to July ٢٠١٤ and after being approved by Medical Ethical Committee of the Department. Thirty healthy subjects were recruited in the study as a study group; another ٣٠ patients diagnosed clinically and electrophysiologically as having carpal tunnel syndrome (CTS) were included as a control group. Bifid median nerve cases were excluded from entering the study. Thorough counseling and a written informed consent was obtained from each subject prior to participating in the study. All recruited subjects were submitted to thorough medical history taking and clinical examination of both wrists, for patients with CTS electrophysiological examination of median nerve was done, then Real-time ultrasound examination using Toshiba medical system Xario ٢٠٠ machine using linear array multi-frequency transducer ١٠-١٢ MHz for estimation of cross sectional area (CSA) of the median nerve at the level of pronator quadratus muscle and at the level of pisiform bone, the study used the trace method, not the ellipse one for accurate measurement of CSA (Figure ١ and ٢). Subtraction of CSA of both levels was performed to obtain the difference. AP and transverse diameters of the median nerve at the level of hamate bone were obtained and flattening ratio was then calculated by dividing transverse diameter by AP diameter (Figure ٣). Dominant and non-dominant sides were examined in normal individuals whereas the only affected side in patients with CTS was examined.

Results of ultrasonography were recorded, tabulated and statistically analyzed. Descriptive statistics were done for all data (study and control group), the data were represented as range, means ± standard deviations (SD).Comparison between different groups was done using student's t-test and Mann Whitney testwhere appropriate using SPSS-٢٠.P value <٠.٠٥ was considered significant.


**Figure ١: cross sectional area calculation of the median nerve at the level of pisiform bone**

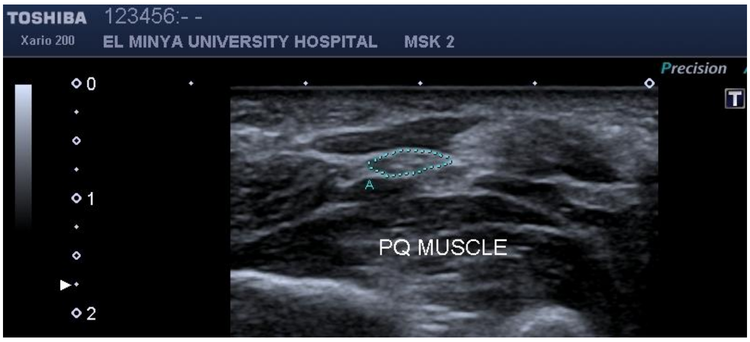


**Figure ٢: cross sectional area calculation of the median nerve at the level of pisiform bone**

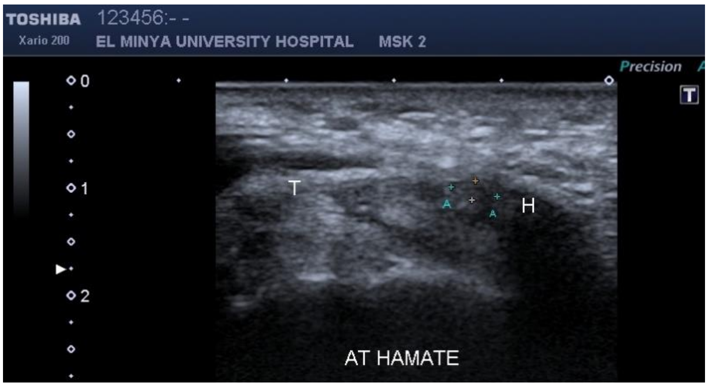


**Figure ٣: Calculation of AP and transverse diameters of median nerve at the level of hamate bone**

## Results

The study was conducted on thirty normal subjects; fifteen males and fifteen females, with their mean age was ٣٦.٧±٤.٨٦ (range ٢٩-٤٥y). Another thirty patients with carpal tunnel syndrome; twelve males and eighteen females with mean age was ٤٣.٩٣±٤.٥١ (range ٣٥-٥٢y).

Descriptive statistics of MN in normal population are shown in (table ١) including dominant and non-dominant hands, there was statistically insignificant difference between two sides.

| | Dominant (n=٣٠) | Non Dominant (n=٣٠) | P value |
|---|---|---|---|
| **(١)CSA at PQ**<br>Range<br>Mean ± SD | <br>(٨-١٠)<br>٩.٣٣±٠.٦١ | <br>(٨-١٠)<br>٩.٢٣±٠.٥٦ | <br>٠.٥١٣ |
| **(١)CSA at PS**<br>Range<br>Mean ± SD | <br>(٩-١٠)<br>٩.٩٣±٠.٢٥ | <br>(٩-١٠)<br>٩.٨±٠.٤١ | <br>٠.١٣٣ |
| **(١)Flattening ratio**<br>Range<br>Mean ± SD | <br>(٢.٢-٢.٧٨)<br>٢.٤٣±٠.١٨ | <br>(٢.٣٦-٢.٨)<br>٢.٥±٠.١٣ | <br>٠.١٢٧ |
| **(٢)PS-PQ CSA**<br>Range<br>Mean ± SD | <br>(٠-١)<br>٠.٦±٠.٤٩ | <br>(٠-١)<br>٠.٥٦±٠.٥ | <br>٠.٧٩٥ |

