

F-ratio, a surrogate marker of carpal tunnel syndrome

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ABSTRACT

الأهداف: لاكتشاف ومعرفة العلاقة بين F-ratio والموجة F، كذلك الدرجة الصغرى للركود (FWML) في مرضى متلازمة النفق الرسغي (CTS).

الطريقة: أجريت هذه الدراسة خلال الفترة ما بين يناير 2006 وحتى يناير 2007م، في قسم الفسيولوجيا الإكلينيكية (وظائف الأعضاء) - مستشفى الملك عبد العزيز الجامعي - الرياض - المملكة العربية السعودية. تمت دراسة نقل الأعصاب الحسية، الحركية، وركود موجة F للأعصاب الوسطى، ونسبة موجة F، في 54 مريضاً يعانون من متلازمة النفق الرسغي (CTS)، و30 في مجموعة التحكم.

النتائج: هنالك 54 مريضاً يعانون من متلازمة النفق الرسغي CTS-14 ذكر يشكلون (26%)، و40 أنثى يشكلن (74%). متلازمة النفق الرسغي (CTS) كانت ثنائية في 32 مريض (59%)، أحادية في 22 مريض (41%). واحداً وخمسون مريضاً (94.4%) يعانون من المتلازمة في اليد اليمنى، 28 مريضاً (51.8%) لديهم اضطراب في توازن الدهون، 20 مريضاً (37%) لديهم ارتفاع في ضغط الدم. في المجموعة التحكم كان ركود موجة (FWML) الصغرى في العصب الوسطى الأيمن 25.46 ± 2.2 ، وفي عصب النفق الرسغي 25.79 ± 1.7 ($p=0.5224$). أما في المجموعة المصابة بالمتلازمة النفق الرسغي (CTS) فقد كان 29.1 ± 3.35 في العصب الوسطى الأيمن، و 26.46 ± 4.35 في العصب النفق الرسغي (CTS)، كانت قيمة الأهمية هي ($p=0.0008$) كان هناك زيادة إحصائية مشابهة معتبرة في ركود العصب الوسطى لوحظت في اليد اليسرى. كما كان هنالك انخفاض معتبر إحصائياً في قيمة F-ratio كان لدى جميع المرضى الذين يعانون من متلازمة النفق الرسغي (CTS) في كلتا اليدين، ($p=0.0001$).

خاتمة: الدراسة الحالية تعرض تطور في درجة الركود للموجة الصغرى (FWML) في الأعصاب الوسطى وانخفاض ذو دلالة إحصائية لـ F-ratio لدى جميع المرضى. كان هناك ارتباط مهم ما بين درجة الركود الصغرى للموجة (FWML) و F-ratio في مرضى متلازمة النفق الرسغي (CTS). يساهم كلاً من درجة الركود الصغرى للموجة (FWML) و F-ratio في تشخيص مرض متلازمة النفق الرسغي (CTS).

Objective: To explore the correlation of F-ratio and F-wave minimal latency (FWML) in carpal tunnel syndrome (CTS).

Methods: This retrospective study was conducted from January 2006 to January 2007 at the clinical physiology lab, King Abdul-Aziz University Hospital, Riyadh, Saudi Arabia. Motor and sensory nerve conduction studies, FMW latencies of median and ulnar nerves, and F-ratio were carried out in 54 CTS patients and 30 controls.

Results: Out of 54 CTS patients, there were 14 were males (26%), and 40 females (74%), CTS was bilateral in 32 (59%), and unilateral in 22 (41%) patients. Fifty-one patients (94.4%) had involvement of the right hand, 28 patients (51.8%) had dyslipidemia and 20 patients (37%) had hypertension. The FWML (ms) in the right median nerve was 25.46 ± 2.2 , and 25.79 ± 1.7 in the right ulnar nerve in the control group ($p=0.5224$), while it was 29.1 ± 3.35 in the right median nerve and 26.46 ± 4.35 in the right ulnar nerve in patients with CTS ($p=0.0008$). A similar statistically significant increase in the median nerve latency was observed in the left hand. A statistically significant reduction in the F-ratio was found consistently in all patients with CTS in both the hands ($p=0.0001$).

Conclusion: The present study reveals prolongation of FWML in the median nerve, and a statistically significant reduction of F-ratio in all CTS patients. A significant inverse correlation was found between FWML and F-ratio in CTS patients. Both FWML and F-ratio support the diagnosis of CTS.

