Predictors of Carpal Tunnel Syndrome: Accuracy of Gray-Scale and Color Doppler Sonography

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OBJECTIVE. The purpose of this study was to retrospectively assess the accuracy of gray-scale and color Doppler sonography in the diagnosis of carpal tunnel syndrome.

MATERIALS AND METHODS. A total of 206 wrists in 151 patients with a clinical suspicion of carpal tunnel syndrome were examined with high-resolution sonography using a 7–15-MHz linear array transducer. The presence of median nerve swelling, edema, and flattening and increased bowing of the flexor retinaculum was evaluated with gray-scale sonography, and the presence of nerve hypervascularization was evaluated with color Doppler sonography. Sensitivity and specificity were calculated for each sonographic feature in comparison with nerve conduction studies as the standard of reference. Multivariate logistic regression analysis was used to determine variables predictive of carpal tunnel syndrome.

RESULTS. Carpal tunnel syndrome was confirmed in 172 wrists at nerve conduction studies. A median nerve cross-sectional area of at least 0.11 cm^2 was calculated as a definition of median nerve swelling. In comparison with nerve conduction studies, nerve swelling showed the highest accuracy (91%) among gray-scale sonography criteria, and the presence of intraneural hypervascularization showed the highest accuracy (95%) among all sonography criteria. Logistic regression analysis showed that nerve hypervascularization was the only variable that independently predicted median nerve entrapment (odds ratio, 16.4; 95% confidence interval, 8.7–31.1; $p < 0.001$).

CONCLUSION. Color Doppler sonography is more accurate than gray-scale sonography for characterizing median nerve involvement in patients with suspected carpal tunnel syndrome.

Carpal tunnel syndrome, a common peripheral entrapment neuropathy, is recognized as one of the most important causes of workplace morbidity [1–4]. Diagnosis of carpal tunnel syndrome is usually based on a combination of clinical signs such as the Tinel sign (tapping over the median nerve producing dysesthesias) and the Phalen sign (wrist flexion producing dysesthesias), and nerve conduction studies [5]. However, the clinical signs are moderately sensitive and specific [6], and false-negative [7] and false-positive [8] results of nerve conduction studies have been reported.

MRI [9–15] and high-resolution sonography [16–21] have emerged as feasible, noninvasive imaging tools for evaluating the median nerve in the carpal tunnel. Both techniques permit perception of nerve compression characteristics, including altered signal, increased cross-sectional area, flattening of the median nerve, and bowing of the flexor retinaculum. The sensitivity and specificity of these diagnostic features vary widely among published studies [17–20, 22, 23], and the critical cutoff value for the nerve cross-sectional area, at which nerve entrapment can be diagnosed, varies considerably, from more than 0.09 [18] to 0.15 cm^2 [24].

Like peripheral nerves, the median nerve is well vascularized with epineural and endoneural microvasculature [25, 26]. Nerve compression caused by elevated pressure in the carpal tunnel is believed to provoke a three-stage process that is initiated with venous congestion of the median nerve followed by nerve edema and then by impairment of the venous and arterial blood supplies [27]. Investigators in recent studies [28, 29] evaluated the blood flow in the median nerve and emphasized the vascular cause of carpal tunnel syndrome. Furthermore, the vascular mechanism of carpal tunnel syndrome was also reported by Sugimoto et al. [30] as the explanation for abnormal enhancement of the median nerve on dynamic contrast-enhanced MRI. To our knowledge, the usefulness of color Doppler sonography in detecting intraneural circulatory disturbance in patients with suspected carpal tunnel syndrome has not

yet been investigated, although color Doppler sonography has been used to evaluate the presence of a persistent median artery in the carpal tunnel [31] and a variety of peripheral nerve abnormalities [32, 33].

The purpose of this study was to assess the accuracy of color Doppler sonography in detecting carpal tunnel syndrome in comparison with nerve conduction studies. We also assessed the accuracy of gray-scale sonography findings in detecting median nerve entrapment and attempted to determine the best independent sonographic indicator of carpal tunnel syndrome.

Materials and Methods
Patients

This study was based on a retrospective analysis of high-resolution sonography of the median nerve. To determine the role of gray-scale and color Doppler sonography in detecting features associated with carpal tunnel syndrome, we reviewed patients' data files stored in a commercially available digital database that included information about patient sociodemographic status, clinical examinations, laboratory tests, radiologic and surgical reports, and postsurgical course.

