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Correlation Between the Severity of Carpal Tunnel Syndrome and Color Doppler Sonography Findings

OBJECTIVE. Carpal tunnel syndrome (CTS) represents one of the most prevalent peripheral entrapment mononeuropathies. The purpose of our study was to assess the potential correlation between intraneural hypervascularization, flexor retinaculum bowing, and median nerve cross-sectional area and the severity of CTS in cases confirmed by nerve conduction study.

SUBJECTS AND METHODS. Sixty consecutive patients with classic or probable symptoms of CTS were enrolled in the study. A control group consisting of 27 healthy volunteers who were never diagnosed with CTS or had any symptoms of CTS was recruited among institution employees. All symptomatic patients were initially examined by a hand surgeon and subsequently referred for sonographic and electrophysiologic examinations.

RESULTS. A total of 90 wrists (in 60 patients) were included in the study. Twenty-eight (31.1%) had mild CTS, 33 had moderate disease, and 29 had severe disease. We detected significant correlation between median nerve hypervascularization and the severity of CTS (p = 0.01, logistic regression) for moderate CTS and (p = 0.04) for severe disease. We also detected a significant correlation in flexor retinaculum bowing and median nerve cross-sectional area with increase in the severity of CTS (p < 0.001 and < 0.008; chi-square test and analysis of variance, respectively).

CONCLUSION. Our study suggests that the severity of CTS strongly correlates with color Doppler sonography findings, and this technique may represent a reliable complementary tool in CTS examination.

arpal tunnel syndrome (CTS) represents one of the most prevalent peripheral entrapment mononeuropathies and usually occurs due to localized compression of the median nerve (MN) in the carpal tunnel. This syndrome was first reported by Phalen [1] in 1950 and since then has been reported to represent up to 90% of all entrapment neuropathies [2, 3]. Clinically, this condition is predominant in middle-aged women, with the overall CTS prevalence reportedly reaching 5.8% in women and only 0.6% in men [4].

From the perspective of occupational health, CTS incidence is reportedly 1% in the general population but reaches up to 5% in certain industrial settings [5], and CTS is also commonly detected in occupations involving high force or repetitive pressure [2]. Other CTS-associated diseases include rheumatoid arthritis, hypothyroidism, diabetes mellitus, Colles fracture, amyloidosis, and acromegaly [6].

Several diagnostic methods are routinely applied in CTS detection, including nerve

conduction studies (NCS) and imaging techniques in addition to clinical signs and symptoms, such as the Phalen sign (dysesthesia after wrist flexion) and Tinel sign (percussion over the median nerve elicits dysesthesia). The current reference standard for CTS diagnosis consists of evaluating clinical symptoms and their location in combination with abnormal median nerve function based on NCS [7]. However, the sensitivity and specificity of the clinical signs is barely moderate [8], and both false-negative and false-positive results of NCS are well documented [7].

Several other imaging techniques have been evaluated in the diagnosis of CTS, such as MRI [9] and sonography. Although both imaging techniques have the advantage of allowing the assessment of anatomic structures adjacent to the MN, the sensitivity and specificity of those techniques varies considerably across published studies [8]. Moreover, MRI is usually a rather costly examination that requires equipment that may not be readily available everywhere. Thus, the practicality

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of using MRI in the initial assessment of suspected CTS may be problematic.

In addition, the general criteria for the severity of CTS vary in the available literature [10]. However, the severity of disease is an important clinical factor that may affect the treatment course and prognostic evaluation [11, 12] and should be routinely recorded. Currently, there are no reliable imaging criteria for the severity of CTS.

The MN is a highly vascularized anatomic structure and circulation impairment of the MN has been proposed as the cause of CTS [13]. To the best of our knowledge, there are no previous reports focusing on the relationship between intraneural hypervascularization and the severity of CTS. The purpose of our study was to assess the potential correlation between intraneural hypervascularization, flexor retinaculum bowing, and median nerve cross-sectional area (CSA) and the severity of CTS in cases confirmed by NCS.

