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ORIGINAL ARTICLE

The Accuracy of Provocative Tests on Diabetic Patients with Suspected Carpal Tunnel Syndome and Comparison with Nondiabetics

Çiğdem Tura Bahadır ¹ ORCID: 0000-0001-6492-3064 Sinan Bahadır ² ORCID: 0000-0002-1037-5645	ABSTRACT					
	Objective: Carpal tunnel syndrome in diabetic patients differ in some aspects from those in the nondiabetic population. The study was designed to evaluate the diagnostic accuracy of widely used provocative tests in the diabetic population in comparison to nondiabetic population.					
	Materials and Methods: 87 nondiabetic and 25 diabetic hands suspicious of carpal tunnel syndrome were included in this retrospective study. The presence of carpal tunnel syndrome is confirmed by nerve conduction studies. The hands were divided into DM- and DM+ groups based on patients' diabetes mellitus history. From patient records, results of Tinel's, Phalen's, Durkan's, median nerve compression, and scratch collapse tests were obtained. Sensitivity, specificity, positive predictive value, and negative predictive values of tests are calculated for each population and then compared with each other.					
	Results: Tinel's test had a higher sensitivity in the diabetic population. Accuracies of Phalen's, Durkan's, median nerve compression, and scratch collapse tests in diabetic patients were similar to those in diabetic patients. None of the tests had a high enough sensitivity to be used alone in either group. Scratch collapse test had very high specificity in both groups but very low sensitivity.					
¹ Department of Endocrinology and Metabolism, Amasya University Faculty of Medicine, Amasya, Turkey. ² Department of Neurosurgery, Amasya University Faculty of Medicine, Amasya, Turkey. Corresponding Author: Sinan Bahadır Department of Neurosurgery, Amasya University Faculty of Medicine, Amasya, Turkey. E-mail: sinanbahadir@windowslive.com	Conclusion: The studied provocative tests have comparable accuracy for carpal tunnel syndrome in diabetic patients to those in nondiabetic patients, with Tinel even having higher sensitivity. But excluding scratch collapse test, none of the tests is strong enough to achieve a diagnosis					
	and none is sensitive enough to rule out a disease. Key words: carpal tunnel syndrome, diabetes mellitus, provocative tests					

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INTRODUCTION

Carpal tunnel syndrome (CTS) is the most frequently seen nerve entrapment with a prevalence of 2-4% in the general population [1]. Diabetes mellitus (DM) is an important risk factor for CTS and the prevalence of CTS in the diabetic population varies between 15-30% [2].

CTS is primarily a clinical syndrome. Diagnosis can be based on clinical presentation, physical and neurological examination, provocative tests, electrodiagnostic studies, magnetic resonance imaging, and ultrasonography [3]. In the past, it was observed that some patients with negative electrodiagnostic study results showed improvement after surgery [4]. This finding led to a need for tests that are applicable in the clinical setting and eventually several provocative tests have been developed [4]. The most commonly used provocative tests in the diagnosis of CTS are Tinel's and Phalen's tests [3]. Besides these, Durkan's test, median nerve compression test (MNCT), and relatively novel scratch collapse test (SCT) are among the provocative tests used for CTS diagnosis [5-7]. Though positive nerve conduction studies (NCS) are regarded as the most objective diagnostic criteria, provocative tests are still in use as part of patient evaluation [8]. Moreover, due to the possibility of false-negative results in electrodiagnostic studies, some physicians rely solely upon provocative tests for the diagnosis [9]. And finally, these tests can be used by general practitioners to refer suspected cases to a specialist.

Since diabetes mellitus is a significant risk factor for CTS, there are several studies on diabetic patients with CTS. It has been shown that CTS in the diabetic population may be different than those in the nondiabetic population in some aspects [10-13]. Regarding demographics, Zyluk and Puchalski found that the involvement of older age people, men, and bilateral hands was higher in diabetic CTS [10]. Regarding pathophysiological properties, Tekin et al found that synovial edema, vascular proliferation, and increased wall thickness were more common in diabetic CTS patients [11]. For electrodiagnostic studies, Tsai et al showed that there were significant differences in distal sensory latency, amplitude, and sensory nerve conduction velocity between diabetic and nondiabetic CTS patients [12]. Regarding the response to surgery, Özer et al demonstrated that diabetic patients

require a greater improvement in Boston Carpal Tunnel Questionnaire (BCTQ) scores to be satisfied [13].

