Value of Second Lumbrical-Interosseous Latency Difference in Diagnosis of Carpal Tunnel Syndrome among Type 2 Diabetes Mellitus Patients with Diabetic Peripheral Neuropathy

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Abstract: Carpal tunnel syndrome (CTS) and diabetic polyneuropathy (DPN) frequently occur concomitantly. Diagnosis of CTS in patients with DPN is important; however, it can be quite challenging in these cases. **Aim of the work:** was to study the value of second lumbrical- interosseous latency difference (2L-INT) latency difference in the diagnosis of CTS in type 2 DM patients with DPN. **Patients and Methods:** This study included 30 patients (60 hands) with type 2 DM. Patients were classified into mild, moderate and severe DPN. Patients were assessed for symptoms and signs of CTS. Electrophysiological evaluation for CTS included the latency difference between the median and ulnar sensory response to the ring finger (DM-DU SLD), latency difference between the median and ulnar motor response (DM-DU MLD) together with the 2L-INT latency difference. **Results:** In this study 20(33%) hands had clinical manifestations of CTS, while 40 (67%) hands had no clinical manifestations suggestive of CTS. There was a highly significant difference ($p<0.01$) as regards the 2L-INT latency difference; and a statistically non-significant difference between the two groups ($p>0.05$) as regards the DM-DU SLD, or DM-DU MLD.2L-INT latency difference was elicited in all the studied hands (100%), as compared to DM-DU MLD elicited in (96.7 %) of hands and DM-DU SLD elicited in (85%)of hands. 2L-INT latency difference had the highest specificity (50%) and accuracy (60%). 2L-INT latency difference had 100% sensitivity among patients with moderate and severe DPN as compared to 66.7% sensitivity in mild DPN patients. It was found to have 71.4% accuracy among patients with mild DPN as compared to 33.3% and 40% accuracy among patients with moderate and severe DPN respectively. **Conclusion:** 2L-INTlatency difference is an easy, and accurate method for the diagnosis of CTS in type 2 DM patients with DPN especially those with severe DPN. We recommend its corporation in their electrodiagnostic workup; whether they complain of clinical manifestations of CTS or not.
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Key words: Carpal tunnel syndrome, diabetic peripheral neuropathy, second lumbrical –interosseous latency difference.

1. Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, which occurs in diabetic patients, with an incidence several-fold that in the general population ***(1).***

Carpal tunnel syndrome (CTS) and diabetic polyneuropathy (DPN) frequently occur concomitantly as DPN is a predisposing factor to entrapment neuropathies ***(2)***. Diagnosis of CTS in patients with DPN is important, as therapeutic interventions directed toward relief of CTS may be effective; irrespective of diffuse neuropathy ***(3).***

Common practice is to apply nerve conduction study (NCS) criteria to diagnose CTS in diabetic subjects without DPN in the same manner as in the nondiabetic population. However, electrophysiological diagnosis of CTS can be quite challenging in cases with DPN. Electrophysiological criteria designed to discriminate CTS in subjects with DPN are available, but their reliability remains uncertain ***(3).***

The second lumbrical- interosseous (2L-INT) latency difference is a motor conduction technique that was initially described as being fairly valuable in the diagnosis of CTS ***(4).*** Over the past years, its value has been conflictingly addressed, as there are studies supporting its high diagnostic sensitivity in CTS ***(5),*** whereas others report a much lower sensitivity ***(6).***

Aim of the work:

Our aim was to study the value of (2L-INT) latency difference in the diagnosis of CTS in type 2 DM patients with DPN.

2.Patients and Methods:

a. This is a cross sectional study conducted at the Physical Medicine & Rehabilitation Department Ain Shams University Hospitals including 30 patients (60 hands) with type 2 DM. The local ethical

committee approved this study and an informed consent was obtained from participating patients.

b. Excluded from the study were patients with other causes of neuropathy, cervical radiculopathy, cervical rib, and previous nerve injuries

d. Patients underwent full history taking and clinical examination. The clinical assessment score of the MDNS was performed and patients were given a clinical score of 0-46***(7)***.

e. Electrophysiological evaluation was performed using Toennies Neuroscreen Plus made by Toennies of Germany. In motor studies, we used parameters of a sweep speed of 5ms/division and a gain of 4mV. In Sensory studies, sweep was adjusted at 2ms and gain at 20uV. The tests were performed at room temperature.

