Sex- and age-related differences in patient-reported outcomes 3 and 12 months after digital nerve repair

*A registry study*

**Author:** Deniz Demirag

Supervisor: Marianne Arner
Co-supervisor: Linda Evertsson
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Introduction: Digital nerve injuries are the most common upper limb peripheral nerve injuries and can lead to sensory dysfunction and problems in daily life. An early nerve repair is the best treatment. Patient-reported outcome measure (PROM) are important for evaluating healthcare but little is known about patient-reported outcome after digital nerve injuries. Targeting individual factors could help clinicians developing future rehabilitation. Aims: To evaluate if there are sex- or age-related differences in patient-reported outcome concerning cold sensitivity, numbness and pain on load, 3 and 12 months after digital nerve repair, and differences between 3 and 12 months. Material and Methods: This is a registry study of 197 patients over 16 years, in Sweden, who answered the patient questionnaire 3 and 12 months after surgery. Exclusion criteria were cognitive problems, undergoing surgery and concomitant hand injuries. Patients were categorised into three age groups; 16-29, 30-60 and over 60 years. A clinically relevant symptom was defined as patient-reported outcome score over 20 of 100. Fisher’s exact test and McNemar’s test were used for analysis. Results: A significant age difference was seen 12 months after surgery, where 77.5% in the youngest age group reported numbness, decreasing by age to 48.5% in the oldest age group (p-value 0.03). No other sex- or age-related differences were found. Conclusions: The results indicate that patient-age has an impact on patient-reported numbness one year after digital nerve repair but does not have an impact on the other patient-reported symptoms. Attention may be payed to younger patients with numbness.

Keywords: Digital nerve injury, Digital nerve repair, PROM, Patient-reported outcome, Subjective outcomes.
<table>
<thead>
<tr>
<th>Abbreviations</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2PD</td>
<td>Two Point Discrimination test</td>
</tr>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>HAKIR</td>
<td>The Swedish national quality registry for hand surgery</td>
</tr>
<tr>
<td>ICD-10</td>
<td>The International Classification of Diseases</td>
</tr>
<tr>
<td>KKA97</td>
<td>Classification of surgical interventions</td>
</tr>
<tr>
<td>MCID</td>
<td>Minimal Clinically Important Difference</td>
</tr>
<tr>
<td>NRS</td>
<td>Numeric Rating Scale</td>
</tr>
<tr>
<td>pp.</td>
<td>Percentage points</td>
</tr>
<tr>
<td>PROM</td>
<td>Patient-reported Outcome Measure</td>
</tr>
<tr>
<td>QuickDASH</td>
<td>Short version of the Disabilities of the Arm, Shoulder and Hand outcome measure</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
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</table>
Introduction

Digital nerves
Digital nerves originate either from the median or the ulnar nerve. Two volar digital nerves in each finger run along the ulnar and radial side of the finger, respectively, with branches that supply the dorsal skin (1). The digital nerves supply for the sensory function in each finger and thumb and are highly important for hand function (2, 3).

Digital nerve injuries
Although digital nerve injuries may be regarded as minor injuries, they can have a crucial impact on daily life. The most common upper limb peripheral nerve injury is the injury of a digital nerve and it is often caused by sharp cuts by broken glass or a knife (2, 4). The index finger and thumb are the most common injured digits (5). The incidence of digital nerve injuries in a middle-sized city in Sweden has been reported to be 6.2/100 000 inhabitants per year, mostly affecting men (75%) and younger individuals with a median age of 29 at time of injury (2). This was also reported in another study where 74% of the patients with digital nerve injuries were men and 57% were between 16 and 35 years old at time of injury (4). Permanent sensory impairment with subjective complaints of incoordination of fine motor function, cold sensitivity and pain with following difficulties in the activities of daily living (ADL) are common (2). Seventy-one percent of the patients with a digital nerve injury have reported ADL problems and 91% complained about reduced function at work. Seventy-nine percent of injured patients lost time from work with a median length of sick leave of 59 days. High costs for the society were also reported (2). A study evaluating the impairment of hand function after a digital nerve injury reported that a loss of sensory function in both digital nerves of the thumb should be considered as a 20% loss of hand function, and a complete loss of sensation in the index or long finger would equal 10% loss each (3).

The best treatment of a digital nerve injury is reported to be a primary, early, nerve repair (4). An injury with a minimal gap between the nerve ends can be treated by a primary end-to-end nerve repair using sutures (6). For larger defects, nerve grafts are considered the gold standard (6). Sensory nerves that are considered as less important for function, such as the cutaneous antebrachial nerve or the sural nerve, are often used as grafts (7).
Factors influencing sensory outcome after nerve injury

Sensory outcome is the patient’s sensory functional status objectively measured by a clinician. An example of a common test of sensory function in the fingers is the Two Point Discrimination test (2PD) (8). Factors influencing sensory outcome after nerve repair have been evaluated in several studies. Type of injury (sharp cut, crush injury, avulsion), level of injury and time between injury to surgery have been reported as important factors (9, 10). However, other authors have not found a significant correlation between sensory outcome and time from injury to surgery (5, 11) and type of injury (12). The recovery of an injured nerve, involving distal nerve degeneration and axon regeneration, takes time. Sensory outcome therefore typically improves with time after digital nerve repair (13). Smoking and concomitant injuries (such as tendon and vascular injuries, fractures) have been reported as negative prognostic factors (12).

