

Comparison of Peak Versus Onset Latency Measurements in Electrodiagnostic Tests for Carpal Tunnel Syndrome

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Purpose: The aim of this prospectively conducted study was to compare the diagnostic accuracy of onset versus peak latency measurements of sensory nerve action potentials in electrodiagnostic studies in diagnosing carpal tunnel syndrome.

Methods: In 156 consecutive patients with clinically defined carpal tunnel syndrome, standardized nerve conduction studies (DIG1, DIG4, PALM3) were performed. Both onset and peak latency were measured. Sensitivity was calculated using the clinical diagnosis as golden standard. Bland–Altman plots were constructed to assess the agreement for quantitative measurements. Overall agreement, positive and negative percent agreement, and Kappa coefficient were computed.

Results: The Bland–Altman plots, positive and negative percent agreement show good overall agreement. The kappa coefficient was 0.850, 0.847, and 0.815 for DIG1, DIG4, and PALM3, respectively.

Conclusions: Onset and peak latencies used in electrodiagnostic tests show a good overall agreement in confirming the clinical diagnosis of carpal tunnel syndrome. Because onset latency measurement represents nerve conduction velocity of the fastest conducting fibers, the use of onset latencies is recommended. In case of uncontrollable stimulus artifacts, peak latencies may be used instead.

Key Words: CTS, NCS, Peak latency, Onset latency, Accuracy.

(*J Clin Neurophysiol* 2014;31: 382–386)

Carpal Tunnel Syndrome (CTS) may be reliably diagnosed clinically; however, most surgeons, at least in the Netherlands, prefer an objective test to confirm the clinical diagnosis before surgery (Claes et al., 2007). Conduction slowing in median sensory nerve fibers across the carpal tunnel is considered the electrophysiological hallmark for the confirmation of the clinical diagnosis of CTS. However, in the usually applied nerve conduction tests in the hand, conduction distances are rather small, and this inherent small distance between stimulus cathode and recording electrode may easily cause stimulus artifacts. Despite modern techniques, these stimulus artifacts may hamper accurately defining the onset latencies needed for the determination of conduction velocities. To avoid this problem, the measurement of peak latencies may be used, because measurement of peak latencies of the sensory nerve action potential (SNAP) is less prone to inaccuracies in the presence of stimulus artifacts (Kiernan et al., 2001; Kouyoumdjian et al., 2000; Salerno et al., 1998; Sander et al., 1999). Unlike onset latency measurements, however, this method does not represent the velocities of the fastest conducting nerve fibers

(Wilbourn, 1994) and can therefore not be used for the computation of nerve conduction velocities. However, this problem is reduced in electrodiagnostic tests in which the median nerve sensory latencies are compared with latencies of other nerves that are presumed to be normal. As a consequence, these latencies may be used as a reference if conduction distances are kept equal (Kasius et al., 2012; Stevens, 1997).

We hypothesized that peak latencies are as accurate as onset latencies in diagnostic tests for CTS. The aim of this prospectively conducted study is to compare the accuracy of peak latency versus onset latency measurement in sensory nerve conduction studies (NCS) to confirm clinically defined CTS.

METHODS

Control Subjects

The control group consisted of 47 healthy asymptomatic volunteers. Only one hand, randomly selected, was studied in each control subject.

Subjects

One-hundred fifty-six consecutive patients with clinically defined CTS were prospectively included in this study. Carpal tunnel syndrome was considered clinically present based on the presence of the following symptoms: paresthesias in the hand in a median nerve distribution, and at least 2 of the following major criteria: (1) paresthesias during night that awaken the patient from sleep, (2) paresthesias relieved by shaking the hand, and (3) aggravation of paresthesias by activities such as driving, bicycling, and holding a telephone or a book. These criteria are based on the Hand Symptom Questionnaire (Stevens et al., 1999) and are an adaptation of the criteria used in other studies (Witt et al., 2004). Patients were not included in the following cases: clinical signs of polyneuropathy or known hereditary neuropathy with liability to pressure palsy, history of trauma or previous surgery of the symptomatic wrist, pregnancy, severe atrophy of the abductor pollicis brevis muscle, history of rheumatoid arthritis or arthrosis of the wrist, known diabetes, hypothyroidism or hyperthyroidism, or alcoholism. One patient was excluded from this study because not all data of each electrophysiological test were complete. In case of bilateral complaints compatible with clinical CTS, only the most symptomatic hand was included for analysis.