Patients with a clinical suspicion of carpal tunnel syndrome who underwent sonographic examinations meeting the following criteria were included in the study: performed between January 2002 and December 2003, performed by one radiologist with 10 years' experience in performing and interpreting sonographic examinations of the peripheral nerves, and performed contemporaneously with full clinical and electrophysiologic examinations of the involved upper extremity. Patients with a history of previous wrist surgery or with a bifid median nerve were excluded.

A digital search resulted in recruitment of 151 consecutive patients (mean age, 58 ± 16 years; age range, 15–90 years). The patient cohort comprised 107 women (mean age, 58 ± 15 years; age range, 15–90 years) and 44 men (mean age, 58 ± 19 years; age range, 22–90 years). Sonographic examinations were unilateral in 96 patients and bilateral in 55 patients who had bilateral symptoms. Therefore, the study cohort comprised 206 wrists. These patients underwent sonography of the carpal tunnel as part of their routine clinical care. Therefore, the patients were asked to give only a verbal consent; a written informed consent was not provided.

Sonography Technique

Gray-scale and color Doppler sonography examinations were performed using a linear 7–15-MHz transducer (HDI 5000, Advanced Technology Laboratories). In the supine and neutral wrist posi-

tion, the course of the median nerve in and proximal to the carpal tunnel was carefully scanned with the transducer in both the transverse and longitudinal planes to investigate the presence of median nerve compression criteria. Sonography was performed by implementing sonography compound imaging and by using a gel standoff pad. Sonographic examinations included measurements of diameters and cross-sectional areas of the median nerve proximal to the carpal tunnel, at the tunnel inlet, and at the tunnel outlet by using digital calipers at the time of the examination. The maximum height of the retinaculum was measured above a line subtended between its radial and the ulnar carpal attachments. Color Doppler sonograms were acquired after modifying the color window dimensions to include the median nerve. Color Doppler sonography settings were adjusted for investigating low-flow vessels. Pulse repetition frequency was set at 800 Hz, and Doppler gain was adjusted to the maximum level that does not produce clutter. Sonograms were digitally saved by means of a PACS.

Gold Standard

The diagnosis of carpal tunnel syndrome was indicated by the patient's history (nocturnal hand discomfort and sensory impairment in the distribution of the median nerve) and clinical examinations (Tinel and Phalen signs). Clinical diagnosis was confirmed by electrodiagnostic testing. Abnormal nerve conduction was defined as a reduction in median nerve sensory conduction velocity of more than 62 msec and prolongation of the distal motor latency of more than 3.9 msec without abnormalities in the ulnar nerve or proximal median nerve parameters.

Image Analysis

The saved digital sonograms of each patient were reevaluated in consensus by two radiologists (with 1 and 1.5 years' experience) who were trained in performing and interpreting sonographic examinations of the peripheral nerves. Neither reviewer participated in the data search, and both were blinded to clinical, electrophysiologic, and surgical outcomes. Median nerve involvement was characterized by evaluating five sonography features on a 2-point ordinal scale: present or absent.

First, the reviewers assessed the presence of nerve edema. The normal median nerve is a bundle of hypoechoic nerve fascicles surrounded by hyperechoic epineural connective tissue, all of which is encased in the hyperechoic perineural sheath [34]. Nerve edema alters the signal produced by nerve components and results in increased hypoechoic signal of the nerve. Next, the reviewers assessed the presence of nerve swelling and nerve flattening. Nerve swelling was defined as an enlargement of the cross-sectional area of the nerve to 0.11 cm^2 or

more within or proximal to the carpal tunnel. The cross-sectional area of the nerve was defined as the area of the nerve bundles in the perineural fibrous tissue. All measurements were rounded to the nearest 0.01 cm^2. Nerve flattening was defined as a decrease in the minor axis combined with an increase in the major axis of the median nerve in the carpal tunnel (at the pisiform or hamate level) with a flattening ratio (nerve's major to its minor axis) of at least 3. The prospectively measured values for cross-sectional area and major and minor axes of the median nerve were used in this study. The maximal value of the nerve cross-sectional area (in or proximal to the carpal tunnel) was used to judge the presence or absence of nerve swelling, and maximal alteration of the major and minor axes of the median nerve, within the carpal tunnel, was used to determine the presence or absence of nerve flattening. In addition, the presence of increased palmar bowing of the flexor retinaculum was determined to be displacement of the palmar apex of the retinaculum 2 mm or more from the straight line between its attachments to the trapezium tubercle and the hamate hook. Finally, color Doppler sonograms were evaluated to determine the presence of any intraneural vascular structures not related to a persistent median artery.