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Carpal tunnel syndrome (CTS) is a common focal peripheral nerve compression.¹ The condition is usually bilateral, although the dominant hand tends to be more severely affected and most cases are idiopathic.^{2,3} The incidence is 139 per 100,000 person/year for men, and 506 per 100,000 person/year for women as reported by Tay in 2006.⁴ The primary diagnostic tool is electrodiagnosis, although 13-27% of patients with CTS symptoms have normal or ambiguous results with electrodiagnosis.^{1,3} Therefore, newer techniques and additional nerve conduction studies (NCS) are being continuously explored to complement and strengthen the diagnosis of CTS. Bodofsky et al¹ in 2005 proposed median sensory and ulnar motor latency difference to be the criteria of choice, and described it as a simple easy sensitive and specific test. In 2007, Wilder et al⁵ determined the motor response derived from a median thenar motor site, and found it to be the best supporting adjunct to the diagnosis of CTS with routine electrodiagnostic tests. Horch et al,⁶ recommended that MRI is accurate and reliable for the diagnosis and follow-up of CTS cases. Ginanneschi et al⁷ in 2007 proposed ulnar nerve stimulation response studies for the diagnosis of CTS.⁷ Wong et al,⁸ in 2004 proposed sonography to be comparable with electrodiagnostic studies for the diagnosis of CTS. The classical electrodiagnostic findings in CTS include: i) Slowing of median motor and sensory velocity across the carpal tunnel, ii) Prolonged distal latency of the median motor nerve, iii) Low amplitude sensory nerve action potential (SNAP), and low amplitude of the median compound motor action potential (CMAP). However, there is no systematic comprehensive published report on the F-wave minimal latency (FWML) and F-ratio values in Saudi patients for the diagnosis of CTS from this region. Therefore, the following study was undertaken. The aim of this work was to measure FWML and F-ratio along with the other parameters to reach an improved and reliable electrodiagnosis of CTS. Also, to provide the reference values in Saudis and to set a future research paradigm.

Methods. This retrospective study was conducted from January 2006 to January 2007 at the clinical physiology lab at King Abdul-Aziz University Hospital, Riyadh, Saudi Arabia in patients referred with a clinical suspicion of CTS from different clinics in King Abdul-Aziz University Hospital as part of their treatment and health care. As a matter of hospital policy, written approval is obtained prior to the NCS from each patient. A total 168 hands were tested from 30 controls and 54 patients. The clinico-epidemiological parameters included age, gender, dominant hand, and comorbidities. All the patients underwent a standardized

NCS that was based on the American Academy of Neurology statement regarding the desired protocol for patients with suspected CTS.⁹ This NCS consisted of 8 cm transcarpal orthodromic median and ulnar sensory peak latencies, median forearm conduction velocities, 8 cm median motor compound muscle action potential, and distal motor latencies. These parameters were measured using standard techniques of supramaximal stimulation and surface electrodes, with precise adjustment of skin temperature. The NCS were performed under the guidance of a neurophysiologist and trained electrodiagnostic technician in all the patients and controls. The inclusion criteria for the control group were healthy adults above the age of 12 years with no history of neurological disease, no injury, or hand trauma. For the CTS group the inclusion criteria comprised pain, paresthesia in the hand, nocturnal awakening due to pain, wasting and weakness of the thenar group of muscles with positive Tinel's and Phalen's signs. The exclusion criteria were age below 12 years, history of trauma, any illness within 6 months, and polyneuropathy.

Procedure. Hands were kept warm prior to test. Skin temperature was monitored with a temperature sensor placed over the dorsum of the hand and temperature was kept around 29°C. The electrodiagnostic tests were carried out in 54 cases who presented with strong clinical findings of CTS. Electromyography was carried out to exclude the root lesion in both the groups. The parameters included for the study were: i) Nerve conduction studies: motor and sensory conduction in median and ulnar nerve was performed according to the standard (electrophysiological methods describe in the mini monograph on CTS).^{8,9} The CMAP was recorded with a surface electrode placed on the abductor pollicis brevis muscle (APB). The reference electrode was placed 3 cm distal to the recording electrode. The distance between the stimulating electrode at the wrist and the recording electrode at the APB muscle was 8 cm. The amplitude of both sensory and motor potentials was also noted. The distal motor latency (DML) of both median and ulnar nerves was recorded. Sensory nerve studies were carried out in an antidromic manner. The stimulation of ulnar and median nerve was carried out at 14 cm from the finger recording electrode. The recording electrode was placed at the index finger for the median nerve and the fifth digit for the ulnar nerve.

