Best Diagnostic Criterion in High-resolution Ultrasonography for Carpal Tunnel Syndrome

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Background: High-resolution ultrasonography (HRUS) has been used to diagnose carpal tunnel syndrome (CTS) in recent years. However, the best diagnostic criterion and optimal cut-off value for HRUS remain controversial.

Methods: This study enrolled 37 patients with idiopathic CTS (61 CTS hands) and 20 healthy subjects (40 normal hands). The subjects underwent nerve conduction studies along with HRUS. Several ultrasonographic measurements with good reliability were compared, including the median nerve cross-sectional areas (CSA) at the pisiform and hook of hamate levels; the flattening ratios (FR) at the pisiform, hook of hamate, and distal radioulnar joint levels; retinacular bowing (RB); and the longitudinal compression sign (LCS). Receiver operating characteristic (ROC) curves were plotted for the optimal cut-off values as well as the sensitivity and specificity.

Results: There was a significant increase in the median nerve CSA at the pisiform and hook of hamate levels, RB, and LCS, but the FR was decreased at the hook of hamate level. The ROC curves demonstrated that the median nerve CSA at the pisiform level was most predictive of CTS; the optimal cut-off value was ≥ 9.875 mm^2, yielding 82% sensitivity and 87.5% specificity.

Conclusions: CTS can be diagnosed by HRUS. The most useful diagnostic criterion is a median nerve CSA of ≥ 9.875 mm^2 at the pisiform level.

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Key words: carpal tunnel syndrome, ultrasonography, diagnosis, median nerve

Carpal tunnel syndrome (CTS), an entrapment neuropathy of the median nerve, is a common disorder of the upper extremity and has a prevalence of 5.8% in women and 0.6% in men.(1) CTS is mainly diagnosed based on symptoms and physical signs and confirmed by nerve conduction studies (NCS). In CTS, the median nerve is swollen at the inlet of the carpal tunnel and flattened in the tunnel and at its outlet.(2,3) Ultrasonography is a noninvasive, convenient, and inexpensive tool for soft tissue imaging. High-resolution ultrasonography (HRUS) has proved reliable for performing measurements of the median nerve and carpal tunnel.(4) HRUS has been applied to CTS diagnosis in recent years, particularly in cases resulting from space occupying lesions. The most consistent finding in HRUS for CTS is a significant increase in the cross-sectional area (CSA) at the pisiform bone level (equivalent to the carpal tunnel

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inlet).(2) Various diagnostic criteria have been published,(2,5-10) and the median nerve CSA at the pisiform level has been cited most often.(2) However, there is no consensus regarding the optimal cut-off value in ultrasonographic measurements for CTS diagnosis. The aim of the present study was to determine the best diagnostic criterion and optimal cut-off value for diagnosing CTS by HRUS.

METHODS

Patients and controls

From June 2006 to May 2007, all patients with classic or probable symptoms of CTS (numbness, tingling, burning, or pain in at least 2 of digits 1, 2, and 3)(11) referred to the Department of Rehabilitation in a tertiary care hospital were recruited. Patients with peripheral neuropathy associated with systemic diseases such as diabetes mellitus, hypothyroidism, gout, and renal failure were excluded. Patients with trauma, pregnancy, or paralysis of the symptomatic wrist/hand were also excluded. The recruited patients signed an informed consent form after receiving a detailed explanation of the study. Patient data was obtained by questionnaire. The patients then underwent NCS and HRUS within 7 days. Concurrently, 20 healthy subjects (40 hands), including hospital employees and people from the community, were tested as controls.

Nerve conduction studies

NCS were performed by one of two examiners with good to excellent inter- and intra-rater intraclass correlation coefficient (ICC, 0.67-0.99) values. We used the Viking IV Electrodiagnostic System (Nicolet Biomedical Inc., Madison, WI, U.S.A.) and followed the NCS guidelines for CTS.(12) The temperature of the tested limbs was maintained at least at 32°C. The median nerve compound motor action potential (CMAP) was recorded at the abductor pollicis brevis with stimulation at the wrist at a distance of 6 cm. The median sensory nerve action potential (SNAP) was recorded at the index finger with stimulation at the wrist at a distance of 13 cm. A wrist-to-palm study (distance, 7 cm) was performed by stimulation at the mid-palm. In addition, a median-ulnar sensory comparison study was performed by recording the SNAP at the fourth digit following stimulation at a distance of 12 cm. Routine ulnar motor and sensory studies and electromyography for selected cases were performed to reveal possible ulnar neuropathy, polyneuropathy, or cervical radiculopathy. A diagnosis of CTS was made when the NCS results met one of the following electrodiagnostic laboratory criteria: motor distal latency (DL) > 4.1 ms, peak sensory DL > 3.5 ms, cross-wrist conduction velocity (CV) < 41 m/s, or fourth digit sensory comparison > 0.4 ms.

