Pathomechanics of Peripheral Nerve Loading

Evidence in Carpal Tunnel Syndrome

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ABSTRACT: Peripheral nerve injury is a common occurrence, with carpal tunnel syndrome (CTS) receiving the most attention. Nerve dysfunction associated with compression syndromes results from an interruption or localized interference of microvascular function due to structural changes in the nerves or surrounding tissues. This article reviews the physiologic, pathophysiologic, and histologic effects of compressing peripheral nerves in animal models, and then examines the evidence for similar processes in humans using CTS as a model.

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PERIPHERAL NERVE STRUCTURE AND FUNCTION

The peripheral nerve consists of hundreds or thousands of cell bodies, located in either the anterior horn of the spinal cord (motor neuron) or the dorsal root ganglia (sensory neuron) and their axons. The axon extends from the cell body to the periphery and, in the case of a myelinated fiber, is wrapped by repeating Schwann cells that cover the length of the axon (Figure 1). Nonmyelinated fibers lie next to the myelinated fibers and are associated with one Schwann cell. These myelinated and nonmyleinated fibers are bundled together and surrounded by a strong membrane known as the perineurial membrane. The bundles are called fascicles, which in turn are typically grouped by a thick sheet of loose connective tissue known as the epineurium. Around each nerve fiber and within the perineurium is an intrafascicular connective tissue called the endoneurium. The thickness of the connective tissue varies along the length of the nerve; this uneven distribution may be related to compressive loading, as evidenced by increased thickness of connective tissue in the nerve near joints and in superficial locations.[1]

Axonal transport and impulse propagation is dependent on a microvascular system that is well developed with vascular plexuses in all connective tissue layers.[2] Axonal transport provides a nutritional delivery and removal system. The large vessels connected to the nerve have a coiled structure and approach the nerve trunk segmentally, so that the vascular supply is uninterrupted during the normal gliding of the nerve trunk during joint motion. Upon reaching the nerve trunk, the vessels branch and run longitudinally within the epineurium and form collateral connections to vessels in the perineurial sheath. Where the vessels pass through the perineurium into the endoneurium, at an oblique angle, they may act as one-way valves.[2] Because there are no lymphatics in the endoneurial space, edema that forms in this space leads to an intrafascicular pressure increase and retards endoneurial blood flow.[3] Epineurial vessels are more easily traumatized than endoneurial vessels.

ISOLATED NERVE AND ANIMAL MODELS OF NERVE TRAUMA

Because of the invasiveness and obvious likelihood of permanent damage with in vivo human experiments, animal models have been developed to examine the effects of compression on the peripheral nerve. The models generally involve isolating peripheral nerve segments and compressing them with clamps, tubes, or other implantable devices to mimic acute or chronic compression.

Acute Effects of Compression

Several studies have demonstrated retarded axonal and epidural flow when an isolated but intact nerve segment is compressed using a small pneumatic cuff. Early studies used very high pressures (e.g., 1,000 mm Hg[4]) and the resultant neuropathy lasted up to

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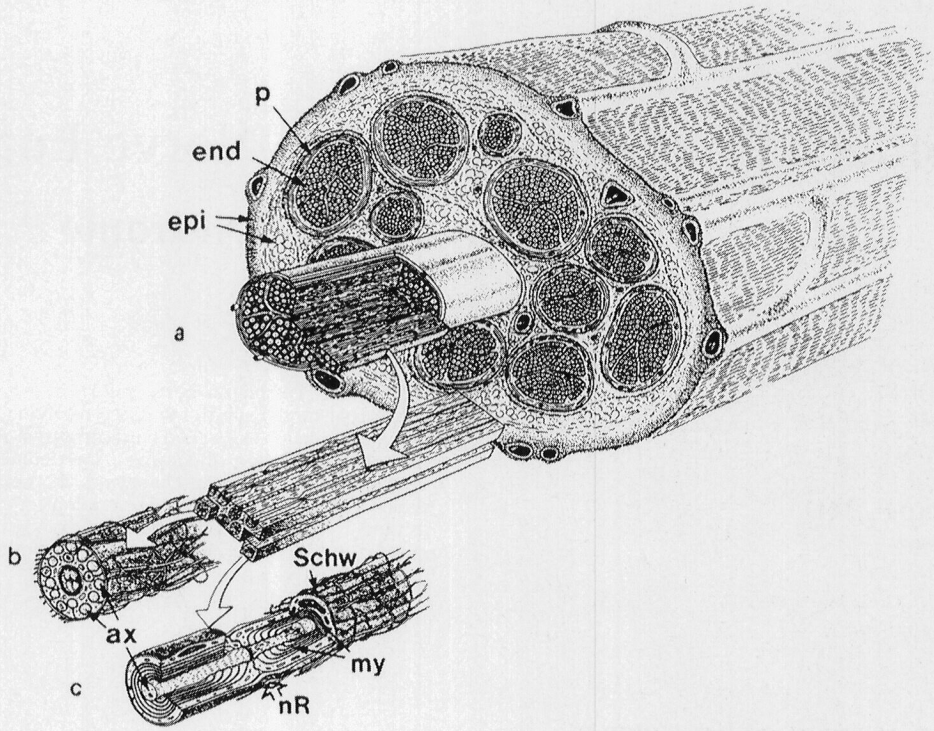