All candidates gave their written informed consent, and the study was approved by the institutional review board.

Electrodiagnostic Tests

Standardized NCS were performed by standardized techniques according to the AANEM summary statement (Jablecki et al., 2002) in all healthy volunteers and in the most symptomatic hand of all patients by the same examiner (J.M.), who was not aware of the

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ISSN: 0736-0258/14/3104-0382

clinical status of the subjects. Nerve conduction studies were performed using a Viking Myograph type IV (Nicolet Biomedical Inc, Madison, WI). Skin temperature was measured before and after each test by means of an infrared thermometer (62 Mini IR Thermometer; Fluke Biomedical, Cleveland, OH). Skin temperature was maintained at a minimum of 31.0°C.

In all antidromic sensory NCS, ring electrodes were applied for recording SNAPs. The proximal recording electrode was placed at the first interphalangeal joint and the distal recording electrode at a distance of at least 3 cm, if feasible. Conduction distances were measured with a precision of 1 mm using a measuring tape. The ground electrode was placed between the proximal recording electrode and the stimulation site and, if necessary, repositioned to reduce stimulus artifacts. Moreover, the hand was manually fixed by the examiner to reduce movement artifacts. Stimulus current was adjusted to obtain supramaximal stimulus conditions. The optimal stimulation site was carefully determined so that with minimal stimulus strength maximal SNAP amplitude could be obtained under supramaximal conditions. If stimulus artifacts were present, repositioning of the anode without changing the position of the cathode by turning the stimulator was performed to try to reduce the stimulus artifact. Signal averaging was applied on all SNAPs at least 3 times or, if necessary, several responses more to obtain a sharp take-off from the baseline. In all tests, latencies were measured at the onset and the peak of the SNAP.

The onset latency was measured at the initial negative deflection of the SNAP. The peak latency was measured at the peak of the negative deflection. Latency markers were manually checked by one and the same electrodiagnostic technologist, using standardized amplification. Filter settings were identical for determining both onset and peak latencies.

Three different types of sensory (two comparison tests, one short-segment study) and one motor NCS were performed in each individual.

1. Median–radial comparison test (DIG1): SNAPs from median and radial nerves were recorded from the first finger after separate stimulation of the median and radial nerve at the wrist, with the same conduction distance. The difference between the thus obtained onset and peak latencies was measured.
2. Median–ulnar comparison test (DIG4): SNAPs from median and ulnar nerves were recorded from the fourth finger after separate stimulation of the median and ulnar nerve at the wrist, with the same conduction distance. The difference between the thus obtained onset and peak latencies was measured.
3. Short-segment study (PALM3): Sensory NCS of the median nerve in the wrist to palm and elbow to wrist segments were performed antidromically. Sensory nerve action potentials were recorded from the third finger after stimulation of the median nerve at the palm, wrist, and elbow, respectively. The stimulation site of the palm was exactly halfway the proximal recording electrode and the mediopalmar line at the wrist. Differences in sensory nerve conduction velocities between wrist to palm segment and elbow to wrist segments were subsequently calculated (Kasius et al., 2012) by using onset and peak latencies.
4. For the sake of completeness and for clinical purposes also, motor NCS were performed in all patients distal motor latency (DML). The median nerve was stimulated at the wrist and at the cubital fossa. Compound muscle action potentials were recorded from the thenar eminence by means of surface electrodes, at a recording distance of 6 cm from the stimulation site at the wrist. Recording position was chosen in a way that enabled recording a compound muscle action potential as maximal as possible with sharp initial negative deflection. A distal motor