Statistical Analysis

Data entry procedures and statistical analysis were performed with a statistical software system (SPSS Version 11.0.0 [SPSS] for Windows [Microsoft]). In the first step, univariate regression analysis was used to examine the relationship of age and sex to carpal tunnel syndrome in comparison with nerve conduction studies. In the second step of analysis, multivariate stepwise logistic regression analysis was used first to determine the threshold value of the median nerve's cross-sectional area that would be predictive of carpal tunnel syndrome. Different values for nerve cross-sectional area ranging from 0.07 to 0.15 cm^2 were evaluated as independent covariates. Then sensitivity, specificity, accuracy, and positive and negative predictive values were calculated on a per-wrist basis—that is, the ability to correctly identify wrists with carpal tunnel syndrome. Finally, multivariate stepwise logistic regression analysis was performed to determine the best sonographic predictors of carpal tunnel syndrome (presence of nerve edema, nerve swelling, nerve flattening, bowing of the flexor retinaculum, or intraneural hypervascularization). Variables were retained in the logistic model if they contributed to the explanatory power of the regression equation ($p < 0.10$). The results were presented as an odds ratio and 95% confidence interval (CI). All p values were two-sided; a p value of less than 0.05 was considered statistically significant.

Results

Univariate regression analysis examining the relationship of age and sex to carpal tunnel syndrome revealed that female sex (odds ratio, 7.9 [95% CI, 4.3–14.4]; $p < 0.001$) and age greater than 50 years (odds ratio, 7.5 [4.2–13.3]; $p < 0.001$) were significantly associated with carpal tunnel syndrome. In particular, age between 50 and 69 years (odds ratio, 4.4 [2.5–8.1]; $p < 0.001$) showed the highest association with carpal tunnel syndrome. Multivariate stepwise logistic regression analysis of nerve cross-sectional area determined the value 0.11 cm^2 as the threshold value that independently predicts carpal tunnel syndrome. Therefore, nerve swelling was defined, in this study, as an enlargement of nerve cross-sectional area to at least 0.11 cm^2.

Nerve conduction studies of 206 wrists in 151 patients revealed 172 wrists in 127 patients with carpal tunnel syndrome. Gray-scale sonography revealed at least one abnormal finding in 181 wrists (Table 1). Color Doppler sonography depicted intraneural blood vessels in 174 wrists and correctly identified carpal tunnel syndrome in 164. All five sonography criteria were present in 65 wrists (32%). Of 172 wrists with carpal tunnel syndrome, 11 met only one sonography criterion for carpal tunnel syndrome—that is, median nerve hypervascularization in seven wrists, nerve swelling in three, and nerve flattening in one. In 153 wrists (89%) with carpal tunnel syndrome, both nerve swelling and nerve hypervascularization were present (Fig. 1), whereas 15 wrists (9%) showed either nerve swelling or nerve hypervascularization. In cases of disagreement between nerve swelling and nerve hypervascularization, the latter correctly correlated with nerve conduction studies in 11 wrists (Figs. 2 and 3) and the former in four.

Examination of the multivariate stepwise logistic regression analysis of sonography criteria showed that nerve swelling was the only gray-scale sonography variable that was independently predictive of the electrophysiologic outcome (odds ratio, 8.7 [95% CI, 5.4–14.2]; $p < 0.001$) for each 1% increase in nerve cross-sectional area. When all sonographic criteria were included, nerve hypervascularization was the only variable that independently predicted median nerve entrapment, with an odds ratio of 16.4 (8.7–31.1; $p < 0.001$) for each 1% increase in nerve hypervascularization.

Discussion

Accurate detection of median nerve entrapment in patients with a clinical suspicion of carpal tunnel syndrome is essential, especially if surgery is contemplated. MRI and sonography have both been advocated as noninvasive diagnostic techniques for the detection of median nerve entrapment. Both provide direct visualization of the median nerve within and proximal to the flexor retinaculum, enabling morphologic assessment of the median nerve, including nerve swelling, edema, flattening, and bowing of the flexor retinaculum.