Sex, age and sensory outcome

Correlation between sex and sensory outcome seems to be less evaluated. However, at least one study suggests that there is no significant correlation between sex and sensory outcome (11). Another important factor influencing sensory outcome is patient age. Numerous studies, including both children and adults, report a correlation between age and sensory outcome, where younger patients show better outcomes (9-14). Weinzweig et al. reported that patients older than 40 years showed significantly poorer sensory outcome than younger patients (11). In median and ulnar nerve injuries, patients younger than 16 years had the best sensory outcome and patients older than 40 had the worst sensory outcome (10). Age over 37 years has also been reported as a negative prognostic factor (12). However, in a more recent review, no significant correlation between age and sensory outcome was found after digital nerve repair (5). In children 0-16 years, no correlation between age and sensory outcome after digital nerve repair has been found (15).

Patient-reported outcome measure

Patient-reported outcome measure (PROM) aims to obtain the patients’ views of their symptoms, their functional status and their health-related quality of life. From initially being developed and used for research, doctors adopted PROMs to enhance the clinical management of individual patients (16). While measures of sensory outcome can provide important objective information about the patient’s sensory function, PROMs can provide additional valuable subjective information. The clinician-assessed sensory outcomes may not fully reflect a
patient’s health status, since the impact of functional limitations on well-being differs for each patient. An outcome perceived as “good” by a clinician may not represent an acceptable outcome from a patient perspective (17). The purposes of collecting patient-reported outcomes are numerous. For instance, most interventions in healthcare aim to reduce symptoms, minimise disability and improve quality of life—aspects only the patients themselves can assess. The measures also avoid observer bias and encourage patients to be more involved in their healthcare (16). In a general healthcare perspective, PROMs can contribute to quality improvement and are considered to be an important way to respond to policies and payments systems emphasizing more patient-centred care (18). In a more clinical view, by analysing PROM data before and after operation, indications for surgery can be evaluated, pre-operative information to patients can be improved and results of different treatment methods can be compared from the patient perspective (19). In patients with rheumatoid arthritis different PROMs are used, by the doctor and patient together, to revise treatments and to plan lifestyle changes (18). In stroke patients, it has been reported that most of the information obtained in PROMs was not captured by the clinical outcome measure (17). In breast cancer patients it has been suggested that the given information to patients prior to treatment, involving treatment choices and post treatment symptoms, could be improved by using PROM data (20). In England, PROMs are reported to be an important aid in clinical decision making, in the same way as clinical investigations (16).

**Digital nerve repair and PROM**

Patient-reported outcome has been less studied than objective sensory outcome after digital nerve repair. Most current PROM studies report on only disability and pain (14, 21, 22). A common PROM questionnaire evaluating disability in the upper extremity is the Disabilities of the Arm, Shoulder and Hand (DASH), describing limitations in upper extremity activities, as well as symptoms (23). The short version of the DASH, called the QuickDASH, consists of 11 questions instead of 30, and has shown equally good psychometric properties (24). A total score of the DASH or QuickDASH however, does not describe the symptoms perceived by patients in detail. Few studies report on specified patient-reported symptoms after digital nerve repair, (2, 25), to the extent of the author’s knowledge.
The Swedish national quality registry for hand surgery (HAKIR), which started in 2010, collects PROM data from all adult patients undergoing digital nerve repair at the seven participating specialized hand surgery departments (26). At surgery, the main diagnosis of the injury and the performed procedure is registered in HAKIR (19) using the International Classification of Diseases-10 (ICD-10) codes (27) and the Classification of Surgical Interventions (KKÅ97) codes (28). The PROM data is collected using a patient questionnaire, designed by HAKIR, and is sent to the patients 3 and 12 months after surgery (19). The patients are requested to report the degree of their perceived severity of seven symptoms in the hand: pain on load, pain on motion without load, pain at rest, stiffness, weakness, numbness/tingling in fingers, cold sensitivity/discomfort on exposure to cold and also the ability to perform ADL. The patient questionnaire is available on the HAKIR website and has been used since the start of the registry in 2010 (19). It was recently validated and psychometrically evaluated, showing construct validity and good data completeness, and was submitted for publication in November 2018 (Personal communication Marianne Arner 15 Nov 2018) (Appendix 1).

Symptoms after digital nerve repair
Cold sensitivity, numbness and pain have been reported to be the most pronounced patient-reported symptoms after nerve surgery (2, 25, 29-31). The HAKIR annual report 2017 reported that the three most pronounced patient-reported symptoms 12 months after surgery in patients with digital nerve injuries were cold sensitivity (mean 48 of 100), numbness (mean 42 of 100) and pain on load (mean 26 of 100) (29). Thorsén et al. showed that 79% of the patients reported cold sensitivity and 97% had trouble with fumbling fingers after digital nerve repair (2). A long term follow-up study showed similar results, where 76% of the patients reported cold sensitivity and 76% reported numbness (25). After digit replant surgery, the results were alike, where 86.7% reported cold sensitivity (30). Cold sensitivity has been reported to be a common and persistent symptom after upper limb peripheral nerve injury and rarely decreasing over time (25).