TABLE 1. Reference Values

Test	Onset		Peak	
	Mean $\pm$ SD	ULN	Mean $\pm$ SD	ULN
DIG1	0.16 $\pm$ 0.19	$\leq$ 0.54 ms	0.21 $\pm$ 0.30	$\leq$ 0.81 ms
DIG4	0.06 $\pm$ 0.14	$\leq$ 0.34 ms	0.02 $\pm$ 0.17	$\leq$ 0.44 ms
PALM3	5.64 $\pm$ 5.96	$\leq$ 17.6 m/s	7.48 $\pm$ 4.56	$\leq$ 16.6 m/s

DIG1, distal sensory latency difference (median–radial nerve); DIG4, distal sensory latency difference (median–ulnar nerve); PALM3, median sensory nerve conduction velocity difference forearm versus wrist (Kasius et al., 2012); ULN, upper limit of normal.

latency of >4.0 milliseconds is considered to be consistent with CTS. The results of the motor nerve studies are not the subject of this article; in general, onset latencies will not be influenced by baseline noise because of the relatively high amplitude of the compound muscle action potential in mild CTS.

Statistical Analysis

Data concerning clinical variables and NCS were processed using Microsoft Office Excel and Access 2003, and all statistical analyses were performed using SPSS Statistics 17.0.

Reference values were obtained from the control group in the same laboratory, using the NCS previously described. Mean differences and standard deviations (SD) were computed, using both onset and peak latencies. The upper limit of normal for the different tests is defined as the mean $\pm$ 2 SD. Upper limit of normal for the different electrodiagnostic tests are listed in Table 1.

The number of patients with an abnormal electrodiagnostic test result for each test according to both onset and peak latencies was estimated using the upper limit of normal, obtained from the reference population. To lower the risk of a false-positive diagnosis, the presence of at least two abnormal comparative electrodiagnostic test results is considered compatible with the electrophysiological diagnosis of CTS (Werner and Andary, 2011).

The sensitivity was calculated using the clinical diagnosis CTS as golden standard. In this study, the latency difference (DIG1, DIG4) and nerve conduction velocity computed (PALM3) from onset latency are defined as the reference test because the onset latency is interpreted to reflect the conduction velocity of the fastest conducting sensory fibers (Wilbourn, 1994). The latency difference and nerve conduction velocity computed from peak latency are regarded as the index test.

To assess the agreement for quantitative measurements (i.e., latency and nerve conduction velocity differences) Bland–Altman plots (Bland and Altman, 1986) were constructed for each test.

Overall agreement between the index and reference test, as well as the positive percent agreement and negative percent agreement were computed. To measure the agreement between the

TABLE 2. Electrodiagnostic Studies Compatible With CTS (i.e., $\geq$ 2 Tests Positive)

	Onset Latency (Reference Test)	
	$\geq$ 2 Abnormal Tests	$<$ 2 Abnormal Tests
Peak latency	$\geq$ 2 Abnormal tests	124
(index test)	$<$ 2 Abnormal tests	5
		27

TABLE 3. Number of Abnormal Tests According to Onset and Peak Latency

	Onset Latency		Peak Latency	
	Abnormal Tests	Sensitivity (%)	Abnormal Tests	Sensitivity (%)
DIG1	126	80.8	118	75.6
DIG4	135	86.5	131	84.0
PALM3	130	83.3	130	83.3

DIG1, distal sensory latency difference (median–radial nerve); DIG4, distal sensory latency difference (median–ulnar nerve); PALM3, median sensory nerve conduction velocity difference forearm versus wrist (Kasius et al., 2012).

index and reference test on a nominal scale (i.e., CTS vs. no CTS), crosstabs were made and the Kappa coefficient was computed.