F-wave studies.⁵ Ten consecutive F-waves were obtained by supramaximal stimulation in both the median and ulnar nerves, and were stimulated at the wrist. The recording surface electrode was placed over the APB for median, and abductor digiti minimi (ADM) for the ulnar nerve. The ground electrode was placed on the dorsum of the hand. F-waves are long latency

responses that are present in many nerves including median and ulnar nerve. It is considered to represent anterior horn cell depolarization caused by antidromic stimulation of motor fibers. Since different anterior horn cells are activated at different times, the shape and latency of F-waves are different from one another. Ten F-waves were obtained, and the shortest latency of F-wave was recorded in each case. The FWML of the APB for median and ADM for ulnar nerve was recorded. The FWML latency difference between the median and ulnar nerve was noted. The F-ratio and proximal latency of the nerve were calculated by using the following formula.¹⁰

$$\text{Proximal latency} = \text{FPROX} - \text{MPROX} - 1 \text{ ms}/2$$

Where one ms is delay in the anterior horn cell

$$\text{F-ratio} = \text{Proximal latency} / \text{MPROX}$$

FPROX = F-latency obtained by proximal stimulation, and MPROX = Motor latency obtained by proximal stimulation

Before performing any median to ulnar FWML difference measurements, ipsilateral ulnar nerve pathology was excluded. A decreased F-ratio indicated a distal nerve lesion such as CTS, while an increased FWML indicated the proximal slowing.⁵ The electrophysiological data were grouped separately for controls and patients. The control data were evaluated with respect to the median and ulnar FWML in the same side. The ulnar FWML was subtracted from the median FWML to calculate FWML difference for each limb separately.

Statistical analysis. The Statistical Package for Social Sciences (SPSS version 10, Chicago) was used for analysis. Descriptive characteristics of the study patients were calculated as mean \pm SD for continuous variables, and as percentages for categorical variables. Student's *t* test was used for comparison between different groups. A *p*-value of <0.05 was considered statistically significant. Pearson's correlation was carried out between the study variables and CTS.

Results. There were 84 subjects, 30 controls, and 54 patients with clinical suspicion of CTS. The clinico-demographic characteristics of the study population are given in Table 1. Electrodiagnostic values of CTS are presented in Tables 2-4. Table 2 explains the comparison of motor conduction velocity (MCV), DML, CMAP amplitude, sensory conduction velocity (SCV), distal sensory latency (DSL), and SNAP amplitude between controls and the CTS group. The MCV in both the right and left median nerve was significantly higher in the control group compared to the CTS group. The DML in both right and left median nerve was lower in the control group compared to the patient group. The amplitude of CMAPs in the CTS group was significantly

Table 1 - Demographics of 54 patients with carpal tunnel syndrome.

Characteristics	n (%)
Age (years, mean \pm SD)	45.32 \pm 5.1
Gender	
Males	14 (26.0)
Females	40 (74.0)
Nationality	
Saudi	54 (100)
Presenting hand	
Unilateral	22 (41.0)
Right	51 (94.4)
Left	35 (64.8)
Bilateral	32 (59.0)
Co-morbidities	
Obesity	14 (26.0)
Dyslipidemia	28 (51.8)
Hypertension	20 (37.0)

Table 2 - Motor and sensory nerve conduction parameters in control versus carpal tunnel syndrome (CTS) group on right side and left side.

Parameters	Control n = 30	CTS n = 54 (86 limbs)	<i>P</i> -value
Motor	Right median nerve		
MCV m/sec	60.27 \pm 5.81	53.22 \pm 9.29	0.0003
DML ms	3.17 \pm 0.49	4.67 \pm 1.23	0.0001
CMAP mv	10.16 \pm 3.89	7.78 \pm 2.93	0.0026
Sensory	Right Control	Right CTS	
SCV m/Sec	53.77 \pm 6.62	31.68 \pm 17.94	0.0001
DSL ms	2.73 \pm 0.55	3.91 \pm 1.27	0.0001
SNAP μ V	31.44 \pm 19.72	20.30 \pm 15.15	0.0097
Motor	Left median nerve		
MCV m/sec	59.45 \pm 6.35	53.20 \pm 8.25	0.0005
DML ms	2.97 \pm 0.57	4.31 \pm 1.35	0.0001
CMAP mv	10.58 \pm 3.78	7.55 \pm 3.35	0.0003
Sensory	Left Control	Left CTS	
SCV m/Sec	54.23 \pm 6.51	38.26 \pm 13.84	0.0001
DSL ms	2.72 \pm 0.56	3.84 \pm 1.11	0.0001
SNAP μ V	34.17 \pm 17.56	25.21 \pm 17.13	0.0305

