Chapter 9

Summary

General Discussion
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Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. CTS may be reliably diagnosed clinically. However, if operative therapy is considered, an objective test is often required to confirm the clinical diagnosis. Electrodiagnostic examination is endorsed as the test of choice, but ultrasonographic examination of the median nerve is applied increasingly.

In this thesis technology assessment, reassessment, and the application of specific nerve conduction tests in confirming the clinical diagnosis CTS will be described (Part I). Furthermore, an exploration of specific cases in which ultrasonographic examination of the median nerve can be useful is performed (Part II).

PART I - Nerve Conduction Studies

Nerve conduction studies (NCS) are important in the electrodiagnostic testing of polyneuropathies and mononeuropathies such as CTS. Since temperature influences different variables of nerve conduction studies, it is recommended to perform NCS with skin temperatures of at least 31°Celsius. This often makes it necessary to warm the limbs prior to electrodiagnostic testing. Since warming cold limbs by hot water immersion may be laborious in certain patients, we examined whether hot packs are as effective as hot water immersion for warming cold limbs in chapter 2. In 10 healthy persons the cold limbs were warmed; in half of patients this was first done by hot packs, then with hot water immersion, and vice versa in the other half of subjects. Motor and sensory NCS of the lower and upper extremities were performed before and after both different warming techniques. Mean temperatures were higher after warming with hot packs compared with hot water immersion and there were no differences in nerve conduction velocities (NCVs). Moreover, subjects preferred hot packs for reasons of convenience. Furthermore, hot packs are safe, clean and easy to use. Another important advantage is that when nerve conduction studies in multiple extremities have to be performed, hot packs may be removed only then when a limb has to be studied in order to keep it at the appropriate temperature. We conclude that hot packs are as effective as and more convenient than hot water immersion for warming cold limbs. All nerve conduction studies in the thesis have been performed with this technique of warming the hand and forearm.
The electrophysiological hallmark of CTS is the decrease in NCV of the median nerve across the carpal tunnel. Often, NCV of the median nerve fibers across the carpal tunnel is compared with those distal from the tunnel i.e. the segment in the palm of the hand. In chapter 3 we tested our hypothesis that comparing the sensory NCV of the median nerve across the wrist with that of the forearm is more sensitive than comparing it with that of the palm in the electrodiagnostic confirmation of CTS. In a prospectively conducted study, we included 157 patients with clinically defined CTS, and reassessed a modification of the classic PALM-test. Reference values were derived from 47 healthy, asymptomatic volunteers. All were tested in the same laboratory according to the same electrodiagnostic test protocol. In all patients, antidromic sensory NCS were performed and the NCV of the median nerve was computed in 3 segments: forearm, wrist, and palm, and recorded from digit 2 and 3. The difference in NCV as well as the ratio of the NCV between the different segments were computed. Sensitivity of comparing the median NCV of the forearm with the wrist segment was 79.6% and 82.8% for the second and third digit, respectively, vs. 65.6% (digit 2) and 65.0% (digit 3) for comparing the NCV of the palm with the wrist. Applying the ratio led to slightly higher sensitivities (82.8% and 85.4% for the second and third digit, respectively). We conclude that this modification of the palmar test is a sensitive and robust method in diagnosing CTS. We recommend to use the sensory NCV of the median nerve of the forearm as a reference, instead of that of the palm. Since the sensitivity of the PALM test recorded from digit 3 is higher compared with the sensitivity of digit 2, we also recommend to record from digit 3.

In the hand the size of the nerve segments in the most commonly used nerve conduction tests in confirming CTS is relatively small. These short distances between stimulus cathode and recording electrode often cause disturbing stimulus artifacts. Consequently, defining onset latencies, as needed for determining NCV, can be difficult. Alternatively, peak latencies may be used. In chapter 4 we compared the diagnostic accuracy of onset versus peak latency measurements of sensory nerve action potentials (SNAPs) in electrodiagnostic studies for diagnosing CTS in a prospectively conducted study that included 156 patients with clinically defined CTS. Standardized NCS were performed (DIG1, DIG4, PALM3) and both onset and peak latency were measured. We constructed Bland-Altman plots to assess the agreement. Overall agreement, positive and negative per cent agreement, and Kappa coefficient were computed. The Bland-Altman plots, positive and negative per cent agreement
show a good overall agreement for all performed sensory NCS. The Kappa was 0.850, 0.847, and 0.815 for DIG1, DIG4 and PALM3, respectively. We conclude that onset and peak latencies in sensory NCS in diagnosing CTS show a good overall agreement, but sensitivities for all three tests are higher for onset latency measurements. Because onset latency represents the fastest conducting fibers, we recommend to use initially onset latencies. If accurate defining of onset latencies is not possible, peak latencies can be used instead.

Despite all efforts, SNAPs can sometimes not be elicited. This occurs especially in severe cases of CTS. Motor NCS are important in the documentation of motor fiber involvement in CTS and even more so if SNAPs cannot be elicited. In chapter 5 we prospectively tested the sensitivity of different motor nerve conduction tests in confirming CTS and compared it with the aforementioned sensory NCS. In 162 consecutive patients with clinically defined CTS we performed the following motor nerve conduction tests: (1) the distal motor latency of the compound muscle action potential (CMAP) of the thenar muscles (DML-APB); (2) lumbrical-interosseous comparison study (2L-INT). For both, terminal latency index (TLI) and residual motor latency were calculated. Sensitivity for the sensory tests was 79.4% (DIG1), 85.2% (DIG4), 81.8% (PALM3). The sensitivity for TLI-APB was 81.3%. All other motor nerve conduction tests showed considerably lower sensitivities. If SNAPs of DIG1, DIG4, and PALM3 could not be elicited, all motor nerve conduction tests are very sensitive (95.8% to 100%). If median nerve SNAPs are not recordable, but a CMAP is recordable to the abductor pollicis brevis muscle, the 2L-INT has no additional value.