The data in the HAKIR annual report for 2017 is based on mean values for groups of patients and has not been corrected for possible registration errors. However, the data still indicates, along with other studies (2, 25) that there is a large group of patients that experience sensory dysfunction after digital nerve repair.
Sex- and age-related differences in PROMs

Numerous studies report differences between women and men in different types of PROMs and different types of conditions, especially concerning pain. However, few studies have reported on differences in PROMs related to age. It has been stated that women report higher levels of pain and experience pain of longer duration than men, in patients with headache, back or abdominal pain as well as musculoskeletal pain (32). However, in a more recent larger review, it has been reported that this not always is the case (33). Racine et al. examined sex differences in the perception of different types of laboratory-induced pain, such as thermal (cold, heat), visceral, pressure and muscle pain, in healthy subjects. It was suggested that women and men have comparable thresholds for cold and ischemic pain, while pressure pain thresholds are lower in women than men (33). Strong evidence was found for that women tolerate less thermal pain and pressure pain. However, the majority of the studies that measured pain intensity and unpleasantness included in the review showed no sex difference in various pain modalities (33). Studies of pre- and postoperative pain and opioid requirements in patients that undergo surgical procedures under general anesthesia, have suggested that women experience higher levels of pain intensity immediately before surgery and after surgery, with larger doses of opioid required postoperatively (34, 35). Women and older individuals (age was not defined), who undergo hip arthroplasty due to osteoarthritis have reported poorer outcome on different PROMs, except for health-related quality of life, where no sex difference was found (36). Brain imaging data has shown that in women, raised levels of sex hormones during the menstrual cycle seem to change functional organization within the hemispheres (37). This indicates that there are functional brain differences between women and men.

Sex- and age-related differences after nerve surgery

There is limited research on sex- and age-related differences after nerve surgery. No significant correlation between age and patient-reported sensory function has been found after different types of nerve surgery (25, 31). In patients reporting cold sensitivity after a peripheral upper limb injury, including digital nerve injuries, no differences between patients over 30 years of age and patients under 30 years were found (25). In patients where the sural nerve was taken as a nerve graft, neither age nor sex were found to correlate with patient-reported outcomes, concerning symptoms at the donor site (31).

There are several studies on the correlation between age and sensory outcome after nerve injury, but little is known about age-related differences in PROM. Sex-related differences in PROM
have been studied, especially concerning perceived pain in different types of conditions. Neither sex- nor age-related differences in PROM have, however, been studied concerning outcomes after surgery with digital nerve repair. Targeting individual factors could help clinicians developing and adapting future rehabilitation programs after digital nerve repair and improve pre-operative information to the patient.

**Aims**

The aim of this study was to evaluate if there are sex- or age-related differences in patient-reported outcome concerning cold sensitivity, numbness and pain on load, 3 and 12 months after digital nerve repair. Secondly, the aim was to evaluate if there are sex- or age-related differences in change between the two time points after nerve repair concerning these symptoms.

**Materials and Methods**

**Study design and study population**

This was a prospective observational registry study of 197 patients between 18 and 87 years of age who underwent digital nerve repair in Sweden between 1st February 2010 and 31st May 2018, and that also answered the patient questionnaire both at 3 and 12 months after surgery. The study included all adult patients, 16 years old and older, that were registered in HAKIR with the ICD code S64.3 “Injury of digital nerve of thumb” and S64.4 “Injury of digital nerve of other finger”, with the KKÅ97 code ACB29 “Suture of another or an unidentified peripheral nerve”.

**Exclusion criteria**

Patients with diagnosed cognitive problems or undergoing repeated surgery are not required to answer the patient questionnaire, according to the general criteria of the HAKIR registry (19), and were therefore excluded from the study. Patients with concomitant injuries, such as tendon injuries, fractures, ligament injuries, nerve injuries of another level, vascular injuries and nerve grafts were also excluded. During the elected time period, 2372 patients had undergone digital nerve repair. From these 2372 patients, the total number of patients analysed was 197 (Figure 1).
Data collection

Since HAKIR is a quality registry, data had already been collected before the start of this project. A file with deidentified data from the period 2010-02-01, the start of HAKIR, to 2018-05-31 was obtained from the registry after ethical approval. The end date was set to 2018-05-31 to allow for time to search the file for potential registration errors, before working with the
data. The obtained data from HAKIR included all patients assessed for eligibility with data on age at time of surgery, sex, main diagnosis of the injury, the performed surgery and data on all patient questionnaire answers 3 and 12 months after surgery. The three symptoms cold sensitivity, numbness and pain on load were collected for analysis, being the most pronounced patient-reported symptoms 12 months after surgery (2, 29). The sex was registered and collected as woman or man, based on the patient’s social security number.

The design of the patient questionnaire is a numeric rating scale (NRS), a type of Likert scale, with a horizontal symmetric and numeric 11-point box scale between 0-100 (38, 39). The scale is supported with numerical descriptors on every ten numbers: 0, 10, 20, 30... 100, with verbal anchors at the ends, where 0, at the left end, is defined as “no problems” and 100, at the right end, is defined as “worst problems imaginable”. The patient was asked to specify their perceived severity of the symptom in question by checking one of the boxes on the NRS, equalizing a ten number.

During the first years of HAKIR, a different scale, a visual analogue scale (VAS; 0-100), was used in the questionnaire. In 2013 the questionnaire design was changed to NRS due to practical difficulties when adapting the questionnaire to usage on tablets and mobile phones. Both VAS and NRS have frequently been used to evaluate postoperative pain intensity in a variety of populations (40). A high correspondence between VAS and NRS results has been established, with a few exceptions (38, 41). Therefore, the data from the VAS and NRS responses was aggregated in this study.

**Age and sex variables**

Patients were categorized into age groups: young adults (age 16 to 29), working-age adults (age 30 to 60) and old adults (age over 60). This grouping was based on clinical significance. The three age limits were selected to obtain three clinically relevant groups of patients with different types of demands in daily life: young individuals before working age, adults in working-age and older persons after working-age. Patients were also categorized into categorical data women and men.
**Patient-reported outcome variable**

The patient-reported outcome of cold sensitivity, numbness and pain on load was categorised into two categories: not clinically relevant symptom and clinically relevant symptom. An outcome score between 0 and 20 was defined as not clinically relevant symptom and an outcome score between 30 and 100 was defined as a clinically relevant symptom. This limit was arbitrarily set but corresponds to the minimal clinically important difference (MCID) of 20 points on a 100 point-scale for the questionnaire QuickDASH (42), which is frequently used for evaluating outcomes after hand surgery. In future text, when presenting or discussing a symptom, the definition clinically relevant symptom will be referred to.

