This work reports the results of an analysis into the course of carpal tunnel syndrome before operation in 479 patients, predominantly women, aged a mean of 58 years, who were scheduled for carpal tunnel operation. The patients were asked to characterise in detail the course of the disease and what determined the decision to undergo surgery.

Results. We identified two specific patterns of CTS course: progressive and preservative/mild. Patients with short-lasting disease suffer first of all from symptoms, but the longer the duration, the more pronounced the functional impairment. In a proportion of patients with longer-lasting disease, spontaneous resolution may occur, for up to a year or more. Bilateral involvement is more common than unilateral and the interval between involvement of the other hand is a mean of 10 months. For most patients the primary motivation to undergo surgery is troublesome symptoms (pain and paraesthesia). Functional impairment is of secondary importance, however, its prominence increases in older patients and in those with longer-lasting disease.

Keywords: carpal tunnel syndrome; natural history; clinical course.

INTRODUCTION

The natural history of carpal tunnel syndrome (course of untreated disease) is not well recognised. Older studies suggested that CTS progressed in time leading to median nerve compromise and subsequent loss of sensation, muscle weakness and functional impairment \(^{1,6}\). This was supported by evidence showing poorer outcomes of operative treatment in patients with longer-lasting disease \(^{1,4}\). However, more recent literature provides different data about the evolution of the disease, showing a proportion of patients who were scheduled for surgery, but who cancelled it due to significant clinical improvement or permanent spontaneous recovery \(^{3,8,9}\).

In the authors’ institution, approximately 300-400 patients with a CTS diagnosis are scheduled for carpal tunnel release yearly, of whom about 20% resign for various reasons. Our institutional CTS register is comprised of more than 1500 records of patients, who have been thoroughly examined before the operation and followed-up for a minimum of 6 months following surgery. We found the history of the disease in a proportion of patients to be long and complex and these findings prompted us to investigate the course of CTS in patients who were referred to our institution \(^{10}\). This article presents the results of the study.
MATERIALS AND METHODS

Over a period of two years (2013-2014), a prospective study was conducted to investigate the history of patients with carpal tunnel syndrome. All patients admitted to the department for carpal tunnel release, besides the standard demographic data and completion of the Levine questionnaire, were also thoroughly asked the following questions:

- Duration of the symptoms
- Age when the first symptoms of CTS occurred,
- Sequence of occurring symptoms and signs
- Undergone treatments and their efficacy
- Presence of comorbidities

In cases of longer-lasting (> 1 year) disease, patients were asked to characterise its course (changes in presence and intensity of symptoms) and what determined the decision to undergo surgery.

The diagnosis of CTS was made based on clinical examination and history. Electrodiagnostic studies were additionally available in 247 patients (52%), confirming the clinical diagnosis.

Statistical calculations were performed for difference between duration of symptoms in bilateral vs unilateral involvement (U-Mann-Whitney test) and for difference in the Levine scores in relation to age and duration of the disease (Kruskal-Wallis test).

A total of 479 patients were included in this study, 397 women (83%) aged a mean of 58 years (range 22-90) and 82 men (17%) aged a mean of 59 years (range 21-86). Social status of the patients: 201 (42%) were employed, 195 (41%) retired, 46 (9%) on disability pension, 20 (4%) were housewives and 17 (3%) were unemployed. This group was the subject of this study.

RESULTS

Age dependent conditions

The mean age of all patients at admission was 58 years (range 21-90), SD=11/12. The mean age of occurrence (appearance) of the first symptoms was 54 years (range 20-89), SD=12 (Table I). The number of patients in age ranges is shown in Table II. The most patients – over 40% – were admitted for surgery from the age range 50-59 years, followed by 60-69 years (25%), 40-49 years (13%) and 70-79 years (12%). The distribution of age ranges at onset of first symptoms was different: in most patients it was in the age range 50-59 years (36%), followed by 40-49 years (23%) and 60-69 years (15%).