FIGURE 1. Drawing of a peripheral nerve showing the various components: (a) fascicles are bundles of nerve fibers surrounded by a membrane called the perineurium (p) and are embedded in the epineurium (epi). Inside a fascicle the myelinated (c) and unmyelinated (b) axons (ax), or nerve fibers, are surrounded by the endoneurium (end). Myelinated fibers are surrounded by the myelin sheath (my), which is formed from Schwann cells (Schw) separated by the nodes of Ranvier (nR). (Reproduced, with modification, from Lundborg G. Nerve Injury and Repair. Edinburgh: Churchill Livingstone, 1988, p 186, with permission.)

months. Lesions were concentrated at the edge of the pneumatic cuff and were attributed to the large pressure gradient at the edges.[4] Later studies, which applied much lower pressures in order to differentiate the effects of mechanical pressure versus ischemia, found that a pressure of 50 mm Hg caused edema to form only in the epineurium, while pressures of 200, 400, and 600 mm Hg caused endoneurial edema as well. Vascular injury at the centre of the compressed segment was related more to duration than magnitude, whereas vascular injury at the edges was related to both duration and magnitude.[5] The authors concluded that "the mechanical force, represented by the shear stresses at the edges, seemed to constitute the basic etiological factor," which may in turn lead to a susceptibility to ischemia, thus beginning a vicious cycle.[5] Further work identified "threshold" levels of compression using inflatable polyethylene cuffs on the rabbit tibial nerve. Epineural venular flow was retarded by a pressure of 20–30 mm Hg and stopped in all specimens by 60 mm Hg. Nerves were completely ischemic by 60–80 mm Hg, and although circulation was restored in the first minute after releasing the pressure, it was sluggish and edema was present.[6]

Perhaps more relevant to nerve compression in humans, fluctuating pressures have been found to have similar effects on nerve function. By examining fluctuating versus constant pressure in the rat tibial nerve, the average pressure during cyclic loading (~20,000 pressure cycles) had similar effects to constant pressure. For example, the action potential amplitude following a 20 to 50 mm Hg fluctuating compression (mean 35 mm Hg) was not significantly different from a constant pressure of 30 mm Hg.[7]

The link between well controlled animal studies and clinical conditions in humans is an important one, and may be best exemplified by inducing increased carpal tunnel pressure in humans. The controlled application of pressure to the palm over the transverse carpal ligament induced pressures of 30, 60, and 90 mm Hg in the carpal tunnel of 16 volunteers and elicited signs and symptoms of carpal tunnel syndrome (CTS) within a short period of time. These signs and symptoms were attributed to an ischemic response rather than mechanical compression.[8] Using a similar model of induced compression, increasing pressure led to a decrease in sensory function.[9] An induced pressure of 40 mm Hg led to a 40% reduction in sensory amplitude and 31% decrease in motor amplitude followed by an immediate recovery, suggesting a threshold of 40–50 mm Hg.[10] In support of the ischemic injury mechanisms, it was noted that hypertensive subjects had a higher

pressure threshold than normotensive subjects (60–70 mm Hg vs. 40–50 mm Hg).

CHRONIC EFFECTS OF NERVE COMPRESSION

Intraneural edema has been observed to persist after animal nerves have been compressed at low pressures for short durations.[5] Using an inflatable miniature cuff, rat sciatic nerves were compressed to 30 or 80 mm Hg (4 or 10.7 kPa) for two hours. The endoneurial pressure remained elevated for 24 hours after the cuff pressure was released.[11] The effects were more pronounced at the higher pressure or if the cuff was inflated for a longer duration (eight hours). These dose-response effects are also observed in longer-term studies.

