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DANIEL L. MENKES, MD*
DANIEL C. HOOD, MD*
ANNEKE C. BUSH ScD† MHS
From the Sections of Neurology and Clinical Investigations†, David Grant United States Air Force Medical Center, Travis Air Force Base, California*

Inversion of the F-waves in Median Neuropathy at the Wrist (Carpal Tunnel Syndrome): An Adjunctive Electrodiagnostic Method

■ The role of F-waves in the diagnosis of carpal tunnel syndrome (CTS) remains controversial. A comparison of ipsilateral-median and ulnar-nerve F-wave minimal latencies (FWML) usually reveals that the median F-wave is shorter than its ulnar counterpart, a pattern that should reverse in CTS associated with median neuropathy at the wrist. Prospective studies were undertaken on 30 controls and 57 patients with symptoms and electrophysiologic evidence of CTS. The mean median FWML minus the ulnar FWML value in the control group was –0.74 msec, with a standard deviation of 0.677 yielding an upper limit of normal of 0.98 msec (mean, + 2.5 SD). In the cases examined, when the median F-wave was absent or the FWML exceeded a normal ipsilateral ulnar FWML by 1 msec, "inversion of the F-waves (FWIN) was documented. CTS was diagnosed when median palm-to-wrist test results were abnormal (compared with ulnar, or abnormal in absolute terms) in patients with symptoms of CTS. Inversion of the F-waves was present in 72 of 95 limbs in the patients, and none of the controls yielding a specificity of 100% or a sensitivity of 76%. The sensitivity of this test was superior to all standard tests of median motor-nerve function and greater than or equal to all other tests for CTS save the mixed-nerve palm-to-wrist comparison. We conclude that inversion of the F-waves is a useful adjunctive test in the diagnosis of CTS. ■

Key Words: Carpal Tunnel Syndrome, F-Waves, Median Nerve, Entrapment Neuropathy, Electromyography

INTRODUCTION

Carpal tunnel syndrome (CTS) is a common condition affecting a significant portion of the population. The etiology of this syndrome is diverse, although a significant number of these conditions result from median-nerve entrapment at the transverse carpal ligament resulting in median neuropathy at the wrist (Spinner et al, 1989). The utility of electrodiagnostic studies is still a matter of controversy, although many practitioners recognize their usefulness in evaluating CTS. A consensus statement regarding the utility of various electrodiagnostic tests in the evaluation of CTS has been published (Jablecki, Andary et al, 1993). F-wave studies were determined to be of uncertain clinical significance, although F-waves have been used to assess the presence of CTS (Macleod, 1987). Measurements in unpublished cadaver studies (Scott, 1995) have demonstrated that the length of the median nerve from the nerve roots to the abductor pollicis brevis (APB) is shorter than the length of the ulnar nerve from the nerve roots to the abductor digiti minimi (ADM). As a lesser distance was involved, it was reasoned that the median-nerve F-wave minimal latencies (FWML) to the APB would be less than that of the ulnar nerve to the ADM.

This study was conducted in two parts. The first was determining whether this trend (median FWML < ulnar FWML) was found prospectively in normal controls and defining the upper limit of normal for this pattern. Once this was defined, any time the F-wave minimal latency difference (F-MLD) between the median FWML and the ulnar FWML exceeded this value, then "inversion of the F-waves (FWIN) was stated as present. A unilaterally absent median F-wave with a present and normal ipsilateral ulnar F-wave was also tallied as an "inversion" for the purpose of statistical analysis. These data are reported in the results section. Patients referred for evaluation of CTS were then studied to determine the specificity and sensitivity of this method as compared with more traditional electrodiagnostic methods using sensory and motor-nerve conduction studies.

