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Research Article

Cut off Values of Median Nerve Dimensions in Carpal Tunnel Syndrome in Egyptian Population. Sonographic Comparison with Normative Values

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Abstract

Objective: To assess the usefulness of superficial ultrasonography of median nerve in accurate differentiation between neuropathic nerve and normal nerve measurement in Egyptian population.

Material and methods: The study was conducted on thirty patients with CTS; twelve males and eighteen females with mean age 43.93±4.51 (range 35-52y), and another thirty normal subjects; fifteen males and fifteen females, with their mean age 36.7±4.86 (range 29-45y). The Cross Sectional Area (CSA) and Flattening Ratio (FR) at different levels on both groups. Data from the study and control groups were compared. The accuracy of the ultrasonographic diagnostic criteria for CTS was evaluated using Receiver Operating Characteristic (ROC) analysis. Results: All measurements showed significant differences between CTS and normal groups except the CSA at pronator quadrates. Using the ROC curve, a cutoff value of CSA >10 mm2 at the level of pisiform and CSA difference > 1 between pisiform and pronator quadrates provided a 100% specificity and high overall diagnostic accuracy 98.89%.

Conclusion: The sonographic cutoff values of the median nerve dimensions in Egyptian population could yield an accurate differentiation between neuropathic and normal median nerve.

Introduction

Median Nerve (MN) is one of the important nerves in the upper limb that originate from the brachial plexus; it travels down through the arm and the forearm until it reach the wrist, where it passes deep to the flexor retinaculum into the carpal tunnel, closer to the transverse carpal ligament than the flexor tendons. Median nerve divides into its terminal motor and sensory branches just above the carpal tunnel. Carpal Tunnel Syndrome (CTS) is one of the most common nerve entrapment syndromes encountered clinically. It affects about 1% of the general population, and mostly seen in persons whose work requires repetitive wrist motion [1]. The carpal tunnel is a narrow unyielding space, therefore; any increase in the compartment pressure can contribute in pathogenesis of CTS [2]. Compression of the median nerve within the carpal tunnel leads to its enlargement which could be expressed as increased Cross-Sectional Area (CSA) [3]. Many studies reported that the increase in the CSA of the median nerve is a significant criterion in the diagnosis of CTS [4-6]. Ultrasonography is generally considered as a convenient non-invasive diagnostic tool having wide availability, rapid performance, and cost effectiveness as compared to other imaging tools used in CTS [7]. Ultrasonography in musculoskeletal system is a growing field used for diagnosis of many musculoskeletal disorders, CTS could be one of these disorders, in which median nerve enlargement at or just proximal to the carpal tunnel was described as characteristic sonographic finding [8,9]. Normally, the median nerve dimensions may be slightly larger at the most distal region, but does not vary greatly throughout its entire length. There is no consensus on the cutoff value that differentiating the normal from neuropathic nerves, most studies conclude a cutoff value ranging from 9mm^2 to 12mm^2 [10,11].

Subjects and Methods

The current study was conducted in Minia University hospital during the period from April 2016 to December 2016 after being approved by the ethical committee of our institution. Thirty patients diagnosed as CTS were referred from the orthopedic clinic and included in the study as a study group; their diagnosis was based on clinical assessment& confirmed by pathological changes in electrophysiological nerve conduction. There was no past history of chronic illness, renal dialysis or diabetes.

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Figure 1: Cross sectional area calculation of the median nerve at the level of pisiform bone.

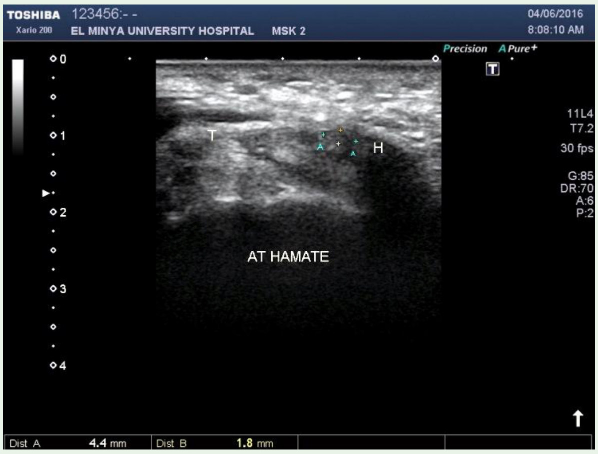

Figure 3: Measurement of AP and transverse diameters of median nerveat the level of hamate bone.