f. Electrophysiological assessment of DPN included: *1)* distal ulnar, and peroneal nerve motor conduction studies in the form of: distal motor latency, distal motor amplitude and nerve conduction velocity; *2*) distal ulnar and sural nerve sensory conduction studies in the form of: distal sensory latency, distal sensory amplitude, and sensory conduction velocity. All sensory nerve conduction studies were antidromic. Nerve conductions (ulnar sensory and motor, peroneal motor, sural sensory) were graded separately: 0 for normal and 1 for abnormal values. Normal values were those between the first and 99th percentiles according to Kimura ***(8)***. Each patient was then given a composite score based on the number of abnormal nerve conductions and the number of points scored on the clinical examination. Mild neuropathy was defined as two abnormalities on nerve conduction and a clinical score of ≤12; moderate neuropathy, included patients with either three or four abnormal nerve conductions and a clinical score of ≤ 29; and severe neuropathy, was defined as abnormalities in all five nerve conductions with clinical scores ≤ 46 ***(7)***.

g. Patients were assessed for symptoms and signs of CTS in the form of nocturnal or activity-related pain and/or paresthesia in the median nerve distribution, hypoesthesia in median nerve distribution with or without weakness ± atrophy of thenar muscles in addition to positive Tinel and/or Phalen's sign ***(9).***

h. Electrophysiological evaluation for detection of carpal tunnel syndrome was done for all the studied patients in the form of: DMSL as compared to DUSL to the ring finger performed antidromically at a distance of 14 cm between the stimulating and recording electrodes to determine the distal median - distal ulnar sensory latency difference (DM-DU SLD). Values ≥ 1 were considered abnormal ***(10)***. (DMML) as compared to the ipsilateral (DUML) recording from the thenar and hypothenar eminences respectively at a distance of 8 cm between the stimulation and active recording electrode to record the distal median - distal ulnar motor latency difference (DM-DU MLD).A value of ≥ 1.5 msec was used for detection of abnormality ***(8)***. Calculation of (2L-INT) latency difference was performed, in which the active recording electrode (G1) was placed just lateral to the midpoint of the third metacarpal with the reference electrode (G2) over the proximal interphalangeal joint of the second digit, median and ulnar nerves were stimulated at the wrist. Identical distances between the stimulation and recording were used (8cm). Distal motor latency of median and ulnar nerves was compared and latency difference was determined. Latency difference ≥0.5 msec was considered abnormal ***(8)***.

i. Statistical analysis was performed by SPSS version 18. We used the chi-squared test for comparison of qualitative data, *t*-test for comparison between two groups as regards quantitative data and ANOVA test to compare between more than two groups as regards quantitative data. The ROC curve was used as a predictor for sensitivity, specificity and accuracy of the three studied methods for the diagnosis of CTS.

P>0.05 =non-significant

P<0.05=significant

3. Results:

This study included 30 patients (60 hands) with Type 2 DM; 16 (53%) were females and 14(47%) were males. Their ages ranged between 46-78 years with a mean ± SD (63.53±11.33). 10 (33%) patients were insulin dependent and 20 (67%) patients were non-insulin dependent. Their known disease duration ranged from 4-30 years with mean ± SD (13.66±0.52). They had DPN of different grades according to the Michigan Diabetic Neuropathy Score ***(7)***; 14(47%) had mild DPN; 6 (20%) had moderate DPN, and 10(33%) had severe DPN.

In this study 20(33%) hands had clinical manifestations of CTS, while 40 (67%) hands had no clinical manifestations suggestive of CTS. There was a statistically non-significant difference (*P*>0.05) between patients with and without clinical manifestations of CTS as regards the age, sex, known disease duration, method of treatment and degree of diabetic neuropathy according to MDNS as shown in (**Table 1&2)**.

Table 1. Table showing the difference between patients with and without clinical CTS as regards the sex, method of treatment and degree of diabetic neuropathy.

		Clinical CTS						Chi-Square	
		Negative		Positive		Total			
		N	%	N	%	N	%	X^2	*p*-value
Sex	**F**	20	50.00	12	60.00	32	53.33	0.536	0.464
	M	20	50.00	8	40.00	28	46.67		
	Total	40	100.00	20	100.00	60	100.00		
Treatment	**I**	12	30.00	8	40.00	20	33.33	0.600	0.439
	D	28	70.00	12	60.00	40	66.67		
	Total	40	100.00	20	100.00	60	100.00		
DPN	**Mild**	20	50.00	8	40.00	28	46.67	0.682	0.711
	Moderate	8	20.00	4	20.00	12	20.00		
	Severe	12	30.00	8	40.00	20	33.33		
	Total	40	100.00	20	100.00	60	100.00		

CTS=carpal tunnel syndrome, DPN =diabetic peripheral neuropathy

Table 2. Table showing the difference between patients with and without clinical CTS as regards the age and disease duration.