Using a wide range of compression cuff pressures (0–300 mm Hg) and durations (0–240 minutes), Dyck et al.[12] found a dose–response relationship between the amount of pressure and the severity of the effect in rat peroneal nerves. Even brief periods of compression resulted in long-lasting (up to 14 days) subperineurial edema. They suggested that the structural changes during a few minutes of compression could not be explained by an ischemic response because these take hours to develop; however, it is conceivable that with prolonged compression, an ischemic injury may be superimposed on the mechanical injury.[12]

There is evidence that previous compression alters the future response of a nerve. This conditioning effect has been found to manifest itself in a number of ways. Using a compression chamber to induce pressure change and a silk suture to create a crush mechanism in the rabbit vagus nerve, histologic examination seven days after injury exhibited migration of the nucleus to the periphery and a statistically significant increase in the percentage of cells showing a dispersion in the Nissl substance at 30, 200, and 400 mm Hg, as well as in the crush condition. There was a decrease in nuclear volume density in all experimental conditions, although less pronounced at 30 mm Hg. This indicated that even at 30 mm Hg, axonal transport is disturbed.[13] These changes may be followed by a change in neuron tubulin transport in the weeks following compression[14] and by functional alteration in the neuron and nerve trunk.[15,16] This alteration in function, or "conditioning lesion effect," has been shown in rat sciatic nerves using small silicone tubes sutured around the nerve and left in place for days[15] or for two hours at specific pressures of 30 and 80 mm Hg.[16] After removal of the compression apparatus, a crush injury is inflicted at some set time (one week in the latter study). These studies have demonstrated a conditioning effect in which the previously compressed nerve demonstrates greater regrowth than the control nerve even with low controlled pressures. Such changes may be involved in conditions such as the double-crush or reverse double-crush syndrome in which one part of the nerve is compressed and leaves a more distal or proximal part of the same nerve more vulnerable to pathologic change.[17]

More recently, a chronic rat model was developed by surgically placing loose fitting polyethylene cuffs of various diameters around the sciatic and sural nerves, so that vascular flow was not visibly occluded. After six weeks, large myelinated axons were reduced in number but thinly myelinated and unmyelinated fibers, though initially reduced, increased beyond control values likely due to a degeneration/regeneration process including regenerative and collateral sprouting of axons. Pathological alterations of the injured nerve included edema and swelling, perineurial sheath hypertrophy, infiltration of fibroblasts and collagen into the intraneurial space, and increased space between axons. These changes are consistent with the cuff studies.[18] Similar biologic responses have been found following low-level compression of spinal nerve roots[19] and the cauda equina.[20]

HISTOLOGIC EVIDENCE IN ANIMALS AND HUMANS

Histologic analysis of a nerve requires a biopsy, and because a nerve biopsy is likely to lead to permanent nerve dysfunction, relatively few histologic studies of human nerve exist. A few case studies of humans with CTS have compared the nerve at the injury site to a nerve either proximal or distal to the injury site.[21,22] At the site of injury, there was thickening of the microvessel walls in the endoneurium and perineurium, epineurial and perineurial edema, as well as thickening and fibrosis. Myelin thinning and evidence of fiber degeneration and regeneration was also found.[21,23] Degeneration followed by regeneration was suggested by a shift to smaller fibers in the unmyelinated nerve population in the superficial branch of the radial nerve in four clinical entrapment cases.[23]

Because of the invasiveness of histologic examination of actual nerve tissue, the neighboring tissues have been examined to offer insights into the effects of chronic compression in humans.

Histology of Tissues Surrounding the Nerve in Humans with CTS

Tissues adjacent to a nerve, such as the synovium within the carpal tunnel, are easier to acquire and have often been studied to provide insight into how these tissues and likely the nerve itself responds to compression.[24–30] Because of the nature of these

studies, it is unusual to have tissue from a normal, uncompressed carpal tunnel.[27] Edema and vascular sclerosis (thickening of the vascular walls) are commonly reported,[26,27] but fibrosis is quite variable from 3% (5 of 177[27]) to 100% (21 of 21[30]) or close to it (96% of 625 cases[28]). The findings from most studies do not support an inflammatory response.[26–29] However, it has been suggested that histologic evidence of long term repetitive stress may present itself in most wrists over time.[31]