Clinical assessment was done by (AFABA), included Phalen's and Tinel's tests at the carpal tunnel, determination of sensory affection, a pinch and grip strength test, and cervical spine neurological examination. The clinical diagnosis was done when positive Phalen's and Tinel's tests in absence of cervical radiculopathy along C6 & C7 roots. Another thirty healthy asymptomatic persons were included in this study as a control group. Exclusion criteria were: presence of bifid median nerve, presence of mass lesions in the carpal tunnel area including ganglion cysts and neurogenic tumors, and persistent median artery. A written informed consent was obtained from each subject prior to participating in the study.

The number of patients required in the study was determined according to data obtained from pilot study. A sample size of 30 persons in each group was determined to provide 99% power for two-tail 't' test at the level of 0.05 significance using G Power 3.1 9.2 software.

All recruited subjects were subjected to Real-time superficial ultrasound examination using Toshiba medical system machine (Xario 200) using linear array transducer and high frequency 12 MHz for estimation of CSA of the median nerve at the level of pronator quadrates muscle and pisiform bone, the study utilized the trace method, for accurate delineation of the CSA (Figure 1 and 2). Subtraction of the CSA at both levels was done to obtain the mathematical difference. AP and transverse diameters of the median nerve at the level of hamates bone were measured in order to calculate the Flattening Ratio (FR) by dividing transverse diameter by AP diameter (Figure 3). Dominant and non-dominant sides were examined in the control group, whereas the affected wrist in patients with CTS was examined.

Figure 2: Cross sectional area calculation of the median nerveat the level of pronator quadratus muscle.

Results of ultrasonography were recorded, tabulated and statistically analyzed. Descriptive statistics were done for all participants; the data were represented as range, means ± Standard Deviations (SD). Comparison between different groups was done using student's t-test and Mann Whitney test where appropriate using SPSS-20. P value <0.05 was considered significant. Inter-rater reliability was assessed and interclass correlation coefficients were obtained.

Table 1: Shows values of MN CSA at pronator quadratus and pisiform boneand the difference in CSA between both levels, and the flattening ratio at hamate level, in dominant and non-dominant sides in normal individuals.

MN variable	Dominant (n=30)	Non Dominant (n=30)	P value
[1]**CSA at PQ**			
Range	(8-10)	(8-10)	0.513
Mean ± SD	9.33±0.61	9.23±0.56	
[1]**CSA at PS**			
Range	(9-10)	(9-10)	0.133
Mean ± SD	9.93±0.25	9.8±0.41	
[1]**Flattening ratio**			
Range	(2.2-2.78)	(2.36-2.8)	0.127
Mean ± SD	2.43±0.18	2.5±0.13	
[2]**PS-PQ CSA**			
Range	(0-1)	(0-1)	0.795
Mean ± SD	0.6±0.49	0.56±0.5	

- (1) Independent sample t test for parametric quantitative data between the two groups
- (2) Mann Whitney test for non-parametric quantitative data between the two groups
- CSA: Cross Sectional Area, PQ: Pronator Quadratus Muscle, PS: Pisiform Bone.

Table 2: Shows comparison between the normal individuals (sixty wrists) and patients with CTS in MN descriptive dimensions and values.

MN variable	Normal (n=60)	CTS (n=30)	P value
[1]Area PQ Range Mean ± SD	(8-10) 9.28±0.58	(8-11) 9.46±1.11	0.305
[1]Area PS Range Mean ± SD	(9-10) 9.86±0.34	(10-20) 14.26±2.91	< 0.001*
[1]Flattening ratio Range Mean ± SD	(2.2-2.8) 2.46±0.16	(2.2-4.3) 3.68±0.71	< 0.001*
[2]PS-PQ Range Mean ± SD	(0-1) 0.58±0.49	(1-10) 4.76±2.34	< 0.001*

- (1) Independent sample t test for parametric quantitative data between the two groups
- (2) Mann Whitney test for non-parametric quantitative data between the two groups.
- *: significant difference at p value < 0.05
- CSA: cross sectional area, PQ: pronator quadratus muscle, PS: pisiform bone.

Table 3: 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.

