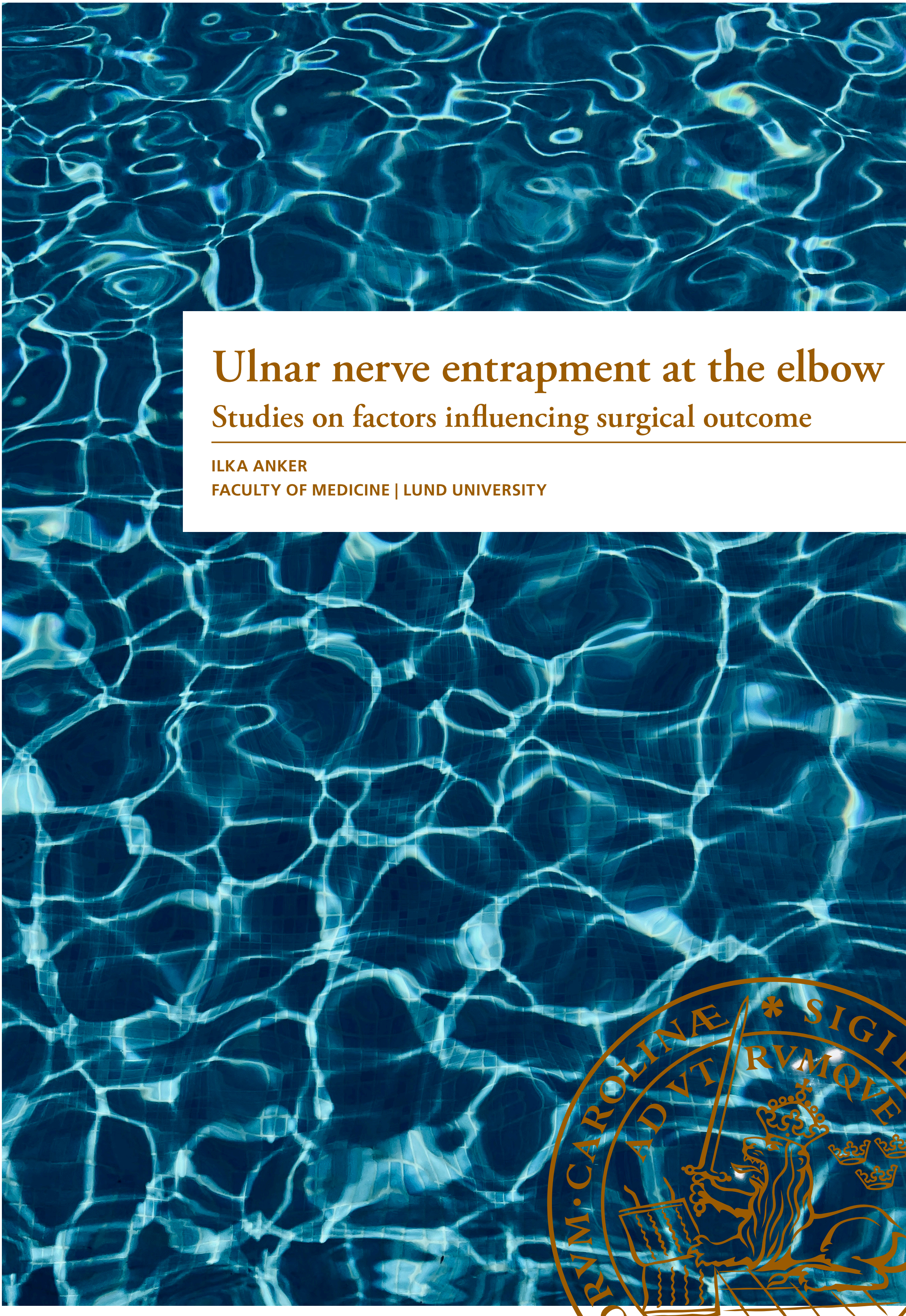
Ulnar nerve entrapment at the elbow - Studies on factors influencing surgical outcome

Anker, Ilka

2021

Document Version:
Publisher's PDF, also known as Version of record



Ulnar nerve entrapment at the elbow

Studies on factors influencing surgical outcome

ILKA ANKER
FACULTY OF MEDICINE | LUND UNIVERSITY

Printed by Media-Tryck, Lund 2021 NORDIC SWAN ECOLABEL 3041 0903

Ulnar nerve entrapment at the elbow

Ulnar nerve entrapment at the elbow is the second most common compression neuropathy in the upper extremity, mainly affecting people of working age. Current literature does not fully support a reliable algorithm on diagnostics, treatment indications and treatment options that can be utilized in a wide patient population, hence these medical choices remain largely surgeon and healthcare center dependent, which may result in increased affliction for patients as well as increased costs for society, due to prolonged time to treatment and incapacity to work.

The aim of this thesis was to advance in essential knowledge concerning ulnar nerve entrapment at the elbow, with primary focus on studying factors that may influence and predict surgical outcome in primary and recurrent cases. The hope is to contribute to creating an evidence-based, standardized process in diagnostics, treatment indications and surgical treatment options for attaining the best possible clinical outcome for the affected patients.

LUND UNIVERSITY

FACULTY OF MEDICINE

Department of Translational Medicine
Department of Hand Surgery

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2021:123
ISBN 978-91-8021-130-7
ISSN 1652-8220

Ulnar nerve entrapment at the elbow

Studies on factors influencing surgical outcome

Ilka Anker

LUND UNIVERSITY

DOCTORAL DISSERTATION

by due permission of the Faculty of Medicine, Lund University, Sweden
To be defended on December 16th, 2021 at 13.00
In Lilla Aulan, Medicinskt Forskningscentrum,
Skåne University Hospital, Malmö, Sweden

Faculty Opponent

Docent Gustav Andersson
Department of Hand- and Plastic Surgery
Norrland University Hospital, Umeå, Sweden

Organization
LUND UNIVERSITY

Faculty of Medicine
Department of Translational Medicine
Department of Hand Surgery

Author Ilka Anker

Document name Doctoral Thesis

Date of issue December 16, 2021

Sponsoring organization

Title and subtitle Ulnar nerve entrapment at the elbow - studies on factors influencing surgical outcome

Abstract

Ulnar nerve entrapment at the elbow (UNE) is the second most common compression neuropathy in the upper extremity. Internationally, there is no clear consensus on diagnostic methods, treatment indications or which surgical procedure offers best clinical outcome, which may increase costs for society. This thesis studies factors that may influence and predict surgical outcome in primary and recurrent UNE, with the aim of contributing to the development of a reliable algorithm for achieving best possible clinical outcome for UNE patients.

In the first part, cases from the Department of Hand Surgery, Skåne University Hospital, were studied retrospectively using a simple doctor-reported outcome measure (DROM). Primary cases treated with simple decompression (SD; n=242) were analysed and cases of primary transposition surgeries and revision transposition surgeries were compared (n=43 and n=44, respectively). In the second part, primary UNE cases from the National Quality Register for Hand Surgery in Sweden (HAKIR; n=1354) were analysed after being linked to the National Diabetes Register (NDR). The third part focused on primary and recurrent UNE cases treated surgically in two of the hand surgery departments reporting to the HAKIR register (n=548). The patient-reported outcome measure (PROM) QuickDASH was primarily used in parts two and three.

In the first part, 78 % of primary SD cases reported being cured or improved after surgery. Sex, smoking, concomitant diseases, and presence of various clinical signs supporting UNE diagnosis did not affect surgical outcome. No difference in outcome was found between UNE diagnosis confirmed by electrophysiology or solely by clinical examination. Cases with electrophysiologically more severe pathology showed worse outcome. Excellent or good outcome (i.e. patients reporting being cured or improved) was reported in 84% of primary and 75% of revision transposition cases. No differences in outcome between primary and revision transposition surgeries was noted. Concomitant systemic diseases, musculoskeletal conditions and carpal tunnel syndrome (CTS) predicted the need for revision surgery. Revision surgeries were characterized by normal electrophysiological findings or less pronounced pathology and a high frequency of preoperative ulnar nerve dislocations compared to primary surgeries. In the second part, no differences were found in surgical outcome between patients with and without diabetes. Men with diabetes had worse outcome after primary SD, which was not seen in women with diabetes. Women showed greater improvement from preoperatively to 12 months postoperatively compared to men, but scored their disability higher than men. Men had better surgical outcome. In the third part ulnar nerve dislocation in UNE was found in 16% of primary and 47% of revision surgeries. Postoperative outcome was worse for UNE cases with dislocation than for those without, but no correlation was found between ulnar nerve dislocation and QuickDASH scores at 12 months postoperatively. Positive correlations were found between postoperative DROM and QuickDASH, giving some support for the possibility of a relationship between DROM and QuickDASH measures. Concomitant diabetes in primary UNE, male sex and increasing age were associated with a worse electrophysiological grading. No differences in postoperative QuickDASH score were found between the various electrophysiological gradings. Primary SD had a better outcome than primary transposition surgeries.