New Animal Models of Repetitive Grasping

Animal models have been developed to evaluate the effects of repetitive grasping. Rats can be trained to perform repetitive grasping for food pellets and are sacrificed at different time points to investigate the effects on nerve tissue.[32,33] Although the rat median nerve anatomy is not identical to human anatomy, the results provide an excellent study in the development of peripheral nerve trauma. Rats were trained to reach for a food pellet four times per minute, tow hours per day, three days per week for three to 12 weeks. Animals reduced their reach rate by five or six weeks, at which time a significant increase in immunoreactive macrophages (ED1+) was found in the median nerve in the carpal tunnel of the reaching limb. At eight to 12 weeks, collagen type I immunoreactivity increased in the epineurium at the wrist and immediately distal to the carpal ligament. Along similar timelines, nerve conduction velocity was modestly but significantly reduced in the reach limb but not in the nonreach limb (47.7 vs. 50.3 m/s, respectively).[32] Using a similar model with high force and high repetition, greater effects were found. Interestingly, unlike the low-force, high-repetition model, significant changes in the contralateral (nonreach) limb were found, perhaps due to systemic effects induced from the other limb.[33]

Vibration Effects

Peripheral neuropathy has also been attributed to vibrational loading. From animal models to human case studies, histologic studies demonstrate damage due to vibration. Although the pathophysiology is not well understood, the evidence suggests that the entire neuron may be involved. In humans, prolonged use of vibrating power tools has been associated with hand-arm vibration syndrome, a complex of symptoms that include both sensory and motor aspects. Once again, animal models allow controlled exposure to vibration and a full histologic assessment of the nerves. In the rat hind limb, acute vibration with characteristics similar to hand tools (peak-to-peak amplitude 0.21 mm, 82 Hz) was applied for four hours in five consecutive days and resulted in prominent and characteristic changes in nonmyelinated nerve fibers.[34] These changes, some of which were reversible after two to four weeks, included a reduction in nonmyelinated fibers, an increase in density in smooth endoplasmic reticulum in the remaining nonmyelinated fibers, and a disruption in the cytoskeletal structure. Using a secondary crush procedure, vibration was to act as a conditioning lesion,[34] similar to prior compression.[13–16,23] However, whereas no ultrastructural changes remained at four weeks, the increased outgrowth associated with the conditioning-lesion effect was still present. Others have found that demyelination occurs early in the process and that axonal loss occurs later.[35] Damage is consistently found to be greatest near the vibration source.[34,35]

Similar findings are observed in human case studies. Biopsy specimens from ten workers exposed to vibrating tools at work, taken from the dorsal interosseus nerve just proximal to the wrist, revealed pathologic changes in all subjects, most notably a breakdown in myelin as well as interstitial and perineurial fibrosis.[36] No controls were considered abnormal, with the exception that one had been treated for Raynaud's phenomenon. These findings indicate that demyelination may be the primary lesion followed by fibrosis with incomplete regeneration. Vibration to the hand can induce structural changes to the nerve proximal to the wrist, thus potentially explaining the generally poor outcomes with carpal tunnel release in these patients.

THE EFFECTS OF JOINT MOTION ON NERVE GLIDING AND STRETCHING

Normal Movement

Motion of the wrist and fingers results in longitudinal[37] and some transverse[38] movement of the median nerve. Observing that their needles would move during nerve testing, McLellan and Swash[37] recorded movement of the median nerve during simple movements of the median nerve at the shoulder and at the wrist. The largest movements occurred during extension of the wrist and fingers during which the median nerve slid distally 7.4 mm on average, whereas flexion of the wrist and fingers resulted in only 1.6 mm of distal movement. When measured at the wrist, the same motions resulted in two to four times the displacement as at the shoulder.[37] A more controlled study with nine cadaver arms found a consistent and linear relationship between median nerve and finger flexor tendon excursion. Full finger flexion required an excursion of 2.3–3.1 cm depending on wrist angle, whereas median nerve displacement was 0.9–1.4 cm.[39] It has been shown that when median nerve excursion is measured at the wrist and elbow, local joint movements are associated with greater excursion,

indicating the potential for strain. Extension of the wrist to 60 degrees accounted for 9.2 mm distal excursion (9.6% strain) whereas flexion to 65 degrees created a proximal excursion of 10.4 mm, resulting in a total excursion of almost 20 mm. At the elbow, the total excursion was 5.6 mm. Full finger motion resulted in almost 10 mm excursion of the nerve at the wrist.[40] Longitudinal sliding and strain of the median nerve may offer the opportunity for trauma in terms of friction and strain; in addition, transverse sliding of the median nerve has been shown to be greater during active motion.[38] Thus, tension may play a role.