Ultrasonography

HRUS was carried out by one of two sonographers using a Sequoia 512 (Acuson, Mountain View, CA, U.S.A.). The patients were examined while sitting upright with their elbows flexed to approximately 120 degrees, fingers semiflexed, and the palm and wrist in the neutral position. The carpal tunnel was scanned with an 8-15 MHz broad linear transducer in both the axial and sagittal planes. The transducer exerted minimal pressure on the skin. Space occupying lesions or anatomic variants were examined if present. Retinacular bowing (RB) was measured as the maximal volar displacement of the flexor retinaculum from a line connecting its attachment to the hook of hamate and trapezoid (Fig. 1).(3,13) Then, an 8-15 MHz small linear transducer was applied to obtain the transverse image of the median nerve. The transducer was held perpendicular to the nerve to obtain the highest echo level. Therefore, the median nerve was observed on the screen as an oval or ellipsoid hypoechoic reticular area with a hyperechoic

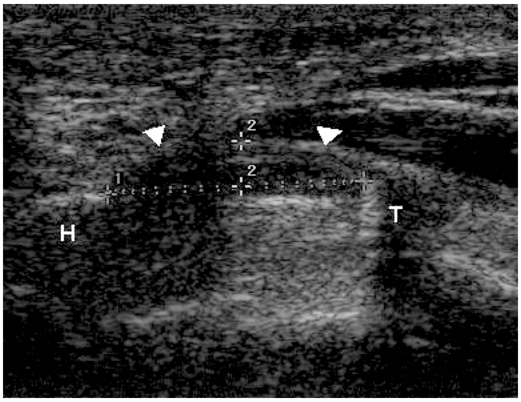

Fig. 1 Measurement of retinacular bowing. By transverse scan at the level of the hook of hamate, maximal volar displacement (between the calipers) of the hyperechoic band-like flexor retinaculum (arrow heads) from the line connects its attachments to the hook of hamate (H) and trapezoid (T).

rim (Fig. 2).(3,13) Its thickness along the long and short axes was measured, and the flattening ratio (FR)(13) was calculated by dividing the thickness along the long axis by that along the short axis. The CSA was obtained by the direct trace method(14) just inside the hyperechoic rim. FRs and CSAs of the median nerve were acquired at the levels of the pisiform and hook of hamate (representing the carpal tunnel inlet and outlet, respectively) and the distal radioulnar joint. The CSA at the pisiform level divided by that at the distal radioulnar joint level was defined as the swelling ratio (SR).(13,15) The median nerve in the carpal tunnel was then scanned in the longitudinal plane to determine the longitudinal compression sign (LCS) resulting from constriction of the flexor retinaculum. While tracing the median nerve longitudinally, the acoustic shadow of the distal radius was fixed as a landmark in the lower part of the image frame. Consequently, 2 carpal bones belonging to the proximal and distal rows were identified (usually the lunate and capitate), and the hyperechoic flexor retinaculum was observed along with the compressive notch (Fig. 3). A nerve with a smooth, even contour was graded LCS 0, equivocal or minimal tapering or a notch was graded 1, definite tapering or a notch was graded 2, and marked narrowing or dipping with a distorted nerve contour was graded 3 (Fig. 3). In most cases, HRUS of a wrist was completed in 10 min.

Reliability of tests

The reliability of the tests was determined by performing repeat NCS and HRUS in every fifth subject within 24 h; both examiners performed these tests.

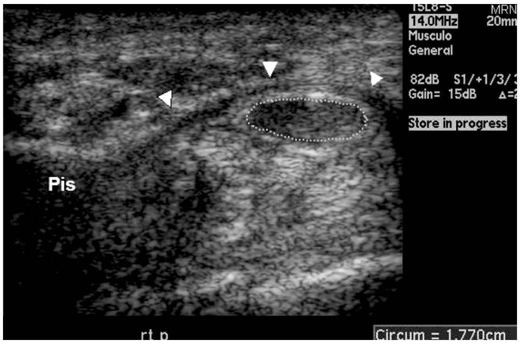

Fig. 2 Median nerve (encircled) in the carpal tunnel. By transverse scan at the level of the pisiform (Pis), the median nerve is observed as an oval or ellipsoid hypoechoic reticular area with a hyperechoic rim beneath the flexor retinaculum (arrow heads).