RESULTS

Study Population

Forty-seven control subjects were evaluated with unilateral NCS: 17 males and 30 females. Twenty-three right and 24 left hands were studied. Mean age was 41.0 (SD, 12.2). The patient population included 156 patients; 35 (22.4%) men and 121 (77.6%) women. Mean patient age was 49.1 (SD, 13.6) years (range, 18–86). The mean age of patients and controls was statistically significant higher in patients ($P < 0.005$).

Electrophysiology

According to the onset and peak latency, 129 (82.7%) and 124 patients (79.5%), respectively had at least 2 abnormal sensory nerve conduction tests (Table 2). For each nerve conduction study, slightly higher sensitivities were found when using onset latency, especially for DIG1 (Table 3). The overall agreement between the index and reference test was 94.9%, 96.2%, and 94.6% for DIG1, DIG4, and PALM3, respectively. The percentage positive agreement was essentially the same for these 3 NCS (93.7%, 96.3%, and 96.7% for DIG1, DIG4, and PALM3, respectively). The percentage negative agreement differed between these 3 tests (100%, 95.2%, and 84.6% for DIG1, DIG4, and PALM3, respectively) with the highest percentage negative agreement for DIG1. The kappa coefficient was 0.850, 0.847, and 0.815 for the 3 NCS (all $P < 0.001$). Despite a high degree of overall agreement, there was an off-diagonal imbalance in the crosstabs. Therefore, we also calculated the AC₁ coefficient (Gwet, 2008). Detailed data are shown in Table 4.

For all 3 NCS, correlations between onset and peak latencies are shown in Fig. 1. The Bland–Altman plots (Bland and Altman, 1986) show a good overall agreement between the index and reference test for all 3 electrophysiologic tests (Fig. 2).

DISCUSSION

The main finding of this study is that the overall agreement according to a nominal scale for the clinical diagnosis of CTS (i.e., present or not) and the percentage positive and negative agreement is equal for onset and peak latencies for all three applied tests. For the PALM3 test, the percentage negative agreement is slightly lower than for the other two sensory NCS. Generally, sensitivities for all three tests are slightly higher for the reference test (i.e., onset latency), especially for DIG1.

We hypothesized that peak latencies are as accurate as onset latencies in electrodiagnostic tests in patients with CTS. In the presence of uncontrollable stimulus artifacts, the peak latency would be a more accurate parameter. Our results confirm this hypothesis for the PALM3 test. This test is, due to the small conduction distances, prone to uncontrollable stimulus artifacts. In addition, in case of SNAPs with small amplitudes, which are frequently found in CTS, baseline noise may hamper accurate determination of the onset latencies. However, we could not demonstrate that peak latencies are as accurate as onset latencies in electrodiagnostic tests in CTS. Sensitivities of onset latency measurements were slightly higher compared with peak latency measurements. An important explanation for this discrepancy may be due to the representation of the fibers of the peak and onset latency. Lew et al. (2005) proposed that in the early phases of CTS, the fastest conducting fibers may be particularly affected. If true, onset latency would be more abnormal compared with the peak latency. However, Prakash et al. (2006) suggested that the medium-range velocity fibers are affected earlier in CTS and, consequently, the peak latency would be more sensitive in diagnosing CTS. Our data do not support this last hypothesis.

Salerno et al. (1999) investigated the reliability of median and ulnar sensory measures of onset and peak latencies among a sample of active workers. They showed higher interexaminer and intra-examiner reliability for peak latency compared with onset latency. However, the reliability of peak and onset latencies in short-segment sensory median NCS was not studied. Moreover, reliability between peak and onset latencies was not tested in a population of subjects with a clinical diagnosis of CTS.