To conclude:

- **Hot packs are as efficient as hot water immersion in warming cold limbs prior to electrodiagnostic testing; it is far less laborious and more practical and it is therefore the preferable procedure.**
- **The modified segmental palmar test is a sensitive, robust, and easily applicable method in diagnosing CTS. The median sensory NCV in the forearm, instead of that in the palm, is recommended to be used as a reference. Since the sensitivity of the PALM test recorded from digit 3 is higher compared with the sensitivity of digit 2, recording from digit 3 is recommended.**
- **Onset and peak latencies show a good overall agreement in confirming the clinical diagnosis of CTS. Since onset latency measurements represent NCV of the fastest conducting fibers, the use of onset latency**
is recommended.

- Sensory nerve conduction tests and terminal latency index have a high sensitivity in the electrodiagnostic confirmation of CTS. If no SNAPs can be elicited, all motor nerve conduction tests have a high sensitivity, but the lumbrical-interosseous comparison test had no additional value.

PART II - Ultrasonography: An Alternative or Additional Test to Nerve Conduction Studies?

NCS may be perceived as unpleasant by some patients. Ultrasonography is painless and it gives additional anatomical and morphological information about the median nerve and its surrounding tissue. Enlargement of the cross-sectional area (CSA) of the median nerve at the inlet of the carpal tunnel is a characteristic finding. Originally, normal values of the CSA of the median nerve are based solely on gender, and range from 9 to 11 mm². Recently, new ultrasonography criteria were developed that take wrist circumference into account, which can predict the upper limit of normal (ULN) more accurately compared to an absolute cut-off point. In chapter 6 we compared the electrodiagnostic confirmation of clinical diagnosis of CTS with ultrasonography, using these new normal values. Furthermore, we determined whether electrodiagnostic examination can be replaced by ultrasonography to confirm the clinical diagnosis of CTS. We prospectively collected 156 patients with clinically defined CTS; all underwent neurological, electrodiagnostic, and ultrasonographic examinations. Upper limit of normal CSA of the median nerve was established using regression equations based on left/right side and circumference of the wrist. Of 156 patients with clinically defined CTS, 130 (83.3%) met the electrodiagnostic criteria of CTS, 26 (16.7%) did not. Ultrasonographic examination adjusted for wrist circumference was abnormal in 89 patients (57.1%), only 3 of these patients had normal electrodiagnostic test results. Ultrasonography was normal in 67 patients (42.9%), within this group 44 patients (65.7%) had abnormal electrodiagnostic test results. We conclude that ultrasonography cannot replace electrodiagnostic examination for the confirmation of the clinical diagnosis of CTS and that it does not have the same diagnostic value as NCS in confirming CTS. However, in case of an abnormal ultrasonographic test result, 96.6% also had abnormal electrodiagnostic test results.
As described in chapter 6 and according to other studies, the CSA of the median nerve is not enlarged in a substantial number of patients with CTS. In chapter 6 we did not include patients with severe thenar atrophy. We hypothesized that the CSA of the median nerve in these patients is not enlarged but in fact may be reduced because of secondary atrophy after severe axonal damage. In chapter 7 we tested this hypothesis in a prospectively collected cohort of 14 patients with clinically and electrophysiologically defined severe CTS. The CSA of the median nerve was measured and compared with controls. Since the patient group appeared to be rather old (mean 71.8 years, range 52-86), we also collected and examined a group of asymptomatic elderly subjects. This group fitted well within the reference values for CSA. The CSA of the median nerve exceeded the ULN in the majority of patients with severe CTS; mean CSA 17.7 mm$^2$ (SD, 5.22). We conclude that atrophy of the median nerve in severe CTS does not explain the negative ultrasonographic test results. Instead, the CSA of the median nerve is enlarged in most patients with severe CTS.

The use of imaging studies for diagnostic purposes in CTS has led to an increase in the recognition of morphological or anatomic anomalies such as bifid median nerves. It is suggested that a bifid median nerve may facilitate compression of the nerve because of larger CSA at the level of the carpal tunnel. Data about frequency, and association with CTS are, however, conflicting. Data about electrophysiological findings and outcome are scarce. In chapter 8 we tested the hypothesis that a bifid median nerve predisposes to the development of CTS and we investigated differences in electrophysiological findings and outcome in a prospectively conducted study with 259 consecutive patients with clinically defined CTS. 54 healthy asymptomatic volunteers were investigated ultrasonographically. We found a bifid median nerve in 41 patients (15.8%), 6 of whom bilateral, so, in patients a bifid median nerve was found in 47 of 518 wrists (9.1%). In contrast, ten control subjects (18.5%) had a bifid median nerve, all unilateral. We found no clinical differences in patients with bifid vs. non-bifid median nerves, but electrophysiological and ultrasonographic abnormalities were more pronounced in patients with non-bifid median nerves. Some outcome measurements show a better outcome after surgical decompression in patients with non-bifid median nerves. We conclude that a bifid median nerve is not an independent risk factor for development of CTS, but some of our data suggest the outcome to be different.
To conclude:

- Ultrasonography cannot replace electrodiagnostic examination for confirmation of the clinical diagnosis of CTS.
- Atrophy of the median nerve does not explain negative ultrasonographic test results. Instead, the CSA of the median nerve is practically always enlarged in patients with severe CTS.
- A bifid median nerve is found in patients as well as in healthy controls and is not an independent risk factor for the development of CTS. However, outcome in patients with a bifid median nerve may be different.