A number of authors have reported the accuracy of sonography criteria of median nerve entrapment [17–23], and several studies have addressed the quantification of the nerve cross-sectional area and its role in diagnosing carpal tunnel syndrome [17–19, 24]. Review of these studies reveals a number of discrepancies in the accuracy of various sonography criteria in diagnosing carpal tunnel syndrome. Although almost all published studies on the sonographic diagnosis of carpal tunnel syndrome agree that nerve swelling is the main sonography criterion indicating carpal tunnel syndrome, the swelling position (i.e., proximal to the carpal tunnel or at the tunnel inlet or outlet) and the critical threshold for nerve cross-sectional area differ considerably among those studies. The sensitivity of nerve swelling ranged from 57% to 89% [17–20, 22, 23, 35], and the nerve cross-sectional area indicating carpal tunnel syndrome ranged from 0.09 to 0.15 cm^2 [18, 24]. The role of retinaculum

bowing and nerve flattening also varied among studies, with sensitivities of 45–81% [17, 23] and 38–65% [17, 18], respectively. The accuracy of nerve edema in the sonographic diagnosis of carpal tunnel syndrome, to our knowledge, has not yet been reported.

This study evaluates the accuracy of five sonographic signs in predicting carpal tunnel syndrome—namely, the four gray-scale sonography morphologic features and intraneural hypervascularization of the median nerve. Gray-scale and color Doppler sonography findings were compared with the widely used standard of reference—nerve conduction studies—in all patients to determine the reviewer-dependent accuracy of sonography in the diagnosis of carpal tunnel syndrome.

Comparison of findings of sonography and nerve conduction studies showed that nerve hypervascularization and nerve swelling yielded the best detectability of carpal tunnel syndrome. However, nerve hypervascularization tended to show a higher accuracy in detecting carpal tunnel syndrome than did nerve swelling because of a substantial increase in specificity and a slight but important increase in positive and negative predictive values. This indicates that color Doppler sonography enables more reliable assessment of median nerve entrapment and therefore helps select candidates for interventional treatment. In fact, color Doppler sonography findings were true-negative in five wrists with a cross-sectional nerve area of 0.11 cm^2 but no electrophysiologic evidence of carpal tunnel syndrome and were true-positive in three carpal tunnel syndrome patients with a cross-sectional nerve area of less than 0.11 cm^2.

The advantage of color Doppler sonography was further shown in that it enabled improved predictability of median nerve entrapment. As opposed to gray-scale sonography, color Doppler sonography enables the detection of functional disturbance rather than morphologic changes in the median nerve. Study results show that the odds of accurate characterization of median nerve involvement in patients with suspected carpal tunnel syndrome using color Doppler sonography were 16 times as high as the odds of diagnosing or ruling out carpal tunnel syndrome using gray-scale sonography. These clinical findings confirm that color Doppler sonography can also be useful when results of clinical examinations or electrophysiologic studies are inconclusive.

Because of its comprehensive perceptibility of the carpal tunnel and its high detectability of criteria associated with carpal tunnel syndrome, MRI is considered the noninvasive

TABLE 1: Detectability of Sonographic Criteria Indicating Carpal Tunnel Syndrome in Comparison with Nerve Conduction Studies

Criteria	Sensitivity (%)	Specificity (%)	Accuracy (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Nerve edema	80 (137/172)	65 (22/34)	77 (159/206)	92 (137/149)	39 (22/57)
Nerve swelling	91 (157/172)	47 (16/34)	89 (183/206)	90 (157/175)	52 (16/31)
Nerve flattening	60 (103/172)	76 (26/34)	63 (129/206)	93 (103/111)	27 (26/95)
Bowing of flexor retinaculum	65 (111/172)	68 (23/34)	65 (134/206)	91 (111/122)	27 (23/84)
Nerve hypervascularization	95 (164/172)	71 (24/34)	91 (187/206)	94 (164/174)	75 (24/32)

Note—Numbers in parentheses are numbers of wrists.

examination of choice for evaluating the carpal tunnel and in particular the median nerve. However, MRI is cost-intensive and may not always be as readily available as sonography. Improved sonography resolution may provide a further advantage over MRI. Like gray-scale sonography criteria, MRI features that indicate carpal tunnel syndrome are not consistently proven in published studies. Several studies [10–12, 36, 37] found that nerve swelling, nerve flattening, and increased signal intensity correlate well with carpal tunnel syndrome, whereas other studies emphasized the role of palmar bowing of the flexor retinaculum [13, 15] and nerve swelling [14] in the diagnosis. In a recent study, Jarvik et al. [9] reported a high sensitivity (91%) combined, however, with a low specificity (38%) of increased signal intensity of the median nerve in detecting carpal tunnel syndrome.