In summary, preoperative electrophysiological grading and age are not clear predictors of surgical outcome after primary SD, but men have a better outcome than women. Concomitant diabetes in primary UNE is associated with a worse electrophysiological grading but does not influence surgical outcome. Ulnar nerve instability is common in UNE, influencing choice of surgical treatment approaches, and possibly surgical outcome, negatively. Concomitant systemic diseases, musculoskeletal conditions and CTS are predictors of revision surgery.

Key words Ulnar nerve entrapment, simple decompression, transposition, revision surgery, electrophysiology, diabetes, nerve dislocation, outcome measures

Classification system and/or index terms (if any)

Supplementary bibliographical information

Language English

ISSN and key title 1652-8220

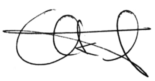
ISBN 978-91-8021-130-7

Recipient's notes

Number of pages 97

Price

Security classification

Signature 

Date 2021-11-10

Ulnar nerve entrapment at the elbow

Studies on factors influencing surgical outcome

Ilka Anker

LUND UNIVERSITY

Coverphoto: *"One who seeks will find",* by Ilka Anker

Faculty of Medicine
Department of Translational Medicine, Department of Hand Surgery

ISSN 1652-8220
ISBN 978-91-8021-130-7
Lund University, Faculty of Medicine Doctoral Dissertation Series 2021:123

Printed in Sweden by Media-Tryck, Lund University
Lund 2021

NORDIC SWAN ECOLABEL
Printed matter 3041 0903

Media-Tryck is a Nordic Swan Ecolabel certified provider of printed material. Read more about our environmental work at www.mediatryck.lu.se

MADE IN SWEDEN

”Two roads diverged in a wood, and I -
I took the one less traveled by,
And that has made all the difference”

Robert Frost

To my all - my family

Sienna, Dante & Tristan
Christian
Elisabeth & Phil
Elisabeth & Ferenc
Magdalena & Ferenc †

Table of Contents

Abstract

Ulnar nerve entrapment at the elbow (UNE) is the second most common compression neuropathy in the upper extremity. Internationally, there is no clear consensus on diagnostic methods, treatment indications or which surgical procedure offers best clinical outcome, which may increase costs for society. This thesis studies factors that may influence and predict surgical outcome in primary and recurrent UNE, with the aim of contributing to the development of a reliable algorithm for achieving best possible clinical outcome for UNE patients.

In the first part, cases from the Department of Hand Surgery, Skåne University Hospital, were studied retrospectively using a simple doctor-reported outcome measure (DROM). Primary cases treated with simple decompression (SD; n=242) were analysed and cases of primary transposition surgeries and revision transposition surgeries were compared (n=43 and n=44, respectively). In the second part, primary UNE cases from the National Quality Register for Hand Surgery in Sweden (HAKIR; n=1354) were analysed after being linked to the National Diabetes Register (NDR). The third part focused on primary and recurrent UNE cases treated surgically in two of the hand surgery departments reporting to the HAKIR register (n=548). The patient-reported outcome measure (PROM) QuickDASH was primarily used in parts two and three.

In the first part, 78 % of primary SD cases reported being cured or improved after surgery. Sex, smoking, concomitant diseases, and presence of various clinical signs supporting UNE diagnosis did not affect surgical outcome. No difference in outcome was found between UNE diagnosis confirmed by electrophysiology or solely by clinical examination. Cases with electrophysiologically more severe pathology showed worse outcome. Excellent or good outcome (i.e. patients reporting being cured or improved) was reported in 84% of primary and 75% of revision transposition cases. No differences in outcome between primary and revision transposition surgeries was noted. Concomitant systemic diseases, musculoskeletal conditions and carpal tunnel syndrome (CTS) predicted the need for revision surgery. Revision surgeries were characterized by normal electrophysiological findings or less pronounced pathology and a high frequency of preoperative ulnar nerve dislocations compared to primary surgeries. In the second part, no differences were found in surgical outcome between

patients with and without diabetes. Men with diabetes had worse outcome after primary SD, which was not seen in women with diabetes. Women showed greater improvement from preoperatively to 12 months postoperatively compared to men, but scored their disability higher than men. Men had better surgical outcome. In the third part ulnar nerve dislocation in UNE was found in 16% of primary and 47% of revision surgeries. Postoperative outcome was worse for UNE cases with dislocation than for those without, but no correlation was found between ulnar nerve dislocation and QuickDASH scores at 12 months postoperatively. Positive correlations were found between postoperative DROM and QuickDASH, giving some support for the possibility of a relationship between DROM and QuickDASH measures. Concomitant diabetes in primary UNE, male sex and increasing age were associated with a worse electrophysiological grading. No differences in postoperative QuickDASH score were found between the various electrophysiological gradings. Primary SD had a better outcome than primary transposition surgeries.

In summary, preoperative electrophysiological grading and age are not clear predictors of surgical outcome after primary SD, but men have a better outcome than women. Concomitant diabetes in primary UNE is associated with a worse electrophysiological grading but does not influence surgical outcome. Ulnar nerve instability is common in UNE, influencing choice of surgical treatment approaches, and possibly surgical outcome, negatively. Concomitant systemic diseases, musculoskeletal conditions and CTS are predictors of revision surgery.

Abbreviations

ANS	Autonomic nervous system
CAMP	Compound muscle action potential
CNS	Central nervous system
CTS	Carpal tunnel syndrome
DASH	Disabilities of arm shoulder and hand
DM1	Diabetes mellitus type 1
DM2	Diabetes mellitus type 2
DROM	Doctor-reported outcome measure
EMG	Electromyography
HAKIR	Swedish National Quality Registry for Hand Surgery
IMT	Intramuscular ulnar nerve transposition
ME	Medial epicondylectomy
MNCV	Motor nerve conduction velocity
MRI	Magnetic resonance imaging
NSC	Nerve conduction studies
PNS	Peripheral nervous system
PROM	Patient-reported outcome measure
PRUNE	Patient-rated ulnar nerve evaluation
QuickDASH	Short version of DASH
RCT	Randomized controlled study
SCT	Subcutaneous ulnar nerve transposition
SD	Simple ulnar nerve decompression
SMT	Submuscular ulnar nerve transposition
SNAP	Sensory nerve action potential
UNE	Ulnar nerve entrapment at the elbow
US	Ultrasonography
2PD	Two-point discrimination

List of papers

This thesis is based on the following papers, referred to throughout the text by their Roman numerals.

Paper I

Outcome and predictors in simple decompression of ulnar nerve entrapment at the elbow

Ilka Anker, Gert S. Andersson, Malin Zimmerman, Helene Jacobsson, & Lars B. Dahlin
Hand & Microsurgery 2018; 7:24-32

Paper II

Subcutaneous and submuscular transposition due to ulnar nerve entrapment at the elbow– analyses of 43 primary and 44 revision cases

Ilka Anker, Gert S. Andersson, Malin Zimmerman, Helene Jacobsson, & Lars B. Dahlin
Hand & Microsurgery 2019;8(1):9-18

Paper III

Ulnar Nerve Entrapment in Diabetes – Patient-reported Outcome after Surgery in National Quality Registries

Malin Zimmerman, Ilka Anker, Anna Karlsson, Marianne Arner, Ann-Marie Svensson, Katarina Eeg-Olofsson, Erika Nyman & Lars B. Dahlin
Plastic and Reconstructive Surgery 2020 Apr 24;8(4):e2740

Paper IV

Ulnar nerve dislocation in ulnar nerve entrapment at the elbow. Influence on surgical outcome

Ilka Anker, Malin Zimmerman, Erika Nyman & Lars B. Dahlin
Hand Surgery and Rehabilitation 2021 Sep 25:S2468-1229(21)00277-2. Online ahead of print.