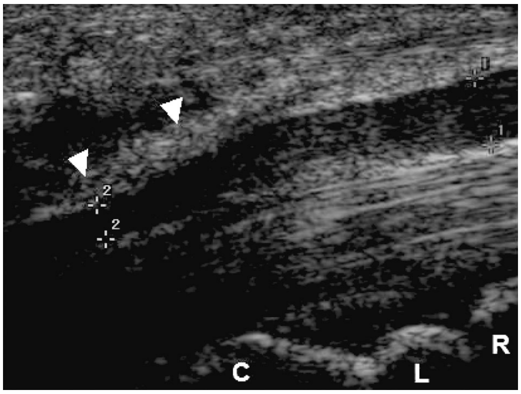

Fig. 3 Longitudinal compression sign, grade 3. The median nerve (between the calipers) is markedly narrowed with a distorted contour and is compressed by the hyperechoic flexor retinaculum (arrow heads). Bony landmarks: distal radius (R), lunate (L), and capitate (C).

Statistical analysis

Statistical calculations were performed using Excel 2003 (Microsoft, Redmond, WA, U.S.A.), SPSS 10.0 (SPSS Inc, Chicago, IL, U.S.A.), and a website for online calculation of weighted kappa.(16) A p value < 0.05 was considered significant. Gender was examined with Fisher's exact test. The Kolmogorov-Smirnov test was applied to determine whether the numeric data was normally distributed. The test revealed that all numeric data had normal distributions. The reliabilities of ultrasonographic variables were tested with $ICC_{(2,1)}$, except for the ordinal LCS, which was measured with weighted kappa. The differences in the means of continuous variables between CTS and normal hands were tested using independent t tests, and the ordinal variables were compared using the Mann-Whitney U-statistic. Useful ultrasonograhic variables were those with significant differences between CTS and normal hands. Receiver operating characteristic (ROC) curves were employed to determine the optimal cutoff values for useful ultrasonographic variables.

RESULTS

This study screened 50 patients. NCS and electromyography showed that 8 patients had CTS in combination with cervical radiculopathy, and 1 patient had cervical radiculopathy. NCS identified Martin-Gruber anastomosis in 1 patient. HRUS showed space occupying lesions in 2 patients predisposing them to CTS: one had flexor tenosynovitis and the other had crystal disposition in the soft tissues (later diagnosed as gout). HRUS also revealed bilateral bifid median nerves in 1 patient. A total of 37 patients with idiopathic CTS (61 diseased hands) were analyzed; 24 patients had CTS bilaterally. CTS was present in 35 right hands and 26 left hands. The duration of CTS ranged from 1-60 months (mean, 19.19 months; standard deviation, 18.49 months).

Patient data

The CTS group included 3 men and 34 women, whereas there were 5 men and 15 women in the healthy group. There were no significant gender differences between the 2 groups. There was no difference in the mean age between CTS patients (44 ± 9.4 years) and healthy subjects (43.7 ± 12.91 years). In addition, there were no differences in the mean height and weight between the 2 groups (height, 157.78 ± 6.36 cm vs. 160.8 ± 6.79 cm; weight, 64.22 ± 14.63 kg vs. 60.1 ± 8.64 kg). However, the CTS patients had a significantly greater body mass index (25.68 ± 5.05) than the healthy subjects (23.23 ± 2.91) ($p = 0.025$).

Nerve conduction studies

Median nerve motor studies revealed that the mean motor DL in the CTS hands (5.1 ± 1.23 ms) was significantly greater than that in the normal hands (3.39 ± 0.36 ms). The motor CV in the CTS hands was significant lower than that in the normal hands (54.97 ± 4.56 m/s vs. 57.88 ± 3.1 m/s). The mean amplitude of CMAP in the CTS hands was lower than that in the normal hands (10.41 ± 4.06 mV vs. 14.15 ± 3.4 mV). Median nerve sensory studies revealed longer onset and peak sensory DLs in the CTS hands compared with the normal hands (onset, 3.42 ± 0.83 ms vs. 2.22 ± 0.25 ms; peak, 4.32 ± 1.01 vs. 2.92 ± 0.3 ms). The sensory CVs in both the wrist to palm and elbow to wrist sections were lower in the CTS hands (33.13 ± 10.13 m/s and 60.32 ± 4.77 m/s, respectively) than the normal hands (56.13 ± 7.79 m/s and 62.83 ± 3.3 m/s, respectively). In addition, the amplitude of SNAP in the CTS hands (29.54 ± 17.08 μV) was significantly lower than that in the normal hands (63.17 ± 22.98 μV). The median-ulnar sensory comparison study showed a greater difference in the median-ulnar latencies in the CTS hands (1.64 ± 1.16 ms) than in the normal hands (0.13 ± 0.16 ms). All comparisons mentioned above had p values < 0.01. CTS was classified as mild in 15 hands, moderate in 36, pronounced in 6, and severe in 3 using the NCS classification system of Wainner.(17) One hand was found to be normal in NCS but had the typical symptoms and signs of CTS.