Subjects and Methods

Patients

Between January 2009 and September 2010, 60 consecutive patients (52 women and eight men, altogether representing 90 affected hands) with classic or probable symptoms of CTS referred to an orthopedic clinic of a tertiary referral hospital, were enrolled in the current study. All patients were initially examined by a hand surgeon, and subsequently referred for sonographic and electrophysiologic examinations. The local ethics committee approved the study protocol.

A control group consisting of 27 healthy volunteers who had never been diagnosed with CTS or had any symptoms was recruited among institution employees. The control group was age-matched to the study group. Both patients and volunteers provided an informed consent for participation in the study and were free to withdraw from the study any time.

Exclusion Criteria

Patients with positive clinical symptoms of CTS and negative NCS results; coexistent neurologic diseases, such as polyneuropathy, proximal median neuropathy, cervical radiculopathy, diabetes mellitus, connective tissue disease, thyroid disease, renal failure, and recent wrist trauma; those with spaceoccupying lesions of the wrist; and those with previous wrist surgery were excluded from the study.

Nerve Conduction Studies and CTS Severity Classification

NCS were performed under the guidance of an electrodiagnostician with a special interest in nerve



Fig. 1—Axial sonogram of median nerve crosssection at carpal tunnel inlet in 42-year-old man shows flexor retinaculum (*asterisks*) and median nerve (*arrowhead*).



Fig. 2—Longitudinal power Doppler sonogram in 36-year-old man shows intraneural blood flow in median nerve.

conduction studies. If the results of NCS were positive, those cases were classified as electrophysiologically-confirmed CTS. Patients were classified as having mild, moderate, and severe CTS according to the MN conduction velocity (cm/s). Mild indicated prolonged (relative or absolute) sensory nerve action potential (SNAP) or mixed nerve action potential (NAP) distal latency (orthodromic, antidromic, or palmar), with SNAP amplitude below the lower limit of the norm. Moderate indicated abnormal median sensory latency as in the mild category plus (relative or absolute) prolongation of median motor distal latency. Severe indicated prolonged median motor and sensory distal latencies, with either an absent SNAP or NAP or low-amplitude or absent thenar compound muscle action potential. Needle examination often reveals fibrillation, reduced recruitment, and motor unit potential changes.

Sonographic Evaluation

All sonographic examinations were performed within 3 days after NCS by a single radiologist with 6 years of experience in musculoskeletal sonography. Both the radiologist and the electrodiagnostician were blinded to each other's assessment at the time of examination.

All examinations were performed with a highfrequency (11-MHz) linear-array transducer with optimized musculoskeletal setting (Nemio 30, Toshiba) for the determination of MN CSA, flexor retinaculum bowing, and MN hypervascularization at the carpal tunnel inlet.

During the examination, subjects were seated facing the radiologist with arms extended, wrists resting on a hard flat surface, and supinated forearms and semiflexed fingers. Axial sonography of the MN was obtained at a single anatomic level: the carpal tunnel inlet at the level of the pisiform and scaphoid bones (Fig. 1). Particular attention was paid to adequate probe orientation to keep the ultrasound beam perpendicular to the MN and to maintain the wrist in a supine position for accurate determination of the MN CSA. The transducer was applied on the wrist with minimal possible pressure because pressure could close small intraneural vessels and inappropriately alter the color Doppler findings. We measured the maximal alteration only, and segmental quantitative nerve measurement was not used.

Low blood flow in the MN sheath was then detected around 2 cm above the carpal tunnel using color and power Doppler sonography because those techniques are the most sensitive for flow detection (Fig. 2). Both power and color Doppler sonography were used (postrepetition frequency at minimum-0.4-0.6 kHz) to obtain the low blood flow images. Specific settings included Doppler depth, 2.5 cm; overall gain equal to 60 dB; time gain compensation, vertical and centered; power Doppler gain, 15-20 dB; and wall filter, set at minimum. We assessed the arteriole blood flow within the nerve sheath visually. Flexor retinaculum bowing was defined as a measurement at 90° from a line drawn from the hook of the hamate bone to the tubercle of the trapezium bone greater than 4 mm.