MCV - motor conduction velocity, DML - distal motor latency, CMAP - compound motor action potential, SCV - sensory conduction velocity, DSL - distal sensory latency, SNAP - sensory nerve action potential

smaller than the control group in both right and left hands.

Median nerve sensory conduction studies. The SCV was slow in the CTS group, and there was a significant reduction in amplitude of SNAP with delayed DSL (Table 2). The FWML of both median and ulnar nerves were studied. The right and left sides were compared in the controls and as well as in the CTS group. In the control group, there was no statistically significant difference in FWML of median and ulnar nerves. In

Table 3 - F-wave minimal latency (FWML), M-wave (MW) latency, and its difference between median and ulnar nerves of the same side in the control group, all values are expressed as mean ± SD.

Motor latencies	Right median	Right ulnar	Left median	Left ulnar
FWML ms	25.46 ± 2.22	25.79 ± 1.72	25.15 ± 2.22	25.22 ± 1.85
MW latency (M proximal) ms	3.17 ± 0.56	2.76 ± 0.28	3.01 ± 0.45	2.60 ± 0.35
FWML difference (ms) between median and ulnar of the same side	0.78 ± 2.01 <i>p</i> =0.5224		-0.11 ± 2.11 <i>p</i> =0.8949	

Table 4 - F-wave minimal latency (FWML), M-wave (MW) latency, and its difference between median and ulnar nerves of the same side in the carpal tunnel syndrome group, all values are expressed as mean ± SD.

Motor latencies	Right median	Right ulnar	Left median	Left ulnar
FWML ms	29.10 ± 3.55	26.46 ± 4.35	28.29 ± 3.12	26.67 ± 3.06
MW latency (M proximal) ms	4.16 ± 1.26	4.18 ± 8.84	4.72 ± 2.84	3.44 ± 3.26
FWML difference (ms) between median and ulnar of the same side	2.53 ± 4.70 <i>p</i> =0.0008		1.47 ± 2.72 <i>p</i> =0.0077	

Table 5 - Pearson's correlations in carpal tunnel syndrome patients between median nerve distal latency, FWML, proximal latency, and F-ratio with nerve conduction parameters (n=86 limbs).

Median nerve	CMAP	MCV	FMWL	DL sensory	SNAP	SCV
Distal latency	-0.289	-0.019	0.374	-0.029	-0.201	-0.401
<i>P</i> -value	0.002	0.845	0.001	0.773	0.039	0.000
FWML	-0.136	-0.299	0.215	0.055	-0.399	-0.433
<i>P</i> -value	0.160	0.002	0.026	0.577	0.001	0.001
Proximal latency	-0.138	-0.306	-0.409	0.073	-0.239	-0.271
<i>P</i> -value	0.155	0.001	0.000	0.462	0.014	0.005
F-ratio	0.129	-0.053	-0.765	0.005	0.246	0.279
<i>P</i> -value	0.185	0.587	0.001	0.957	0.011	0.004

CMAP - compound motor action potential, MCV - motor conduction velocity, FMWL - F-wave minimal latency, DL - distal latency, SNAP - sensory nerve action potential, SCV - sensory conduction velocity

the CTS group, the difference between FWML value of median and ulnar nerves was significant (Tables 3 & 4).

