

## Grey-scale sonography and sonoelastography for diagnosing carpal tunnel syndrome

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### Abstract

Carpal tunnel syndrome (CTS) is a common peripheral entrapment neuropathy of the median nerve at wrist level, and is thought to be caused by compression of the

median nerve in the carpal tunnel. There is no standard quantitative reference for the diagnosis of CTS. Grey-scale sonography and sonoelastography (SEL) have been used as diagnostic tools. The most commonly agreed findings in grey-scale sonography for the diagnosis of CTS is enlargement of the median nerve cross-sectional area (CSA). Several authors have assessed additional parameters. "Delta CSA" is the difference between the proximal median nerve CSA at the pronator quadratus and the maximal CSA within the carpal tunnel. The "CSA ratio" is the ratio of CSA in the carpal tunnel to the CSA at the mid forearm. These additional parameters showed better diagnostic accuracy than CSA measurement alone. Recently, a number of studies have investigated the elasticity of the median nerve using SEL, and have shown that this also has diagnostic value, as it was significantly stiffer in CTS patients compared to healthy volunteers. In this review, we summarize the usefulness of grey-scale sonography and SEL in diagnosing CTS.

**Key words:** Carpal tunnel syndrome; Cross-sectional area; Gray-scale sonography; Diagnosis; Median nerve; Sonoelastography; Elasticity

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**Core tip:** The diagnostic value of grey-scale sonography and sonoelastography in carpal tunnel syndrome (CTS) is reviewed. Sonography can potentially allow a noninvasive screening, and could therefore be a preferable first-line approach to detect pathological changes of the intracarpal tunnel contents. This review summarizes the current knowledge of sonographic findings as a diagnostic tool in CTS.

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## INTRODUCTION

Carpal tunnel syndrome (CTS) is a common compression neuropathy of the median nerve at wrist level, with an estimated prevalence of 50 cases per 1000 population per year<sup>[1]</sup>. The main symptoms of CTS include numbness and tingling in the area of the median nerve distribution and weakness in the opposition of the thumb.

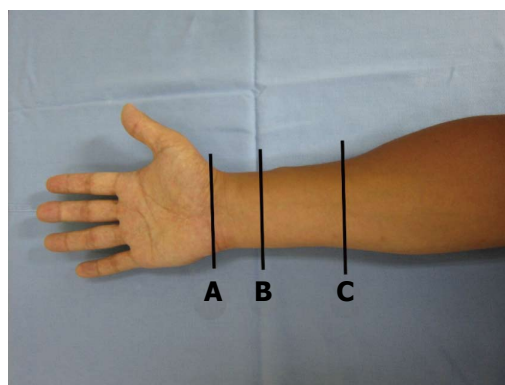
The median nerve in the carpal tunnel lies between the transverse carpal ligament superiorly and the flexor tendons and carpal bones inferiorly<sup>[2]</sup>. CTS is thought to be caused by compression of the median nerve within its surrounding structures, including the transverse carpal ligament, finger flexor tendons, and tenosynovial tissue<sup>[3,4]</sup>. Therefore, it is important to investigate morphological changes in the intracarpal tunnel contents in order to understand the pathophysiology of CTS.

Sonography can provide information on anatomical abnormalities of the median nerve and intracarpal tunnel contents, which are causative factors in CTS. Sonoelastography (SEL) is a modality for quantitatively measuring the elasticity of soft tissue through conventional grey-scale sonography with estimated Young's modulus or semi-quantitative values as strain ratios, and promising preliminary results have been obtained for SEL in the diagnosis of liver, breast, pancreas, prostate, and thyroid masses using the appropriate cut-off values<sup>[5-9]</sup>. Recently, several studies have investigated the elasticity of the intracarpal tunnel contents to clarify the pathophysiology of CTS using SEL<sup>[10-15]</sup>.

In this review, we summarize the usefulness of grey-scale sonography and sonoelastography in diagnosing CTS.