Pathologic Movement of Median Nerve

The concept of "tethering" of the median nerve has associated decreased nerve excursion with increased strain in the nerve. A reduction in transverse sliding of the median nerve in the carpal tunnel has been observed in CTS patients versus controls (1.75 mm vs. 0.37 mm) during full motion of the index finger. No sliding was noted in one third (ten of 30) of the CTS wrists.[41] In another study, finger motion from extension to flexion caused the median nerve to move radially 3.24 mm in normal subjects, whereas in CTS patients the motion was limited to 1.02 mm.[42]

Longitudinal sliding or strain may be of more importance simply because of the larger potential for strain. By measuring the differential sensory latency between two points multiplied by a theoretical conduction velocity of 60 m/s, nerve displacement was calculated for various postures. Regardless of whether the elbow was flexed, wrist flexion resulted in half the excursion in CTS patients, whereas the ulnar nerve was unaffected.[43] Interestingly, repeated low level strain of rat brachial plexus for one hour resulted in abnormalities in histology, nerve conduction and grasp strength while continuous strain did not.[44] With elongation of 5–10% there is a slowing of venular flow but not in arterioles or capillaries, whereas all microcirculation stopped by 11–18% (the latter is beyond the threshold of nerve viability).[45] Median nerve stretching has been incorporated into a clinical stress test, by extending the wrist and hyperextending the index finger, CTS symptoms are elicited if positive.[46]

HUMAN STUDIES OF CARPAL TUNNEL PRESSURE

Efforts to examine the effects of external loading on pressure adjacent to the median nerve in the human carpal tunnel have involved measuring hydrostatic pressures, contact pressures and modeling of the structures within the carpal tunnel. The difference between hydrostatic and contact pressure lies in the methods of measurement. Both have been called "carpal tunnel pressure," but we reserve that term for measures of hydrostatic pressure. Hydrostatic pressure is measured by a catheter of some sort (wick, slit, perforated) and may be done in vivo, whereas contact pressure is typically measured using a bulb or balloon device in cadavers.

Carpal tunnel pressure (CTP) is typically higher in CTS patients,[47–51] although there may be an adaptation in chronic advanced cases.[52] Resting CTP in patients typically exceeded 30 mm Hg. A comparison is found in Table 1. Elevated CTP has been suggested as a criterion for surgery, although it is not widely used.[53] Surgery, specifically the transection of the transverse carpal ligament, reduces carpal tunnel pressure.[49,50,53] Two studies have shown resting CTP to decrease from about 43 mm Hg to about 5 mm Hg after endoscopic release.[50,53] During surgical release of CTS, the compressed segment of the nerve may exhibit disturbed microcirculation, which is immediately restored after transection of the transverse carpal ligament. Nerve function is also usually immediately restored following surgery, indicating an ischemic response in the early stages of compression syndrome.[3]

Wrist, finger, and forearm postures influence CTP in a predictable manner. The lowest CTP is typically found in a neutral or slightly flexed wrist posture[54] and increases with deviation from this posture in flexion and extension,[47,49,51,52,54] as well as in both

TABLE 1. **Mean Hydrostatic Carpal Tunnel Pressure in CTS Patients and Controls in Extended, Flexed, and Neutral Wrist Postures**

	Carpal Tunnel Pressure (mm Hg)					
	Patients			*Controls*		
Study	*Extension*	*Neutral*	*Flexion*	*Extension*	*Neutral*	*Flexion*
Keir et al.[56]				37	9	31
Rojviroj et al.[47]	33	12	27	13	3	9
Luchetti et al.[102]		26			13	
Szabo and Chidgey[52]	51	10	32	28	5	16
Okutsu et al.[50]	222	43	192	158	14	144
Thurston and Krause[103]	32	8	19			
Werner et al.[104]	105	31	75			
Gelberman et al.[49]	110	32	94	30	2.5	31

radial and ulnar deviation.[55,56] Pressure changes are greater in extension than in flexion.[56,57] In CTS patients, the effects of posture are heightened (Table 1). CTP is also altered by finger posture[56,58] and forearm posture.[58,59] Wrist motion with the fingers extended significantly increased CTP in healthy volunteers, attaining pressures upwards of 70 mm Hg by 40 degrees of wrist extension, whereas metacarpophalangeal joint flexion of 45 degrees resulted in only 30 mm Hg of pressure.[56] It has also been reported that pressures increase significantly with gripping when compared to a relaxed hand, particularly when the wrist was in extension.[50,51,53,60] The forearm posture of 45 degrees pronation ("midprone") is associated with lowest CTP.[58,59] These studies suggest that rehabilitative splints which maintain a more neutral wrist posture may be beneficial[54] and that wearing a flexible brace while working may not provide protection and may actually increase pressure in the carpal tunnel.[61]