**Statistical analysis**

Sex, age and outcome were analysed as nominal categorical data. The age groups were analysed together as a single variable, providing an overall p-value. Data was presented as proportions (percent, %) and the difference between two proportions was presented as percentage points (pp.).

Statistical methods employed were Fisher’s exact test and McNemar’s test. In order to determine whether there were sex- or age-related differences in patient-reported outcome, Fisher’s exact test was used (43). Fisher’s exact test is preferably used for small number of participants (<1000), as in this study, and is applicable when there are two nominal variables and the aim is to investigate whether the proportion of one variable is different depending on the value of the other variable (43). In order to assess whether there were sex- or age-related differences in change between 3 and 12 months, McNemar’s test was used (43). McNemar’s test is applicable when the outcome variable is binary (no clinically relevant symptom and clinically relevant symptom) and is used to assess whether there is a significant change or significant difference in proportions over time for paired or matched data (43). A p-value <0.05 was considered to be statistically significant. All statistical analyses were performed using IBM® SPSS Statistics® for Macintosh version 25.0.

**Ethical considerations**

When performing a registry study, the main concern is the patient’s autonomy and the right to privacy. Registration in the quality registry HAKIR was done according to the rules of quality registries in the laws of patient data, Patientdatalagen (SFS 2008:355) (26) and according to
the Declaration of Helsinki (44). All patients who are registered in HAKIR have received appropriate information to ensure their autonomy: information about the registry, secrecy management and voluntary participation and termination. Written registry information was handed to the patient at the hand surgery clinic. The information was also available on the HAKIR website, on posters and in brochures in the waiting room of the hand surgery clinic. In May 2018, HAKIR updated documents and information according to the new General Data Protection Regulation. The data was obtained from the registry by the supervisors. The integrity of the patient was protected by the fact that only information relevant to the study was obtained from the registry and that all obtained data was deidentified before analysis. Since this was a registry study, there was no risk of physically harming the patient. The results of this study will provide knowledge about patient-reported outcome after digital nerve repair which may help improve treatment. An ethical approval to perform this registry-based study on data from HAKIR was obtained by the Stockholm Ethical Review Board in 2017 (Dnr. 2017 2023-31).

Results

Patient characteristics

Patient characteristics are described in Table 1. Data for a total number of 197 patients was analysed. The median patient age was 47 years (range 18-87) and 51.8% were men. Most patients were in the age group “working-age adults” 30-60 years old (61.9%). In the age group “young adults” 16-29 years, women made up for more than half of the age group (55%) (Figure 2). In the age groups “working-age adults” 30-60 years and “old adults” over 60 years, the men made up for more than half of each age group (52.5% and 57.1% respectively).

<table>
<thead>
<tr>
<th>Table 1: Patient characteristics.</th>
<th>Population size (n=197)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>95</td>
</tr>
<tr>
<td>Men</td>
<td>102</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
</tr>
<tr>
<td>Young adults 16-29 years</td>
<td>40</td>
</tr>
<tr>
<td>Working-age adults 30-60 years</td>
<td>122</td>
</tr>
<tr>
<td>Old adults &gt;60 years</td>
<td>35</td>
</tr>
</tbody>
</table>
Data on patient-reported symptoms is described in Table 2. Numbness was the most pronounced clinically relevant patient-reported symptom three months after surgery (66%), closely followed by cold sensitivity (65%). Twelve months after surgery, the most pronounced clinically relevant patient-reported symptom was cold sensitivity (70.3%), closely followed by numbness (65%). Clinically relevant levels of pain on load was reported in almost half of the patients (3 months 45.9% and 12 months 45.4%).

Table 2: Patient-reported symptoms.

<table>
<thead>
<tr>
<th></th>
<th>3 months after surgery</th>
<th></th>
<th>12 months after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td><strong>Cold sensitivity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not clinically relevant&lt;sup&gt;a&lt;/sup&gt;</td>
<td>63</td>
<td>35%</td>
<td>58</td>
</tr>
<tr>
<td>Clinically relevant&lt;sup&gt;b&lt;/sup&gt;</td>
<td>117</td>
<td>65%</td>
<td>137</td>
</tr>
<tr>
<td>Total answers</td>
<td>180</td>
<td>100%</td>
<td>195</td>
</tr>
<tr>
<td>Missing</td>
<td>17</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>Numbness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not clinically relevant</td>
<td>67</td>
<td>34%</td>
<td>69</td>
</tr>
<tr>
<td>Clinically relevant</td>
<td>130</td>
<td>66%</td>
<td>128</td>
</tr>
<tr>
<td>Total answers</td>
<td>197</td>
<td>100%</td>
<td>197</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Pain on load</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not clinically relevant</td>
<td>106</td>
<td>54.1%</td>
<td>107</td>
</tr>
<tr>
<td>Clinically relevant</td>
<td>90</td>
<td>45.9%</td>
<td>89</td>
</tr>
<tr>
<td>Total answers</td>
<td>196</td>
<td>100%</td>
<td>196</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

<sup>a</sup> not clinically relevant = patient-reported outcome <20/100)
<sup>b</sup> clinically relevant = patient-reported outcome >20/100)
<sup>c</sup> percent of total answers
Sex- and age-related differences in patient-reported outcomes

Proportions of patients with clinically relevant symptoms of cold sensitivity, numbness and pain on load in relation to sex and age are shown in Table 3. Differences between sexes were analysed with Fisher’s exact test, as well as the overall difference between the age groups. A statistically significant overall difference between the age groups was seen in numbness 12 months after surgery (p-value 0.03; Figure 2b). Highest proportions of patients were seen in the youngest age group (16-29 years), decreasing by age to lowest proportions in the oldest age group (over 60 years). A similar difference was seen in pain on load at 12 months, although not significant (p-value 0.1) (Figure 2c). This difference was not seen in cold sensitivity at 12 months (Figure 2a). No other statistically significant differences were found.