MATERIALS AND METHODS

Inclusion Criteria

Thirty normal controls (15 were men) and 57 patients with symptoms of CTS were examined prospectively with standard electrophysiologic

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Address reprint requests and correspondence to Daniel L. Menkes, MD, 60th Medical Group/SGOMU, David Grant USAF Medical Center, 101 Bodin Circle, Travis AFB, CA 94535

Table 1 Normal Subject Data

Test	*Latency* (msec)	*Amplitude* (uV)	*Conduction Velocity* (msec)
Median D2-wrist SNAP	distance dependent	>6	>44
Ulnar D5-wrist SNAP	distance dependent	>4	>45
Palm-to-wrist (median and ulnar)	<1.8	>10	>47
Median-mixed ulnar-mixed	<0.4	N/A	N/A
Median-to-APB CMAP	<4.5	>4500	N/A
Median F-wave minimum latency	height dependent	N/A	N/A
height = 60 in	<28		
height = 65 in	<29		
height = 72 in	<31		
Ulnar-to-ADM CMAP	<4.0	>5000	N/A
Ulnar F-wave minimum latency	height dependent	N/A	N/A
height = 60 in	<29		
height = 65 in	<30		
height 72 in	<32		

Note: There were no differences between this set of normative data and the control data ($p > 0.05$)

methods, including sensory and motor-nerve conduction studies as well as palmar mixed-nerve studies (Baker et al, 1990). This study had the approval of our institution's Committee on Human Studies. The controls were examined and were noted to have no history of neurologic disease and normal results on neurologic examination. The data regarding the cases and controls are summarized in Table 1. Exclusion criteria for controls were as follows: age outside the range of 18–80 years, history of neurologic disease, hand symptoms, history of hand surgery or hand trauma, abnormal neurologic exam results, or refusal to participate in this study. Patients were excluded for the following reasons: refusal to participate, abnormalities in nerve conduction in nerve distributions other than the median nerve, absence of CTS symptoms, hematologic abnormalities precluding needle electromyography, and age outside the range of 18–80 years. Inclusion criteria for the cases also required that CTS be present as defined by the palm-to-wrist, mixed-nerve conduction study criteria stated in the following paragraphs. Those who qualified for a diagnosis of CTS and met study criteria were asked to enroll. All persons included in the analysis had symptoms and electrophysiologic evidence of CTS as defined by an abnormality of the median compound nerve-action potential (CNAP) and no abnormalities in its ipsilateral ulnar-nerve counterpart. Patients with symptoms of CTS who had no electrophysiologic abnormalities were excluded from this analysis as they did not demonstrate median-nerve pathology at the wrist as defined by electrophysiologic testing.

General Methodology

Verbal informed consent was obtained prior to the performance of every test as required by our institution's Committee on Human Studies. All hands were warmed prior to testing. Surface skin temperature was measured with a temperature probe placed over the dorsum of the hand in order to ensure that this value always exceeded 32.0°C. The normal values used in all electrophysiologic methods are listed in Table 1, which are the normative values used at Massachusetts General Hospital.

Nerve Conduction Studies

Motor and sensory-nerve conduction studies were performed according to the standard electrophysiologic methods described in the AAEM minimonograph on CTS (Ross and Kimura, 1995). Sensory-nerve conduction studies were all performed in an orthodromic manner. Digital stimulation over the fifth digit (ulnar nerve) and the index finger (median nerve) was performed by placing the cathode over the proximal finger crease and the anode over the distal finger crease. Fixed distances were not used because the anatomic landmark of the second wrist crease was used. Motor-nerve conduction studies were performed to the APB (median nerve) and to the ADM (ulnar nerve). Palmar mixed-nerve studies were conducted and the latencies analyzed as described in a previous publication (Jack-

son and Clifford, 1989). At a fixed distance of 8 cm, the median and ulnar mixed nerves were orthodromically and supramaximally stimulated and the average of eight responses was recorded.

F-wave Studies

Ten consecutive F-waves were obtained by supramaximal, random rates of stimulation in both the median and ulnar nerves. The filter settings and stimulator orientation were the same as those used in motor-nerve conduction studies. The shortest response of the series defined the FWML of each nerve examined. These F-wave minimal latency values were subjected to an independent blinded review to validate the original measurements. No significant differences were noted on the blinded review, so the original data were used in the analysis as this is how the test is performed in routine clinical practice.

Needle electromyography was performed using a concentric disposable needle electrode in all cases studied. A case was not further examined if no fibrillation potentials were noted in the APB. (Presence of fibrillation potentials in this muscle would result in the study of at least two additional C8–T1 innervated muscles and the pronator teres to exclude diagnoses other than CTS. Had this occurred in any of the individuals examined, they would have been excluded from the analysis.) Needle electromyography was not performed on normal subjects in accordance with the protocol approved by the Committee on Human Studies.