	Clinical CTS						T-Test	
	Negative			Positive				
	Mean	±	SD	Mean	±	SD	t	*p*-value
Age (years)	61.2	±	5.43	64.35	±	10.84	-1.5	0.14
Disease duration (years)	14.250	±	11.017	12.500	±	9.333	0.609	0.545

CTS =carpal tunnel syndrome

Comparison between hands with clinical manifestations of CTS and those without, showed a significant difference ($p<0.01$) as regards the 2L-INT latency difference; however there was statistically non-significant difference between the two groups ($p>0.05$) as regards the DM-DU SLD, and DM-DU MLD as shown in (**Table 3**).

Table 3. Comparison between hands with clinical manifestations of CTS and those without as regards DM-DU SLD, DM-DU MLD and 2L-INT latency difference.

	Clinical CTS		T-Test	
	Negative	Positive		
	Mean±SD	Mean±SD	*t*	*p*-value
DM-DU SLD (msec)	1.558±0.783	2.047±0.961	-1.897	0.064
DM-DU MLD (msec)	1.950±1.175	2.572±2.028	-1.475	0.146
2L-INT LD (msec)	0.949±0.866	1.700±1.019	-2.983	0.004

CTS=carpal tunnel syndrome, DM-DU SLD=distal median –distal ulnar sensory latency difference, DM-DU MLD=distal median-distal ulnar motor latency difference, 2L-INT LD=second lumbrical –interosseous latency difference, msec=milliseconds.

2L-INT latency difference was elicited in all the studied hands (100%). The sensory response to the ring finger could not be elicited in 9 hands (15%). The compound motor action potential could not be elicited from the thenar eminence in 2 hands (3.3%) due to severe wasting of the thenar eminence.

2L-INT latency difference was positive for CTS in 36 hands (60%) and negative for CTS in 24 hands (40%). Among hands with elicited sensory response DM-DU SLD was positive for CTS in 40 hands (78%). Among hands with elicited motor response DM-DU MLD was positive for CTS in 36 hands (62%). Hands with negative clinical CTS were positive for CTS when elicited by 2L-INT latency difference in 50 % of hands, in 55% by DM-DU MLD and in 70% by DM-DU SLD.

Sensitivity, specificity and accuracy of the different studied electrophysiologic diagnostic methods for CTS are shown in **Table 4**. 2L-INT latency difference showed the highest specificity

(50%) and accuracy (60%). Sensory study in the form of DM-DU SLD showed the highest sensitivity (100%).

Table 4.Roc curve showing the sensitivity, specificity and accuracy of the different studied methods, including DM-DU MLD, DM-DU SLD and 2L-INT latency difference in the diagnosis of CTS.

		Clinical CTS						Chi-Square		Roc curve				
		Negative		Positive		Total								
		N	%	N	%	N	%	X^2	*p*-value	Sens	Spec.	PPV	NPV	Accuracy
DM-DU SLD	Negative	11	30.56	0	0.00	11	21.57	8.866	0.003*	100.00	30.56	37.50	100.00	50.98
	Positive	25	69.44	15	100.00	40	78.43							
DM-DU MLD	Negative	18	31.0	4	6.9	22	37.9	2.736	0.098	77.8	45.0	38.9	81.8	55.2
	Positive	22	37.9	14	24.1	36	62.1							
2L-INT latency difference	Negative	20	33.3	4	6.7	24	40.0	5.000	0.025*	80.0	50.0	44.4	83.3	60.0
	Positive	20	33.3	16	26.7	36	60.0							

CTS=carpal tunnel syndrome, DM-DU SLD=distal median –distal ulnar sensory latency difference, DM-DU MLD=distal median-distal ulnar motor latency difference,2L-INT LD=second lumbrical –interosseous latency difference.

Studying the sensitivity, specificity and accuracy of the different studied methods in the diagnosis of CTS among patients with different stages of DPN showed 2L-INT latency difference to have 100% sensitivity among patients with moderate and severe DPN as compared to 66.7% sensitivity in mild DPN patients. It was found to have 75% specificity and 71.4% accuracy among patients with mild DPN as compared to 33.3% and 40% accuracy among patients with moderate and severe DPN respectively as shown in (**Table 5**).

Table 5. ROC curve showing the sensitivity, specificity and accuracy of the different studied methods for the diagnosis of CTS in patients with mild, moderate and severe DPN.