Paper V

Preoperative electrophysiology in patients with ulnar nerve entrapment at the elbow - prediction of surgical outcome and influence of age, sex and diabetes

Ilka Anker, Erika Nyman, Malin Zimmerman, Ann-Marie Svensson, Gert S. Andersson & Lars B. Dahlin
**Frontiers in Clinical Diabetes and Healthcare, section Diabetes Clinical Epidemiology 2021 (submitted)*

Thesis at a glance

Paper I

Outcome and predictors in simple decompression of ulnar nerve entrapment at the elbow

Objectives: To evaluate outcome and potential predictors of outcome after simple decompression in ulnar nerve entrapment at the elbow (UNE).

Methods: All surgically treated UNE cases (from 2004-2008) at our department were studied retrospectively. From 285 primary surgeries, 242 primary simple ulnar nerve decompressions were included. Medical records, including electrophysiological protocols, were reviewed and postoperative outcome was graded: 1) cured/improved and 2) unchanged/worsened symptoms, based on a patient-reported and surgeon-evaluated outcome.

Results: Of the 242 simple decompressions (122 males and 120 females; median age 50.5 years), 101 cases were students, retired, unemployed, or on long-term sick-leave and 112 had manual, blue-collar work. 189 cases were cured or improved, while 53 cases experienced no change in, or even worsened symptoms. Gender, smoking, or associated diseases did not affect outcome, while a tendency was observed for higher age, a manual occupation and experiencing constant symptoms over intermittent. Out of 196 electrophysiologically examined cases, 155 showed signs of ulnar nerve affection (56 reduced conduction velocity; 19 conduction block; 80 axonal degeneration; the last two groups had significantly worse outcome).

Conclusion: Patients with a preoperatively electrophysiologically diagnosed nerve conduction block or axonal degeneration have a higher risk of not being cured or improved after simple decompression in UNE. Older patients, those with a manual profession, and constant symptoms of UNE tend to improve less after surgery.

Paper II

Subcutaneous and submuscular transposition due to ulnar nerve entrapment at the elbow– analyses of 43 primary and 44 revision cases

Objectives: To study outcome of subcutaneous (SCT) and submuscular (SMT) ulnar nerve transpositions due to ulnar nerve entrapment at the elbow (UNE), analysing both primary and revision surgeries, aiming to identify predictors of revision surgery.

Methods: All surgically treated UNE cases (2004-2008) at our department were studied retrospectively. The initial surgically treated study population included 285 primary surgeries and 52 revision surgeries. Forty-three of the former (15 SCT and 28 SMT) and 44 (7 SCT and 37 SMT) of the latter were transpositions, which were included. Medical records, including electrophysiological protocols, were reviewed and the postoperative outcome was graded as: 1) cured/improved, and 2) unchanged/worsened symptoms, based on a patient-reported and surgeon-evaluated outcome.

Results: The frequency of concomitant systemic diseases, musculoskeletal conditions and CTS was higher in revision that in primary surgery cases. Both primary and revision SMT cases had a high frequency of ulnar nerve dislocation. Primary SMT cases had a higher frequency of ulnar nerve impact found through electrophysiological examination, while revision SMT cases had normal electrophysiological findings or reduced ulnar nerve conduction velocity. Satisfaction rate was 79-93% in primary transposition surgeries and 73-86% in revision transposition surgeries.

Conclusion: Patients with comorbidity with other systemic diseases, musculoskeletal conditions or CTS have a greater risk of UNE relapse and need for revision surgery. Surgeons should assess any tendency for intraoperative ulnar nerve dislocation at primary surgery for UNE, proceeding with a concomitant transposition of the nerve to minimize the need for revision surgery.

Paper III

Ulnar Nerve Entrapment in Diabetes: Patient-reported Outcome after Surgery in National Quality Registries

Objectives: To evaluate patient-reported outcome in patients with ulnar nerve entrapment at the elbow (UNE), with and without diabetes, to assess potential sex differences and compare surgical treatment methods.

Methods: Data on patients operated for UNE (2010-2016; n = 1354) from the Swedish National Registry for Hand Surgery were linked to the Swedish National Diabetes Register. Symptoms were assessed preoperatively, at three and 12 months postoperatively by QuickDASH and HQ-8 (specific hand surgery questionnaire-8 questions). Only simple decompressions were included when comparing groups.

Results: Men with diabetes reported higher postoperative QuickDASH scores than men without diabetes. Women scored their disability higher than men at all time (with QuickDASH), but showed greater improvement between preoperative and 12-months-postoperative values. Patients operated with transposition scored higher on QuickDASH at 12 months than patients who had simple decompression.

Conclusions: Women with diabetes benefit from simple decompression for UNE to the same extent as women without diabetes. Men with diabetes risk benefiting less from simple decompression than women do. Ulnar nerve transpositions had a higher risk of residual symptoms than simple decompression.

Paper IV

Ulnar nerve dislocation in ulnar nerve entrapment at the elbow. Influence on surgical outcome

Objectives: To assess occurrence of symptomatic ulnar nerve dislocation and its influence on surgical outcome after primary and revision surgeries in ulnar nerve entrapment at the elbow (UNE).

Methods: Influence of pre- or intraoperative ulnar nerve dislocation on postoperative outcome was assessed in 548 surgically treated cases (defined as treated nerves) from two hand surgery departments reporting to a National Quality Registry for Hand Surgery, using a patient-reported (PROM; QuickDASH, before and at three and 12 months postoperatively) and a doctor-reported outcome measure (DROM; i.e. grading at last visit into cured-improved or unchanged-worsened, median follow-up time 3.0 months).

Results: A documented pre- or intraoperative ulnar nerve dislocation was found in 109/548 (20%) cases, more often among revision (35/75, 47%) than primary surgeries (74/473, 16%). Cases with dislocation reported a higher QuickDASH score at 12 months. A linear regression model, adjusted for age and sex, predicted higher QuickDASH scores at 12 months postoperatively for cases with dislocation. Cases defined as unchanged-worsened at the median follow-up time of three months predicted worse QuickDASH scores than cured-improved cases at three and 12 months. Primary surgeries had better outcome (DROM grading) than revision surgeries, but QuickDASH scores did not differ.

Conclusions: Presence of a clinically relevant ulnar nerve dislocation results in worse outcome, perhaps associated with transposition surgery. Nerve dislocation needs attention when treating UNE patients.

Paper V

Preoperative electrophysiology in patients with ulnar nerve entrapment at the elbow - prediction of surgical outcome and influence of age, sex and diabetes

Objectives: To evaluate influence of preoperative electrophysiological grading on outcome in ulnar nerve entrapment at the elbow (UNE) and to analyse how age, sex and in particular diabetes affect such grading.

Method: Electrophysiological protocols for 406 UNE cases, surgically treated at two hand surgery units reporting to the Swedish National Quality Register for Hand Surgery (HAKIR; 2010-2016), were retrospectively assessed, and graded as normal, reduced conduction velocity, conduction block or axonal degeneration. Outcome after primary and revision surgery was evaluated using QuickDASH and a doctor-reported outcome measure (DROM).

Result: No differences in QuickDASH or DROM were found between the four groups with different electrophysiological grading preoperatively, or at three and 12 months postoperatively. Dichotomizing electrophysiological grading into normal and pathologic electrophysiology, cases with normal electrophysiology had worse preoperative QuickDASH score than cases with pathologic electrophysiology, while postoperative QuickDASH scores did not differ. Presence of conduction block or axonal degeneration indicated a worse outcome, according to DROM grading. Primary surgeries had electrophysiologically more pronounced nerve pathology than revision surgeries. Older age, men, and presence of diabetes accorded with more severe electrophysiological nerve affection. In the linear regression analysis, increasing age and presence of diabetes were associated with a higher risk of a worse electrophysiological classification. Female sex was associated with a better electrophysiological grading.

Conclusion: We conclude that older age, male sex, and diabetes are associated with more severe preoperative electrophysiological nerve affection. Preoperative electrophysiological grade of ulnar nerve affection may influence surgical outcome.

Populärvetenskaplig sammanfattning

De flesta människor har upplevt en s.k. änkestöt, vilket är en smärtsam elektrisk stötliknande känsla som ögonblickligen sprider sig längs underarmen ner i handen och särskilt i lillfingret. Strukturen som påverkas i samband med ett sådant slag är ulnarisnerven.