Statistical Methods

Statistical analysis was undertaken by our institution's statistician, who did not participate in the data collection. The data set for the patients and controls can be found in Table 2. The control data were evaluated with respect to the median and ulnar FWML in the same arm. The ulnar FWML was subtracted from the median FWML to calculate an F-wave minimal latency difference (F-MLD) for each independent limb. The mean and standard deviation for this F-MLD was then calculated for each side. As the median and ulnar FWML are independent measurements in each limb, their difference also yields an independent measurement. Therefore, an overall F-MLD was calculated by combining the F-MLD from both sides. This is the only parameter for which the sides were combined. In all other statistical analyses and comparisons, the right side was randomly selected and assessed for any significant differences when comparing ipsilateral-median and ulnar-nerve parameters or when comparing the two groups.

The patients were compared with the controls with respect to age, height, and gender. In addition, the ulnar FWML was compared in the right limbs of both the patients and the controls. The ulnar FWML was compared with the subject age in the patients to assess any correlation of age and ulnar FWML. Our analysis also did not combine limbs as these are not truly independent measurements. Therefore, all data were recorded separately for the right and left limbs. Data were analyzed with respect to symptoms, side of involvement, and results of conventional studies used in the diagnosis of CTS. These tests included F-wave inversion (FWIN), orthodromic median sensory D2-wrist studies (D2-wrist), median motor to APB distal motor latency (DML), and the presence of isolated fibrillation potentials in the APB (FAPB). These parameters were analyzed with respect to sensitivity and specificity for each side separately. In addition, these tests were analyzed with respect to the palm-wrist nerve comparison, (the gold standard). (See Tables 3–5).

Table 2 Data Sets for Patients and Controls

	Controls (n = 30)	*Patients* (n = 57)
Age (years)	31.2 + 3.11	47.5 + 14.9
Gender	15 men	28 men
Height		
men	68.8 + 2.1	69.4 + 2.9*
women	65.4 + 2.5	62.7 + 2.2*
F-wave data		
right median FWML	25.5 + 2.2	
right ulnar FWML	26.2 + 2.4	26.9 + 2.4
left median FWML	25.5 + 1.8	
left ulnar FWML	26.2 + 2.2	27.0 + 2.5

*n = 27 for both men and women

Results

Blinded Review

Twenty-nine of the 30 control data sets for both the right and left limbs were subjected to a blinded review (one data set was unavailable for review). No statistically significant difference was noted in the FWML values between the blinded and unblinded review ($p = 0.14$). The unblinded data were used in the statistical analysis as this is how the test is performed in routine clinical practice (see Discussion).

Controls

The median FWML tended to be shorter than that of the ulnar in the ipsilateral arm bilaterally ($p < 0.05$). Given no significant side-to-side differences, and because the F-MLD was an independent measurement for each limb, these values were averaged in the controls so that the mean and standard deviation of the overall F-MLD could be calculated. The resulting mean

Table 3 Proportion of Abnormalities Noted

	Right Limb	*Left Limb*
Patients (total)	53	42
F-wave inversion	40	32
Absent F-wave (% of inversions)	10% (4/40)	6.3%(2/32)
Abnormal D2-wrist SNAP	38	34
Prolonged DML to APB	32	24
FAPB	10	4

Note: None of these values were abnormal in a limb that was classified as being normal (median palm-wrist results were normal)

Table 4 Comparison of Symptoms with Disease

Symptomatic Side	*Total Patients*	*CTS on R*	*CTS on L*
Bilateral	43	42*	39
Right only	11	11	N/A
Left only	3	N/A	3

*One patient had symptoms bilaterally but did not permit study of the right upper extremity.

Table 5 Ipsilateral Method Comparison

	F-wave Inversion	*Prolonged D2-Wrist*	*Prolonged DML*	*FAPB*
Right FWIN absent	N/A	6	1	1
Right D2-wrist normal	9	N/A	0	0
Right DML normal	9	6	N/A	1
Right FAPB absent	31	28	23	N/A
Left FWIN absent	N/A	5	2	0
Left D2-wrist normal	6	N/A	1	0
Left DML normal	10	11	N/A	0
Left FAPB absent	28	30	20	N/A

Data based on number of cases in which the test above each column detected CTS while the tests listed in the table did not.