## GREY-SCALE SONOGRAPHY

The most commonly agreed findings in grey-scale sonography for the diagnosis of CTS is the enlargement of the median nerve cross-sectional area (CSA). Nerve enlargement is thought to result from large myelinated fibers at the periphery of the fascicles, interfascicular epineurial fibrosis, and/or perineurial thickening under chronic nerve compression<sup>[16]</sup>. Table 1 gives the diagnostic accuracy of using the CSA from previous studies and includes the CSA cut-off values used and the location where the CSA was measured. The reported CSA cut-off values in the carpal tunnel measured by sonography ranged from 8.5 to 12 mm<sup>2</sup>. The majority of studies measured the CSA at the tunnel inlet, which is described as being level with the pisiform bone in some studies. The findings of these studies revealed a wide variation in sensitivity (62%-99%) and specificity (57%-100%). In a meta-analysis, the single CSA test for CTS was reported to have 87.3% sensitivity and 83.3% specificity, with an area under the receiver operating characteristic curve of 0.93<sup>[17]</sup>. However, a limitation of



**Figure 1 Demonstration of probe location at the forearm.** The cross sectional area of the median nerve was measured (A) level with the pisiform bone (B) level with the proximal third of the pronator quadratus and (C) level with a point 12 cm proximal to the pisiform bone.

this analysis was that measurements were obtained in different proportions of patients at different points along the carpal tunnel.

In order to overcome the limitations arising from individual anatomical differences when using the CSA to diagnose CTS, Klauser *et al.*<sup>[18]</sup> assessed "delta CSA", which is the difference between the proximal median nerve CSA at the level of the pronator quadratus and the maximal CSA within the carpal tunnel, resulting in a threshold of 2 mm<sup>2</sup>. However, there are few studies using "delta CSA" for diagnosing CTS<sup>[18-20]</sup>, and further research is needed to validate this diagnostic parameter. Other studies reported the diagnostic accuracy of a ratio between a CSA in the carpal tunnel and a proximal CSA at the mid forearm (the "CSA ratio")<sup>[19,21-25]</sup>. These two parameters allowed a more accurate detection of CTS than CSA alone. Tables 2 and 3 summarize the previously reported diagnostic accuracies of these two parameters. Probe locations at the forearm in major studies are shown in Figure 1, and representative grey-scale sonographic images of a CTS patient are shown in Figure 2.

Other characteristic parameters of CTS have been reported, including the thickness of the transverse carpal ligament, palmar bowing of the flexor retinaculum, flattening of the median nerve, and decreased longitudinal excursion on dynamic assessment, all of which can aid in the sonographic diagnosis of CTS<sup>[26-28]</sup>. In addition, it is recognized that hypervascularity and hypoechogenicity of the median nerve are present in CTS with a larger CSA, and investigation of the vascularity of the median nerve using Doppler sonography has been used as an adjunct to the diagnosis of CTS<sup>[29,30]</sup>. Despite these characteristic findings, few validated quantitative scoring systems have been created for assessing hypervascularity and hypoechogenicity of the median nerve as a reference standard for CTS diagnosis<sup>[31]</sup>.

## SONOELASTOGRAPHY

There are two major stress applications in SEL;

**Table 1** Summary of previous studies reporting the diagnostic value of the median nerve cross-sectional area in carpal tunnel syndrome