There is a vast amount of studies on idiopathic CTS in the literature. However, to the best of our knowledge, despite potential differences between diabetic and nondiabetic population, there isn't a study that evaluated the accuracy of provocative tests in the diabetic population.

In this study, the primary aim was to evaluate the accuracy of provocative tests in the clinical assessment of CTS in the symptomatic diabetic patients. Secondary aim was to compare the findings with those in nondiabetic patients.

MATERIALS AND METHODS

A retrospective study of consecutive patients referred to a single neurosurgeon for suspected CTS from November 2020 to November 2021 was performed upon approval by the institutional review board (Amasya University Ethical Commitee of Non-Invasive Clinical Research, Date: 07.10.2021, No: 143). Because of the study's retrospective nature, requirement for informed consent is waived.

The patients were extracted from hospital records with a preliminary diagnosis of CTS. The inclusion criteria were: hands with characteristic symptoms for CTS (paresthesia, pain, weakness, or clumsiness at the distribution site of median nerve; aggravation of symptoms by sleep, repeated movements of hands or wrist, prolonged fixed position; relief of symptoms by shaking hands or position change) and evaluation by provocative tests and electrodiagnostic studies. The exclusion criteria were: age younger than 18 years old, less than 1 month of symptom duration, previous history of fracture, laceration, or operation in the symptomatic hand, cervical radiculopathy, inflammatory joint disease, renal insufficiency, thyroid function disorders, pregnancy, and missing demographic, clinical and/or examination data.

In Tinel's test, the distal wrist crease is tapped 4-5 times and the onset of symptoms is considered positive [14]. In Phalen's test, the wrist is held in palmar flexion while the elbow is extended and considered positive if the symptoms appear

within one minute [15]. For Durkan's test, the examiner applies moderate compression with his/her two thumbs on the flexor retinaculum of the symptomatic hand for 30 seconds [5]. MNCT was performed while the elbow is extended, the forearm is supinated, and the wrist is flexed at 60° [6]. With his/her thumb, the examiner applies pressure on the carpal tunnel [6]. In SCT test, with elbows in 90° flexion and forearms in 90° pronation, the patient resists with bilateral shoulder external rotation to the force applied on the lateral side of forearms [7]. In the presence of allodynia secondary to nerve entrapment, a temporary decrease in muscle resistance occurs following a gentle swipe of the nerve entrapment area with the examiner's fingers, and the test is considered positive [7].

Demographic data and past disease history (including laboratory and imaging studies when necessary) of the patients; and presenting symptoms, examination findings, and NCS results of symptomatic hands were extracted from the hospital's patient database and were recorded. The hands were divided into DM- (non-diabetic) and DM+ (diabetic) groups based on the absence or presence of DM, respectively. Then the groups were subdivided into two subgroups as CTS- and CTS+ based on the absence or presence of CTS based on electrodiagnostic studies.

Statistical Analysis

Continuous data are expressed as mean \pm standard deviation, categorical data are expressed as count and frequency. Continuous data were evaluated either by unpaired t-test or Mann-Whitney U test based on the distribution of data which was analyzed by the Shapiro-Wilk test.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of evaluated provocative tests were calculated for DM- and DM+ groups separately. Intergroup comparison was performed by Fisher's exact test. P<0.05 was considered statistically significant.

RESULTS

The retrospective data search yielded 183 hands (110 patients) that were evaluated by electrodiagnostic studies for preliminary diagnosis of CTS. 54 hands were excluded for thyroid function disorders, extremity and peripheral nerve pathologies, and

compressive cervical disc herniation. Demographic data of 80 patients and 129 hands that were included in the study are summarized in Table 1. Diabetic patients were older and have a higher body mass index (BMI) compared to nondiabetic patients, but symptom duration did not differ between the two groups. The incidence of bilateral symptoms was also similar in both groups but electrodiagnostically confirmed bilateral CTS was significantly more frequent in diabetic patients. CTS was confirmed electrodiagnostically in all but two hands (95.2%) in the DM+ group whereas this rate was lower (73.6%) in nondiabetic hands (P=0.040).