Ultrasonography

The results of HRUS are summarized in the Table 1. There was good to excellent reliability for the CSA at the pisiform level, RB, and LCS. However, variable ICCs were noted with the FR at all 3 levels, CSA at the hook of hamate and distal radioulnar joint levels, and SR. Because the lower limits of the 95% confidence intervals of these ICCs were less than 0.34 (detailed data not shown), these variables were not analyzed. In the CTS hands, the CSAs at all 3 levels in these hands were significantly greater than those in the normal hands ($p < 0.001$). However, the FR at the hook of hamate level in the CTS hands was lower than that in the normal hands.

Table 1. Comparison of Ultrasonographic Variables with Reliability

	Normal hands (N = 40)	CTS hands (N = 61)	p	Reliability
P-FR	2.92 ± 0.59	2.82 ± 0.59	0.436	0.664-0.896
P-CSA (mm^2)	9.22 ± 1.75	12.87 ± 4.21	< 0.001	0.865-0.959
H-FR	3.76 ± 1.01	3.28 ± 0.58	0.008	0.576-0.836
H-CSA (mm^2)	8.83 ± 1.67	11.95 ± 3.74	< 0.001	0.6-0.883
RU-FR	2.45 ± 0.50	2.26 ± 0.57	0.093	0.604-0.734
RU-CSA (mm^2)	6.89 ± 1.25	10.45 ± 4.71	< 0.001	0.436-0.932
RB (mm)	1.87 ± 0.56	2.64 ± 0.78	< 0.001	0.745-0.952
Swelling ratio	1.21 ± 0.23	1.30 ± 0.33	0.088	0.47-0.831
LCS	0 (0-1)	1.5 (1-2)	< 0.001	0.751-0.926

Abbreviations: CTS: carpal tunnel syndrome; P: pisiform level; FR: flattening ratio; CSA: cross-sectional area; H: hook of hamate level; RU: distal radioulnar joint level; RB: retinacular bowing; LCS: longitudinal compression sign.

All values in both groups are the mean ± standard deviation, except for median values (interquartile range) in the case of LCS; all reliability values are the range of intraclass correlation coefficients ($ICC_{(2,1)}$), except for weighted kappa in the case of LCS.

The RB and LCS values were significantly greater in the CTS hands than in the normal hands ($p < 0.001$). Only variables having good to excellent reliabilities were further analyzed. These were defined as useful ultrasonographic variables and included CSA at the pisiform level, RB, and LCS. The ROC curve of the pisiform CSA revealed that the area under the curve (AUC) was 0.901 ($p < 0.001$) with an optimal cut-off value of 9.875 mm^2, yielding 82% sensitivity and 87.5% specificity (Fig. 4). For the LCS, the ROC curve demonstrated that the AUC was 0.842 ($p < 0.001$) with an optimal cut-off value of ≥ 1.5, yielding 50% sensitivity and 95.8% specificity. Furthermore, the ROC curve of RB showed that the AUC was 0.781 ($p < 0.001$) with an optimal cut-off value of ≥ 2.11 mm, translating into 77% sensitivity and 75% specificity. The median nerve CSA at the pisiform level had the best diagnostic accuracy.

DISCUSSION

Space occupying lesions and anatomic variants

One of the advantages of ultrasonography is its ability to demonstrate several areas of anatomy simultaneously. Therefore, ultrasonography is recognized as a good tool for detecting space occupying lesions and anatomic variants. Tenosynovitis, crystal or amyloid deposition, ganglia, soft tissue tumors, neurogenic tumors, accessory muscles, bifid median nerves, and persistent median arteries have been reported to cause CTS.(3,18) Early detection of these underlying conditions could be helpful in planning treatment, which could be quite different from that of idiopathic CTS. In our series, 3 patients were diagnosed with CTS due to space occupying lesions or anatomic variants by HRUS. These included one case each of tenosynovitis, gout, and bifid median nerve, accounting for 7.5% (3/40) of all CTS patients.