Ref.	CSA cut-off (mm <sup>2</sup> )	CTS wrists	Control wrists	Location	Sensitivity (%)	Specificity (%)	AUC
Duncan <i>et al.</i> <sup>[47]</sup>	9	102	68	Pisiform	82	97	NA
Lee <i>et al.</i> <sup>[48]</sup>	15	100	56	Scaphoid tuberosity and the pisiform	88	96	NA
Sarria <i>et al.</i> <sup>[26]</sup>	11	64	42	Hook of hamate	75	57	NA
Swen <i>et al.</i> <sup>[49]</sup>	10	63	20	Pisiform	70	63	NA
Nakamichi and Tachibana <sup>[50]</sup>	12	414	408	Mean location of the proximal, mid and distal tunnel	67	97	NA
Wong <i>et al.</i> <sup>[51]</sup>	9.8	35	35	Tunnel inlet	89	83	0.91
Kele <i>et al.</i> <sup>[52]</sup>	11	110	55	Tunnel inlet	74	98	NA
Altinok <i>et al.</i> <sup>[53]</sup>	9	40	40	Pisiform	65	93	NA
El Miedany <i>et al.</i> <sup>[54]</sup>	10	96	156	Tunnel inlet	98	100	NA
Keleş <i>et al.</i> <sup>[55]</sup>	9.3	35	40	Middle carpal tunnel	80	76	0.833
Ziswiler <i>et al.</i> <sup>[56]</sup>	10	78	23	The largest CSA	82	87	0.89
Mallouhi <i>et al.</i> <sup>[57]</sup>	11	172	None	Maximal CSA in the carpal tunnel	91	47	NA
Wiesler <i>et al.</i> <sup>[58]</sup>	11	44	86	The distal wrist crease	91	84	NA
Naranjo <i>et al.</i> <sup>[59]</sup>	9.7	80	25	Tunnel inlet	86	48	0.78
Kaymak <i>et al.</i> <sup>[60]</sup>	12	34	38	Pisiform	88	66	0.84
Kwon <i>et al.</i> <sup>[61]</sup>	10.7	41	41	Tunnel inlet	66	63	0.75
Pinilla <i>et al.</i> <sup>[62]</sup>	6.5	40	30	Tunnel inlet	89.5	93	NA
Sernik <i>et al.</i> <sup>[28]</sup>	10	40	63	Pisiform	85	92.1	NA
Visser <i>et al.</i> <sup>[63]</sup>	10	265	137	Tunnel inlet	78	91	0.90
Ashraf <i>et al.</i> <sup>[64]</sup>	9.3	70	80	Middle carpal tunnel	80	77.5	0.796
Klauser <i>et al.</i> <sup>[18]</sup>	12	100	93	Maximal CSA in the carpal tunnel	94	95	0.9896
Pastare <i>et al.</i> <sup>[65]</sup>	9	97	None	Tunnel inlet	62	100	0.842
Mohammadi <i>et al.</i> <sup>[66]</sup>	8.5	132	32	Tunnel inlet	97	98	NA
Ghasemi-Esfe <i>et al.</i> <sup>[29]</sup>	10.5	85	49	Pisiform	69	94	NA
Roll <i>et al.</i> <sup>[19]</sup>	10.3	83	83	Pisiform	80.4	90.6	0.899
Kang <i>et al.</i> <sup>[23]</sup>	9.5	110	38	Distal wrist crease	96	92	0.988
Ulaşlı <i>et al.</i> <sup>[67]</sup>	10.5	95	48	Maximal CSA in the carpal tunnel	91	81	0.934
Fowler <i>et al.</i> <sup>[42]</sup>	10	55	30	Pisiform	89	90	NA
Kantarci <i>et al.</i> <sup>[35]</sup>	9.5	60	36	Tunnel inlet	60	91.7	0.844
Miyamoto <i>et al.</i> <sup>[37]</sup>	11	43	44	Pisiform	82	75	0.85
Ooi <i>et al.</i> <sup>[68]</sup>	9.8	95	30	Pisiform	92	90	0.95

CSA: Cross-sectional area; CTS: Carpal tunnel syndrome; AUC: Area under curve; NA: Not available.