Variable	Optimal Cutoff	AUC	P value	Sensitivity	Specificity	PPV	NPV	Accuracy
CSA PQ	>10	0.527	0.705	26.67	100	100	73.2	75.6
CSA PS	>10	**0.986**	**<0.001***	96.67	100	100	98.4	**98.89**
F. Ratio	>2.8	**0.843**	**<0.001***	83.3	100	100	92.3	**94.4**
PS-PQ	>1	**0.990**	**<0.001***	96.67	100	100	98.4	**98.89**

CSA: Cross Sectional Area, PQ: Pronator Quadratus Muscle, PS: Pisiform Bone, PPV: Positive Predictive Value, NPV: Negative Predictive Value.

Table 4: Simple discriminant functional analysis for prediction of CTS showing that flattening ratio has higher accuracy than other variables.

	Wilk's lambda	P value	Constant	Coefficient	Sectioning point	Accuracy (%)
CSA at PQ	0.988	0.305	-11.751	1.258	0.04	66.7
CSA at PS	0.406	<0.001*	-6.583	0.581	0.42	88.9
F. Ratio	0.375	<0.001*	-6.655	2.316	0.47	94.4
PS-PQ CSA	0.332	<0.001*	-1.407	0.711	0.5	88.9

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 normal

Results

The study group included twelve males and eighteen females with mean age 43.93±4.51 (range 35-52y), whereas the normal subjects were fifteen males and fifteen females, with their mean age 36.7±4.86 (range 29-45y).

The descriptive statistics of MN dimensions in normal subjects showed statistically insignificant difference between the dominant and non-dominant hands (Table 1).

Accordingly, the data form dominant and non-dominant sides in normal individuals were merged into one group containing sixty wrists, then; their values were compared with the study group (Table 2). There was statistically significant difference between all values among both groups expect the CSA area at pronator quadratus muscle.

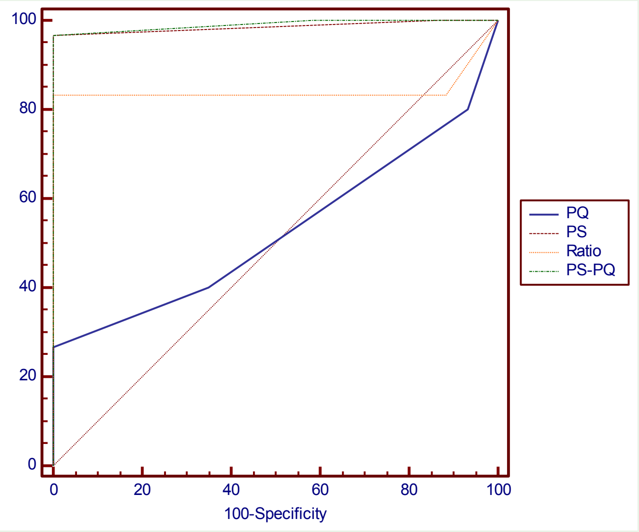

Figure 4: Receiver Operating Characteristic (ROC) graph showing sensitivity, specificity and area under the curve for MN variables.

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Table 5: Multiple discriminate 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.

	Wilk's lambda	P value	Constant	Coefficient	Sectioning point	Accuracy (%)
CSA at PS	0.285	<0.001*	- 3.477	-0.093	0.55	93.3
F. Ratio				1.202		
PS-PQ CSA				0.543		

CSA: Cross Sectional Area, PQ: Pronator Quadratus Muscle, PS: Pisiform Bone
Multiple discriminant functional analysis
Discriminant score = -3.314 + (-0.093 x PS) + (0.1.127 x Ratio) + (0.57 x PS-PQ)
If the discriminant score > sectioning point → it means CTS
If the discriminant score < sectioning point → it means normal

Table 6: 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.

	Wilk's lambda	P value	Constant	Coefficient	Sectioning point	Accuracy (%)
F. Ratio	0.281	<0.001*	- 4.337	1.204	0.55	93.3
PS-PQ CSA				0.443		

CSA: Cross Sectional Area, PQ: Pronator Quadratus Muscle, PS: Pisiform Bone
Stepwise multiple discriminant functional analysis
Discriminant score = -4.181 + (1.13 x Ratio) + (0.469 x PS-PQ)
If the discriminant score > sectioning point → it means CTS
If the discriminant score < sectioning point → it means normal

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 different values and corresponding sensitivity and specificity, a summary of their relationship is shown in a ROC curve graph (Figure 4). Using this graph, an optimal cutoff point is used for determination of normal MN dimensions from neuropathic MN (Table 3).

Simple discriminate functional analysis, multiple discriminate functional analysis and Stepwise multiple discriminate functional analysis were obtained for CTS prediction (Tables 4-6).

