USE OF ULTRASONOGRAPHIC TESTING IN DIAGNOSIS OF CARPAL TUNNEL SYNDROME

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ABSTRACT

Background: Carpal tunnel syndrome (CTS) is among the most common disorders of the upper extremity. At the moment electrodiagnostic testing (EDX) is often identified as a gold standard for CTS diagnosis. Recent studies show that ultrasonographic testing may become an alternative confirmatory tool for the disorder.
Aim: To compare the cross sectional area (CSA), wrist-to-forearm ratio (WFR) and the elasticity of the median nerve (MN) between patients with CTS and healthy subjects and to evaluate diagnostic usefulness of these measurements in diagnosis of CTS.
Materials and Methods: Patients diagnosed with CTS as well as healthy volunteers were examined by two observers, experienced radiologist and medical resident with 1 year of experience. Both were blinded to the diagnosis. Standard measurements of CSA of the MN were performed. Elasticity of the nerve was measured using strain ratio elastography. In order to evaluate the diagnostic utility of ultrasound, recently proposed diagnostic algorithm was tested (Goldberg G, 2016). QuickDASH questionnaire was used to evaluate the ability of ultrasound and EDX to assess symptom severity of CTS patients.
Results: 27 wrists with CTS and 25 healthy wrists were analyzed. CSA and WFR were significantly higher in CTS patients than in healthy volunteers. However, there was no significant difference in elasticity of the MN in our sample. There was no correlation between the MN conduction velocity, clinical symptoms and ultrasound measurements. Logistic regression revealed that ultrasound measurements had weak relationship between prediction and grouping. Diagnostic algorithm had specificity of 81.5% and sensitivity of 24%.
Conclusion: Currently there is no reliable ultrasonographic diagnostic algorithm. Further ultrasound studies are needed for the development of better diagnostic tools combining various diagnostic techniques.

***Keywords*:** carpal tunnel syndrome, cross sectional area, elastosonography, strain ratio, quickDASH

INTRODUCTION

Carpal tunnel syndrome (CTS) is among the most common disorders of the upper extremity. One of the recent studies show that it affects around 8% active workers with higher rates in females and older age people [1]. Main symptoms of CTS are numbness, tingling, weakness and pain that in severe cases can cause disability of the arm and interfere with person's daily living activities and result in decreased quality of life.
At the moment electrodiagnostic testing (EDX) is often identified as a gold standard for CTS diagnosis [2] together with clinical symptoms and is widely used if surgical treatment is planned. EDX confirms a clinical diagnosis of CTS with a high degree of sensitivity (56% to 85%) and specificity (at least 94%) [3]. Another useful technique in examining CTS is ultrasound. Enlargement of the median nerve (MN) at the distal wrist crease is sensitive (65% to 97%) and specific (73% to 98%) [4], however pathological size of the cross sectional area (CSA) is still debated. Combining measurements of strain elastography

and CSA of the MN may improve diagnostic accuracy [5]. Novel ultrasonography techniques such as shear wave elastography shows promising results in CTS diagnostics with high sensitivity and specificity as well (93%, 89% respectively) [6]. Elastography may be usefull not only for establishing the diagnosis, it also allows to evaluate severity of CTS [7].

These results shows that ultrasound may be a good alternative to EDX because it is less expensive, causes no pain and requires shorter waiting time for the patients to be examined. As about 60% of patients at diagnosis show objective clinical deficit and 80% slowing of distal motor latency of the MN [8], more easily available ultrasonographic testing may shorten the waiting time and help to diagnose CTS earlier.

The goal of this study is to compare the CSA, wrist-to-forearm ratio (WFR) and the elasticity of the MN between patients with CTS and healthy subjects and to evaluate diagnostic usefulness of these measurements in diagnosis of CTS.

MATERIALS AND METHOD

Study protocol was approved by local institutional ethics committee. Written informed consent was obtained from all participants.

Population and procedure

Between December 2015 and March 2016 we examined 26 subjects (27 wrists with CTS and 25 healthy hands). As one participant had one hand with CTS and the other without, he was assigned to both control and patients groups. Table 1 shows the main characteristics of patient and control group included in this study. All patients were symptomatic and had electrodiagnostically proven CTS. Subjects meeting electrophysiological criteria for polyneuropathy were excluded. Other exclusion criteria for both groups were prior wrist trauma, operation, diabetes mellitus and rheumatic diseases.

Table 1. Demographic data of healthy volunteers and patients with CTS

Characteristic	Control group (n=13)	CTS group (n=14)	P Value
Sex (n)[1]			0.385
Female	9 (69.2)	12 (85.7)	
Male	4 (30.8)	2 (14.3)	
Age (y)[2]	59.2 9.7	57.7 9.8	0.867
Height (cm)	166.9 7.1	162.4 8.1	0.128
Weight (kg)	75.2 13.8	78.3 20.5	0.720
BMI[3]	27.1 5.2	29.6 6.8	0.449

1Data are numbers of patients or volunteers with percentages.
2 Data are means ± standard deviations.
3 Body mass index (kg/m2).