- **(١ ) Independent sample t test for parametric quantitative data between the two groups**
- ***(٢) Mann Whitney test for non-parametric quantitative data between the two groups***

**Table ١:** shows values of cross sectional area at pronator quadratus muscle and pisiform bone, flattening ratio at hamate level and difference in cross sectional area (CSA) between pronator quadrates (PQ) muscle and pisiform (PS) bone levels, in dominant and non-dominant sides in normal individuals.

*CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone*

As the difference of dominant and non-dominant sides in normal individuals was statistically insignificant, the study merged them in one group in order to compare their values with those obtained from CTS patients (Table ٢). There was statistically significant difference between two groups in all values expect CSA area at pronator quadratus muscle.

| | Normal (n=٦٠) | CTS (n=٣٠) | P value |
|---|---|---|---|
| **(١)Area PQ**<br>Range<br>Mean ± SD | <br>(٨-١٠)<br>٩.٢٨±٠.٥٨ | <br>(٨-١١)<br>٩.٤٦±١.١١ | <br>٠.٣٠٥ |
| **(١)Area PS**<br>Range<br>Mean ± SD | <br>(٩-١٠)<br>٩.٨٦±٠.٣٤ | <br>(١١-٢٠)<br>١٤.٢٦±٢.٩١ | <br>< ٠.٠٠١* |
| **(١)Flattening ratio**<br>Range<br>Mean ± SD | <br>(٢.٢-٢.٨)<br>٢.٤٦±٠.١٦ | <br>(٢.٢-٤.٣)<br>٣.٦٨±٠.٧١ | <br>< ٠.٠٠١* |
| **(٢)PS-PQ**<br>Range<br>Mean ± SD | <br>(٠-١)<br>٠.٥٨±٠.٤٩ | <br>(٢-١٠)<br>٤.٨±٢.٢٩ | <br>< ٠.٠٠١* |

- ***(١)Independent sample t test for parametric quantitative data between the two groups***
- ***(٢)Mann Whitney test for non-parametric quantitative data between the two groups***
- ****: significant difference at p value < ٠.٠٥***

**Table ٢:** shows comparison between the normal individuals and patients with CTS in MN descriptive dimensions and values.

*CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone*

The receiver operating characteristic (ROC) curve was performed to find out the value of MN variables obtaining maximum sensitivity and specificity. The continuous measurement scale in the current study results in the differentcut-off values and different corresponding sensitivity andspecificity, a summary of their relationship is shown in aROC curve graph (Figure ٤). Using this graph, an optimal cutoff point is used for determination of normal MN dimensions from neuropathic MN (Table٣).

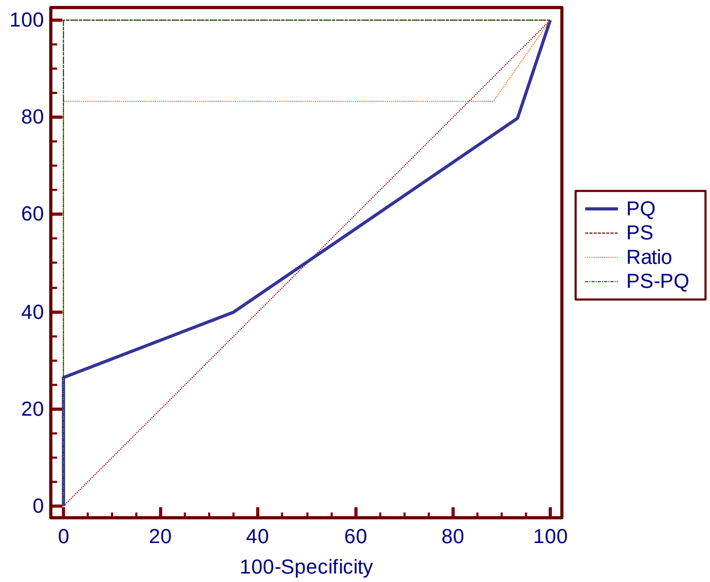


**Figure ٤: Receiver operating characteristic (ROC) graph showing sensitivity, specificity and area under the curve for MN variables.**
*PQ: cross sectional area at pronator quadratus muscle, PS: cross sectional area at pisiform bone*