DPN			Clinical						Chi-Square		ROC curve				
			Negative		Positive		Total								
			N	%	N	%	N	%	X^2	*p*-value	Sens	Spec.	PPV	NPV	Accuracy
DM-DU SLD	Mild	Negative	10	35.71	0	0.00	10	35.71	8.772	0.003	100.00	50.00	44.44	100.00	64.29
		Positive	10	35.71	8	28.57	18	64.29							
	Moderate	Negative	1	8.33	0	0.00	1	8.33	0.856	0.355	100.00	12.50	36.36	100.00	41.67
		Positive	7	58.33	4	33.33	11	91.67							
	Severe	Negative	0	0.00	0	0.00	0	0.00							
		Positive	8	72.73	3	27.27	11	100.00							
DM-DU MLD	Mild	Negative	6	42.9	2	14.3	8	57.1	2.486	0.115	66.7	75.0	66.7	75.0	71.4
		Positive	2	14.3	4	28.6	6	42.9							
	Moderate	Negative	0	0.0	0	0.0	0	0.0			100.0	0.0	33.3		33.3
		Positive	4	66.7	2	33.3	6	100.0							
	Severe	Negative	0	0.0	0	0.0	0	0.0			100.0	0.0	25.0		25.0
		Positive	6	75.0	2	25.0	8	100.0							
2L-INT latency difference	Mild	Negative	6	42.9	2	14.3	8	57.1	2.486	0.115	66.7	75.0	66.7	75.0	71.4
		Positive	2	14.3	4	28.6	6	42.9							
	Moderate	Negative	0	0.0	0	0.0	0	0.0			100.0	0.0	33.3		33.3
		Positive	4	66.7	2	33.3	6	100.0							
	Severe	Negative	0	0.0	0	0.0	0	0.0			100.0	0.0	40.0		40.0

CTS=carpal tunnel syndrome, DM-DU SLD=distal median –distal ulnar sensory latency difference, DM-DU MLD=distal median-distal ulnar motor latency difference, DPN=diabetic peripheral neuropathy

4.Discussion:

This study was performed on 30 patients (60 hands) with DPN. Diabetic patients with symptoms of CTS have clinical manifestations suggestive of that pathology; however commonly it is attributed to the presence of DPN.The aim of our study was to assess the 2L-INT latency difference as a method for the diagnosis of CTS among patients with DPN in order not to miss its diagnosis and to provide treatment for that relatively easily curable condition.

Patients were diagnosed according to the MDNS for classification of DPN ***(7)***. MDNS is an easy method for classification of the different grades of DPN.It combines both an easy outpatient clinical assessment score and a NCS evaluation.It was found to be comparable to the more complicated Mayo Clinic protocols ***(11)*** and San Antonio Consensus Statement ***(12)*** for diagnosis and staging of DPN. 14(47%) of the patients had mild DPN, 6 (20%) had moderate DPN and 10(33%) had severe DPN.

In this study, 20 out of the 60 studied hands (33%) had clinical CTS. Among the hands that had no clinical CTS manifestations we detected CTS electrophysiologically in approximately 50% of those hands. Dyck and his colleagues ***(13)*** found that approximately 25% of patients with diabetes had electrophysiologic abnormalities characteristic of CTS without any clinical manifestations of CTS. Our greater percentage could be attributed to involving only patients with DPN in our study who are more liable to the development of CTS as opposed to their study in which they included patients with or without DPN. Another study by Kim and colleagues ***(14)*** reported electrophysiologic CTS only in 6.5% of

patients with no clinical CTS manifestations. They included patients with diabetes mellitus without evidence of DPN. Their electrophysiologic evaluation for CTS only included abnormal sensory nerve conduction study of the index finger-wrist and /or palm-wrist segment.

A study by Perkins and colleagues ***(3)*** based on the ratios between median to ulnar: distal motor latency, distal sensory latency, amplitude of elicited compound motor action potential, amplitude of elicited sensory action potential, distal motor conduction velocity, distal sensory conduction velocity, proximal motor conduction velocity and proximal sensory conduction velocity to diagnose CTS in patients with DM came to the conclusion that NCS did not reliably distinguish the presence or the absence of CTS in patients with DPN. They advised that therapeutic decisions in patients with clinical criteria for CTS should be made independent of NCS findings. They advised that a trial of therapy should be strongly considered in patients with both diabetes and clinical CTS without undue reliance on electrodiagnostic results ***(3)***.