A limitation of most hydrostatic pressure studies is that the location of the measuring tip of the catheter is not known; moreover, it most likely moves with wrist deviation. CTP has been shown to be greatest in the distal aspect of the tunnel.[60,62]

Fingertip Loading and CTP

In healthy humans, increasing fingertip force up to 12 N causes an increase in CTP independently from wrist extension angle and to a greater magnitude.[63] Further evaluation of finger forces revealed that the same force at the fingertip when using a pinch grip resulted in twice the carpal tunnel pressure than a simple finger press in the same posture.[64] A low pinch force of 5 N elevated CTP above the 30-mm Hg critical threshold,[64] providing support to workplace studies linking repeated or sustained pinch grip use with increased risk of CTS.[65,66]

Contact Pressure

Just as with the isolated nerve studies, the nature of the compression appears important to fully describe the trauma to the median nerve. Contact pressure and hydrostatic pressure (CTP) involve two different mechanisms of nerve compression and occur differentially with different hand postures. For example, contact pressure acts primarily in wrist flexion, whereas hydrostatic pressure has a greater effect in wrist extension.[55] To examine contact pressure, bulb or balloon systems were use in cadavers to examine the effects of posture,[48,57,67,68] tendon force,[57,68] and location within the tunnel.[67,68] Using a distensible bag in cadavers (considered controls) and CTS patients, Tanzer[67] found pressures to be greatest in the proximal carpal tunnel with much greater pressures in flexion than extension. Using a similar system, Smith et al.[68] found that greater tendon loads produced higher pressures and tendon loading combined with wrist flexion resulted in the greatest pressures compared to wrist neutral or extended postures. Furthermore, with wrist flexion of 45 degrees, loading of the finger flexor tendons resulted in a 2.5-fold increase in contact pressure over all other conditions.[55] Although similar pressure increases were found with radial and ulnar deviation, the highest contact pressures on the median nerve are found independently in flexion and in ulnar deviation.[55]

Modeling Nerve Compression

Mechanical compression of the median nerve has been estimated using modeling techniques, most notably, likening the tendons wrapping around the transverse carpal ligament to a belt wrapping around a pulley.[69] The forces exerted on the pulley, assumed equal to the compressive force on the median nerve, was proportional to the tension in the belt divided by the radius of the pulley.[69] This model was refined by recreating tendon trajectories through the carpal tunnel in healthy volunteers.[70] Using magnetic resonance imaging (MRI) data, detailed examination of the tendon trajectories demonstrated the value of the original belt-pulley model and also proved it to be oversimplified in several respects. Friction within the carpal tunnel, excluded from the original belt-pulley models, appears to be important and is currently being evaluated for tendons under various conditions.[71–73]

ANATOMICAL RELATIONSHIPS

Hydrostatic pressure within the carpal tunnel can be altered either by decreasing the volume of the compartment, or by increasing the volume of its contents.

Carpal Tunnel Cross-sectional Area

To fully understand and model CTP and mechanical compression, there is a need to determine the shape of the carpal tunnel. In general, in the neutral wrist, the carpal tunnel is smaller at its distal end than at its proximal end in controls,[74–81] but not necessarily in CTS wrists.[76] The carpal tunnel has also been said to be an hourglass shape with a "waist."[82] Measuring the cross-sectional area of the carpal tunnel can be done with MRI, an improvement in soft-tissue contrast over computed tomography (CT) of earlier studies.[74]

Carpal tunnel cross-sectional area measures depend on the measurement method, location within the tunnel, the posture and the population being investigated (Table 2). The area is slightly smaller than a 5-cent piece in the average wrist. The size of

TABLE 2. Mean Carpal Tunnel Cross-sectional Area in CTS Patients and Controls in Full Extension, Full Flexion, and Neutral Wrist Postures