Discussion

In the current study, the authors chose the studied parameters to be objective and easily applicable for the purpose of procedure reproducibility, the parameters did not need special technique or high experience to be performed, the measurement of the MN was obtained from axial plane only with the transducer placed perpendicular on the distal forearm and the wrist.

The entrapment of the MN occurs between the transverse carpal ligament and carpal bones, with subsequent CSA enlargement which occurs at the level of proximal carpal tunnel (the level of pisiform); the MN size appears to be not affected at more proximal level above the carpal tunnel (the level of pronator quadratus). To the best of the authors' knowledge, there is no consensus on cutoff values between normal MN dimensions and neuropathic ones, most of the published studies suggested a range cutoff value of CSA at pisiform from 9 to 12mm^2 [11].

The current study showed statistically significant difference between study and control groups in CSA of the MN at pisiform bone. Many studies were in the same line with this result; Klauser et al. [12] studied CSA of the MN among normal and CTS patients and found that, the mean CSA at PS was 9.0± 1.5 in the healthy volunteers, and 16.8 ± 5.8 in the patients with CTS and (P < 0.001). Buchberger et al. [13] also found the mean CSA was higher (14.5 mm^2) in CTS patients compared with (7.9 mm^2) in the healthy control group. Also, Duncan et al. [14] found that the mean CSA of the MN at proximal carpal tunnel in CTS patients and healthy control group were 12.7mm^2 and 7mm^2, respectively. Furthermore Yesildag et al. [15] examined one hundred and forty-eight wrists of 86 patients with CTS and 76 wrists of 45 normal patients; they reported that the mean CSA was 14.9±4.7 in CTS patients and7.8±1.6 in normal control group.

The mean difference between CSA at PQ and at PS (PS-PQ) in the current study was 0.58±0.49 in healthy group, and 4.8±2.29 in CTS patients (P< 0.001), using cutoff value >1 there was high specificity 100% and overall accuracy 98.89%. This result is in agreement to Klauser et al., [12] who assessed the CSA difference between the pisiform level and the pronator quadraus level and found that, the mean difference between PS-PQ was 0.25±0.43 in the healthy volunteer, and 7.4±5.6 in the CTS group (P<0.01), they utilized cutoff value of 2mm^2 or greater in CSA difference with a sensitivity of 99% and a specificity of 100%.

In the current study, the mean value of FR was 3.68±0.71in CTS patients compared with 2.46±0.16in normal group, using 2.8 as a cutoff value; there was high specificity 100 % and overall accuracy 94.4 %.Using simple discriminate functional analysis for CTS prediction, the FR had higher accuracy for a single variable than other parameters.

Many studies assessed the FR as differentiating parameter between neuropathic and normal MN. Aiman et al. [16], who studied Sonographic evaluation of median nerve performed in 50 wrists of 25 asymptomatic volunteers, reported that FR of MN in CTS was 4.04ranged from 2.1 to 6.08. Duncan et al. [14] found that FR was 3.17in CTS patients and 2.72 in asymptomatic normal controls. Buchberger et al. [13] accepted that a FR cutoff value of 3 was significant for CTS. On the other hand, Sarria et al. [17] and Wong et al. [18] had not found any significant differences in FR between CTS patient and normal control groups and they concluded poor diagnostic value of the FR.

In the current study, using cutoff value of CSA at pisiform in CTS patients >10mm^2 yielded high specificity 100% and overall accuracy 98.89%. This is in agreement with Ziswiler et al. [19] who utilized

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cutoff value of 10 mm^{2}at pisiform and achieved sensitivity (82%) and specificity (87%), Other studies showed variable cutoff values, Yesildag et al. [15] reported that the suggested cutoff point of CSA at pisiform using ROC analyses was 10.5 mm^2, with sensitivity and specificity found were 89% and 93% respectively. Kang et al. [20] derived a cutoff value of 9.5 mm^2 for CSA and achieved sensitivity of 96.4% and specificity of 92.1%.Chen et al. [21] who reported that the mean CSA of CTS at PS was 14.0±4.3, used higher cutoff value = 12.5.

Conclusion and Recommendation

According to the results of this study we concluded that: The sonographic cutoff values of the median nerve dimensions in Egyptian population could yield an accurate differentiation between neuropathic and normal median nerve using cutoff value of CSA >10 mm^2 at the level of pisiform and CSA difference > 1.Meta-analysis of all published studies in different populations is recommended to get a consensus on a universal cut off values.

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