Statistical Analysis

Statistical analysis was performed using SPSS, version 16, and R project statistical software. The statistical calculation was performed by using the chi-square test, analysis of variance, and logistic regression. A p value ≤ 0.05 was considered statistically significant.

Results

A total of 60 patients representing 90 CTSaffected wrists were enrolled in the study; 82

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(91.1%) were women and 8 (8.9%) were men. Of the 90 assessed hands, 52 were right hands and 38 were left hands. The average age of patients was 45.2 years. In the control group, 27 volunteers were recruited, and both wrists of each subject were evaluated. Four volunteers (14.8%) were men, 23 (85.2%) were women. The average age was 41.9 years.

Severity and Laterality of CTS

Twenty-eight hands (31.1%) were affected with mild CTS, 33 (36.7%) with moderate CTS, and 29 (32.2%) with severe disease. Twenty-two (39.3%) patients had unilateral CTS (18 in the right hand and four in the left hand), and 34 (60.7%) patients were diagnosed with bilateral CTS.

Correlation Between Flexor Retinaculum Bowing and Severity of CTS

A total of 48 (53.3%) hands showed flexor retinaculum bowing (6 [6.7%] in the mild, 20 [22.2%] in the moderate, and 22 [24.4%] in the severe category of CTS). We detected a significant correlation between flexor retinaculum bowing and increase in the severity of CTS (p < 0.001 by chi-square test).

Correlation Between Median Nerve Cross-Sectional Area and the Severity of CTS

The mean \pm SD of the CSA was 11.07 \pm 2.08 mm² (range, 7–16) in mild CTS, 11.73 \pm 1.56 mm² (range, 9–15) in moderate, and 12.59 \pm 1.7 mm² (range, 10–16) in severe CTS. We detected a significant correlation between MN CSA and the severity of CTS (p < 0.008 by 95% CI analysis of variance) (Fig. 3). The Mann-Whitney U test showed significant differences between severe CTS CSA levels and both moderate and mild CTS (p = 0.04 and 0.005, respectively).

Correlation Between Median Nerve Hypervascularization and Severity of CTS

Forty-nine (54.4%) cases showed hypervascularization of the MN. We detected significant correlation between MN hypervascularization and the severity of CTS (p = 0.01 by logistic regression) for moderate CTS and (p = 0.04) for severe disease. In addition, we detected highly significant correlation between MN CSA and MN hypervascularization (p = 0.0001 by logistic regression) (Fig. 4). The statistical difference in CSA between the two groups (hands showing hypervascularization vs hands in which hypervascularization is absent) was highly significant (p < 0.0001 by Mann-Whitney U test). We found no correla-



Fig. 3—Boxplot shows gradual increase in crosssectional area (CSA) with patients stratified for severity of CTS. Bold black lines = medians, whiskers = error bars.

tion between MN hypervascularization and patient age or flexor retinaculum bowing.

Control Group

In the control group, no hypervascularization was detected in any of the subjects. The CSA ranged from 5 to 8, with average of 6.19 ± 0.73 . There was no correlation in the control group between CSA and any of the variables (flexor retinaculum bowing, subject age, hand laterality, subject sex). When compared with the study group, the CSA was significantly different (< 0.0001 by unpaired Student *t* test).

The presence of hypervascularization and of flexor retinaculum bowing was significantly different between the control and the subject groups (p < 0.0001 and 0.0002, respectively, by chi-square test), suggesting that hypervascularization and flexor retinaculum bowing occur more commonly in patients affected with CTS compared with control subjects.