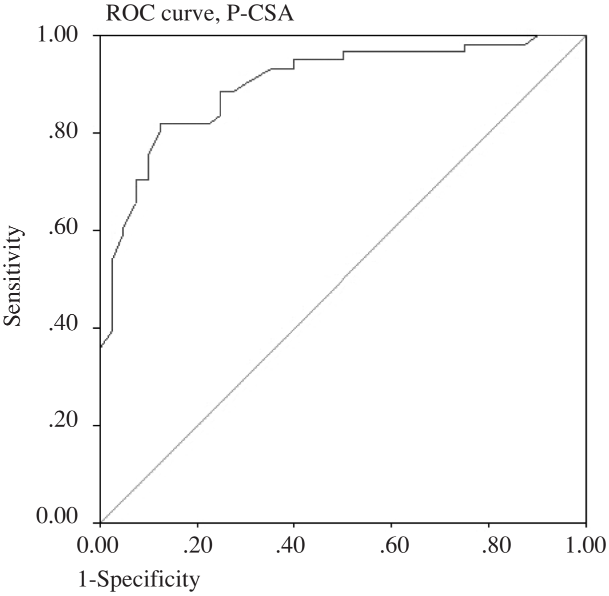

Fig. 4 Receiver operating characteristic (ROC) curve of the cross-sectional area at the pisiform level (P-CSA). Area under the curve was 0.901 ($p < 0.001$) and the optimal cut-off value was ≥ 9.875 mm^2, yielding a sensitivity of 82% and a specificity of 87.5%.

Patients with unilateral CTS and/or with a palpable mass at the wrist are particularly likely to have a space occupying lesion;(2) HRUS is suggested in these patients.

Cross-sectional area

Advancements in the resolution of ultrasonography have enabled detailed scanning and precise measurements of peripheral nerves. Several ultrasonographic measurements have been reported to be diagnostic of CTS, including the CSA and FR at the pisiform and hook of hamate levels, SR, RB, and qualitative nerve compression sign.(2,6) Among these, the CSA at the pisiform level was found to be the most predictive of CTS; the critical values varied mostly between 9 and 11 mm^2, yielding sensitivities of 70% to 94% and specificities of 65% to 97%.(2,7,9) In the present study, the diagnostic criterion i.e., the CSA at the pisiform level, had an optimal cut-off value of ≥ 9.875 mm^2 (sensitivity, 82% and specificity, 87.5%). This was very close to the results obtained by Swen et al.(19) (CSA, 10 mm^2; sensitivity, 70%; and specificity, 63%) and Wong et al.(5) (CSA, 9.8 mm^2; sensitivity, 89%; and specificity, 83%). The pathophysiology of median nerve swelling is thought to be the result of a cascade of events after compression, including damming of the axoplasmic flow, endoneurial edema, inflammation, demyelination, remyelination, and finally perineurial thickening.(20)

Flattening ratio

An increased FR at the hook of hamate level has been reported as a diagnostic criterion. Buchberger et al. reported a cut-off value of 4.2, while Keberle et al. reported it to be 3.4.(13,15) However, the controversy surrounding the increased median nerve flattening at the hook of hamate level continues. Some recent studies showed increased FRs at the hook of hamate level,(8,21,22) whereas others did not.(9,23) Nakamichi and Tachibana reported with a good reliability that this variable was significantly lower in CTS hands than in normal hands by measuring frozen slices from amputated wrists.(23) Duncan et al. noted that the FR was highly variable and had a poor predictive value for CTS.(14) The present study yielded similar results, in that variable ICCs were noted in the FR measurements at all 3 levels. Therefore, the FRs were not further analyzed with ROC curves.