Provocative tests used in the clinical setting and thus evaluated in this study were Tinel's test, Phalen's test, MNCT, Durkan's test, and SCT. The sensitivity, specificity, PPV, and NPV of tests were summarized in Table 2.

The most sensitive test in both groups was Phalen's test with no significant difference between groups (70.5% for DM-, 76.3% for DM+). The least sensitive test was SCT in both groups. Regarding sensitivity, only Tinel's test was different between groups (P=0.035), however, it was the second least sensitive test.

SCT was the most specific test in both groups (95.7% for DM-, 100.0% for DM+). No test varied significantly regarding specificity between the two groups. The second most specific test in DM- was Tinel's test (73.9%).

Both in DM- and DM+ groups, SCT had the highest PPV (92.3% and 100.0%, respectively). Excluding SCT, the overall highest PPV in DM- group was 78.3% (Durkan's test) while the overall smallest PPV in the DM+ group was 86.7% (Durkan's test). Still, only MNCT showed a significant difference between DM- and DM+ groups (75.6% vs 95.8%, respectively; P=0.457).

Overall NPVs were very low in both groups. The highest NPVs were achieved with Phalen's test (33.3%) and SCT (5.7%) in DM- and DM+ groups, respectively.

DISCUSSION

The study revealed a few important findings. None of the provocative tests had a significantly worse sensitivity in the diabetic group compared

	Nondiabetic patients (n=55)	Diabetic patients (n=25)	Р
Gender (M:F)	15:40	3:22	0.158
Age (years) (median, range)	47 (28-76)	56 (19-72)	0.002*
BMI (median, range)	27.43 (21.29-47.27)	35.11 (24.14-47.66)	0.001*
Symptomatic hands (n,%)	87 (79.0%)	42 (84.0%)	0.524
Bilateral symptoms (n)	32	17	0.465
Confirmed bilateral CTS	21/32	16/17	0.037*
Duration of diabetes mellitus (median, range)	Not applicable	10 years (2 years – 22 years)	
Type of diabetes (Type I:Type II)	Not applicable	1:24	
Diabetic neuropathy (n)	Not applicable	7	
Diabetic vasculopathy (n)	Not applicable	2	
Diabetic nephropathy (n)	Not applicable	1	
	Nondiabetic hands (n=87)	Diabetic hands (42)	
Confirmed CTS (n,%)	64 (73.6%)	40 (95.2%)	0.040*
Symptom duration (months) (median, range)	12 (1-240)	12 (1-240)	0.479
Motor weakness (n,%)	9 (10.3%)	5 (11.9%)	0.770
Sensory disturbance (n,%)	29 (33.3%)	15 (35.7%)	0.844
Tenar atrophy (n,%)	7 (8%)	21 (50%)	0.095
Number of Tinel's test performed (n)	87	42	
Number of Phalen's test performed (n)	82	40	
Number of Durkan's test performed (n)	48	23	
Number of MNCT performed (n)	86	42	
Number of SCT performed (n)	87	40	

* Statistically significant

M: male, F: female, BMI: body mass index, CTS: carpal tunnel syndrome, MNCT: median nerve compression test, SCT: scratch collapse test

Table 2. Sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) of the tests when used alone.

	Sensitivity (%)		Specificity (%)		PPV (%)			NPV (%)				
	DM-	DM+	Р	DM-	DM+	Р	DM-	DM+	Р	DM-	DM+	Р
Tinel	26.6	47.5	0.035*	73.9	50.0	0.490	73.9	95.0	0.100	26.6	4.5	0.033*
Phalen	70.5	76.3	0.644	42.9	0.0	0.502	78.2	93.5	0.075	33.3	0.0	0.076
Durkan	51.4	61.9	0.580	61.5	0.0	0.200	78.3	86.7	0.681	32.0	0.0	0.152
MNCT	54.0	57.5	0.839	52.2	50.0	1	75.6	95.8	0.046*	29.3	5.6	0.049*
SCT	18.8	13.2	0.587	95.7	100.0	1	92.3	100.0	1	29.7	5.7	0.005*

* Statistically significant

MNCT: median nevre compression test, SCT: scratch collapse test

to nondiabetic group. In fact, Tinel's test had a significantly higher sensitivity in the diabetic group. Regarding specificity, two groups didn't differ in any provocative tests. SCT had the highest specificity in both groups. One important issue is almost all of the symptomatic hands in diabetic patients had electrodiagnostically confirmed CST, which is close to PPV of provocative tests, excluding SCT. The most sensitive test was Phalen's test in both groups. Durkan and MNCT did not excel in any parameter in any group and are not the best candidates to be used as standalone tests. The sensitivity of SCT was very low in both groups compared to the literature. However, it had a very high specificity and PPV.