F-ratio. In the control group, the F-ratio of the median nerve on the right side was 7.5±1.61, while on the left side it was 7.58±1.46. In the CTS group, the right median F-ratio value was 5.57±1.30, while in left median it was 5.71±1.76. The result of F-ratio of both the median nerves in patients with CTS group was highly significantly reduced as compared to the control group (*p*=0.0001). Moreover, the F-ratio showed a positive correlation with SNAP and SCV, and a negative correlation with M-wave latency (Table 5). The proximal latency of median nerves in the control group was 22.74±2.23 on the right and 21.82±2.47 on the left side. In the CTS group, this was 23.94±3.10 on the right, and 22.99±4.16 on the left, with no significant

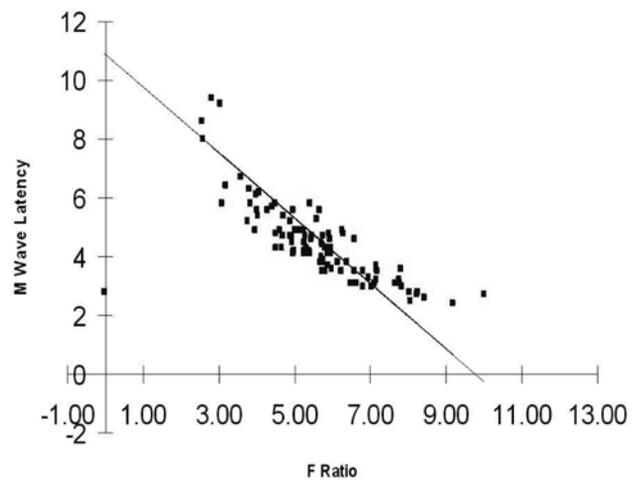


Figure 1 - Relationship between M-wave latency and F-ratio (*r* = 0.5844, *p*=0.0001).

difference. Regression analysis between M-wave latency as an independent variable, and F-ratio as a dependant variable was highly significant (Figure 1).

Discussion. Carpal tunnel syndrome is a common clinical problem¹¹ due to median nerve entrapment leading to demyelination in the carpal tunnel. Even with a good history and physical examination at times it may be difficult to diagnose.¹² The electrophysiological studies are now regarded as the gold standard diagnostic tests. It has a high degree of sensitivity and specificity.¹³ However, newer techniques are being continuously tried to support and improve the diagnosis of CTS, for instance ultrasonography, MRI, ulnar NCS, F-ratio, and FWML studies, especially where traditional NCS fail.¹⁴⁻¹⁶ However, Cho et al¹⁷ emphasized that comparison of distal motor or sensory latency of the median nerve to the ulnar nerve along with amplitude of the response is the most sensitive test for the diagnosis of CTS.

The present study reveals that in Saudi patients, CTS was more common in females. A similar predominance of female gender for the prevalence of CTS is reported by McDiarmid et al.¹⁸ The right hand was also more commonly affected in the present study, which again is in agreement with previous research.^{4,19} Patients were in their fourth to fifth decades of life. Obesity was not predominant, while hypertension and dyslipidemia were some other co-morbidities. The NCS performed in the present study revealed that in patients with clinical suspicion of CTS there was a delayed motor and SCV of the median nerve with normal conduction in the ulnar nerve, delayed DML of the median nerve, decreased amplitude of CMAP from the APB muscle and prolonged or absent median SNAP. The results of the present study are comparable with the results of previous work.¹¹ In the present study, in the control group there was minimal reduction in FWML of the median nerve as compared to the ulnar nerve. While in the CTS group of patients, the FWML of the median nerve was longer than the ulnar nerve. This difference in latency was highly significant ($p=0.001$) and could be explained on the basis of either demyelination or axonal loss occurring in the distal course of the median nerve.

A decreased F-ratio of the median nerve was found in all cases of CTS, indicating a distal nerve lesion such as CTS.¹¹ The other parameter studied was the proximal latency of the median nerve. The value of proximal median nerve conduction velocity in our study consistently showed no reduction in the CTS group as compared to the control group. Similar findings were observed by Wilson et al.²⁰ Chang et al,²¹ in 2006 recommended systematic steps in improving and complimenting the diagnosis of CTS, such as extended NCS, F-ratio, and

distal latencies in the median and ulnar nerve should be carried out if the routine electrodiagnostic tests are ambiguous, and finally sensory latency differences between median - radial for thumb, and medial - ulnar nerve for ring finger should be taken into account. They also reported that extended NCS will increase the diagnostic efficiency by 20%.²¹

The present study has the limitation that the number of patients is small. Larger studies are needed to strengthen the interpretations. Only one ethnic group was considered, and more ethnic groups should be evaluated to generalize the interpretations. The present study suggests that FWML of median and ulnar nerves with F-ratio of median nerve compliments the diagnosis of CTS, and can be taken into consideration in establishing the diagnosis of CTS. The present study has also provided the reference values of F-ratio and FWML in Saudi patients.

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