	Cross-sectional Area (mm^2)							
	Patients				*Controls*			
		Neutral				*Neutral*		
Study	*Ext*	*Prox*	*Dist*	*Flex*	*Ext*	*Prox*	*Dist*	*Flex*
Jarvik et al.[105]			185				203	
Monagle et al.[106]		348	310			333	265	
Cobb et al.[84]			185				183	
Horch et al.[86]	161	168	143	135	180[D] 160[P]	178	152	144[D] 154[P]
Yoshioka et al.[79]					187[D] 151[P]	173	158	138[D] 145[P]
Skie et al.[78]					175		152	136
Winn and Habes*[77]		201	193			184	169	
Merhar et al.*[75]		298	217			257	219	
Bleecker et al.*[107]		190				253		
Dekel et al.*[74]		184	188			246	231	

Data were acquired by MRI or CT (asterisks).
Prox/P = proximal (level of pisiform); Dist/D = distal (hook of hamate).

the tunnel has been reported to be smaller[74,83] or larger[77] in CTS wrists.[75,84] The proximal carpal tunnel is smaller in female controls than male controls (213.7 ± 4.8 mm^2 vs. 279.9 ± 8.3 mm^2). Female CTS patients (184.1 ± 4.0 mm^2) had smaller carpal tunnel cross-sectional areas than both male and female controls.[83] The shape of the carpal tunnel changes with flexion and extension, although the magnitude of the area change and the direction of the change depends on the level within the tunnel. Additionally, there are unresolved issues with the ability of MRI to obtain true cross-sectional images at different wrist postures and along different axes.[85]

In general, the studies find that wrist flexion results in a decrease in cross sectional area at both proximal and distal ends of the tunnel (primarily due to decrease in tunnel width). Wrist extension, however, has a differential effect on area. At the level of the pisiform (proximal end) the area decreases primarily due to a flattening effect, whereas at the distal end of the tunnel (hook of hamate) the area increases.[78,79,86,87]

Carpal Tunnel Volume

The examination of carpal tunnel volume has evolved with the imaging techniques and, in theory, should be directly related to CTP. The difficulty in the measure is the use of MRI or CT slices to create the volume. Carpal tunnel volumes are dependent on the proximal and distal boundaries of the tunnel, which may be arbitrary or have some error associated with imaging method. Early MRI-determined volumes were compared to silicone molds[81,88] and overestimated the molds by 20–25% with reported volumes of 5.8 ± 1.2 cm^3 [81] and 4.2 ± 0.7.[88] Using the radial styloid process as the proximal end of the tunnel, values from 7.6 to over 11 cm^3 have been reported in CTS and control wrists.[89–91] More recently, smaller volumes were found in a mixed study of men and women (3.9 cm^3 for the tunnel proper and 5.5 cm^3 using the radial styloid as a boundary). Volumes were reduced in flexion and extension and were significantly smaller in women.[85]

Tissues Compromising the Space Within the Carpal Tunnel

For the purposes of modeling CTP, the effective volume of the carpal tunnel may be reduced by incompressible structures within the tunnel (e.g., tendon). Several case studies have reported anomalous muscles[92] or growths in the carpal tunnel that, after removal, resulted in the loss of CTS symptoms.[93] Given the small size of the tunnel and the nine tendons that pass through it, researchers have quantified the occupied space in the carpal tunnel by calculating ratios of the contents (e.g., tendon and muscle) to the tunnel in area or volume.[81,84,85]

Lumbrical Muscle Incursion into the Carpal Tunnel

The lumbrical muscles enter the distal end of the carpal tunnel as the deep flexor tendons from which they originate, and slide proximally into the carpal tunnel when the fingers are flexed.[80,92,94–96] Yii and Elliot[96] investigated lumbrical muscle incursion in 35 hands (32 patients) during decompression surgery. By pulling on the flexor digitorum profundus (FDP) tendons, the fingers were drawn into full flexion, and in all 32 of their patients, three or more lumbricals moved into the carpal tunnel with mean incursion values of 17, 21, 16, and 11 mm for the index, middle, ring, and little fingers, respectively.[96] In a detailed study using five cadaver wrists, a stainless steel suture was placed at the origin of each lumbrical

muscle to allow measurement from radiographs, while the fingers were manipulated into four different postures: 100%, 75%, and 50% flexion, and full extension, resulting in mean lumbrical incursions of 29.8, 25.5, 13.9, and 0 mm for the four postures, respectively.[94]