The cut off value for considering an abnormal DM-DU SLD we used was 1 msec as opposed to 0.5 msec used by many authors as 1 msec latency difference was recommended by Werner and Andary ***(10)*** among patients with DPN as it showed more specificity than the 0.5msec value which yielded many false positive results.

In this study there was a statistically significant difference between patients with clinical manifestations of CTS and those without CTS (p<0.01) as regards the 2L-INT latency difference; however there was a statistically non-significant difference between the two groups of patients as regards the DM-DU SLD or the DM-DU MLD.

In our study we failed to elicit a sensory response from the fourth digit in 9 out of 20 (45%) of hands with severe sensori-motor demyelinating and axonal DPN. A previous study by Noel ***(15)*** described failure to elicit a sensory action potential from the second digit on stimulation of the median nerve at the wrist in 9 out of 11 (81%) of patients with a severe sensori-motor demyelinating and axonal DPN. This could be attributed to the large reduction in the number of active fibres ***(15)***. In contrast to 2L-INT latency difference which could be elicited from all our studied hands (100%).

In our study 2L-INT latency difference could detect CTS in two hands with clinical CTS who had no elicited response from the thenar eminence due to severe CTS; as the abductor pollices brevis muscle is the most radial and first muscle to atrophy ***(16).*** Thus showing superiority to DM-DU MLD in the diagnosis of severe CTS associated with wasting of the thenar eminence. In a study by Löscher and colleagues ***(17)*** 31 out of 36 hands could elicit a 2L –INT latency difference and could diagnose CTS although median motor and sensory responses could not be elicited through the standard median nerve conduction studies.

In this study, 2L-INT latency difference was capable of diagnosis of CTS among patients with DPN with a sensitivity of 80%, this came in accordance with Yagci and colleagues ***(18)*** who stated that CTS could be identified in patients with DPN using the 2L –INT latency difference with a sensitivity of 88.4% at a distance of 8cm between the stimulating and active recording electrodes at a cut off value of 0.4 msec and using the DM- DU SLD with a sensitivity of 54% at a stimulating distance of 12-13 msec at a cut off value of 0.5 msec ***(18).***

Badry and colleagues ***(19)*** used 2L-INT latency difference to diagnose CTS among patients with end stage renal disease on renal dialysis with uremic neuropathy. The frequency of carpal tunnel syndrome among their studied patients using standard nerve conduction parameters was 51.4%; however, the frequency increased substantially to 83.8% when 2L-INT latency difference was included in the criteria for the diagnosis. They concluded that 2L-INT latency difference is a sensitive test to predict CTS in presence of peripheral neuropathy.

2L-INT latency difference could diagnose CTS in patients with DPN at a specificity and accuracy of 50% and 60% respectively; which was more than the specificity and accuracy of the DM-DU SLD which showed a specificity and accuracy of 30.6% and 51% respectively and the DM-DU MLD which showed a specificity and accuracy of 45% and 55.2% respectively.

We studied the sensitivity, specificity and accuracy of the 2L –INT latency difference in diagnosis of CTS among the different grades of DPN (mild, moderate and severe) in comparison to the other methods we used.

Among patients with mild DPN, 2L-INT latency difference showed (66.7%) sensitivity. This value is equal to DM-DU SLD and DM-DU MLD.2L-INT latency difference specificity was (75%) equal to DM-DU MLD however less than DM-DU SLD. Its accuracy was (71.4%) equal to DM-DU MLD and more than DU-DM SLD.

Among patients with moderate DPN, 2L-INT latency difference showed (100%)sensitivity. This value is equal to the DM-DU SLD and DM-DU MLD.2L-INT latency difference together with DM-DU MLD specificity was less than DM-DU SLD. Its accuracy was (33.3%) equal to DM-DU MLD and less than DU-DM SLD.

Among patients with severe DPN, 2L-INT latency difference showed (100%) sensitivity. This

value is equal to the DM-DU MLD and more than DM-DU SLD.2L-INT latency difference together with DM-DU MLD and DM-DU SLD showed no specificity among patients with severe DPN. Its accuracy was (40%); more than DM-DU SLD (25%)and DU-DM MLD (25%).

6.Conclusion:

We can conclude from this study that 2L-INTlatency difference is an easy, and accurate method for the diagnosis of CTS in type 2 DM patients with DPN especially those with severe DPN. We recommend its corporation in their electrodiagnostic workup whether they complain of clinical manifestations of CTS or not.

Conflict of interest:

The authors have no conflict of interest to declare**.**

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