Duration of symptoms

The mean duration of symptoms at admission exceeded 4 years and was slightly (a mean of 6 months) longer in men than in women. The number of patients in particular ranges of symptom duration is shown in Table III. Most patients – 209 (44%) –

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>479</td>
<td>397 (83%)</td>
<td>82 (17%)</td>
</tr>
<tr>
<td>Age (range) SD</td>
<td>58 (21-90)</td>
<td>58 (22-90)</td>
<td>58 (21-86)</td>
</tr>
<tr>
<td>SD</td>
<td>11.4</td>
<td>11.2</td>
<td>12.3</td>
</tr>
<tr>
<td>Duration of symptoms to the operation (years). Range, SD</td>
<td>4.3 (1/4 - 30)</td>
<td>4.3 (1/4 - 30)</td>
<td>4.8 (1/4 - 30)</td>
</tr>
<tr>
<td>Age at appearing the first symptoms (range) SD</td>
<td>54 (20-89)</td>
<td>54 (21-89)</td>
<td>54 (20-82)</td>
</tr>
<tr>
<td>Handness declared Right/Bilateral/Left</td>
<td>446 / 21 / 12</td>
<td>93% / 4% / 3%</td>
<td>-</td>
</tr>
<tr>
<td>Affected hand at admission Both / Right / Left</td>
<td>289 / 143 / 47</td>
<td>60% / 30% / 10%</td>
<td>-</td>
</tr>
<tr>
<td>Smoking habit Yes/No %</td>
<td>78 / 399</td>
<td>17% / 83%</td>
<td></td>
</tr>
</tbody>
</table>
had the disease from 1 to 5 years, followed by 101 (12%) patients having symptoms for 6 months to 1 year. The distribution of ranges was similar for men and women (Table III).

Duration of symptoms in relation to age ranges is shown in Table IV. The longest duration – a mean of 5 years (SD=5.8) had patients in the age range 60-69 years. The shortest duration, less than one year had the youngest group of patients (20-29 years). Surprisingly, the oldest patients (>80 years, n=21) had relatively short disease duration, lasting a mean of 2 years.

### Course characteristics

Patients with symptoms lasting less than one year (n=138) were younger than average (a mean of 39 years, range 21-58) and had a relatively regular course of the disease. The complaints from the onset were moderate or severe, reaching a plateau after one month on average. The symptoms underwent only slight variability and were troublesome enough to seek medical advice promptly, and remained stationary until admission. Eleven of these patients (8%) had received one intracarpal steroid injection, which brought resolution of symptoms for 3-6 months. Eighty-five patients (61%) also reported weaker grip and poorer hand function but these signs, in their opinion, were of secondary importance, compared to the symptoms.

Patients with the disease lasting over one year (n=341) were asked to characterise its course, what determined changes of the course (if any) and the decision to undergo surgery. Of 209 patients with the disease lasting from 1 to 5 years, a majority – 142 (68%) – reported their complaints to be constant and relatively mild for a long time, followed by exacerbation at a mean of one year before admission. This directly determined their decision to seek medical advice and undergo surgery. Ninety-seven of these 142 patients (68%), besides symptoms, also reported slightly weaker grip and poorer function of the affected hand. Twelve of the 209 patients (6%) had noticeable thenar muscle atrophy.

In the remaining 67 patients the course of the disease was variable, with periods of exacerbation and resolution, depending on circumstances such as: season (usually more severe in autumn/winter), overuse due to work, sport or recreational activities. Twenty-four of these 67 patients (36%) experienced spontaneous resolution of symptoms for as much as one year. The majority of these patients were

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<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 - 29</td>
<td>6 (1%)</td>
<td>4 (1%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>30 - 39</td>
<td>21 (4%)</td>
<td>17 (4%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>40 - 49</td>
<td>63 (13%)</td>
<td>52 (13%)</td>
<td>11 (13%)</td>
</tr>
<tr>
<td>50 - 59</td>
<td>194 (41%)</td>
<td>166 (43%)</td>
<td>28 (35%)</td>
</tr>
<tr>
<td>60 - 69</td>
<td>113 (25%)</td>
<td>92 (24%)</td>
<td>21 (26%)</td>
</tr>
<tr>
<td>70 - 79</td>
<td>57 (12%)</td>
<td>43 (11%)</td>
<td>14 (17%)</td>
</tr>
<tr>
<td>80 - 89</td>
<td>20 (4%)</td>
<td>18 (4%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>&gt;89</td>
<td>1 (-%)</td>
<td>1 (-%)</td>
<td>-</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at appearing the first symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 - 29</td>
<td>12 (2%)</td>
<td>10 (2%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>30 - 39</td>
<td>48 (10%)</td>
<td>40 (10%)</td>
<td>8 (10%)</td>
</tr>
<tr>
<td>40 - 49</td>
<td>109 (24%)</td>
<td>85 (21%)</td>
<td>24 (29%)</td>
</tr>
<tr>
<td>50 - 59</td>
<td>174 (37%)</td>
<td>149 (39%)</td>
<td>25 (31%)</td>
</tr>
<tr>
<td>60 - 69</td>
<td>74 (15%)</td>
<td>62 (17%)</td>
<td>12 (15%)</td>
</tr>
<tr>
<td>70 - 79</td>
<td>46 (10%)</td>
<td>37 (9%)</td>
<td>9 (11%)</td>
</tr>
<tr>
<td>80 - 89</td>
<td>12 (2%)</td>
<td>10 (2%)</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>
Forty-four patients, aged a mean of 67 years (range 63-79) had the disease for longer than 10 years. In almost all of these patients the complaints were stationary and relatively mild for a long time, with periods of exacerbation and resolution, depending on various factors. All of these patients reported weaker grip, reduced sensation and impaired dexterity of the hand, which became noticeable 1-3 years before making any decision about treatment. Forty of these patients (91%) had thenar muscle atrophy.