Ulnarisnerven är en av de tre stora nervgrenarna i människans arm. Nerven kan drabbas av olika sjukdomar, där den vanligaste är s.k. neuropati, dvs nervinklämning, som av anatomiska skäl oftast sker i armbågsnivå där ulnarisnerven löper i en fåra på insidan av armbågen, överbryggat av en ledbandsstruktur. Inklämning av ulnarisnerven i armbågsnivå är den näst vanligaste neuropatin i armen efter s.k. karpaltunnelsyndrom, som drabbar medianusnerven i handledsnivå. Ulnarisnervpåverkan och inklämning diagnosticeras genom värdering av den drabbade patientens beskrivning av sina besvär sammantaget med specifika undersökningsfynd, som verifierar diagnosen. Symptomen kan emellanåt vara svårtolkade och därmed kan tiden mellan symptomdebut och behandling bli lång. Vissa undersökningsmetoder kan stötta diagnosen, exv. s.k. neurografisk undersökning, som kan kartlägga och gradera nervfunktionen. Internationellt sett finns dock ingen tydlig samstämmighet om vilka diagnostiska metoder, behandlingskriterier och behandlingsmetoder som ger bäst slutresultat för den drabbade, vilket kan leda till ökade samhällskostnader pga. sjukfrånvaro, eftersom majoriteten av de drabbade är i arbetsför ålder.

Denna avhandling fokuserar på att studera faktorer som kan påverka slutresultatet efter kirurgisk behandling vid både primär och sekundär ulnarisnervpåverkan i armbågsnivå med syfte att bidra till utvecklandet av ett vetenskapligt baserat flödesschema för att uppnå bästa möjliga behandlingsresultat hos drabbade patienter.

I den första delen studerades fall som opererats på Handkirurgiska kliniken, Skånes Universitetssjukhus. 242 primära fall som hade opererats med nervfriläggning (s.k. enkel dekompression) analyserades och 43 primära fall som opererats med nervflyttning (s.k. transposition) jämfördes med 44 fall som opererades med nervflyttning pga. återfall. Ett enkelt doktor-rapporterat utvärderingsinstrument (s.k. DROM) användes för att utvärdera behandlingsresultaten efter kirurgi. I den andra delen studerades 1354 primära fall av ulnarisnervpåverkan från den Svenska Handkirurgiska Kvalitetsregistret

(HAKIR), efter att dessa sammanfogats med det Svenska Nationella Diabetesregistret (NDR), medan den tredje delen fokuserade på 548 primära och sekundära fall från två Handkirurgiska kliniker som ingår i HAKIR-registret. I dessa delar användes framför allt ett beprövat patient-rapporterat utvärderingsinstrument (s.k. PROM; patientenkäter) för att utvärdera behandlingsresultaten efter kirurgi, som kallas QuickDASH, med vilken högre poäng talar för mer uttalad nervpåverkan.

I den första delen uppgav 78% som opererats med nervfriläggning att de upplevde sig botade eller förbättrade av behandlingen. Kön, närvaro av andra sjukdomar, rökning och olika undersökningsfynd som stöttar diagnosen ulnarisnervpåverkan, påverkade inte resultaten av operationen. Ingen skillnad hittades mellan fall där diagnosen ulnarisnervpåverkan ställts enbart med hjälp av undersökningsfynd eller om det bekräftats med nervfunktionsmätning. Sämre resultat av operation noterades bland de fall som hade en uppmätt mer uttalad nervpåverkan. Utav fallen som opererats med nervflyttning uppgav 84% av de primära fallen och 75% av de sekundära fallen att de upplevde sig botade eller förbättrade efter operation. Ingen skillnad hittades mellan de primära och sekundära fallen vad gäller resultaten av operation. Närvaro av andra sjukdomar och karpaltunnelsyndrom ökade risken att få återfall av ulnarisnervpåverkan. Bland de sekundära fallen återfanns hög andel som hade ökad rörlighet av ulnarisnerven ur sin fåra och över det beniga utskottet på armbågens insida (s.k. dislokationstendens) före operationen. Dessa fall uppvisade samtidigt normala fynd vid mätning av nervfunktionen, eller enbart en lindrig påverkan av nervfunktionen. I den andra delen noterades ingen skillnad vad gäller resultat av operation mellan fall med eller utan samtidig diabetesdiagnos. Män med diabetes hade sämre utgång av operation med nervfriläggning, vilket inte noterades bland kvinnor med diabetes. Kvinnor upplevde sina symptom av ulnarisnervpåverkan vara mer uttalade än män, men hade större förbättring 12 månader efter operation jämfört utgångsläget före operation. Samtidigt noterades män ha bättre resultat av behandlingen än kvinnor. I den tredje delen återfanns ökad rörlighet av ulnarisnerven hos 16% av primära och 47% av sekundära fall med ulnarisnervpåverkan. Fallen med ökad rörlighet av ulnarisnerven före operation hade sämre resultat av operation, men inget statistiskt samband (s.k. korrelation) fanns mellan ökad nervrörlighet och QuickDASH poäng 12 månader efter operation. Ett positivt statistiskt samband fanns mellan DROM och QuickDASH poäng efter operativ behandling, vilket bedöms ge ett visst stöd till relationen mellan dessa två utvärderingsinstrument. Närvaro av samtidig diabetesdiagnos vid primär ulnarisnervpåverkan, manligt kön och stigande ålder noterades ha ett samband med sämre uppmätt nervfunktion. Ingen skillnad fanns mellan olika grader av mätbar påverkan av nervfunktionen och QuickDASH poäng efter operation. Primära fall av ulnarisnervpåverkan som opererades med nervfriläggning hade bättre resultat av operativ behandling jämfört med primära fall som opererades med nervförflyttning.

Sammantaget bedöms ålder och graden av mätbar påverkan av nervfunktionen inte tydligt påverka resultatet av kirurgisk behandling bland fall med primär ulnarisnervpåverkan som opererades med nervfriläggning, medan män visar bättre resultat efter operation än kvinnor. Samtidig diabetesdiagnos bland fall med primär ulnarisnervpåverkan är förknippat med mer uttalad påverkan av nervfunktionen, men det påverkar inte utgången av operationen. Ökad rörlighet av ulnarisnerven är vanlig vid ulnarisnervpåverkan, det påverkar behandlingsvalen och kan också påverkan resultaten av kirurgisk behandling negativt. Närvaro av andra sjukdomar och karpaltunnelsyndrom ökade risken att få operationskrävande återfall av ulnarisnervpåverkan.

Introduction

Most people have experienced hitting their so-called "funny bone" on the medial side of the elbow, resulting in an immediate, painful, electrical shock-like sensation down the arm. This "funny bone" is in reality not a bone, but the structure affected by the contusion is the ulnar nerve.

The ulnar nerve is one of the three major peripheral nerves in the upper extremity, together with the median and the radial nerves. Peripheral neuropathy is a condition which affects the function of these peripheral nerves, the most common cause being chronic compression (1). Compression neuropathy of the ulnar nerve is commonly referred to as ulnar nerve entrapment which, for anatomical reasons, occurs primarily at elbow level (i.e. UNE; ulnar nerve entrapment at the elbow). UNE is the second most common compression neuropathy in the upper extremity (2, 3) and diagnosis is often based on patient history, symptoms and clinical signs. Symptoms in UNE can at times be challenging to assess, due a varying degree of symptoms such as sensory- and motor loss, implying that the time between onset of symptoms and initiation of treatment may be long. At the time this project was initiated in 2011, there was no clear consensus, either nationally in Sweden or internationally, concerning diagnostic methods, indications for surgery and on which surgical procedure led to the best clinical outcome (4). Current literature does not fully support a reliable algorithm that can be utilized in a wide patient population, and hence choices regarding diagnostics and treatment remain largely surgeon and healthcare center dependent. This may result in high costs for society, due to incapacity to work and paid sick-leave, since a majority of the affected patients are of working age.

The overall aim of the present thesis is to advance in essential knowledge concerning UNE, with primary focus on studying factors that may influence and predict surgical outcome in primary and recurrent UNE. The hope is, through this knowledge, to contribute to creating an evidence-based, standardized process in diagnostics, treatment indications and surgical treatment options for attaining the best possible clinical outcome for UNE patients. A unified global strategy may reduce the time between onset of UNE symptoms and treatment and thus contribute to easing affliction for patients on an individual level as well as reducing costs for society from a socioeconomic perspective.