ULTRASONOGRAPHIC MEASUREMENTS ACQUISITION

Experiment was conducted by two observers. First observer was a radiologist with 30 years of experience and the second was a medical resident with 1 year of experience. Both were blinded to the diagnosis of CTS and measurements of each other.

All subjects were comfortably seated and asked to rest their arm on the table with elbow flexed 90° and fingers kept relaxed. A slight flexion of the wrist was maintained during the measurement. First, CSA of the MN was measured at the distal wrist crease (CSA-D) which corresponds to the proximal inlet of the carpal tunnel at the scaphoid-pisiform level. Next, it was measured in the forearm by tracing the MN 12 cm proximally (CSA-P). While scanning in the transverse plane, using conventional B-mode ultrasonography, the hyperechoic boundary of the nerve was traced by a continuous line and the CSA was acquired.

Representative ultrasonographic image is shown in Figure 1. WFR was calculated dividing the CSA-D by CSA-P value. All ultrasound images were acquired using Phillips EPIQ 7 ultrasound system and L12-5 linear array transducer.

Elasticity of the MN was measured using strain elastography. Measurements were taken at the distal wrist crease. Low-frequency compression of the tissues was applied manually by the hand-held ultrasound transducer. Ellipse located on CSA of the MN was used as a region of interest (ROI), the adjacent tissue to the right of the MN at the same depth was used as the reference. Representative ultrasonographic image is shown in Figure 2. Relative strain was measured and strain ratio was calculated using Philips QLAB software's Q-App Elastography Quantification (EQ) application, which compares the strain values between two user-defined areas of tissue in the elastrogram. Because manual compression was used and some differences in tissue displacement depending on different levels of pressure may occur, the strain ratio was measured three times and mean value was used for data analysis and comparison, with higher strain ratio number meaning higher stiffness.

ULTRASONOGRAPHIC DIAGNOSTIC ALGORITHM

As ultrasonographic screening is potential time and health care costs saving method, we decided

Figure 1. Transverse image. CSA-D measurement using continuous trace.

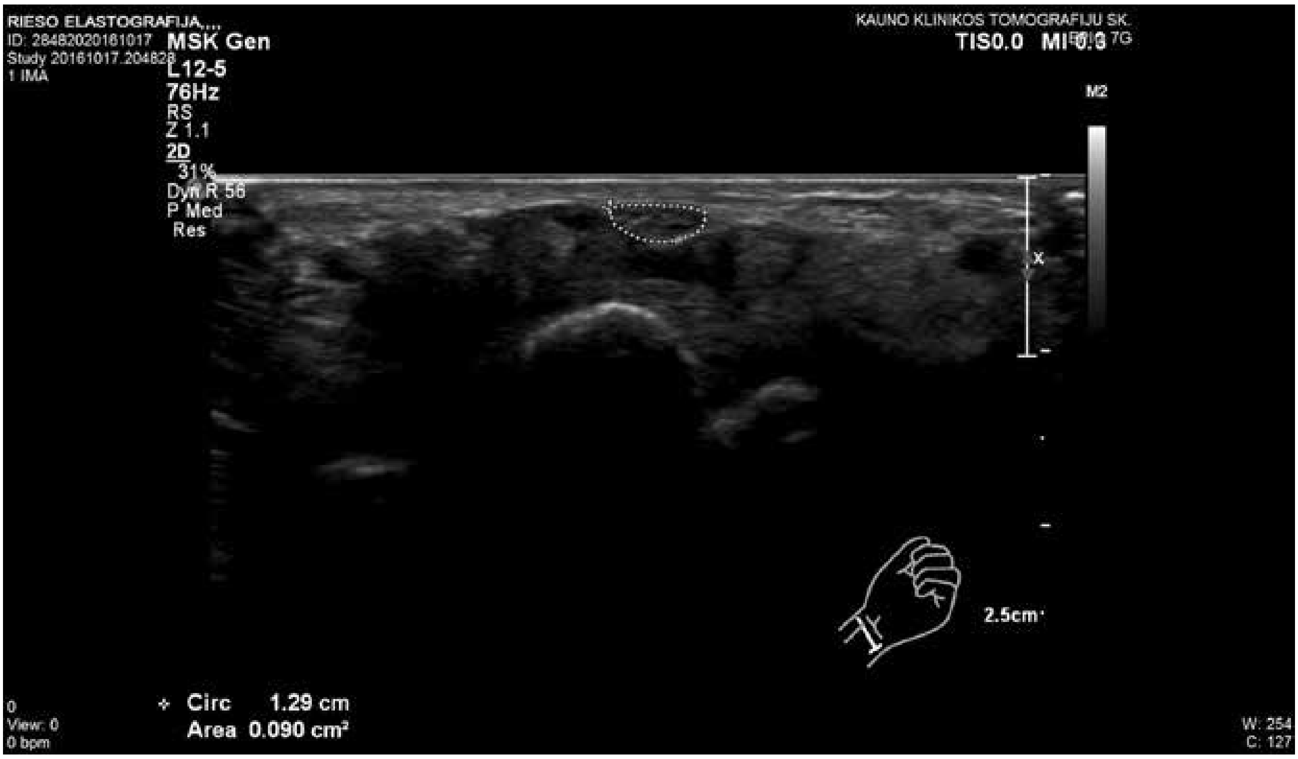
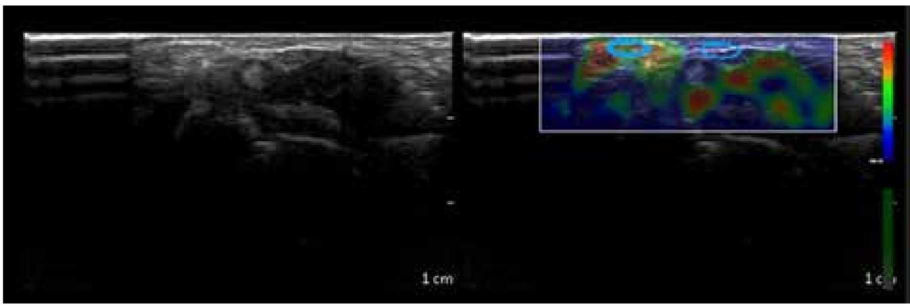