Other relationships

Twenty three of 132 patients (17%) with the disease lasting over 5 years, reported season-dependent complaints: they became more severe in colder seasons (autumn, winter) and milder in warmer seasons. A proportion of these patients noticed withdrawal of symptoms when going on holiday (in winter) to warm-climate countries and recurrence of symptoms after returning home.

Fifty-six of the 341 patients (16%) with the disease lasting over 1 year elected for surgery after inclined to undergo operation at the behest of family members or family doctor, and their direct motivation was neither stronger symptoms nor poorer grip or hand function.

In the group of 88 patients with the disease lasting 5-10 years, its course was stationary and relatively mild for a long time, followed by exacerbation at a mean of one year before admission in half of the patients. In the other half, the direct motivation to seek medical advice and undergo surgery was noticeable weakness and functional impairment of the hand, without exacerbation of symptoms (i.e. pain, numbness). A proportion of these patients also reported reduced sensation in the affected fingers, and 34 (39%) presented with thenar muscle atrophy. As in the previous group, some experienced spontaneous resolution of symptoms for even more than one year. Eighteen of 88 patients (20%) received at least one steroid injection into the carpal tunnel before surgery, which caused resolution of symptoms for periods ranging from 6 months to 4 years. Eleven patients (12%) had been earlier/already scheduled for surgery, but then cancelled due to spontaneous cessation of symptoms.

Forty-four patients, aged a mean of 67 years (range 63-79) had the disease for longer than 10 years. In almost all of these patients the complaints were stationary and relatively mild for a long time, with periods of exacerbation and resolution, depending on various factors. All of these patients reported weaker grip, reduced sensation and impaired dexterity of the hand, which became noticeable 1-3 years before making any decision about treatment. Forty of these patients (91%) had thenar muscle atrophy.

### Table III. — Duration of symptoms (ranges)

<table>
<thead>
<tr>
<th>Duration of symptoms (ranges)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>3-6 months</td>
<td>37 (8%)</td>
</tr>
<tr>
<td>6-12 months</td>
<td>101 (21%)</td>
</tr>
<tr>
<td>1-5 years</td>
<td>209 (44%)</td>
</tr>
<tr>
<td>5-10 years</td>
<td>88 (18%)</td>
</tr>
<tr>
<td>10-20 years</td>
<td>36 (8%)</td>
</tr>
<tr>
<td>&gt;20 years</td>
<td>8 (1%)</td>
</tr>
</tbody>
</table>

### Table IV. — Duration of symptoms in relation to age ranges

<table>
<thead>
<tr>
<th>Age ranges</th>
<th>Duration of symptoms (years, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>20 - 29</td>
<td>0.8 (0.7)</td>
</tr>
<tr>
<td>30 - 39</td>
<td>3.3 (2.8)</td>
</tr>
<tr>
<td>40 - 49</td>
<td>3.9 (4.4)</td>
</tr>
<tr>
<td>50 - 59</td>
<td>4.6 (5.0)</td>
</tr>
<tr>
<td>60 - 69</td>
<td>5.0 (5.8)</td>
</tr>
<tr>
<td>70 - 79</td>
<td>4.8 (6.5)</td>
</tr>
<tr>
<td>80 - 89</td>
<td>2.0 (2.3)</td>
</tr>
<tr>
<td>&gt;89 (one patient)</td>
<td>1.5</td>
</tr>
</tbody>
</table>
reaching pensionable age (in the authors’ country this is 62 years for women and 67 for men). The complaints in these patients were moderate and did not significantly disturb their ability to work, but were troublesome enough to undergo surgery after retirement.

For a proportion of patients with the disease lasting longer than 5 years, the motivation to undergo surgery was positive electrophysiological tests, obtained after referral from the family doctor or neurologist (in the authors’ institution, nerve conduction studies are not routinely performed in patients suspected of CTS). These patients made the decision to operate regardless of their complaints being mild and constant for many years.