| Variable | Optimal Cutoff | AUC | P value | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|---|---|
| **CSA PQ** | >١٠ | ٠.٥٢٧ | ٠.٧٠٥ | ٢٦.٦٧ | ١٠٠ | ١٠٠ | ٧٣.٢ | ٧٥.٦ |
| **CSA PS** | >١٠ | ١ | <٠.٠٠١* | ١٠٠ | ١٠٠ | ١٠٠ | ١٠٠ | ١٠٠ |
| **F. Ratio** | >٢.٨ | ٠.٨٤٣ | <٠.٠٠١* | ٨٣.٣ | ١٠٠ | ١٠٠ | ٩٢.٣ | ٩٤.٤ |
| **PS-PQ** | >١ | ١ | <٠.٠٠١* | ١٠٠ | ١٠٠ | ١٠٠ | ١٠٠ | ١٠٠ |

**Table ٣:** shows area under the curve (AUC), optimal cut-off point, sensitivity, specificity, identified normal MN from neuropathic MN with overall accuracy using receiver operating characteristic (ROC) method.

*CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone, PPV:positive predictive value , NPV:negative predictive value*

Simple discriminate functional analysis, multiple discriminate functional analysis and Step wise multiple discriminate functional analysis were obtained for CTS prediction (tables ٤-٦):

| | Wilk's lambda | P value | Constant | Coefficient | Sectioning point | Accuracy (%) |
|---|---|---|---|---|---|---|
| **CSA at PQ** | ٠.٩٨٨ | ٠.٣٠٥ | -١١.٧٥١ | ١.٢٥٨ | ٠.٠٤ | ٦٦.٧ |
| **CSA at PS** | ٠.٣٩٥ | <٠.٠٠١* | -٦.٦٨٧ | ٠.٥٩٠ | ٠.٤٣ | ٨٨.٩ |
| **F. Ratio** | ٠.٣٧٥ | <٠.٠٠١* | -٦.٦٥٥ | ٢.٣١٦ | ٠.٤٧ | ٩٤.٤ |
| **PS-PQ CSA** | ٠.٣٢٠ | <٠.٠٠١* | -١.٤٤٢ | ٠.٧٢٥ | ٠.٥١ | ٨٨.٩ |

**Table ٤:** Simple discriminant functional analysis for prediction of CTS showing that flattening ratio has higher accuracy than other variables.

*CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone*
*Simple discriminant functional analysis*
*Discriminant score = constant + (coefficient x measure)*
*If the discriminant score > sectioning point → it means CTS*
*If the discriminant score < sectioning point → it means norma*

<table>
<tr><th></th><th>Wilk's lambda</th><th>P value</th><th>Constant</th><th>Coefficient</th><th>Sectioning point</th><th>Accuracy (%)</th></tr>
<tr><td>CSA at PS</td><td rowspan="3">٠.٢٨٠</td><td rowspan="3"><٠.٠٠١*</td><td rowspan="3">-٣.٣١٤</td><td>-٠.٠٩٣</td><td rowspan="3">٠.٥٦</td><td rowspan="3">٩٤.٤</td></tr>
<tr><td>F. Ratio</td><td>١.١٢٧</td></tr>
<tr><td>PS-PQ CSA</td><td>٠.٥٧</td></tr>
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**Table ٥:** Multiple discriminant functional analysis for prediction of CTS showing highest accuracy obtained from combination of cross sectional area at pisiform, flattening ratio and the CSA difference at pronator quadratus and pisiform.

*CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone*
*Multiple discriminant functional analysis*
*Discriminant score = -٣.٣١٤ + (-٠.٠٩٣x PS) + (٠.١.١٢٧x Ratio)+(٠.٥٧x PS-PQ)*
*If the discriminant score > sectioning point → it means CTS*
*If the discriminant score < sectioning point → it means normal*

<table>
<tr><th></th><th>Wilk's lambda</th><th>P value</th><th>Constant</th><th>Coefficient</th><th>Sectioning point</th><th>Accuracy (%)</th></tr>
<tr><td>F. Ratio</td><td rowspan="2">٠.٢٨١</td><td rowspan="2"><٠.٠٠١ *</td><td rowspan="2">- ٤.١٨١</td><td>١.١٣</td><td rowspan="2">٠.٥٦</td><td rowspan="2">٩٤.٤</td></tr>
<tr><td>PS-PQ CSA</td><td>٠.٤٦٩</td></tr>
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**Table ٦:** Stepwise multiple discriminant functional analysis for prediction of CTS revealed that highest accuracy obtained from combination of

Cross sectional area difference at pronator quadratus and pisiform and flattening ratio.
*CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone*
*Stepwise multiple discriminant functional analysis*
*Discriminant score = -٤.١٨١ + (١.١٣x Ratio)+(٠.٤٦٩x PS-PQ)*
*If the discriminant score > sectioning point → it means CTS*
*If the discriminant score < sectioning point → it means normal*

## Discussion

The entrapment of the median nerve MN occurs between the transverse carpal ligament (TCL) ventrally and carpal bones dorsally, so this compression causes an enlargement of the median nerve cross-sectional area (CSA) at the level of pisiform (PS) while no affection of CSA at the level of PQ, this obtained in our study as the mean normal median nerve CSA value at PQ was ٩.٢٨±٠.٥٨ and in CTS patients was ٩.٤٦±١.١١ with non-significant P value, while, CSA of normal MN at PS was ٩.٨٦± ٠.٣٤, and in CTS patients CSA was ١٤.٢٦± ٢.٩١ with P value < ٠.٠٠١.