Retinacular bowing

Buchberger et al. and Keles et al. demonstrated that RB is a CTS diagnostic criterion with a cut-off value of 3.7 mm.(9,24) Sarria et al. reported an RB cut-off value of 2.5 mm.(25) In this study, this cut-off value was 2.11 mm, although the sensitivity (77%) and specificity (75%) were not satisfactory. Increased RB in CTS hands is assumed to occur owing to raised intracarpal tunnel pressure. Idiopathic CTS is thought to result from increased soft tissue volume in the carpal tunnel, mostly in the form of noninflammatory synovial fibrosis.(26)

Longitudinal compression sign

LCS of the median nerve is frequently noted in CTS hands. Kele et al. reported that a median nerve CSA of > 11 mm^2 in the proximal carpal tunnel in combination with qualitative LCS (positive or negative) was highly predictive of CTS (sensitivity, 89.1% and specificity 98%).(6) Wiesler et al.,(10) did not perform measurements on the longitudinal scan because of its inconsistent reliability. The present study is the first to introduce a semi-quantitative scale for the longitudinal scan (LCS 0, 1, 2, and 3). We used an 8-15 MHz small linear transducer, instead of transducers with relatively low frequencies (maximal 11-12 MHz), which had been used in previous studies.(6,10) This facilitated demonstration of detailed changes in the nerve contour. The LCS provided fair to good diagnostic accuracy according to ROC curves (cut-off value ≥ 1: sensitivity, 91.7% and specificity, 62.5%; cut-off value ≥ 2: sensitivity, 50% and specificity, 96.8%). However, the LCS might still be useful for diagnosing CTS if its value were 2 or 3 (cut-off value ≥ 2: positive predictive value, 96%). The potential drawback of performing LCS using a small transducer would be its inability to display the whole carpal tunnel in a bigger wrist in a single image frame. Further studies are necessary to elucidate the usefulness of LCS.

HRUS vs. NCS

A review of several studies(2,5-9,21,22) indicated that the diagnostic accuracy of HRUS was similar or slightly lower than that of NCS. Nevertheless, Koyuncuoglu et al. reported that CSAs at the pisiform level were greater than 10.5 mm^2 in 30.51% of NCS-negative CTS hands.(27) They concluded that HRUS was of value in diagnosing CTS in NCS-negative hands. In our series, the only NCS-negative CTS hand could be diagnosed with HRUS; although its pisiform CSA was 9.1 mm^2, its RB was 2.3 mm with LCS grade 2. In NCS-negative patients presenting with symptoms and signs compatible with CTS, HRUS may be a useful complementary diagnostic tool.

HRUS for follow-up

In addition to diagnosis, HRUS has been used to follow up the carpal tunnel and median nerve status postoperatively. Lee at al. found that the CSAs of both the carpal tunnel and median nerve were greater 8 months after surgery, but there was no significant change in the FR.(28) The role of HRUS in the screening of recurrent CTS is unclear and requires further studies.

Limitations of this study

The main limitations of the present study were the relatively small sample size and inadequate blinding of the examiner to clinical information. In addition, the severity of CTS was relatively mild according to NCS grading. As a result, the conclusions may not be applicable to all CTS patients.

Conclusion

HURS is a good diagnostic tool for CTS. The best ultrasonographic diagnostic criterion for idiopathic CTS is a median nerve CSA of ≥ 9.875 mm^2 at the pisiform level, yielding 82% sensitivity and 87.5% specificity. Larger series may be necessary to elucidate follow-up values of HRUS in the median nerve and carpal tunnel.

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高解像力超音波診斷腕隧道症候群之最佳標準

王琳毅 梁秋萍 黃郁琦 洪禎雯 張舜雯 彭亞蘋

背 景： 近年來高解像力超音波被用於診斷腕隧道症候群。但最佳的超音波診斷標準與適切分界值仍有爭議。

方 法： 共納入 37 位自發性腕隧道症候群病人 (61 隻病手) 與 20 位正常人 (20 隻正常手)，均接受神經傳導檢查及高解像力超音波。比較具良好信賴度之超音波測量值，包括正中神經在豌豆骨及在鉤狀骨旁的截面積，在豌豆骨、鉤狀骨，和遠端撓尺關節旁的扁平率、支持帶彎曲，與縱向壓迫徵。描繪接受者操作特徵曲線 (ROC curve) 以定出適切分界值、敏感度和特異度。

結 果： 有腕隧道症候群的手，正中神經在豌豆骨及在鉤狀骨旁的截面積、支持帶彎曲，與縱向壓迫徵皆較大。但在豌豆骨旁的扁平率較小。ROC curve 顯示正中神經在豌豆骨旁的截面積最能預測腕隧道症候群，適切的分界值是 ≧ 9.875 mm^2。(敏感度 82%，特異度 87.5%)。

結 論： 腕隧道症候群可以高解像力超音波診斷，最有用的診斷標準是正中神經在豌豆骨旁的截面積 ≧ 9.875 mm^2。

(長庚醫誌 2008;31:469-76)

關鍵詞： 腕隧道症候群，超音波，診斷，正中神經

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