In all categories, except pain on load 12 months after surgery, the proportion of women reporting clinically relevant symptoms were slightly higher than the proportion of men. These were not statistically significant differences. The resulting difference between the proportion of women and the proportion of men reporting numbness was 4.7 pp., both 3 and 12 months after surgery. The resulting difference between the proportion of women and the proportion of men reporting cold sensitivity was 4.6 pp. at 12 months.
Table 3: Differences in clinically relevant patient-reported symptoms. Clinically relevant symptom = patient-reported outcome >20/100. Number of patients (n) that reported clinically relevant cold sensitivity, numbness and pain on load in each sex- and age group, with corresponding proportion of patients (%) on total number of patients that answered the question in each group. Total number (total n) of patients that reported the clinically relevant symptom at the two time points, with corresponding proportion of patients (total %) on total number of patients that answered the question.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age group</th>
<th>3 months after surgery</th>
<th>12 months after surgery</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n (% within sex)</td>
<td>n (% within age group)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Women</td>
<td>Men</td>
<td>Total n (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16-29 yrs.</td>
<td>30-60 yrs.</td>
<td>&gt;60 yrs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16-29 yrs.</td>
<td>30-60 yrs.</td>
<td>&gt;60 yrs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16-29 yrs.</td>
<td>30-60 yrs.</td>
<td>&gt;60 yrs.</td>
</tr>
<tr>
<td>Cold sensitivity</td>
<td>Women</td>
<td>61 (66.3)</td>
<td>56 (63.6)</td>
<td>117 (65)</td>
</tr>
<tr>
<td>Numbness</td>
<td>Women</td>
<td>65 (68.4)</td>
<td>65 (63.7)</td>
<td>130 (66)</td>
</tr>
<tr>
<td>Pain on load</td>
<td>Women</td>
<td>45 (47.4)</td>
<td>45 (44.6)</td>
<td>90 (45.9)</td>
</tr>
</tbody>
</table>

a P-values were calculated using Fisher’s exact test (2-sided).
b Statistically significant value (<0.05) in bold.

Yrs. = years
Cold sensitivity and differences between 3 and 12 months

Differences between the proportions of patients reporting cold sensitivity at the two time points 3 and 12 months after surgery were analysed with McNemar’s test. Crosstabulation was used, resulting in numbers and proportions of patients, in each category, who had a change in reporting clinically relevant or not clinically relevant cold sensitivity between the two time points. Total proportions of patients reporting cold sensitivity at 3 and 12 months are shown in Table 4, with the resulting difference between the total proportions. No statistically significant differences between the two time points were found in either women and men, or in the age groups.

Although not significant, there was a slightly higher proportion of patients reporting cold sensitivity at 12 months compared to 3 months in all categories, except for the age group 16 to 29 years. The resulting difference between the proportion of women reporting cold sensitivity at 12 months and at 3 months was 6.5 pp. (p-value 0.2), while the same difference in men was 3.5 pp. (p-value 0.6). The resulting difference between the proportion of patients in the oldest age group at 12 months and at 3 months was 7.1 pp. but was not significant (p-value 0.08).

Table 4: Clinically relevant cold sensitivity at 3 and 12 months. Clinically relevant = patient-reported outcome $>20/100$. Cold sensitivity at 3 and 12 months is presented as total proportions (percent, %) of patients reporting clinically relevant cold sensitivity in the specific category and at the specific time point. The difference between 3 and 12 months is presented as the resulting difference (percentage points, pp.) between the total proportions of patients at 3 and 12 months.

<table>
<thead>
<tr>
<th></th>
<th>3 months %</th>
<th>12 months %</th>
<th>Difference pp.</th>
<th>P-value*</th>
</tr>
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<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>66.3</td>
<td>72.8</td>
<td>6.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Men</td>
<td>63.2</td>
<td>66.7</td>
<td>3.5</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-29 yrs.</td>
<td>68.6</td>
<td>68.6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>30-60 yrs.</td>
<td>64.6</td>
<td>71.7</td>
<td>7.1</td>
<td>0.08</td>
</tr>
<tr>
<td>&gt;60 yrs.</td>
<td>61.3</td>
<td>64.5</td>
<td>3.2</td>
<td>1</td>
</tr>
</tbody>
</table>

*P-values were calculated on total patients in each category using McNemar’s test (2-sided) with binomial distribution. yrs. = years
Numbness and differences between 3 and 12 months

Differences between the proportions of patients reporting numbness at the two time points 3 and 12 months after surgery were analysed with McNemar’s test. Crosstablulation was used, resulting in numbers and proportions of patients, in each category, who had a change in reporting clinically relevant or not clinically relevant numbness between the two time points. Total proportions of patients reporting numbness at 3 and 12 months are shown in Table 5, with the resulting difference between the total proportions. No statistically significant differences between the two time points were found in either women and men, or in the age groups.