Furthermore, MRI may require the IV injection of contrast material to evaluate the vitality of the median nerve [15, 30], and sonography does not require contrast material. Instead, color Doppler sonography, a convenient integral adjunct to gray-scale sonography, tends to show the pathologic intraneural vasculature, thus permitting recognition of hypervascularization in the median nerve even before the development of nerve swelling and edema. This indicates that color Doppler sonography may allow early detection of median nerve involvement in carpal tunnel syndrome and therefore enable early initiation of suitable treatment, which may well improve prognosis.

Successful implementation of color Doppler sonography, however, is predicated on the correct choice of Doppler parameters and the correct application of the transducer on the patient's forearm. Generating a reliable color

Doppler sonogram of the median nerve can be achieved, in our experience, by limiting the Doppler window to the median nerve and maximizing Doppler gain to a level that does not produce clutter that hampers the image. Furthermore, it is important to scan the median nerve without applying any pressure to the median nerve through the transducer, which may cause compression of the tiny intraneural vascular structures and render them occult.

In this study, the sensitivity of nerve flattening and that of bowing of the retinaculum in the detection of carpal tunnel syndrome were concordant with previous studies, although the sensitivity of nerve swelling was somewhat higher. All patients in our study were examined with a linear transducer with a 7–15-MHz frequency using sonographic compound imaging and a gel pad on the patient's forearm. Although it was not formally assessed in this
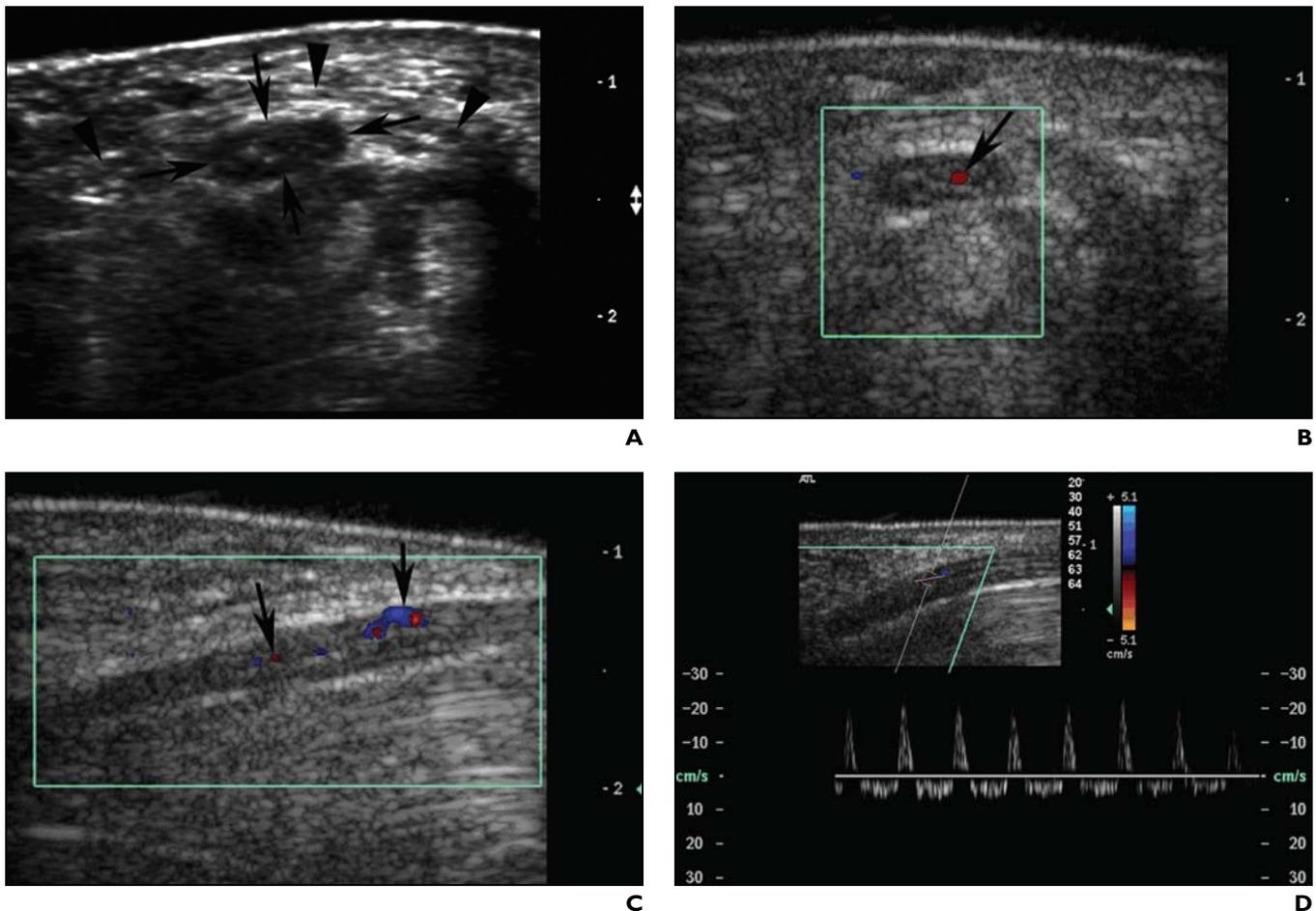