F-MLD was –0.734 msec with a standard deviation of 0.677 (range, –2.4–0.5). Restated, the median FWML never exceeded the ipsilateral ulnar FWML by more than 0.5 msec in control subjects. Defining the upper limit of normal as mean +2.5 SD, the cut-off value is 0.98 msec (approximately 1 m-sec). This value of mean +2.5 SD was chosen as 1.0 msec because it can be easily recalled in routine clinical practice. When an individual had an F-MLD of 1.0 msec or greater, it was considered to be a reversal of the normal pattern of FWML, or "inversion of Fs." If the F-wave was absent in the median nerve and the ipsilateral ulnar nerve was of normal minimum latency in absolute terms and with respect to the other side, it was considered to have the same significance as an inversion. This situation only occurred in 4 of 40 right limbs and 2 of 32 left limbs. None of the normal subjects had F-wave inversion or an absent median F-wave.

No significant differences were found for the F-MLD from side to side (Table 6). The F-MLD did not vary with respect to height, age, or subject gender ($p > .05$). As stated in the Methods section, the right limb was used in all statistical analyses save the original definition of F-wave inversion. Men tended to have median and ulnar F-wave minimal latencies and heights greater than those of the women ($p < 0.05$). When men and women of similar stature were compared, this gender difference did not reach statistical significance ($p > 0.05$).

Side-to-side comparisons for the median and ulnar nerves were studied. The median FWML had a mean side-to-side difference of 0.01 msec with a standard deviation of 0.92 msec. The values for the ulnar nerve were 0.03 msec for the mean and 0.77 for the standard deviation. The upper limit of normal for the mean F-wave side-to-side difference using mean +2.5 SD is 2.31 msec for the median nerve and 1.96 msec for the ulnar nerve.

Patients

The patients and controls were compared for statistically significant differences with respect to age, height, gender, and ulnar F-wave minimum latency.

Table 6 Control Data Controls

						95% C.L.	
	n	*Range*		*Mean*	*S.D.*	(lower)	(upper)
Side-to-side difference (median F-wave)	30	–2.1	1.9	–0.01	0.92	–1.81	1.79
Side-to-side difference (ulnar F-wave)	30	–1.9	1.9	–0.03	0.77	–1.54	1.48
Left F-wave MLD* (median-ulnar)	30	–2.5	0.5	–0.74	0.76	–2.23	0.75
Right F-wave MLD* (median-ulnar)	30	–2.3	0.5	–0.72	0.6	–1.9	0.46

MLD represents the F-wave minimum-latency difference. Combining right and left MLD yields an upper limit of normal of 0.98 msec (Mean, +2.5 S.D.)

Of these parameters, only age was significantly different at the 95% confidence level. The ulnar FWML did not differ between patients and controls and did not correlate well with the subjects' age (r = 0.28). Therefore, the median-to-ulnar F-wave comparison is valid despite the age differences as further explained in the Discussion section.

Symptoms were present in both limbs in 43 of the 57 patients, on the right side only in 11 patients, and on the left side only in 3 patients. One individual who had bilateral symptoms discontinued the test after her left arm was studied. Therefore, data from her right arm were not available for further analysis. All of the remaining 42 patients who had bilateral symptoms had CTS of the right arm but only 39 of 43 had it on the left. All patients with unilateral symptoms (11 right-sided) had CTS.

F-wave inversion was present in 40 of 53 affected right limbs and in 32 of 42 left limbs. Abnormalities of the D2-wrist sensory-nerve action potential (SNAP) were noted in 38 of 53 affected right limbs and in 34 of 42 left limbs. A prolonged Distal Motor Latency (DML) was noted in 32 of 53 patients on the right side and 24 of 42 patients on the left. Fibrillations of the abductor pollicis brevis (FAPB) were noted in 10 of 53 patients on the right and 4 of 42 on the left. The sensitivity of these tests in the right upper extremity were 75% for FWIN, 72% for the D2-wrist SNAP, 60% for the DML, and 19% for FAPB. On the left, these values were 76% for FWIN, 81% for the D2-wrist SNAP, 57% for the DML, and 9% for the FAPB. Side-to-side sensitivity differences meet statistical significance only for the FAPB ($p < 0.05$).