Background

Anatomy

The nervous system

The human nervous system is a complex biological signalling system that coordinates corporal functions through electrochemical impulses. It comprises two parts: the central nervous system (CNS), which consists of the brain and spinal cord, and the peripheral nervous system (PNS), which consists of the different nerves and ganglia emanating from the CNS (5). The CNS is responsible for processing and storing information, as well as initiating responses to stimuli. The PNS is made up of the cranial nerves III-XII and 31 pairs of spinal nerves, which connect the CNS with the head, limbs and organs (6).

The PNS is in turn divided into the somatic nervous system (SNS) and the autonomic nervous system (ANS), which are composed of both sensory nerves that transmit signals from sensory organs to the CNS and motor nerves from the CNS to effector organs, such as glands and muscles. The SNS is under voluntary control through skeletal muscles, while the ANS is outside voluntary control and regulates visceral functions, such as breathing, blood pressure, heart rate, digestion and reproduction (5). The ANS is comprised of the sympathetic and parasympathetic divisions, activated in situations of distress (fight-or-flight) and idleness (rest-and-digest), respectively, as well as the enteric division that is the intrinsic nervous system of the gastrointestinal tract (7, 8).

The peripheral nerve

A nerve cell (i.e. neuron) in the PNS typically consists of a cell body (i.e. soma) from which processes called dendrites and a single axon extend. The cell body of a motor neuron is located in the spinal cord, while the cell bodies of sensory neurons are located in the dorsal root ganglia adjacent to the spinal cord. Dendrites commonly conduct electrical signals to the cell body. Axons are commonly known as nerve fibres and end in presynaptic terminals where the electrical signals that spread from the cell body along the axon are converted into chemical signals that act on the effector organ. Nerve fibres in the PNS are normally wrapped in a myelin sheath by Schwann cells surrounding them, a lipid-rich substance that acts as insulation and increases the speed at which electrical signals are spread along the axon. The speed with which an electrical impulse is conducted along a large-diameter myelinated axon (e.g. motor neurons innervating skeletal muscles or most sensory neurons) is 15-120 m/s, compared to 2 m/s or less in unmyelinated small-diameter axons (5).

Each myelinated nerve fibre is covered by a protective basal membrane. The connective tissue components surrounding both myelinated and unmyelinated nerve fibres are called endoneurium, which in some respect also has a protective function. Several nerve fibres are then bundled together to form a fascicle, which is covered by another connective tissue layer called the perineurium, made up of flattened cells with tight junctions, which in turn also have important protection tasks. The nerve itself comprises several fascicles embedded in a third protective layer called the epineurium, which consists of looser connective tissue. The amount of the three tissue components varies both among different nerves and along a specific nerve. For example, more tissue components are present in superficial nerves than in more deeply located nerves as well as at points where nerves cross joints, reflecting the need for protection. Within the nerve, blood vessels travel along the fascicles, as the nerve fibres need a high energy supply (9) (Figure 1).

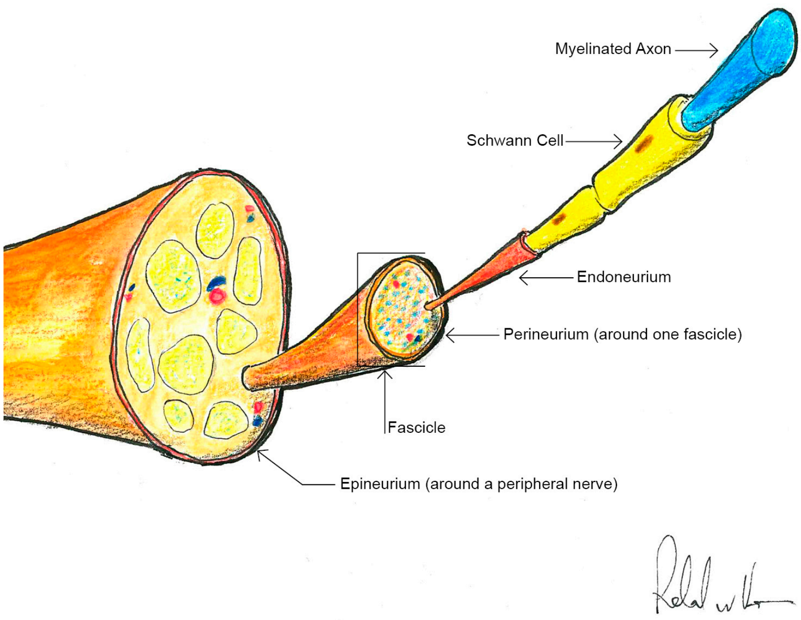


Figure 1. Anatomy of the peripheral nerve. Artist Roland van Veen, with permission.

The ulnar nerve

The brachial plexus is a network of spinal nerves (part of the PNS) that originate from the lower four cervical nerves (C5-C8) and the first thoracic nerve (Th1) (Figure 2). Upon exiting from the spinal cord, they form the three major peripheral nerves of the upper extremity; the median nerve, the radial nerve and the ulnar nerve. The ulnar nerve has its origin in the C8 and Th1 spinal nerves (10).

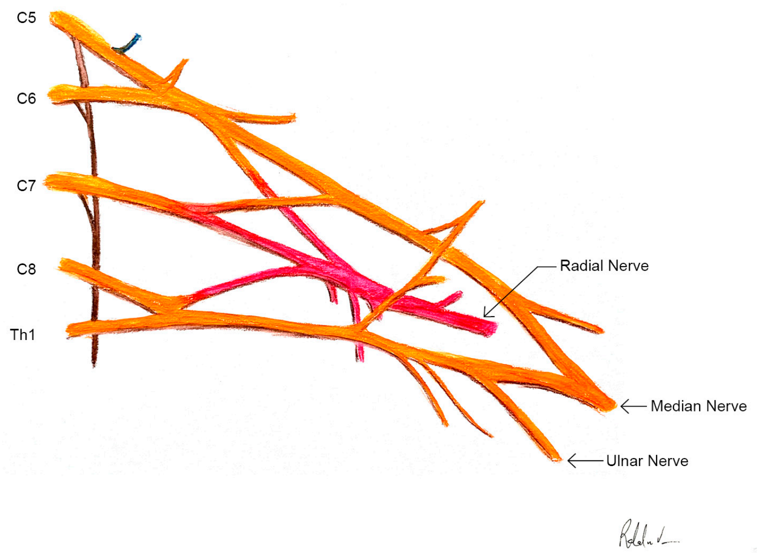
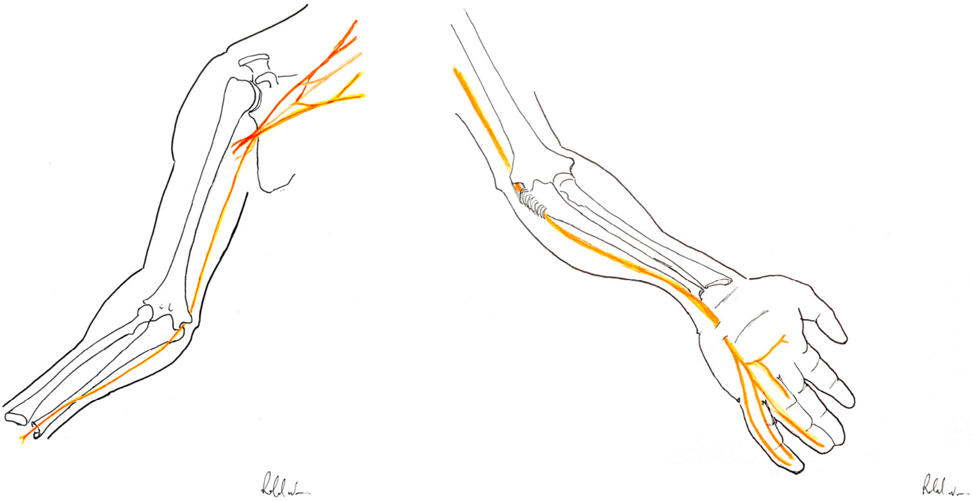
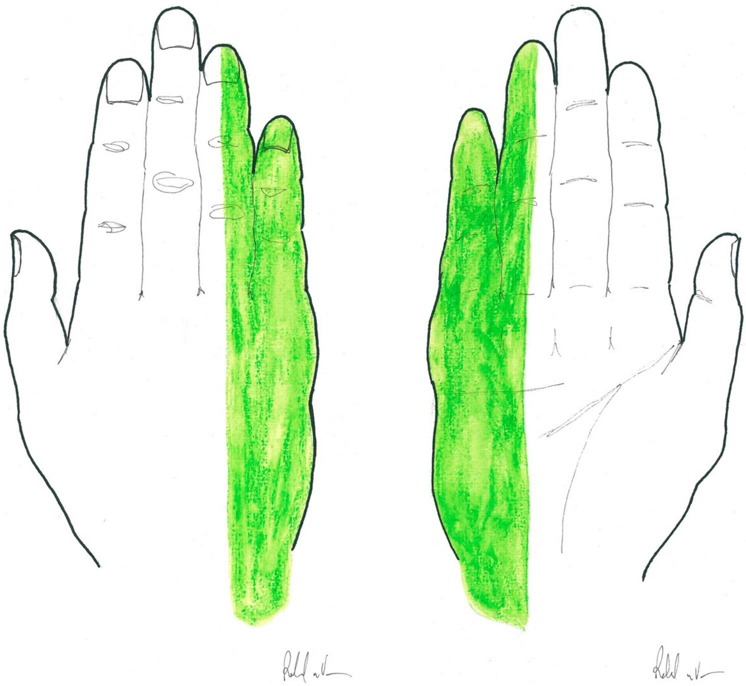