There have been a few studies investigating the difference or correlation between onset and peak latencies in CTS (Prakash et al., 2006; Salerno et al., 1999; Sander et al., 1999). Sander et al. (1999) suggested that the use of peak latency may be simpler, more rapid, and may be more reliably computerized. There are, however, some differences between these studies and our study. First, the nerve conduction techniques are different, for example, antidromic versus orthodromic stimulation (Sander et al., 1999). Second, we investigated the agreement between peak and onset latency for 3 different sensory NCS (DIG1, DIG4, PALM3) instead of only PALM (Sander et al., 1999) or DIG1 (Prakash et al., 2006). Third, we investigated the agreement between onset and peak latencies purely in sensory fibers instead of mixed nerve

TABLE 4. Agreement Between Index (Onset) and Reference (Peak) Test

	Overall Agreement (%)	PPA (%)	PNA (%)	Kappa		AC ₁ Coefficient (Gwet, 2008)
				Value	P	
DIG1	94.9	93.7	100	0.850	<0.001	0.9221
DIG4	96.2	96.3	95.2	0.847	<0.001	0.9486
PALM3	94.6	96.7	84.6	0.815	<0.001	0.9239
>2 abnormal tests	96.8	96.1	100	0.896	<0.001	0.9538

DIG1, distal sensory latency difference (median–radial nerve); DIG4, distal sensory latency difference (median–ulnar nerve); PALM3, median sensory nerve conduction velocity difference forearm versus wrist (Kasius et al., 2012); PPA, percentage positive agreement; PNA, percentage negative agreement.

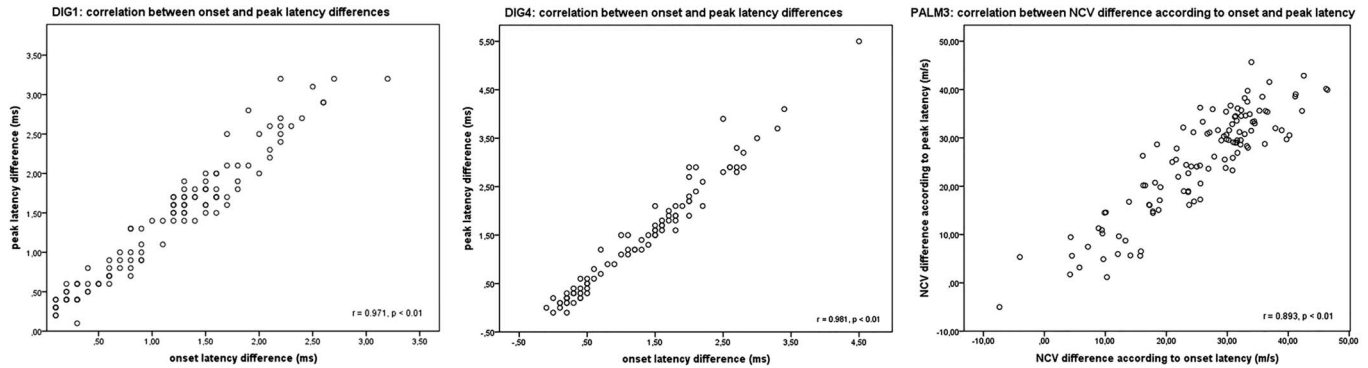


FIG. 1. Correlation between peak and onset latencies. DIG1, distal sensory latency difference (median–radial nerve); DIG4, distal sensory latency difference (median–ulnar nerve); PALM3, median sensory nerve conduction velocity difference, forearm versus wrist (Kasius et al., 2012).

conduction (Sander et al., 1999). Fourth, unlike Sander et al. (1999), we included all patients with clinically definite CTS, irrespective of the results of the NCS. This may account for some differences in sensitivities. The computed sensitivities from the different NCS are lower compared with reported data from other studies (Jablecki et al., 2002; Prakash et al., 2006), which is possibly partially caused by different inclusion criteria. However, the aim of our study was to investigate the correlation and agreement between the onset and peak latency, instead of just computing sensitivities or specificities (Prakash et al., 2006). Because only healthy subjects were examined as controls, specificity could not be calculated.