In the youngest age group, 16 to 29 years, there was a higher proportion of patients reporting numbness at 12 months compared to at 3 months. The resulting difference between these proportions was 12.5 pp. but not statistically significant (p-value 0.2). In the oldest age group, over 60 years, there was a lower proportion of patients reporting numbness at 12 months compared to at 3 months. The resulting difference between these proportions was 20 pp. but not statistically significant (p-value 0.9).

Table 5: Clinically relevant numbness at 3 and 12 months. Clinically relevant = patient-reported outcome >20/100. Numbness at 3 and 12 months is presented as total proportions (percent, %) of patients reporting clinically relevant numbness in the specific category and at the specific time point. The difference between 3 and 12 months is presented as the resulting difference (percentage points, pp.) between the total proportions of patients at 3 and 12 months.

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
<th>12 months</th>
<th>Difference</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>68.4</td>
<td>67.4</td>
<td>-1</td>
<td>1</td>
</tr>
<tr>
<td>Men</td>
<td>63.7</td>
<td>62.7</td>
<td>-1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-29 yrs.</td>
<td>65</td>
<td>77.5</td>
<td>12.5</td>
<td>0.2</td>
</tr>
<tr>
<td>30-60 yrs.</td>
<td>65.6</td>
<td>65.6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>&gt;60 yrs.</td>
<td>68.6</td>
<td>48.6</td>
<td>-20</td>
<td>0.9</td>
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</tbody>
</table>

*P-values were calculated on total patients in each category using McNemar’s test (2-sided) with binomial distribution.
yrs. = years
Pain on load and differences between 3 and 12 months

Differences between the proportions of patients reporting pain on load at the two time points 3 and 12 months after surgery were analysed with McNemar’s test. Crosstabulation was used, resulting in numbers and proportions of patients, in each category, who had a change in reporting clinically relevant or not clinically relevant pain on load between the two time points. Total proportions of patients reporting pain on load at 3 and 12 months are shown in Table 6, with the resulting difference between the total proportions. No statistically significant differences between the two time points were found in either women and men, or in the age groups.

The proportion of women reporting pain on load at 12 months was lower compared to at 3 months. The resulting difference between these proportions was 4.1 pp. but not statistically significant (p-value 0.6). The proportion of men reporting pain on load at 12 months was higher compared to at 3 months. The resulting difference between these proportions was 4 pp. but not statistically significant (p-value 0.5).

Table 6: Clinically relevant pain on load at 3 and 12 months. Clinically relevant = patient-reported outcome >20/100. Pain on load at 3 and 12 months is presented as total proportions (percent, %) of patients reporting clinically relevant pain on load in the specific category and at the specific time point. The difference between 3 and 12 months is presented as the resulting difference (percentage points, pp.) between the total proportions of patients at 3 and 12 months.

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
<th>12 months</th>
<th>Difference</th>
<th>P-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>47.4</td>
<td>43.3</td>
<td>-4.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Men</td>
<td>44</td>
<td>48</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-29 yrs.</td>
<td>57.5</td>
<td>57.5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>30-60 yrs.</td>
<td>44.2</td>
<td>45</td>
<td>0.8</td>
<td>1</td>
</tr>
<tr>
<td>&gt;60 yrs.</td>
<td>37.1</td>
<td>34.3</td>
<td>-2.8</td>
<td>1</td>
</tr>
</tbody>
</table>

aP-values were calculated on total patients in each category using McNemar’s test (2-sided) with binomial distribution.

yrs. = years
**Discussion**

Digital nerve injuries are the most common upper limb peripheral nerve injury and can lead to sensory dysfunction, resulting in limitations managing daily activities (2). This was a prospective observational registry study of patients who had undergone digital nerve repair. The aim was to evaluate if there were sex- or age-related differences between patient-reported outcomes, 3 and 12 months after digital nerve repair. Patient-reported outcomes evaluated were cold sensitivity, numbness and pain on load. This study also aimed to evaluate if there were any differences in change between the two time points. The results indicated that patient age has an impact on patient-reported numbness one year after surgery but does not seem to have an impact on the other patient-reported outcomes. The results also indicated that there are no sex-related differences, and no sex-related differences in patient-reported cold sensitivity, numbness and pain on load, related to the time after digital nerve repair.

**Sex and patient-reported outcome**

No significant differences were found between women and men in patient-reported outcomes in this study. There is limited research on sex-related differences after nerve surgery. In patients where the sural nerve was taken as a nerve graft, sex was not found to correlate with patient-reported outcomes (31), which is in line with this current study. The evaluated patient-reported outcomes in the study mentioned, however, concerned the nerve donor site, which might differ from the site of a digital nerve injury. Previous studies on sex differences concerning perceived pain in other conditions, however, seem to report inconsistent results (32-35). In opposite to previous reviews, Racine et al. showed strong evidence that women tolerate less cold pain than men but concluded that there is no evidence for sex differences in most pain modalities (33). It has also been suggested that women report higher levels of pain before and after surgery (34, 35). Weis et al. suggested that altering levels of sex hormones in the course of women’s menstrual cycle have an impact on brain hemispheric functions, resulting in behavioural differences between women and men (37). Whether the menstrual cycle could have an impact on how women experience their symptoms, remains unknown, but may be a possible reason to the inconsistent results of sex differences in patient-reported outcome. Although, sex differences in patient-reported outcome seem to remain unclear and results seem to vary between different type of conditions.
Age and patient-reported outcome

A significant overall age difference was found at 12 months after surgery, where more younger patients reported numbness than older patients, with decreasing proportions by each age group. This finding contradicts previous research on correlation between age and clinical sensory outcome, where the younger patients obtained better outcomes (9-14). However, few studies have reported on differences in PROMs related to age and no previous studies have been evaluating the differences between age and patient-reported outcome after digital nerve repair. In patients reporting cold sensitivity after a distal upper limb injury, no differences between patients over 30 years of age and under 30 years were found (25), which are in line with the results of cold sensitivity in this study. Greene et al. suggested that older patients (age was not defined) who have undergone hip arthroplasty report poorer outcome on different PROMs (36), which is the opposite to the difference found in this study.