Figure 2. Anatomy of the brachial plexus. Artist Roland van Veen, with permission.

In the upper arm, the ulnar nerve runs posteromedially, along the humerus and adjacent to the brachial artery. Proximal to the medial epicondyle, it pierces the medial intermuscular septum of the triceps muscle at an aponeurotic band called the arcade of Struthers. At elbow level, it passes behind the medial epicondyle in the cubital tunnel, defined by the so-called ligament of Osbourne as its roof and with the joint capsule and medial collateral ligament of the elbow acting as its floor (Figure 3). The ulnar nerve then enters the two heads of the flexor carpi ulnaris muscle in the anterior compartment of the forearm. At wrist level the ulnar nerve courses through the Guyon canal, where it enters the hand radially of the pisiform bone (Figure 4). The ulnar nerve provides sensory innervation of the little finger and the ulnar half of the ring finger and hand as well as motor innervation of the following muscles: flexor carpi ulnaris, flexor digitorium profundus of the little and ring fingers, adductor pollicis, deep head of flexor pollicis, palmaris brevis, hypothenar muscles (m. abductor digiti minimi, m. flexor digiti minimi, m. opponens digiti minimi) and the majority of the interossei muscles (11) (Figures 5 and 6).



Figures 3 and 4. The course of the ulnar nerve along the arm. Artist Roland van Veen, with permission.



Figures 5 and 6. The sensory innervation of the hand by the ulnar nerve. Artist Roland van Veen, with permission.

Pathology

Peripheral neuropathy

Peripheral neuropathy is a condition affecting the function of peripheral nerves and is usually classified as hereditary or acquired. Hereditary neuropathies of the PNS (e.g. Charcot-Marie-Tooth disease) are infrequent (12). Acquired neuropathies are more common and may be due to metabolic changes (e.g. diabetes, thyroid disease, renal failure), nutritional factors (e.g. vitamin deficiency, celiac disease, alcoholism), autoimmune inflammation (e.g. Guillain-Barré syndrome, systemic lupus erythematosus (SLE), vasculitis), ischemia, exposure to toxins and traumatic events (13). Peripheral neuropathies can involve motor or sensory neurons independently or together, resulting in widespread clinical manifestations, such as altered sensation, pain, muscle weakness and muscle atrophies, depending on the affected nerves. The neuropathies may present themselves acutely or chronically, as well as in the form of mononeuropathy, localized to one nerve, or polyneuropathy, affecting several nerves diffusely and symmetrically (14).

Ulnar nerve neuropathy

The most common cause of peripheral mononeuropathies is chronic compression, commonly occurring in fibro-osseous tunnels as nerves cross joints, which can take place at several sites along the course of the nerves (1). Compression neuropathy of the ulnar nerve is commonly referred to as ulnar nerve entrapment, which primarily occurs at elbow level (i.e. UNE; ulnar nerve entrapment at the elbow) and secondarily at wrist level in the Guyon canal. Around the elbow there are five potential sites where the ulnar nerve may become entrapped: 1) the arcade of Struthers; 2) the medial intermuscular septum; 3) the medial epicondyle; 4) the cubital tunnel; and 5) the superficial and deep fascias of the flexor-pronator muscle mass. Among these the cubital tunnel (below the ligament of Osbourne) is the most common site (15). As the elbow is moved from full extension to full flexion, the ulnar nerve elongates between 4.7-8.0 mm (16, 17) and is subjected to traction, compression and frictional forces, e.g. a cubital tunnel volume decrease of 50%, an increase in extraneural pressure of 50% and an increase in intraneural pressure of 4-17 mm Hg (16, 18, 19). Since the semi-rigid ligament of Osbourne acts as a type of roof over the cubital tunnel, these dynamic changes may facilitate occurrence of UNE.

Ulnar nerve entrapment at the elbow

Risk factors

UNE is the second most common compression neuropathy of the upper extremity, after carpal tunnel syndrome (CTS) (2, 3) with incidence rates ranging between 21 and 30 per 100 000 inhabitants and year (20, 21). UNE is mainly considered to be idiopathic, although risk factors, such as older age, male sex, smoking, lower socioeconomic status, vibration exposure, heavy manual, stationary and repetitive work, multiple occasions of minor pressure on the cubital tunnel and concomitant CTS, have all been shown to predispose to the condition (2, 21-26). Diabetes is a known risk factor for compression neuropathies in general and also increases the risk of primary UNE (3, 22, 27, 28). High body mass index (BMI), on the other hand, has not consistently been found to increase the risk of, or association with, UNE (2, 3, 22, 29). Acute trauma to the elbow, old trauma with soft tissue scarring or arthropathic diseases can also affect the ulnar nerve causing UNE symptoms.

Diagnostics

Clinical examination

UNE diagnosis is often based on patient history, symptoms and clinical signs. Symptoms include sensory and motor loss to a varying extent, depending on the degree of nerve affection, as well as possible mild to severe pain. Early stages of UNE may present with solely sensory symptoms of numbness and paraesthesia in the ulnar fingers and ulnar part of the hand and are commonly accentuated at night-time or be brought on by different positional activities, such as flexion of the elbow. These sensory symptoms can be revealed by physical examination (e.g. with light touch, two-point discrimination (2PD) and Semmes-Weinstein monofilament testing) in the form of impaired sensation in the little finger, the ulnar part of the ring finger and the ulnar part of the hand, including the dorsal part of the hand. A more pronounced affection of the ulnar nerve includes loss of motor symptoms in the form of muscle weakness of ulnar-innervated muscles, which can be detected through testing muscle strength. The Wartenberg sign is observed when the little finger cannot actively be adducted, due to weakness of the third palmar interosseous muscle, and is therefore deviated from the hand. The Froment sign is found as a compensatory flexion in the interphalangeal joint of the thumb during key-pinch, due to weakness of the adductor pollicis muscle. In severe cases of UNE muscle atrophies can be observed and in the final stage a claw hand deformity occurs, i.e. Duchenne sign (15, 30) (Figure 7). Pain around the elbow can also occur in the various stages of UNE.

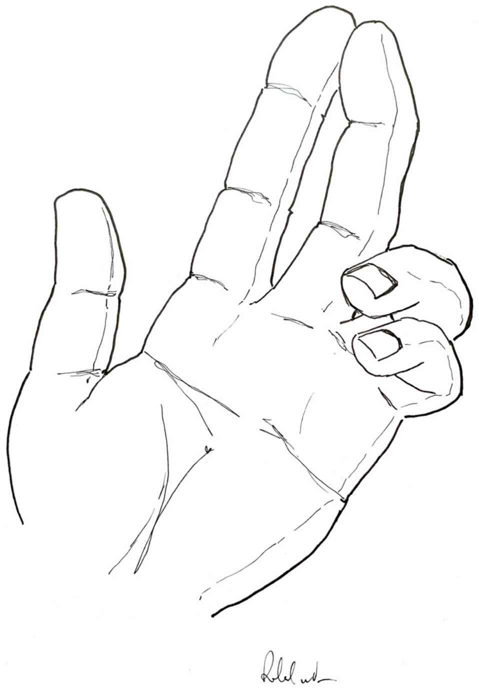


Figure 7. Claw hand deformity in the final stage of severe ulnar nerve entrapment at the elbow.
Artist Roland van Veen, with permission.