Finger Flexor Muscle Belly Incursion into the Carpal Tunnel

On the other, proximal, side of the carpal tunnel, flexor muscles may enter the carpal tunnel during finger or wrist extension. Wrist extension causes a great increase in CTP, but this has yet to be adequately explained by changes in CT area or volume (see above), suggesting a potential role of the finger flexor muscle bellies entering the tunnel with wrist extension.[56] The potential of this hypothesis was demonstrated with cadavers[97] and the actual mechanism demonstrated.[98]

Holtzhausen et al.[98] conducted a large (54 females, 51 males) study of cadaver hands and found that with the wrist in a neutral posture and fingers extended, only 8% of the male specimens showed excursion of muscle into the proximal carpal tunnel, while 46% of female specimens did. Despite a very wide range in incursion values, the largest incursion of muscles was seen in the female cadavers with 16 mm (past the proximal edge of the carpal tunnel) for the FDP of the ring finger and 15 mm for the flexor digitorum superficialis (FDS) of the index finger. These results provide support for a similar mechanism to that of the lumbrical muscles, and also explain the increase in CTP with extended fingers and extended wrists.[56] The most distal portion of the finger flexor muscle fibers were found to be a mean (standard deviation) distance of 4.9 (9.5) mm and 9.3 (8.6) mm proximal to the pisiform bone for the FDS and the FDP, respectively. Using known models for tendon and muscle excursion,[99,100] it was demonstrated that the flexor muscles enter the carpal tunnel with wrist extension.[97] Therefore, in both symptomatic and asymptomatic wrists, an increase in the contents of the compartment can occur due to incursion of the lumbrical muscles in finger flexion[94,95] or finger flexor muscles in wrist extension.[92,93,98,101]

SUMMARY

Several conclusions can be derived from the literature regarding the role of tissue loading in the pathogenesis of peripheral nerve injury, many specific to CTS.

First, from isolated nerve studies, increased extraneural pressure can inhibit intraneural microvascular blood flow, axonal transport, and nerve function within minutes or hours. Increased pressure can also lead to endoneurial edema and damage to myelin. Pressures as low as 20 mm Hg (2.7 kPa) can retard epineurial blood flow while pressures of 30 mm Hg (4.0 kPa) have been shown to limit axonal transport and cause nerve dysfunction and endoneurial edema.

Second, even brief-duration, low-magnitude extraneural pressure can initiate a nerve injury and repair process that can last from weeks to months. Some studies have offered dose–response relationships between pressure and duration, but critical values have yet to be clearly defined. The process of nerve injury by compression includes endoneurial edema, demyelination, inflammation, axonal degeneration, fibrosis, new axonal growth, remyelination as well as perineurial and endothelial thickening.

Third, vibration applied for four or five hours a day for five days to a rat hindlimb has been shown to induce similar effects as nerve compression, including intraneural edema, changes in the structure of myelinated and unmyelinated fibers, and functional disturbances. In humans exposed to vibrating hand tools at work, permanent damage to the nerves of the fingers as well as the nerve trunks proximal to the wrist. The relationships among the exposure duration, vibration magnitude, and the structural changes in the nerve are not well understood.

Fourth, in healthy people, finger, wrist, and forearm deviations from neutral posture elevate carpal tunnel pressures in a dose–response manner. A similar dose–response relationship also exists for fingertip loads, either in a pulp press or pinch grip. CTP associated with a pinch grip increases to the critical pressure of 30 mm Hg with 5 N of fingertip force. Although CTPs in hand-intensive industrial tasks are not known, these findings may explain the association of repetitive forceful pinch grip to CTS in industry.

Fifth, measurements of carpal tunnel area and volume have begun to clarify the effects of finger and wrist postures on tunnel shape and contents. Ultimately, these studies are likely to provide an explanation for the effects of hand and wrist postures on contact and hydrostatic pressure within the carpal tunnel.

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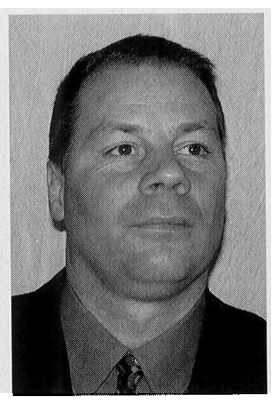

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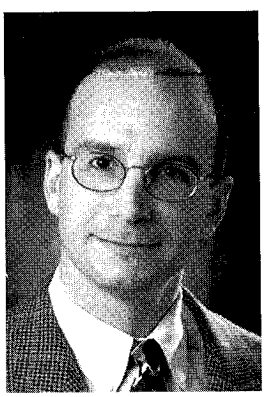

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