When comparing the difference between 3 and 12 months, in each age group, no significant differences were found. However, there was a higher proportion of patients, in the youngest age group, reporting numbness at 12 months compared to at 3 months, with a resulting insignificant difference of 12.5 pp. An interesting difference was also seen in the oldest age group, where there was a lower proportion of patients at 12 months compared to at 3 months, with a resulting insignificant difference of 20 pp. This indicates that the younger patients might experience worse problems with numbness one year after surgery compared to three months after, but that the older patients experience the opposite. However, since these are insignificant differences, they need to be studied further. This also indicates that there might be an actual difference between these age groups, though this was not analysed. One possible reason why the younger patients in this study report poorer outcome could be higher expectations on the outcome because of different demands in daily life, requiring high sensory function. Previous studies that reported better outcomes in younger patients evaluated the objective sensory outcome, which could differ from the patient’s subjective view. It has been reported that there is no significant correlation between patient-reported cold sensitivity and objective sensory recovery (25), which indicates that the patient’s point of view might differ from the objective sensory outcome.

Additional findings

When looking at patient characteristics, some incidental findings were seen. There were high proportions of patients reporting clinically relevant symptoms one year after digital nerve
As much as 70% of the patients reported cold sensitivity. The high levels correlate well with previous literature, where 76 to 79% of the patients reported cold sensitivity (2, 25). In the HAKIR annual report 2017 the patient-reported mean value of cold sensitivity was 48 of 100 on the patient questionnaire (29), which also indicates that patients experience problems with cold sensitivity. One possible reason to these high levels of reported cold sensitivity might be cold climate or cold working environment. This was suggested in a Canadian study where patient-reported cold sensitivity was as highest during the winter months of December, January and February (25). A Swedish study found that cold exposure was related to reported neurovascular hand symptoms, such as cold sensitivity, and suggested that cold climate might be a risk factor for these type of symptoms (45). Another possible affecting factor might be type of work. Different types of work demand different levels of sensory function in the hand. For instance, patients with manual labour might report more symptoms than those with non-manual occupations.

**Strengths and Limitations**

A strength in this study was that patient-reported data was collected at 3 and 12 months after surgery, which allowed for analysis of differences in change during a long follow-up period. Another strength is that the questionnaire used has been validated. Although, since it is a self-reporting questionnaire there might exist information-bias. Compared to previous PROM studies (25, 30, 31), the number of patients that got analysed in this study was high. However, statistically there was a small number of patients, and the methods employed were therefore chosen to match the small population size to avoid potential type I and II errors (43).

Although an acceptable population size was used, there were few patients analysed in some subcategories. For example, in the age group over 60 years, three months after surgery, only 13 patients reported pain on load. Many patients were excluded, due to e.g. concomitant injuries and not answering the questionnaire at both time points. There was also a low response rate to the questionnaire in general with only 40% of the included patients answering at 3 or 12 months. Although the employed methods were matched to the small population size, there might still exist a type II error due to the small number of patients in the sub categories, making the results unreliable (43). Furthermore, a large drop out of patients that did not answer the questionnaire enhance the risk for possible non-responder bias. Patients that did answer the questionnaire might differ from those who did not. For instance, those patients who answered may be more
disappointed with their sensory function and therefore more prone to answer the questionnaire to express their dissatisfaction.

Confounding factors, such as smoking, diabetes and neuropathy, were not collected and therefore not accounted for in this study. It is also unknown if some of the patients had gone through rehabilitation after the surgery, which, in that case, might have had an impact on the reported outcome of that patient.

The limit of clinically relevant symptom, over 20 of 100, was set based on previous literature on another 100-point scale questionnaire (42). However, this cut off limit has not been used before for the patient questionnaire in the current study. Furthermore, the individual reported differences in change between the two time points were not considered. An individual change from, for example, 100 to 30 on the questionnaire, was in this study analysed as no difference, since both reported outcomes were over the cut off limit. In order to answer the second aim better, different statistical methods could have been employed, using no cut off limit. There is also a possibility that the categorising of the age variable in this study had an impact on the results. The age groups were analysed as one single variable, testing the probability for all age groups, and not the probability between the age groups themselves. This answered the question if there was a difference or not, though it did not say between which specific age groups.

**Clinical Applications**

The results of this study suggested that it is mostly the younger patients experiencing problems with numbness one year after surgery. This finding could be considered when developing a rehabilitation program, by, for instance, focusing on numbness in the younger patients. It could also be incorporated into the pre-operative information to the younger patients and act as a guidance when implementing follow-ups. By identifying these younger patients with numbness problems, and developing a rehabilitation program for them, the perceived numbness might get better and might lead to less problems in ADL and shorter periods of sick leave. However, clinical applications should not be based on the current study solely and further studies are needed.