Discussion

Our study shows that a clinical sign routinely used in CTS diagnosis (flexor retinaculum bowing) is significantly dependent on the severity of CTS as defined by NCS criteria. In addition, our data confirm a correlation between increased MN CSA and the increased severity of CTS and increased MN CSA in the case of MN hypervascularization. All these findings suggest that CTS can be objectively stratified in terms of disease severity, and such stratification may lead clinical decisions in terms of treatment and prognosis. The comparison with healthy volunteers confirmed a statistically significant increase in CSA in CTS-affected patients.



Fig. 4—Boxplot shows difference in cross-sectional area (CSA) in patients with and without median nerve hypervascularization. Bold black line = median, whiskers = error bars.

In clinically confirmed CTS, rapid resolution of subjective symptoms often occurs after carpal tunnel release surgery, which suggests the involvement of an ischemic component [14]. From the pathophysiologic perspective, during the early compression of MN, the subsequent effect is a blockage of the venous outflow, leading to MN hyperemia and edema [15, 16]. Such obstruction of the venous outflow due to external compression can lead to blood accumulation and edema, with a subsequent increase in compartment pressure and decrease in arterial supply by the vasa nervorum [16] leading to the ultimate ischemic injury [15, 16]. The blockage of the venous outflow would lead to a lesser signal detected on Doppler sonography; however, compensatory dilatation of perineural veins will cause hyperemia and ultimate signal increase on Doppler sonography.

Although NCS is considered the reference standard in the diagnosis of CTS, with a sensitivity range of 80-92% and specificity range of 80-99% [16], false-positive [17] and falsenegative [18] results of NCS are well recorded. Our results show that NCS is capable of stratifying NCS-confirmed CTS patients into groups with variable severity of CTS, and this stratification corresponds with objective findings (MN CSA, hypervascularization) on color Doppler sonography. This indicates that color Doppler sonography is an accurate tool in the assessment of MN entrapment and may facilitate the selection of appropriate candidates to undergo either invasive surgical treatment or conservative medical therapy.

Further advantages of sonography include its noninvasiveness, speed, convenient handling, price, and performance capacity, suggesting its potential role as an inexpensive and quick guide for therapeutic intervention [8]. Its usefulness in the diagnosis of CTS has already been assessed, and the study has shown that the odds of MN involvement detection were 16 times higher when color Doppler sonography was used compared with gray-scale sonography [8] because unlike gray-scale sonography, color Doppler sonography allows the detection of functional rather than morphologic disturbances.

Another advantage of color Doppler sonography is its ability to detect intraneural hypervascularization early before MN swelling or edema, which could be beneficial for patients in the early stages of carpal tunnel syndrome and may enable the use of alternative clinical management instead of more invasive procedures [8]. Our data clearly suggest that in patients with a lesser severity of CTS (mild category on basis of NCS), the edema and hypervascularization are less common, and such patients may be ideal candidates for nonsurgical treatment.

In addition, color Doppler sonography may be especially useful for postsurgery followup of patients. Although surgery is usually a highly successful treatment, in some cases the incomplete resection of the flexor retinaculum can lead to the recurrence of symptoms [19]. This eventuality can also be assessed by sonography rather than NCS along with objectively monitoring the decrease of swelling and blood flow restoration in MN.

The disadvantages of color Doppler sonography include the dependence of its accuracy on operator experience and its decreased ability to display morphologic disturbances. A limitation of our study is that the most accurate measurement of MN CSA is by using continuous boundary trace of the nerve rather than measurement at a single level, although previous studies evaluating both methods have produced comparable results [20].

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In conclusion, our study suggests that the severity of CTS strongly correlates with color Doppler sonography findings, and this technique may represent a complementary tool in CTS examination. Our data also warrant future studies exploring the precise causative role of intraneural vascular pressure in CTS and assessing color Doppler sonography evaluation of CTS treatment outcome because of its potential to guide clinical decisions and predict patients' eventual outcomes.

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