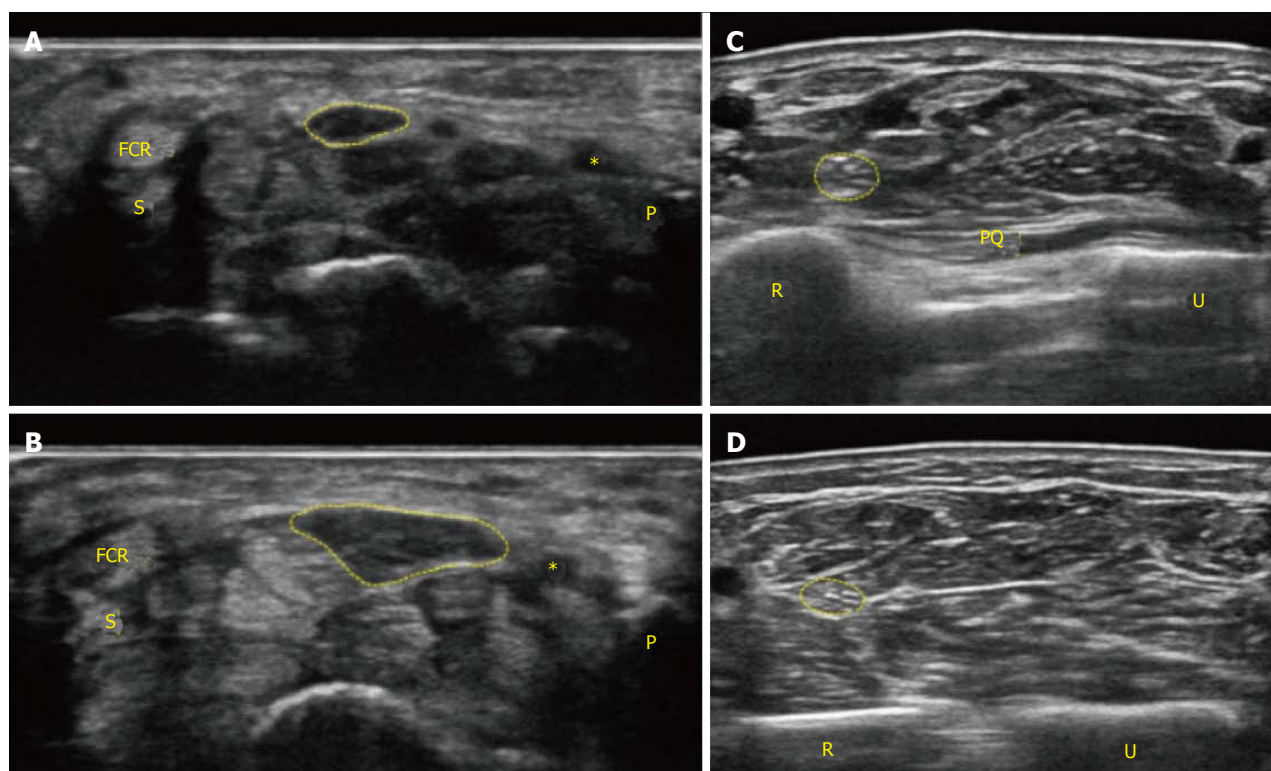
**Table 2** Summary of studies reporting the diagnostic value of the delta cross-sectional area of the median nerve for carpal tunnel syndrome

Ref.	delta CSA cut-off (mm <sup>2</sup> )	CTS wrists	Control wrists	Location	Sensitivity (%)	Specificity (%)	AUC
Klauser <i>et al.</i> <sup>[18]</sup>	2	100	93	Maximal CSA in the carpal tunnel/proximal third of the pronator quadratus	99	100	0.9988
Roll <i>et al.</i> <sup>[19]</sup>	4.16	83	83	Pisiform/6 cm proximal to the distal wrist crease	82.4	87.5	0.886
Tajika <i>et al.</i> <sup>[20]</sup>	2	50	81	Pisiform/distal radioulnar joint	100	99	0.996

CSA: Cross-sectional area; CTS: Carpal tunnel syndrome; AUC: Area under curve.

compression elastography and shear-wave elastography. Compression elastography, also described as static strain elastography, is based on the principle that the compression of tissue produces strain. Displacement is calculated in real time by repeated manual compression to the tissue using a hand-held sonographic transducer. The displacement is then converted to a color-coded strain distribution map, which is often superimposed over the conventional B-mode image or displayed next to it. Most compression elastography systems provide both a visual representation of pressure and a quantitative measurement in the form of the strain ratio, which is an index of the relative elasticity between an objective region of interest (ROI) and a reference ROI. Compression

elastography can draw the calculation area as a relatively free shape (*e.g.*, elliptical or bowing). The strain is lower in firmer tissues. However, compression elastographic assessment is subject to a number of technical difficulties. The compression force for measurements of tissue strain can be regulated by freehand, and the probe should always be held perpendicular to the objectives so that the appropriate strain is adjusted with reference to the feedback indicator. This is necessary because the nonlinear compression force can result in the elasticity of the objectives being measured incorrectly. To minimize intra- and inter-observer variation and to avoid transient temporal fluctuations, Yoshii *et al.*<sup>[32,33]</sup> developed a cyclic compression apparatus with automatic vibratory