Figure 2. Transverse image. Strain ratio measurement.



to test one of the recently proposed ultrasonographic diagnostic algorithms for CTS (Goldberg G, 2016). It was based on analytic literature review and suggests that patients who present with typical or atypical symptoms without clinical signs of motor axon deficiency should be first examined by ultrasound and if their CSA is larger or equal 9 mm^2 and/or WRF is higher or equal than 1.4 should be tested eletrodiagnostically. The goal of the test is to assess potential of the algorithm in clinical practice by evaluating its sensitivity and specificity.

ULTRASOUND AND EDX RELATIONS WITH DISABILITY OF THE ARM IN CTS GROUP

Each CTS patient was asked to fill QuickDASH, one of a hand-specific questionnaires that may help to determine functionality in patients with CTS. We decided to use validated lithuanian version of QuickDASH questionnaire because its results well correlates with Boston Carpal Tunnel Questionnaire which is most widely used for evaluating CTS severity [9]. QuickDASH questionnaire was used in order to compare ultrasonographic and EDX results with the disability of the arm in CTS group.

STATISTICAL ANALYSIS

All data analysis was performed using SPSS Statistics Version 23 (IBM). First of all, the ultrasonographic measurements were compared between groups to check the hypothesis that strain ratio of the MN, WFR and CSA-D are significantly higher in patient group than in control group. Independent samples Mann-Whitney U test was used for this. As majority of the patient group had mild CTS, it was not possible to compare ultrasonographic measurements between different degrees of CTS. To evaluate the relation between EDX and ultrasonographic measurements in patient group Spearman's rank order correlation was used. MN conduction velocity (MNCV) from wrist to second digit (as it is one of the first indicators of CTS), CSA-D, WFR and strain ratio index were compared. To test how well would MNCV and ultrasound measurements predict diagnosis on their own, without the use of algorithm, logistic regression was used. Algorithm was tested by counting true positives and negatives, false positives and negatives and calculating specificity and sensitivity. Results between examiners were compared using related samples Wilcoxon signed rank test.

RESULTS

According to radiologist, patient group had statistically higher CSA-D with the mean of 9.8 mm^2 versus control group 8.4 mm^2 ($p=0.016$). WFR was statistically higher in patient group as well with the mean of 3.3 versus control group 1.6 ($p=0.047$). There was no significant difference in elasticity of the MN in our sample, with mean strain ratio 1.6 in patient group and 1.4 in control group ($p=0.109$). We found no correlation between MNCV and ultrasonographic measurements ($p>0.05$).

There was no statistically significant difference between experienced radiologist's and resident's CSD-D ($p=0.935$), but there was statistically significant difference between doctor's and resident's CSA-P measurements ($p=0.045$), followed by statistically significant difference between WFR ($p=0.03$). There was no statistically significant difference between strain ratio measured by the doctor and by the resident ($p=0.437$).