**Levine symptom and function scores in relation to age and duration of the disease**

Patients aged ≥59 years had Levine function scores statistically significantly higher (suggesting greater functional impairment) than younger patients (Kruskal-Wallis test, p=0.04). There were no statistically significant differences in symptom Levine scores (Table V).

Patients with the disease lasting longer than 5 years had Levine function scores statistically significantly higher than those with shorter duration (Kruskal-Wallis test, p=0.01). There were no statistically significant differences in symptom Levine scores (Table V).

**Bilateral and unilateral manifestation**

The majority of patients in the study – 446 (94%) – was right-handed, 21 (4%) were both-handed (dominant hand not determined) and in 12 (2%) patients the left hand was dominant. At admission 289 patients (60%) had bilateral CTS; the right hand was involved in 143 (30%); and the left hand in 47 (10%). For 289 patients with bilateral manifestation, the first symptoms appeared in the right hand in 141 (49%), in the left hand in 109 (38%) and simultaneously in both hands in 39 (13%) patients. The interval between involvement of the other hand was 10 months on average (range from 0 months/simultaneous onset to 8 years). Eighty-one patients (28%) with bilateral manifestation had received carpal tunnel decompression for one wrist and were admitted for operation on the second hand.

The duration of symptoms differed in bilateral vs unilateral involvement. Patients (n=289) with bilateral manifestation had the disease lasting statistically significantly longer than those (n=190) with unilateral involvement – a mean of 6.2 years (range 3 mo - 30 y) vs 3.8 years (range 3 mo - 25 y) (U-Mann Withney test, p<0.001). This finding may be explained by “summation” of the periods of symptoms in patients with subsequent involvement in one and then the other hand, with a time interval between.

**Appearance of individual symptoms at onset**

For most patients – 374 (79%) – the first noticeable symptom was a feeling of numbness in one or more fingers, followed by the pain in the hand in 64 (13%). The remaining symptoms/signs: hand weakness and decreased sensation occurred less frequently as first signs and only single patients experienced swelling, stiffness and pain in the whole upper limb at first. The second symptom to appear for most patients (n=213, 44%) was: pain in the hand and feeling of reduced sensation in 106 (22%); numbness of fingers in 84 (18%); and hand weakness in 64 (13%). In the vast majority of patients (n=404, 84%) the symptoms appeared in the night. The second symptom appeared about 1 month after the first one (range 0 months/simultaneous onset - 5 months).

**Distribution of paraesthesia in the digits**

Ninety per cent of patients felt numbness/tingling on the pulp of the middle finger, 80% in the index and 70% in the thumb and ring finger. Half of the patients had paraesthesia immediately in 2-3 digits and 30% reported paraesthesia in the little finger

**Ninety patients (20%) reported occurrence of CTS in family members**

Most commonly – in 32 cases (35%) – the mother of the patient suffered from or underwent treatment for CTS, followed by the sister of the patient in 28 cases (31%).
DISCUSSION

This work reports the results of an analysis into the course of carpal tunnel syndrome before operation. In certain aspect it parallels the natural history of the syndrome, as in the vast majority of patients (n=341) it was not managed for a minimum one year. One may question whether the findings from this study are relevant, but we have failed to find any similar article in the literature. We would like to emphasise the following findings and observations:

– Most patients (40%) were referred for carpal tunnel surgery in the age range 50-59 years, with a mean age of 58 years. Onset of the disease (appearance of first symptoms) occurred four years earlier on average, at a mean age of 54 years. This finding is, however, only statistical, because time interval between symptom onset and surgical referral is related strongly to the individual pattern of the course (see below).

– We can identify two specific patterns of CTS course:

  – Progressive course. Relatively short-lasting (less than one year) disease characterised by constant and fairly severe symptoms (mostly pain in the hand), which are troublesome enough to seek medical help and prompt surgery.

  – Preservative/mild course. This is characterised by mild and non-troublesome symptoms, being stationary for many years, however undergoing some fluctuations (exacerbation and resolution) according to various circumstances. In about a half of these patients, the symptoms exacerbate spontaneously at some point/moment, which prompts them to seek medical help and prompt surgery.

Comorbidities

Three hundred and twenty-one patients (67%) had at least one comorbidity. The commonest comorbidity reported by 98 patients (20%) was cervical spine arthritis. This figure, however, should be treated with caution, as it comes from patients’ declaration only, and was not objectively confirmed. 70 patients (15%) declared a history of hypothyroidism, 59 (12%) were diabetics and 49 (10%) suffered from rheumatoid arthritis. Forty-five patients (9%) reported fracture of the distal radius at the same wrist sustained within 2 years of development of CTS.