The additional findings in this study, along with the HAKIR annual report and previous literature indicate that there is a large group of patients experiencing sensory problems up to
one year after digital nerve repair (2, 25, 29). However, at the present, there is no national consensus on follow-up or rehabilitation for these patients in Sweden (Personal communication Marianne Arner 14 Dec 2018). It is usually up to the patients themselves to contact the hand surgery department if experiencing any problems after surgery. The high proportion of patients experiencing sensory dysfunction in this study indicates that there is a need for more standardised follow-ups and rehabilitation in order to improve the perceived disability in these patients. Since such high proportions of patients experience cold sensitivity, numbness and pain on load, these symptoms could act as a guidance and as a part of criteria for knowing which patients to follow up.

**Equity**

This study evaluated if there are sex- or age-differences and is thereby illustrating important aspects of equity. However, aspects like gender and educational and socioeconomical background were not accounted for when obtaining the data. The sex of the patient was defined only as woman or man, based on the social security numbers in the registry, and accounts were not taken for perceived gender. The proportions of women and men analysed in this study were almost equal. It is plausible to think that educational and socioeconomical background might have had an impact on the response rate of the questionnaire. For instance, lack of reading skills or Swedish skills could have prevented patients from answering the questionnaire, resulting in risk of selection bias. At the present, only a Swedish and an English version of the questionnaire is available, and it was only recently translated to English. Patients under 16 years of age and patients with cognitive problems were excluded. This makes the results of this study only applicable to Swedish-speaking cognitive healthy adults. The results are applicable to both women and men, although only by biological means.

**Future Studies**

In this study, only patients answering the questionnaire both 3 and 12 months after surgery were included, which lead to analyses of a small number of patients, with less reliable results. In order to draw more general conclusions, analysing larger data materials would be required. One way to widening the population base and to increase the response rate could be through translation of the patient questionnaire. In order to guide future rehabilitation efforts, evaluating the correlation between patient-reported outcome after digital nerve repair and other potential influencing factors would be beneficial. For instance, analysing information about the patient’s
In order to provide an extended view of influencing factors, the type of work and hobbies compared to differences in patent-reported outcome might give an extended view of influencing factors. This could help the clinician to give better and more customised information to the individual patient. It would also be of interest to evaluate the effects of different rehabilitation programs on patient-reported outcome and the correlation between objective sensory outcome and patient-reported outcome after digital nerve injury. Since concomitant injuries (e.g. tendon injuries) and smoking have been reported as negative prognostic factors for objective sensory outcome (12), it would be of interest to evaluate if these factors also have similar impact on patient-reported outcome. For instance, to evaluate if there is a correlation between smoking and experiencing sensory problems after digital nerve repair. If a correlation would exist, it could be incorporated into the prognostic information given to the patient. Additionally, this study indicated that there is a difference between the age groups. However, the study did not state between which age groups this difference was found. This would be of interest to evaluate in future studies and could be done by using another statistical method for the analysis. Another way to analyse the age variable is to categorise the ages into, for example, 5-year groups (16-20 years, 21-25 years etc.). Further research on more specific age differences could aim to optimise the rehabilitation program by adapting the rehabilitation after certain age groups.

**Conclusions**

One year after digital nerve repair, up to approximately two thirds of the patients still experienced problems with cold sensitivity, numbness and pain on load. The results suggest that patient-age has an impact on patient-reported numbness one year after surgery but does not seem to have an impact on the other patient-reported symptoms. Furthermore, the results indicate that there are no sex-related differences, and no age-related differences in change over time, in the three patient-reported symptoms. The results emphasise the importance of follow-ups and rehabilitation and that attention may be payed to younger patients with numbness. However, further research is needed.

**Acknowledgements**

The author wishes to thank supervisor Marianne Arner and co-supervisor Linda Evertsson for their valuable guidance, commitment and availability. Their insightful feedback has increased the quality of this work. Appreciations go also to co-supervisor Lars Dahlin for valuable comments and thoughts.
References


24. Gummesson C, Ward MM, Atroshi I. The shortened disabilities of the arm, shoulder and hand questionnaire (QuickDASH): validity and reliability based on responses within the full-length DASH. BMC Musculoskelet Disord. 2006;7:44.


Postoperative questionnaire

☐ 3months postop  ☐ 12 months postop

Date of birth (social security no) (yyyy-mm-dd):  

Patient questionnaire HQ-8 (arm/hand)

Date (yyyy-mm-dd):  

I am (please indicate your writing hand):  ☐ Left handed  ☐ Right handed  ☐ Ambidextrous

Arm/hand that was operated on:  ☐ Left  ☐ Right

This questionnaire reports on problems that you have had this past week in the hand/arm that was operated on. Please tick the alternative that best corresponds to any of your problems.

1. Pain on load

   No problems  0 10 20 30 40 50 60 70 80 90 100  

2. Pain on motion without load

   No problems  0 10 20 30 40 50 60 70 80 90 100  

3. Pain at rest

   No problems  0 10 20 30 40 50 60 70 80 90 100  

4. Stiffness

   No problems  0 10 20 30 40 50 60 70 80 90 100  

5. Weakness

   No problems  0 10 20 30 40 50 60 70 80 90 100  

6. Numbness / tingling in fingers

   No problems  0 10 20 30 40 50 60 70 80 90 100  

7. Cold Sensitivity (discomfort on exposure to cold)

   No problems  0 10 20 30 40 50 60 70 80 90 100  

8. Ability to perform daily activities

   No problems  0 10 20 30 40 50 60 70 80 90 100  

9. How would you rate the result of your operation overall?

   Complete 0 10 20 30 40 50 60 70 80 90 100  

10. How would you rate the care that you received at the clinic during your treatment?

    Complete 0 10 20 30 40 50 60 70 80 90 100  

Version 1 (2018-10)