**Figure 2** Transverse images in a 79-year-old female with carpal tunnel syndrome. A: A conventional grey scale sonographic image shows the cross-sectional area of the median nerve (CSA) corresponding to the circle in the normal side with an area of 8 mm<sup>2</sup> at the level of the pisiform bone; B: CSA in the carpal tunnel syndrome (CTS) side shows 21 mm<sup>2</sup> at pisiform bone level; C: CSA in the CTS side shows 7 mm<sup>2</sup> at the proximal third of the pronator quadratus level; D: CSA in the CTS side shows 6 mm<sup>2</sup> at a point 12 cm proximal to the pisiform bone. In this case, the calculated “delta CSA” and “CSA ratio” were 14 mm<sup>2</sup> and 3.5, respectively. \*: Ulnar artery. FCR: Flexor carpi radialis; P: Pisiform bone; S: Scaphoid bone; PQ: Pronator quadratus muscle; R: Radius; U: Ulnar.

**Table 3** Summary of studies reporting the diagnostic value of the cross-sectional area ratio of the median nerve for carpal tunnel syndrome

Ref.	CSA ratio cut-off	CTS wrists	Control wrists	Location	Sensitivity (%)	Specificity (%)	AUC
Hobson-Webb <i>et al</i> <sup>[21]</sup>	1.4	44	18	Distal wrist crease/12 cm proximal in the forearm	100	NA	NA
Visser <i>et al</i> <sup>[22]</sup>	2	265	137	Tunnel inlet/forearm	69	90	0.83
Roll <i>et al</i> <sup>[19]</sup>	1.70	83	83	Pisiform/6 cm proximal to the distal wrist crease	80.4	81.2	0.842
Kang <i>et al</i> <sup>[23]</sup>	1.34	110	38	Distal wrist crease/12 cm proximal in the forearm	99.9	100	0.988
Mhoon <i>et al</i> <sup>[24]</sup>	1.4	192	50	Distal wrist crease/12 cm proximal in the forearm	97	28	0.789
Fu <i>et al</i> <sup>[25]</sup>	1.3	46	44	Tunnel inlet/outlet	91	93	0.98

CSA: Cross-sectional area; CTS: Carpal tunnel syndrome; AUC: Area under curve; NA: Not available.

equipment.

Shear-wave elastography employs a directional force that leads to shear deformation propagating as a shear wave. Shear-wave elastography, also termed dynamic elastography, is based on the measurement of the propagation velocity distribution of a directional shear wave produced by an ultrasound pulse<sup>[34]</sup>. The velocity of the shear waves can be measured and used to evaluate tissue elasticity because the shear waves travel faster in harder materials: Young modulus (E) can be calculated as a function of shear velocity (Cs) and material density ( $\rho$ ) using the equation  $E = 3\rho Cs^2$ <sup>[34]</sup>. This technique allows for quantitative measurements that can be expressed in kilopascals or in centimeters per second. A disadvantage of shear-wave elastographic

evaluation is that only limited ROI shapes (e.g., a 5 mm × 5 mm box or a 1 mm × 1 mm circle) are currently available for the quantitative measurement of elasticity.

The diagnostic significance of median nerve stiffness using SEL has also been investigated (Table 4). Kantarci *et al*<sup>[35]</sup> found that the median nerve at the carpal tunnel inlet was significantly stiffer in CTS patients than in healthy volunteers using shear-wave elastography. They evaluated the median nerve elasticity within a defined 2 mm diameter circle at the carpal tunnel inlet in the longitudinal image, and reported that a 40.4 kPa cut-off value on shear-wave elastography gave a high diagnostic accuracy. Two further studies evaluated the elasticity of the median nerve by compression elastography<sup>[36,37]</sup>. The median nerve in CTS patients

**Table 4** Summary of studies reporting the diagnostic accuracy for carpal tunnel syndrome of the median nerve elasticity determined using sonoelastography

Ref.	Type of sonoelastography	CTS wrists	Control wrists	Location	Sensitivity (%)	Specificity (%)	AUC
Orman <i>et al</i> <sup>[36]</sup>	Compression	74	45	Pisiform-scaphoid	84	54	NA
Miyamoto <i>et al</i> <sup>[37]</sup>	Compression	43	44	Pisiform-scaphoid	82	68	0.78
Kantarci <i>et al</i> <sup>[35]</sup>	Shear wave	60	36	Tunnel inlet	93.3	88.9	0.956

CTS: Carpal tunnel syndrome; AUC: Area under curve; NA: Not available.

was significantly stiffer than that in healthy volunteers in both studies. These studies also evaluated the diagnostic value of median nerve elasticity. Orman *et al*<sup>[36]</sup> reported that an appropriate median nerve strain cut-off value could detect CTS with 84% sensitivity and 54% specificity, although this was not a significant improvement over conventional grey-scale sonography.