Fig. 1—72-year-old woman with nerve conduction studies and surgically proven carpal tunnel syndrome.
A, Gray-scale sonogram at carpal tunnel inlet depicts mild swelling of median nerve (*arrows*) with cross-sectional area of 0.11 cm^2 in addition to severe nerve edema and slight palmar bowing of flexor retinaculum (*arrowheads*).
B and **C,** Transverse (**B**) and longitudinal (**C**) color Doppler sonograms at carpal tunnel inlet show intraneural abnormal vasculature (*arrows*).
D, Spectral Doppler waveform of intraneural vascular structure indicates presence of arterial flow in nerve.
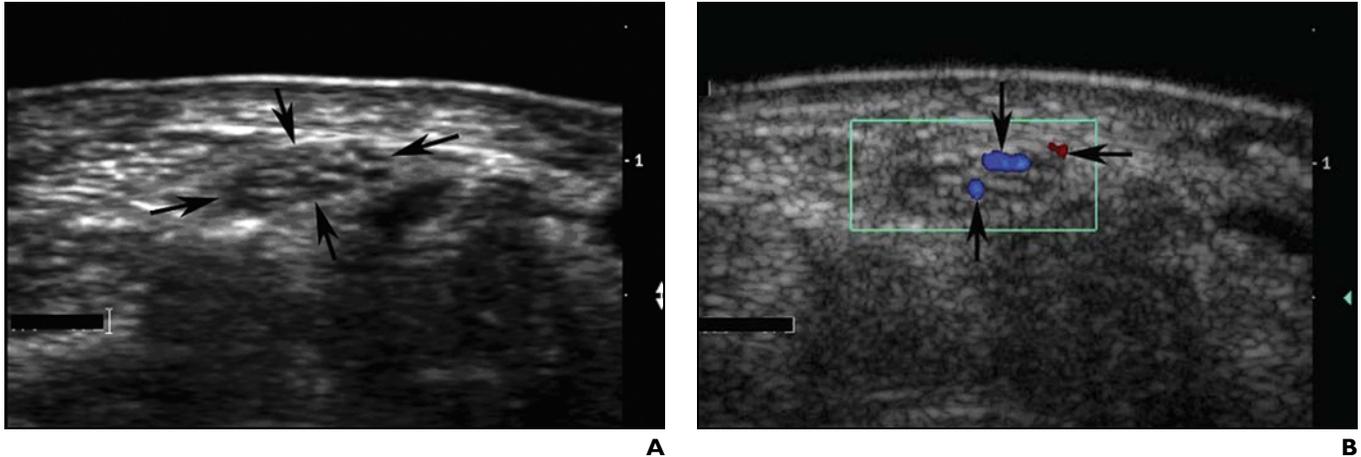
Fig. 2—67-year-old man with nerve conduction studies and surgically proven carpal tunnel syndrome.
A, Gray-scale sonogram at carpal tunnel inlet depicts normal median nerve (*arrows*) with cross-sectional area of 0.09 cm^2 and no evidence of nerve edema or increased palmar bowing of flexor retinaculum.
B, Transverse color Doppler sonogram at carpal tunnel inlet shows intraneural abnormal vasculature (*arrows*), an advantage of color Doppler over gray-scale sonography.
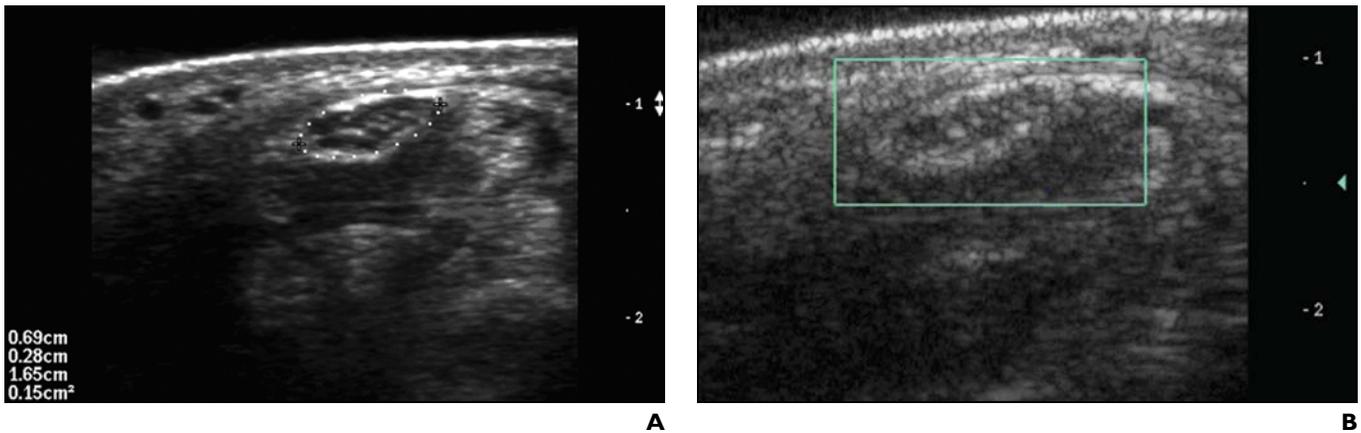