This result was in line with Klauser et al.,[١٣], who found that, the mean CSA at PS was ٩.٠± ١.٥ in the healthy volunteers, and ١٦.٨ ± ٥.٨ in the patients with CTS and (*P* < ٠.٠٠١).

Buchberger et al.,[١٤] also found the mean CSA was higher (١٤.٥ mm$^{٢}$) in CTS patients compared with (٧.٩ mm$^{٢}$) in the healthy control group, also, Duncan et al.,[١٥] found that the mean CSA in CTS patients and healthy control group were ١٢.٧mm$^{٢}$ and ٧mm$^{٢}$, respectively.

The present result also, was in line with Yesildag et al., (٢٠٠٤)[١٦] who examined one hundred and forty-eight wrists of ٨٦ patients with CTS and ٧٦ wrists of ٤٥ normal patients, they reported that the mean CSA was ١٤.٩±٤.٧ in CTS patients and ٧.٨±١.٦ in normal control group.

The mean difference between CSA at PQ and at PS (PS-PQ) in our study was ٠.٥٨± ٠.٤٩ in healthy group, and ٤.٨±٢.٢٩ in CTS patients (P< ٠.٠٠١), the cutoff value was >١ that shows sensitivity and specificity of ١٠٠٪. The CSA difference between PS- PQ was reported by Klauser et al.,[١٣] they found that, the mean difference between PS-PQ was ٠.٢٥±٠.٤٣ in the healthy volunteer, and ٧.٤±٥.٦ in the CTS group (*P*< ٠.٠١), they utilized cutoff value of ٢mm$^{٢}$ or greater in CSA difference at PS-PQ with a sensitivity of ٩٩٪ and a specificity of ١٠٠٪.

In the current study, the mean value of flattening ratio FR was ٢.٢±٢.٨ in normal group and ٢.٢±٤.٣ in CTS patients, this in agree with Yesildag et al., (٢٠٠٤)[١٦] who reported that, FR was ٢.٩± ٠.٤ in CTS group and ٢.٥ ± ٠.٥ in normal group. However, we reported that, FR of normal MN was ٢.٤٣±٠.١٨ range (٢.٢-٢.٧٨) slightly higher in dominant than that of non- dominant one, and the difference was not statistically significant (*P* >٠.٠٥), this result was in line with Aiman et al., ٢٠٠٩[١٧], who studied Sonographic evaluation of median nerve performed in ٥٠ wrists of ٢٥ asymptomatic volunteers, they obtained mean CSA of normal MN was ٩.٧٠ ±٢.٢٥, and reported that FR of normal MN was ٤.٠٤, range ٢.١٦-٦.٠٨, the mean FR of median nerve was slightly higher in dominant hand than in non-dominant one, but the difference was not statistically significant (*P* >٠.٠٥).

Duncan et al.,[١٥] found that FR was ٣.١٧in CTS patients and ٢.٧٢ in asymptomatic normal controls. Buchberger et al.,[١٤] accepted that a FR of ٣ mm was significant for CTS.

However, Sarria et al.,[١٨] and Wong et al.,[١٩] had not found any significant differences in FR between CTS patient and normal control groups and they suggested that its diagnostic value was poor.

In the present study cutoff value of CSA at PS in CTS patients was >١٠, this is partially in line with Chen et al., ٢٠١١[٢٠] who reported that CSA of CTS at PS was ١٤.٠±٤.٣, but with higher cutoff value ١٢.٥. Furthermore; the result was in agreement with Yesildag et al., (٢٠٠٤)[١٦] who reported that the cut-off point of CSA at PS using ROC analyses was ١٠.٥ mm$^{٢}$, with sensitivity and specificity found were ٨٩٪ and ٩٣٪. Also, Ziswiler et al.,[٢١] derived a cutoff value of ١٠ mm$^{٢}$ and achieved sensitivity (٨٢٪) and specificity (٨٧٪) values. Kang et al.,[٢٢] derived a cut-off value of ٩.٥ mm$^{٢}$ for CSA and achieved sensitivity of ٩٦.٤٪ and specificity of ٩٢.١٪.

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