This study has several shortcomings. Because both peak and onset latency measurements were done by the same examiner, expectation bias is not completely ruled out. However, at the time the NCS were performed, normal values were not known.

Patients with severe atrophy were not included in this study. The authors believe that this does not influence a potential spectrum bias because, first, severe atrophy is not frequently found in an average CTS population. Second, severe atrophy is associated with electrophysiologically more severe CTS (Nora et al., 2004) and consequently more often unrecordable SNAPs. In this study, we were interested in the agreement between latency measurements. Unrecordable SNAPs provide no additional information on this issue.

In addition, patients were statistically significant older than the controls. However, because comparative tests of different nerves or different segments of the same nerve were used of the same object, we consider this finding not of significant importance.

Peak latencies cannot be used to compute absolute nerve conduction velocities. However, for the electrophysiological diagnosis of CTS, differences in peak latencies and nerve conduction velocities give an accurate reflection of the abnormalities of the nerves. It is important to emphasize that, when peak latencies are used, one needs to use other normal values. These data are shown in Table 1. As recommended by Jablecki et al. (2002), each laboratory has to make their reference values when using peak latencies.

Our study is the first report on the comparison of the accuracy of onset and peak latencies in three sensory tests in CTS. Both methods may be used in electrodiagnostic tests to confirm the clinical diagnosis of CTS, and both show a good correlation and overall agreement. Tests using peak latency are often much more simple in dealing with stimulus artifacts and may also be of advantage in automatically measuring latencies. In contrast, only onset latency measurement represents nerve conduction velocity of the fastest conducting fibers and has to be used to determine classical nerve conduction velocity. Since sensitivities for all three tests are higher for onset latency measurements and because onset latency represents the fastest conducting fibers, we recommend to use initially onset latencies. If, despite all efforts to reduce the stimulus

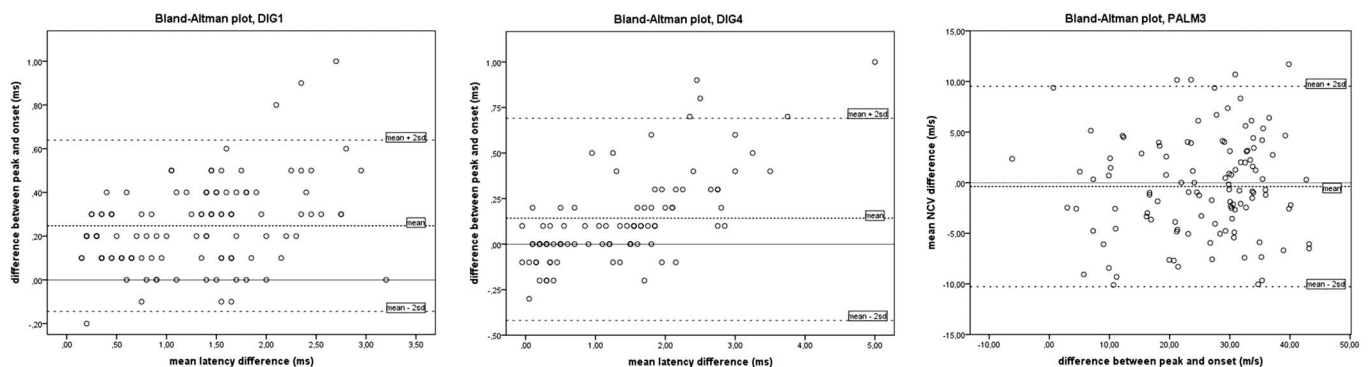


FIG. 2. Bland–Altman plots (Bland and Altman, 1986). DIG1, distal sensory latency difference (median–radial nerve); DIG4, distal sensory latency difference (median–ulnar nerve); PALM3, median sensory nerve conduction velocity difference, forearm versus wrist (Kasius et al., 2012).

artifact, accurately defining of onset latency is not possible, we suggest the use of peak latencies.

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