Table 5 summarizes the frequency with which another test correctly identified CTS when the reference test did not. Using FWIN as the standard on the right limb, 6 additional cases were noted by D2-wrist SNAP and 1 instance each by DML and FAPB. On the left, 5 additional cases were detected by D2-wrist SNAP, 2 by DML, and none by FAPB. If D2-wrist SNAP on the right were used as a standard, 9 additional cases were noted by FWIN and no cases were noted by DML or FAPB; on the left, the values were 6 cases identified by FWIN, 1 case by DML, and no cases by FAPB. Using DML as the standard for the right, 9 other cases were detected by FWIN, D2-wrist SNAP found 6 cases, and FAPB found only 1 case. Values for the left were 10 cases detected by FWIN, 11 cases by DML, and no cases by FAPB. FAPB was never found in isolation; it was noted in 1 instance on the right when D2-wrist SNAP was the only other abnormality.

Discussion

Carpal tunnel syndrome is a common presenting complaint. The method by which the subset of patients with median-nerve compression should be separated from this group is controversial, although electrodiagnostic testing plays a major role. One of the six criteria specified for the detection of CTS needs to be addressed: the requirement of testing those with symptoms as the "gold standard" in diagnosis. This subject has been extensively debated in the past (Brown et al, 1994). A syndrome is a collection of signs and symptoms that does not specify the underlying pathophysiology; not every limb with symptoms that qualify for a diagnosis of CTS has electrophysiologic evidence of it. If symptoms are used as the gold standard for this diagnosis, then all electrodiagnostic techniques will demonstrate low sensitivity and specificity. Conversely, electrophysiologic evidence of CTS implies compression of the median nerve at the wrist with resultant demyelination (Ochoa et al, 1971, 1972). Electrophysiologic testing has proven very useful in the diagnosis of CTS associated with median-nerve entrapment, yet the value of F-wave testing compared with other conventional tests has not been adequately defined. Our investigation demonstrates that F-wave inversion is equal or superior to all other electrodiagnostic tests in diagnosing CTS save palm-to-wrist studies (the reference standard).

Several aspects of this investigation merit discussion. The only statistically significant difference between the patients and the controls was the age of the subjects. This would have been relevant had there been a difference between the ulnar F-wave minimum latency in the two groups since this is the standard by which the ipsilateral median F-wave is determined to be abnormal. This value is virtually identical between the two groups as noted in Table 2. The ulnar F-wave minimal latency poorly correlated with age as noted in the Results section but correlated well with height; therefore, the ulnar FWML depends more on an individual's height rather than age. Because the height and the ulnar FWML are similar among the patients and controls, the F-wave comparison test is still valid despite the differences in age.

As stated in the Methods section, a blinded review was conducted of the control data set. No statistically significant difference was noted between the unblinded and the blinded analysis. The patients were not analyzed in this manner because the cut-off value was not known prior to the original statistical analysis (the control set was acquired concurrently). This method best approximates actual use of the test in routine electrodiagnostic practice as the electromyographer is not blinded as to which nerve is being studied.

The median-nerve FWML tends to be shorter than that of the ulnar nerve. Measurements in cadaver studies have demonstrated that the median nerve is shorter than the ulnar nerve in a small series studied (Scott, 1995). Therefore, the F-MLD should be a

negative number in most normal patients examined. Indeed, not a single normal limb in our study had an F-MLD of greater than 0.5 msec. Ten sequential F-waves were chosen because the FWML from ten stimuli approximates that obtained from 100 stimuli (Fisher et al, 1994). Any process that causes demyelination of the median nerve and spares the ulnar nerve would thus alter the normal pattern until the median FWML became longer than that of its ipsilateral ulnar counterpart. When this value is 1 msec or greater, pathology affecting the median nerve is suggested. The F-wave comparison will not localize the abnormality to the wrist segment, as the FWML becomes prolonged with pathology affecting any portion of the nerve. The median sensory index-finger–to–wrist conduction study has the same limitation; its absence cannot differentiate between median-nerve pathology at the wrist or at a more proximal location. An independent confirmatory test must therefore be used to localize the site of pathology to the wrist, such as a median-to-ulnar mixed-nerve comparison. An important precondition to performing any median-to-ulnar nerve-comparison test is the absence of ipsilateral ulnar-nerve pathology. A test of median-nerve conduction that crosses the transverse carpal ligament, such as the palm-to-wrist study, should also be performed. Therefore, ulnar-sensory, mixed, motor, and F-wave studies are routinely performed in our laboratory for comparison with their ipsilateral median counterparts.