Electrophysiological studies

As mentioned earlier, in the authors’ institution, nerve conduction studies are not routinely performed on patients suspected of CTS. However, many patients referred to our institution by other doctors (general practitioners, neurologists) have already undergone these tests. Two hundred and forty-seven patients (51%) presented with results of electrophysiological examination, of which 109 (44%) showed mild, 99 (40%) moderate and 39 (16%) severe conduction disturbances in the median nerve (according to previously described classification) (11). The correlation between electrophysiological findings and clinical variables was not analysed, but we found that patients with severe conduction disturbances had the disease lasting >5 years and they were older than average (a mean of 66 years, range 58-89).
medical advice. Regardless of the mild course of the disease, in a proportion of patients functional impairment of the hand slowly develops, which was shown in higher Levine function scores. This finding suggests that decompression of the carpal tunnel should be considered in these patients, regardless of their mild and non-troublesome symptoms.

- Patients with short-lasting disease (less than one year) suffer first of all from symptoms, without meaningful functional impairment of the hand. The longer the duration of the disease, the more frequent signs became troublesome (weaker grip, poorer function, sensory deficit – expressed in higher Levine function scores) constituting a greater motivation than the symptoms to undergo surgery. In a proportion of patients with longer-lasting (>1 year) disease, a spontaneous resolution of symptoms may occur, lasting one year or more. All of these patients were eventually referred for operation due to recurrence of symptoms, but we can speculate that other patients may experience permanent recovery. This is also supported by scientific evidence (2,5,7,8).

- The most common sequence of the individual symptoms appearing at the onset of CTS included feelings of numbness in digits, followed by pain in the hand. Not surprisingly, the symptoms appeared during the night in the vast majority of patients.

- Bilateral involvement is more common than unilateral. These patients have statistically longer-lasting disease, and involvement of the other hand occurs a mean of 10 months later. Simultaneous onset in both hands is less frequent.

- For most patients the primary motivation to undergo surgery is troublesome symptoms (pain and paraesthesia). Functional impairment is of secondary importance, however its prominence increases in older patients and in those with longer-lasting disease. For some patients, other factors determine the decision, such as family persuasion, family doctor’s advice or positive electrophysiological tests. Some patients, regardless of troublesome symptoms, postpone the operation until after retirement.

- Comorbidities are frequent in CTS patients; surprisingly, the history of cervical spine arthritis being the most common, followed by hypothyroidism, diabetes and rheumatoid arthritis. Positive familial history in 20% of the patients seems also to be an interesting finding.

A study of the literature provides no comparable studies. Single reports concern investigation into the natural history of the syndrome. Pensy et al. (2011) compared outcomes of patients who underwent and who cancelled carpal tunnel surgery. The patients were followed-up 6 years after enrolment. Thirty-six patients did not proceed with surgery despite having been scheduled for operation and 24 patients received carpal tunnel release. Overall improvement was noted in both groups when compared to baseline. The improvement in symptom Levine scores was greater in surgical patients, but functional Levine scores were not different. These findings suggest non-progressive course and spontaneous (partial or absolute) recovery in a proportion of CTS patients (8).

Padua et al. (2001) reported results of a one-year observation of 196 CTS patients with a mean age of 52 years and a mean duration of symptoms of 29 months. Assessments included Levine scores, specific clinical scale (History and Objective, HiOb) and electrophysiological studies. The patients had relatively mild disease, with average symptom and function Levine scores of 2.5 and 1.8, respectively. At the follow-up examination, about half of the patients remained stationary with regard to all considered parameters, 30% improved and 20% deteriorated. The authors found short (but not precisely how short) duration of symptoms to be a significant predictor of clinical improvement and younger age to be a predictor of electrophysiological improvement (7).

Ortiz-Corredor et al (2008) reported results of a two-year observation of 132 CTS patients with a mean age of 49 years. The measurements comprised HiOb clinical scale and nerve conduction studies. At the final clinical assessment, almost half (48%) of the patients recovered, 29% remained constant and 23% deteriorated. In the nerve conduction studies, 67% cases were unchanged, 25% improved and 8% deteriorated. The authors conclude that progressive course of CTS is not a rule, and that a proportion of patients may recover without treatment (5).
None of the quoted studies investigated the history of CTS patients as thoroughly as our own. Therefore we believe that our findings may be interesting for several medical disciplines, not only for hand surgeons. The limitation of this study is that we have not provided outcomes of surgery in the examined patients. This would, however, exceed the size of one article, and will be the subject of the next study.

REFERENCES