A logistic regression analysis was conducted to predict diagnosis of CTS using only CSA-D and WFR measurements. A test of the full model against a constant only model was statistically significant, indicating that the predictors as a set reliably distinguished between patient and control groups (chi square = 11.588, $p<0.003$ with df= 2). Nagelkerke's R^2 of 0.266 indicated a weak relationship between prediction and grouping. Prediction success overall was 67.3% (72% for control group and 63% for CTS group) compared to constant only model's 51.9%. Adding strain ratio to the model didn't make a significant improvement in prediction making overall prediction success just a little higher 69.2% (76% for control group and 63% for CTS group, chi square = 11.643, $p<0.009$ with df = 3, Nagelkerke's $R^2 = 0.268$).

According to radiologist, in patient group there were 22 hands whom would be correctly send to the EDX using proposed algorithm (indications for EDX is CSA-D ≥ 9 mm^2 and WFR ≥ 1.4 mm^2), and 5 hands would have been falsely declared as healthy. That gave the algorithm specificity of 81.5%. In control group there were 19 false positive hands and 6 true negative hands, which gave the algorithm sensitivity of 24%. Resident doctor also showed similar specificity (100%) and sensitivity (40%) as a radiologist.

QuickDASH results varied from 13.6 to 65.9, the higher result meaning the greater disability. In CTS group disability of the arm was significantly higher in subjects with slower nerve conduction velocity. However, CSA-D, WFR and nerve stiffness were not significantly higher in people with greater disability of the arm.

DISCUSSION

In our study we got similar results when comparing CSA and WFR between patient and control group like other studies [6,14-16] as there was a statistical difference between the groups, despite higher CSA values in our control group when compared to other studies 6.3-7.9 mm^2 [6,14].

Table 2. Mean CSA-D, CSA-P, WFR and elastographic values for patients and control group by both examiners

Diagnostic Test	Radiologist		P Value	Resident		P Value
	Control group (n=13)	CTS group (n=14)		Control group (n=13)	CTS group (n=14)	
CSA-D	8.4 ± 2.2	9.8 ± 2.1	0.016	8.1 ± 1.7	11.0 ± 3.5	0.001
CSA-P	5.3 ± 1.8	4.6 ± 2.0	0.608	5.0 ± 1.0	4.1 ± 2.6	0.016
WFR	1.6 ± 0.4	3.3 ± 3.7	0.047	1.7 ± 0.7	3.7 ± 2.8	0.000
Strain ratio	1.4 ± 0.6	1.6 ± 0.6	0.109	1.5 ± 0.6	3.3 ± 0.4	0.410

Previous studies have shown that stiffness of the MN in CTS patients is significantly higher than in healthy subjects [5,12,13]. However, we didn‘t find difference in nerve stiffness between the groups. It could be due to different methods applied by other authors in measuring elasticity of the MN, for example, using acoustic coupler with a standardized elasticity. The fact that most of our CTS cases have mild CTS also could have influenced the results. However, one of the recent studies that used similar technique as ours shows that strain elastography do not exclude patients with mild CTS [10]. Also, anthropometric factors such as body mass index may affect the results [11].

Findings about ability of ultrasound to distinguish between different degrees of CTS are controversial. According to some authors, ultrasound should be able to distinguish between different degrees of CTS [7], some concludes that it cannot categorize disease severity [10]. Limited number of studies using same methods exists, so it is not yet possible to evaluate true diagnostic value of strain ratio elastography.

We found no relations between sensory MN conduction velocity and ultrasound measurements despite other authors findings [17,18,19]. Disability of the arm is related to nerve conduction changes but not with ultrasonographic measurements. Other studies had similar results [20,21]. It appears that changes in nerve physiology have more effect on function than changes in anatomy which is represented in these findings.

When testing the ability of CTS diagnosis prediction, we found that in our model CSA and WFR of the MN had a poor value of prediction. And we didn‘t achieve good results with elasticity of the MN too, in our sample there was no correlation between elasticity and CTS as reported by other authors [5,6]. We found that the proposed algorithm for diagnosing CTS lacked sensitivity. These results fall behind greatly when compared to sensitivity of clinical provocative tests such as Phalen's test (57%-91%) [22] and conventional EDX (56% to 85%) [3]. Though some other studies found that ultrasound measurements had a good sensitivity [6] it seems that EDX would still be a first choice for diagnosing CTS as it has a potential to diagnose between diseases that could imitate CTS.

Ultrasound still holds its potential as easy to master technique when compared to EDX. Resident doctor in our study performed similarly to experienced radiologist. This could aid greatly in the accessibility for diagnosing CTS. This and other advantages like relatively low cost of examination, provision of anatomic images of the MN and surrounding structures, makes ultrasound a valuable technique, but further improvements of the method are needed, as at the moment ultrasonographic algorithm lacks sensitivity for a screening test. Further studies are needed for the development of better diagnostic tools combining various diagnostic modalities.

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