The F-wave comparison has additional advantages over other traditional electrodiagnostic methods in that it tests the motor fibers and is thereby less subject to temperature effect than tests of sensory fibers. Few electromyographers record temperature throughout the performance of electrodiagnostic testing, which has a greater effect on sensory and mixed-nerve testing. Thus, the F-wave method is more practical in routine electrophysiologic testing. As most electromyographers obtain F-waves in routine practice, additional information without additional electrophysiologic testing is provided by this method. FWIN can also serve as an independent confirmation of abnormalities detected on sensory or mixed-nerve conduction studies. Our findings demonstrate that FWIN is at least as sensitive as the D2-wrist SNAP study; thus, it should be employed in the routine evaluation of CTS. As a test of motor-nerve function, FWIN is clearly superior to tests of median DML or FAPB. Other median-to-ulnar nerve comparisons using the lumbrical method have been advocated (Preston and Logigian, 1992). However, it is difficult to be certain that the surface Compound Muscle Action Potential (CMAP) recorded is from the lumbrical muscle being evaluated. FWIN does not have this limitation because the F-waves recorded from the APB and ADM are easily evoked and are reproducible.

The origin of the F-wave has been extensively reviewed elsewhere (Young and Shahani, 1978). As 1- to 5% of the largest and thus fastest conducting fibers contribute to this response, they are an indirect measure of the function of these fibers. Any process that results in either demyelination or axonal loss with secondary myelin loss can contribute to a prolongation of the FWML, and any process that affects all of the largest motor fibers should be reflected in the F-wave minimum latency. Complete loss of these fibers would result in an absent F-wave as well as a reduction in CMAP amplitude. Conversely, even if a small percentage of these large fibers survive the pathologic insult, the F-wave minimum latency will be normal. One of our patients had a prolonged D2-wrist SNAP, a normal DML, and a normal FWML but had fibrillations in the APB. This can be explained by demyelination affecting some but not all of the median-nerve fibers at the wrist. The sparing of some large motor axons and the loss of smaller axons explains the presence of FAPB and the absence of FWIN.

As the largest axons are the most heavily myelinated, it stands to reason that electrophysiologic tests of large fibers will appear abnormal first, as previously reported (Lang et al, 1995). The palm-to-wrist not only tests these largest fibers but also examines a short distance across the site of pathology. Therefore, the pathologically involved segment comprises a larger proportion of the nerve tested. As such, this test is most likely to detect incipient demyelination and was thus chosen as our reference standard. FWIN detected more cases of CTS than D2-wrist SNAP, but this did not reach statistical significance in our study ($p > 0.05$). A larger series may demonstrate its superiority as an electrodiagnostic test. The sensitivity and specificity of digital-nerve studies in CTS have been previously examined (Kothari et al, 1995). The D2-wrist SNAP was measured as an onset latency, which reflected the fastest conducting fibers. Had peak latency been used, a greater degree of demyelination would have been required to show abnormal results, which would have yielded a more impressive comparison for FWIN. In our study, FWIN was clearly superior to DML or FAPB because a greater degree of motor-fiber involvement is usually required to produce abnormalities in those tests. As such, FWIN is the most sensitive and specific test of motor-nerve involvement in CTS, comparable or perhaps superior to digital-sensory-nerve testing.

In summary, the F-wave inversion method is the most sensitive and specific of all electrodiagnostic tests of median-nerve function used in this study save the palm-to-wrist mixed-nerve comparison test. It can be used without learning a new electrodiagnostic

technique. Because it has a sensitivity greater than or equal to D2-wrist testing, it should be employed in all electrodiagnostic evaluations for CTS. It can serve as confirmatory test when the median palm-to-wrist mixed nerve action potential is abnormal and ipsilateral ulnar nerve studies are within normal limits. We strongly advocate the use of this test in this context.

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