Common provocative clinical tests that support UNE diagnosis are the Tinel´s test (i.e. nerve percussion test over the ulnar nerve in the cubital tunnel) with a sensitivity of 62-70%, the elbow flexion-pressure test with a sensitivity of 61-98% and the glenohumeral internal rotation elbow flexion test with a sensitivity of 87% (31-33).

A specific problem that may affect the ulnar nerve, due to its anatomy, is hypermobility of the nerve during elbow flexion and extension, which may cause the nerve to dislocate partially (i.e. subluxation) or completely over the medial epicondyle. Ulnar nerve dislocation is reported to occur in 24 - 46 % of asymptomatic individuals (i.e. healthy controls) (34-37) assessed by high-resolution ultrasonography or clinical evaluation. Other studies have found similar frequency of ulnar nerve instabilities in UNE patients (20 - 46 %) (38, 39). It has also been noted that hypermobile ulnar nerves have a larger diameter than nerves that do not dislocate (37).

Classification

Severity of UNE has been classified by McGowan and modified by Dellon as: 1) purely subjective symptoms, but no objective clinical findings, 2A) sensory loss (as tested with 2PD), motor weakness, but good strength in intrinsic muscles, 2B) sensory loss (as tested with 2PD), motor weakness and notable atrophy of intrinsic muscles and 3) severe sensorimotor deficit, marked muscle atrophies and claw hand deformity (40), and is still commonly used in clinical praxis. However, this classification of severity has limitations and does not reflect neurobiological alterations in the peripheral nerve during compression. Studies on intraneural topography of the ulnar nerve at the elbow have shown that the sensory fibres together with the motor fibres to the intrinsic muscles are located more superficially within the nerve, while motor nerve fibres to the remaining ulnar innervated muscles are located more deeply, which is believed to explain the different clinical stages of UNE (9).

Diagnostic testing

Diagnostic testing is commonly performed to further confirm a suspected UNE diagnosis as determined from history and physical examination. They can aid in diagnosing the structure and functionality of nerve fibres as well as the progression of ulnar neuropathy by showing a progression from dynamic ischemia to demyelination and finally axonal loss in the ulnar nerve. The most common diagnostic test is electrophysiological examination, followed by ultrasonography (US) and magnetic resonance imaging (MRI). All have been shown to be effective in UNE diagnostics in different ways, although some studies question whether one test is superior to the others (41).

Electrophysiology

Electrophysiological examinations are commonly used in UNE diagnostics and research. The method consists mainly of two techniques; nerve conduction studies (NCS) and electromyography (EMG). NCS in turn comprises of motor and sensory nerve conduction studies, where the distally propagated compound muscle action potential (CMAP) and orthodromic sensory nerve action potential (SNAP) are, respectively, assessed and action potential amplitudes, conduction velocity and motor onset and sensory latency are measured. As part of NCS, F-waves may also be recorded. F-waves are a type of late motor response, which can be used to estimate conduction velocity along long lengths of a nerve between the limb and spine. It can be a sensitive indicator of peripheral nerve pathology in cases where motor and sensory NCS are insufficient. Needle-EMG measures and evaluates the electrical activity of a muscle and the motor nerve cell controlling it (42).

In UNE diagnostics, the ulnar nerve is commonly stimulated at the wrist level, then below and above the elbow and a response is recorded from the abductor digiti minimi muscle. F-waves and orthodromic sensory response of the ulnar nerve to stimulation are recorded from the little finger. In many departments of Clinical Neurophysiology, the ulnar nerves are also examined with a short segment (8 mm - 3 cm) stimulation across the cubital tunnel, so-called inching technique (Figures 8 and 9). Several studies have analysed long- and short-segment stimulation as well as recordings from other muscles, but no consensus has been reached on optimal electrodiagnostic procedures for best diagnostic value in UNE (43-45).

Figure 8. The set-up for electrophysiological testing. Photographer Malin Zimmerman, with permission.

Figure 9. Performance of electrophysiological testing. Photographer Malin Zimmerman, with permission.

Common electrodiagnostic criteria for ulnar neuropathy are a decrease in conduction velocity to <50 m/s, a relative drop in conduction velocity of ≥10 m/s across a measured interval around the elbow or a <20% reduction in action potential amplitude (46, 47). False-negative cases (i.e. clinical UNE with normal electrophysiological data) can result from variable compression of different ulnar nerve fascicles and close to normal conduction velocities in unaffected large nerve fibres during testing. Diagnostic error is also attributable to variable elbow position, skin temperature, and amount of soft-tissue padding around the elbow (46, 47). NCS are the first tests to show abnormality in UNE, with a drop in conduction velocity due to decreased ulnar nerve perfusion and a subsequent successive focal demyelination of the nerve, while needle-EMG is needed to detect more severe stages of UNE with axonal degeneration (42). Padua et al developed a classification for UNE based on electrophysiological findings that reflect the electrophysiological progression of the neuropathy: 1) Negative UNE; normal findings on all tests; 2) Mild UNE; slowing of ulnar motor nerve conduction velocity (MNCV) across elbow and normal ulnar SNAP; 3) Moderate UAE; slowing of ulnar MNCV across elbow and reduced amplitude of ulnar SNAP; 4) Severe UNE; slowing of MNCV across elbow and absence of ulnar SNAP and 5) Extreme UNE; absence of hypothenar motor and sensory response. (48) This classification, with varying degrees of modification, is used in several departments of Clinical Neurophysiology with respect to local reference values.

Electrophysiological examinations in UNE have a sensitivity of 73-96% (43, 44, 49) and are useful in supporting UNE diagnosis, localizing the site of nerve compression and estimating the severity of entrapment. Some studies have found electrophysiological assessments to be possible predictors of surgical outcome in UNE (50) but, on the other hand, an earlier review found no differences in surgical outcome based on electrophysiology protocols (4).

Ultrasonography

Ultrasound (US) uses sound waves for imaging, by means of which it has been shown that ulnar nerves in UNE patients are larger in diameter compared to healthy controls (51). The use of US in UNE diagnostics is not as common as electrophysiology, although there is a correlation between ultrasonographic and electrodiagnostic findings, and a sensitivity of 70-90% for US in diagnosing UNE (51-55). In a recent study, UNE patients with normal electrodiagnostic findings had an enlarged cross-sectional area of the ulnar nerve at the elbow, as demonstrated by US, indicating presence of UNE (56). Another study has even found that precubital US measurements are a good predictor of treatment outcome (55). However, unlike electrodiagnostic examination, US studies cannot provide functional information for evaluating nerve conduction. Even though the role of US is not clearly established in UNE diagnostics, it is believed to be advantageous in comparison with electrophysiology because it is more comfortable for the patient and requires shorter time to perform (52).

Magnetic resonance imaging

Using MRI in diagnostics, allows soft tissue details to be evaluated. The most frequent MRI findings in UNE are a combination of high signal intensity and nerve enlargement, found in 63% of UNE cases, but the method has not been shown to be capable of differentiating between grades of UNE (57). Using MRI neurography, the ulnar nerve in UNE patients has been found to be 50% larger in diameter in comparison to healthy controls. The method has also been shown to be capable of discriminating between mild and severe UNE, with a diagnostic sensitivity of 83-90% (57, 58), suggesting that there is clinical value in using MRI neurography as a sole diagnostic method.

Treatment and outcome

Conservative treatment

UNE can be treated either conservatively or surgically. A recent Cochrane review study shows that there is still no standardized, evidence-based process through diagnostics and treatment for patients with suspect UNE. Hence, treatment decisions are strongly doctor- and health-centre-dependent rather than evidence-based (4). The same Cochrane review study also concluded that we still do not know when conservative treatment is superior to surgical treatment and vice versa (4).