Fig. 3—40-year-old woman with negative results of nerve conduction studies.
A, Gray-scale sonogram at carpal tunnel inlet depicts median nerve swelling with cross-sectional area of 0.15 cm^2, nerve edema, and palmar bowing of flexor retinaculum. Area inside dotted oval is region of interest.
B, Transverse color Doppler sonogram at carpal tunnel inlet reveals no intraneural abnormal vasculature, thus correlating with nerve conduction studies better than gray-scale sonography correlated with those studies.

study, our impression is that the resulting high-quality, high-resolution sonograms enabled precise measurements of median nerve cross-sectional area and therefore better characterization of nerve involvement.

A main limitation of our investigation is related to its retrospective design. Only patients with nerve conduction studies were included. Because nerve conduction studies are performed in patients with a high clinical suspicion of carpal tunnel syndrome, most of our patient population indeed had electrophysiologic proof of carpal tunnel syndrome. Although carpal tunnel syndrome is a common health problem, the ratio of carpal tunnel syndrome patients in our investigation may not correspond to that in society. However, the study results are in con-

cordance with data reporting the peak prevalence of carpal tunnel syndrome in women older than 50 years [38, 39]. Another limitation of this study is the lack of a quantitative analysis of the number or density of abnormal intraneural blood vessels. However, a histopathologic study of human sural nerves [40] found no significant correlation between the number of epineural and endoneural blood vessels and no significant correlation between the number of epineural and endoneural blood vessels and the severity of the neuropathy, despite significant correlation between an increased number of epineural and endoneural blood vessels and neuropathy. A further limitation of our study is that quantitative analysis of nerve measurements was not performed on a segmental ba-

sis—that is, proximal to the carpal tunnel, at the pisiform level, and at the hamate level. Rather, only data on maximal alteration were included in the statistical analysis.

In summary, we conclude that color Doppler sonography contributed more than gray-scale sonography to the perception of the circulatory status of the median nerve and consequently to the advantageous characterization of nerve involvement in patients with clinically suspected carpal tunnel syndrome. This could have a considerable impact on the early diagnosis of median nerve compression and on patient selection for carpal tunnel decompression. Hence, color Doppler sonography supports the role of sonography as a noninvasive means of evaluating patients with suspected carpal tunnel syndrome.

Gray-Scale and Color Doppler Sonography of Carpal Tunnel Syndrome

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