CTS is principally a clinical syndrome where an asymptomatic patient cannot be diagnosed with the disease despite having a positive NCS, which should be considered as median neuropathy at the wrist [9]. Though NCS is regarded as the most reliable diagnostic tool for CTS, provocative tests have still been in use for clinical evaluation [3].

The accuracy of provocative tests in idiopathic CTS has been widely studied in the literature [4, 6, 7, 16-23]. When the diagnosis is based on electrodiagnostic studies, sensitivity, specificity, PPV, and NPVs of these tests show great variation across different reports [4, 6, 7, 16-23]. Such studies either excluded diabetic patients, or didn't look for DM at all, or only evaluated those with neuropathy. So, the accuracy of provocative tests in diabetic patients remained unclear.

One of the oldest and most widely used provocative tests is Tinel's test [14]. Tinel's sign is defined as a phenomenon observed during the regeneration following demyelination in peripheral nerve injuries [18, 24]. In their prospective study which didn't exclude any diabetic patients, Tetro et al compared Tinel's, Phalen's, Durkan's, and MNCT tests and found a sensitivity and specificty values of 75% and 91%, respectively, for Tinel's test [6]. They also hypothetically found Tinel's test's PPV and NPV ranging between 29-89% and 78-99%, respectively [6]. In Mondelli et al's and El Miedany et al's studies which both excluded diabetic patients, Tinel's sensitivity (30% and 41%, respectively) was much lower than Tetro et al's findings, but specificity (65% and 90%, respectively) was similar [18, 20]. In a recent study by Kasundra et al which included diabetic patients, Tinel's test had a sensitivity and specificity of 78.5% and 91.3%, respectively [3]. In another prospective study by Küçükakkaş et al, which also included diabetic patients, Tinel's test showed a sensitivity of 89%, a specificity of 41%, a PPV of 59%, and an NPV of 80% [25]. This variation in sensitivity of Tinel's test might have resulted from inclusion of diabetic patients. But in 2020, in a prospective study conducted on symptomatic patients that included diabetic patients, Zhang et al found Tinel's test's sensitivity as 47%, specificity as 56%, PPV as 90%, and NPV as 11% [23]. Tinel's sensitivity in our study was also higher in diabetic hands which can be attributed to ongoing neuronal injury in diabetic patients.

The purpose in Phalen's test is to provoke symptoms by inducing ischemia with compression of the median nerve which is already under compression and has a lower threshold for mechanical pressure [17]. Tetro et al found a lower sensitivity and specificity values (61% and 83%, respectively) for Phalen's test compared to Tinel's test [6]. They found PPV and NPV for Phalen's test ranging between 1679% and 68-98%, respectively, depending on the prevalence of the disease [6]. Mondelli et al and El Miedany et al found similar, albeit slightly lower, sensitivity values for Phalen's test (59% and 47%, respectively) compared to Tetro et al's study, but specificity values varied greatly (93% and 17%, respectively) [18, 20]. Zhang et al found Phalen's test had a sensitivity of 50%, specificity of 33%, PPV of 86%, and NPV of 7% [23]. Kasundra et al found higher sensitivity (84.9%) and specificity (73.9%) values for Phalen's test compared to previous studies [3]. Küçükakkaş et al's findings, showed similar sensitivity, specificity, PPV, and NPV for Phalen's test (86%, 57%, 66%, and 81%, respectively) to those in previous reports [25]. Similarly, in our study, Phalen's test showed no significant difference between diabetic and nondiabetic hands.

Durkan's test has a similar mechanism to Phalen's test. Its sensitivity and specificty were found as 75% and 93%, respectively, by Tetro et al [6]. Its PPV ranged between 35-91%, and NPV ranged between 79-99% [6]. In their prospective study where diabetic patients were not excluded and only symptomatic patients were included, Kaul et al found sensitivitity and specificity of Durkan's test as 52.5% and 61.8% respectively, much lower than Tetro et al's findings [17]. PPV and NPV of Durkan's test were 66.6% and 47.2%, respectively, according to same study [17]. Küçükakkaş et al found sensitivity of 96% and a specificity of 67% for Durkan's test [25]. They found similar PPV (73%) and NPV (94%) to Tetro et al's findings [25]. In Zhang et al's study, Durkan's test had a sensitivity of 71%, similar to literature; specificity of 22% that is very low compared to previous studies; PPV of 89%; and NPV of 8% [23].