We reported different findings for CTS diagnosis using compression elastography. In our study, we used a reference medium with a constant elasticity for quantitative assessment. On the basis of a receiver operating characteristic analysis, a logistic combined model with both median nerve stiffness and the CSA was providing a sensitivity of 81% and a specificity of 91%, with an area under receiver operating characteristics curve of 0.91<sup>[37]</sup>.

## FUTURE PERSPECTIVE

The general approaches for diagnosing CTS are combinations of clinical provocation tests and nerve conduction studies (NCS)<sup>[1]</sup>. However, studies of Phalen's maneuver reported a wide range of values for sensitivity of 10% to 71% and specificity of 55% to 86%<sup>[38]</sup>. The sensitivity of Tinel's sign ranged from 9% to 89% and a specificity of 55% to 96%<sup>[38]</sup>. Whereas, Graham *et al*<sup>[39]</sup> developed original clinical diagnostic criteria for CTS by analyzing selected highly ranked predictors from clinical provocation tests and symptoms. They reported that what they call "CTS-6" (numbness in the median nerve distribution, nocturnal numbness, weakness/atrophy of the thenar musculature, Tinel's sign, Phalen's test, loss of 2-point discrimination) contributed to the diagnostic model of CTS. The correlation between the probability of CTS predicted by CTS-6 and a panel of expert clinicians was 0.71<sup>[39]</sup>.

However, there is no quantitative gold standard of reference for CTS diagnosis. NCS has been widely used in the quantitative diagnosis of CTS. But, NCS tests have a reported sensitivity of 56% to 85%<sup>[40]</sup>, and the false-negative rate for NCS testing has been reported to be between 16% and 34%<sup>[41]</sup>. By comparing sonography with NCS using CTS-6 as the reference standard, Fowler *et al*<sup>[42]</sup> showed that sonography could be used to confirm the diagnosis of CTS with better specificity and equal sensitivity as those of NCS. It could therefore be an alternative method to NCS in clinical practice to use sonography as a first-line approach for CTS screening because it is non-invasive, allows real-time access, and is cost-effective<sup>[43]</sup>.

Previous studies have shown that sonography can be useful also to monitor therapeutic response following surgery<sup>[44,45]</sup> and corticosteroid injection<sup>[15,46]</sup>. Smidt *et al*<sup>[44]</sup> reported that CSA of the median nerve at least 6 mo after surgery decreased from 14 mm<sup>2</sup> to 11 mm<sup>2</sup> in a patient group with a good outcome, whereas CSA remained almost the same in a group with a poor outcome. Kim *et al*<sup>[45]</sup> found CSA decreased in the first 3 wk after surgery. These findings indicate that measurement of CSA may provide clinicians with a tool to estimate the response to CTS surgery.

Palpation-guided injection into the carpal tunnel is often performed in general clinical practice. The major risk of the palpation-guided injection is damaging the intracarpal intact structures including the median nerve, flexor tendons and vessels. Moreover, if the injected steroid is not adequately placed inside the carpal tunnel, patients cannot obtain therapeutic effectiveness. Therefore, in order to improve the accuracy of the injection, a sonography-guided technique should be useful. Comparing a sonography-guided group to a palpation-guided group, the improvement in symptom in the sonography-guided group at 12 wk after injection was higher than that in the palpation-guided group<sup>[46]</sup>. The average time to symptom relief was also shorter in the sonography-guided group<sup>[46]</sup>. We measured the stiffness of the intracarpal tunnel contents by using SEL. The stiffness of the intracarpal tunnel contents surrounding the median nerve in CTS patients was higher than that of healthy volunteers but decreased 6 wk after corticosteroid injection<sup>[15]</sup>.

In addition to diagnostic tools, grey-scale sonography and SEL could be key skills for objectively assessing the response and predicting the prognosis following therapeutic intervention and operative treatment in CTS.

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