MNCT attempts to combine Phalen's and Durkan's tests in one test. Tetro et al found MNCT to be more sensitive (86%) than both Tinel's, Phalen's and Durkan's tests, but only more specific (95%) than Phalen's test [6]. It also had a higher PPV and NPV (94% and 87%, respectively) than Phalen's test when the hypothetical prevalence rate was 0.5 [6]. On the other hand, Cheng et al, in their prospective study, reported a much lower sensitivity (44%), but a similar specificity (99%) for the test [7]. Zhang et al found a similar sensitivity (84%) to Tetro et al's findings accompanied with a very low specificity 11% [23]. They also found a PPV of 89% and NPV of 8% [23].

In the relatively novel SCT test, the exact mechanism is unknown, it is thought to be related to the cutaneous silent period where inhibitory spinal reflexes play a role [7]. Cheng et al initially a sensitivity of 64% and a specificity of 99% for SCT in their paper where they introduced the test [7]. They also found a PPV of 99% and a MPV of 82% fort he test [7]. They found the test significantly more sensitive than both Tinel's test and MNCT [7]. In a prospective study by Simon et al, in which diabetic patients were not excluded, SCT had a sensitivity of 28%, specificity of 75%, PPV of 81%, and NPV of 20% [22].

Such a variety among studies regarding provocative tests -including ours- may arise from study design, selected population, measurement and evaluation methods, and statistical methods [18]. A high level of sensitivity in a population consisting of patients with severe and classical symptoms would not be achievable in a population that includes less typical cases [17]. On the other hand, when the control group is composed of healthy subjects, there can be specificity bias [17]. In a study by Gerr et al [26], the specificity of Phalen's test was 97% when the control group consisted of healthy subjects, however, it dropped to 61% when the control group is composed of patients with symptoms but didn't have CTS. Similarly, Descatha et al [27] found that provocative tests were not effective screening tools in patients that don't have complaints severe enough to seek healthcare. For these reasons, it is essential to interpret the findings of provocative test studies with the study population in mind.

Though some studies included diabetic patients in their cohorts while evaluating the accuracy of provocative tests, none had compared the findings between these two group of patients. The findings of this study showed that some tests's accuracy may differ between these patients.

The study is not deprived of limitations: First, since the study is retrospective, blindness could not be achieved. However, apart from SCT, all the tests depend on patients's responses and examiner's bias hardly affects the results. Second, there might have been selection bias since only symptomatic hands were evaluated. However, since these tests aren't screening tests for healthy subjects but tests that are performed on patients with complaints, we think that this type of study population conforms to clinical practice better. Third, since both symptomatic hands were included in the study, the samples are not completely independent. Finally, the diabetic group had a relatively low number of samples compared to non-diabetic group. Besides, conditions which are frequently seen in the diabetic population like neuropathy, hypertension, and hyperlipidemia, or disease related conditions such as blood glucose control status, treatment type, or type of DM might have impaired the homogeneity of this group. Also, it must be noted that in the diabetic group, only 2 hands turned out to be CTS negative and this low value might have affected the reliability and generalizability of specificity and NPV of tests in this group.

CONCLUSION

Provocative tests in diabetic patients are as accurate as in the nondiabetic population. Excluding SCT which has a very high specificity, none of the tests are sensitive and specific enough to be used alone for the clinical diagnosis of CTS, regardless of diabetes mellitus. In populations similar to those of the study, SCT can be used as a diagnostic tool. On the other hand, no negative results of these tests can rule out the disease.

Author contribution

Study conception and design: ÇTB and SB; data collection: ÇTB and SB; analysis and interpretation of results: SB; draft manuscript preparation: ÇTB and SB. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Amasya University Ethical Commitee of Non-Invasive Clinical Research (Protocol no: 143/Date: 07.10.2021).

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Conflict of interest

The authors declare that there is no conflict of interest.

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