Conservative treatment is commonly recommended initially in mild cases of UNE and includes patient education (i.e. avoiding direct pressure over the medial aspect of the elbow, activity modification and repetitive triceps strengthening exercises) and the use of a nocturnal orthosis with the elbow semiflexed at an angle of approximately 30 degrees (Figure 10). Studies on conservative treatment of UNE show that 59- 90% of patients with mild to moderate UNE are improved by conservative treatment alone (21, 59-61). Corticosteroid injections, as part of conservative treatment for UNE, have also been evaluated but are not superior to placebo (62). Dellon et al found that patients with mild UNE had a 21% probability of requiring later surgery and patients with moderate and severe UNE a 33% and 66% probability, respectively, concluding that conservative treatment should be reserved for patients with mild UNE (59).

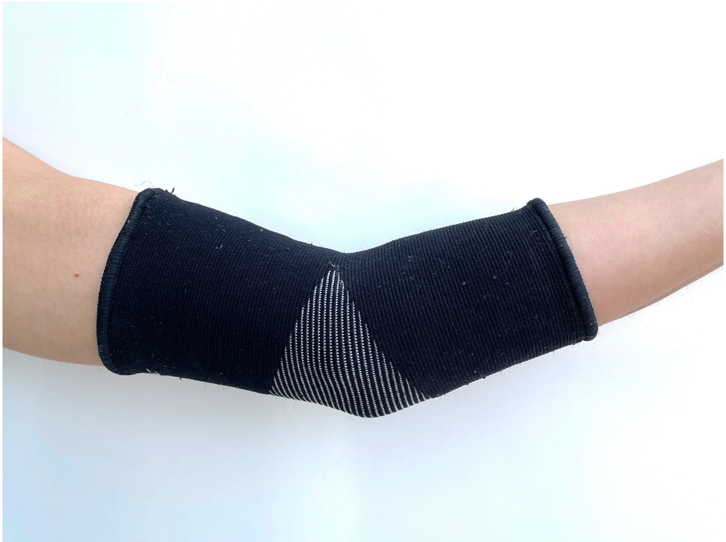


Figure 10. Orthosis with semiflexed elbow, as used in conservative treatment of UNE. Author's own photograph.

Surgical treatment

Surgical treatment is generally recommended when conservative treatment has failed, in more severe cases of UNE, in cases with ulnar nerve dislocation and in recurrent UNE. Surgical treatment includes open or endoscopic simple decompression (SD), subcutaneous transposition (SCT), intramuscular transposition (IMT), sub-muscular transposition (SMT) or medial epicondylectomy (ME).

Simple decompression may be performed by releasing fascial structures superficial to the ulnar nerve (i.e. the ligament of Osbourne, the arcade of Struthers, the superficial and deep fascia of the flexor carpi ulnaris muscle and the fascia between the medial triceps and medial intermuscular septum) over a distance of 10-12 cm. The ulnar nerve is retained on its bed to minimize complications in the form of devascularization and nerve dislocation (15, 63) (Figure 11). In transposition surgery, the ulnar nerve is decompressed as in SD, but over a longer section, circumferentially dissected from its bed and then placed anteriorly of the medial epicondyle. In SCT, the nerve is embedded in subcutaneous tissue after transposition, in IMT the nerve is placed in a tract created through the flexor-pronator muscle mass and in SMT it is placed beneath the flexor-pronator muscle. Both compression and tension on the ulnar nerve are reduced by transposition. Decision on which type of transposition to perform is mainly dependent on the severity of UNE and patient factors, such as amount of subcutaneous tissue (15). In ME, the ulnar nerve is initially decompressed as in SD, after which an osteotomy is used to remove the medial aspect of the medial epicondyle and the flexor-pronator origin is then reattached to the periosteum. The insertion of the medial collateral ligament is preserved (15, 64).

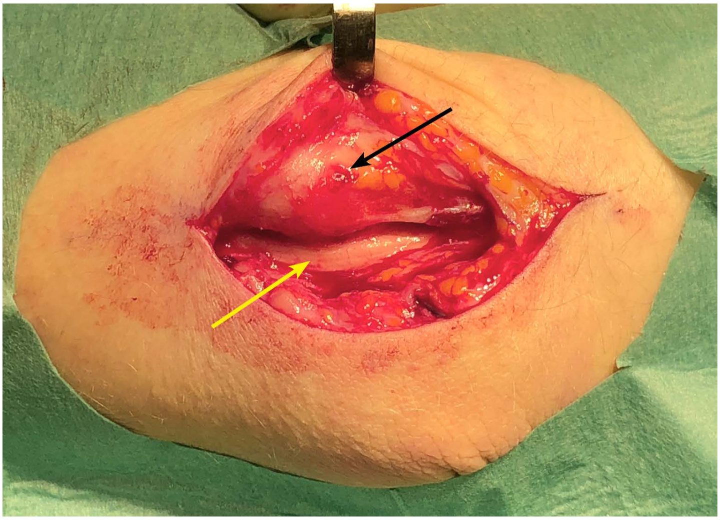


Figure 11. Simple decompression of the ulnar nerve at the elbow. Yellow arrow indicates the decompressed ulnar nerve and black arrow the medial epicondyle. Author's own photograph with permission from the patient.

Numerous studies have shown that outcome after open SD in primary UNE is similar to both endoscopic SD (65) and transposition surgery in the form of SCT and SMT (4, 66). In multiple prospective RCT studies, outcome classified as excellent or good, have been found in 61-84% of cases after open SD and in 62-83% after SCT or SMT (67). Studies on endoscopic SD have shown excellent or good outcome in 87-94% of cases, although such studies are few in number and have generally been smaller (68). A major complication risk of ME is postoperative elbow instability and as many as 45% of patients have also been found to have persistent postoperative elbow pain (69). A review study on ME concluded that the quality of existing studies is insufficient to allow firm conclusions to be drawn regarding the efficacy of the surgical technique compared to SD and transposition surgeries (70). However, a recent study found better outcome after SD compared to ME (71). Although several studies have focused on surgical outcome in UNE, possible factors that might influence and predict outcome have not been sufficiently highlighted.

Simple decompression is a surgically less invasive technique, is easier to perform, has a lower risk of postoperative complications (67, 72, 73, 74) and has also proved to be more cost effective (75). It has, therefore, commonly been considered the gold standard treatment in primary UNE. Nevertheless, transposition surgery is frequently chosen as the surgical method if partial or total ulnar nerve dislocation is present preoperatively, if ulnar nerve dislocation arises intraoperatively when performing primary SD, or in UNE cases with recurrent symptoms in need of revision surgery. It is not generally known whether ulnar nerve dislocation in itself influences surgical outcome and its role as a predictor of outcome remains to be clarified (34, 35, 37-39).

UNE relapse

UNE relapse, in terms of persistent or recurrent symptoms, occurs in 3-19% of cases (76-78). Persistent symptoms may be due to intraneural pathology in the ulnar nerve or to incomplete release of the structures compressing the nerve, while recurrence may be related to perineural scarring and adhesions of the nerve to the medial epicondyle after primary surgery (79, 80). As there are few studies on UNE relapse focusing on possible predictors of relapse and outcome of revision surgery, there is a need to investigate this further. The few studies that have been carried out have found clinically mild UNE, age < 50 years, female sex, concomitant CTS and previous elbow fracture or dislocation to be predictors of UNE recurrence (76-78). Diabetes has not consistently been shown to increase the risk of UNE relapse in need of surgical revision, hence its role in possible UNE relapse remains to be clarified (81). Primary UNE cases surgically treated with SCT have been found to have a lower recurrence rate than cases treated with SD, SMT or ME, respectively (82). Recurrent UNE is mainly treated with ulnar nerve transposition. Generally, 73-82% of the patients report satisfactory results, the main improvement being reduction in pain, whereas return of sensibility and motor function are more unpredictable and variable (79, 80).

Outcome measures

A vast number of different outcome measures are used to follow up and evaluate surgical treatment in UNE (83, 84). Most modern studies use various patient-reported outcome measures (PROMs), which assess hand function, health status and patient satisfaction, for postoperative follow-up and evaluation [e.g. DASH (Disability of Arm, Shoulder and Hand questionnaire), QuickDASH (the shortened version of the DASH), PRUNE (patient-rated ulnar nerve evaluation), Bishop score, MHQ (Michigan Hand Outcomes Questionnaire), EQD5 (EuroQol 5 dimensional instrument), SF-36 (36-item short-form health survey), SF-12 (12-item short-form health survey), CTQ (carpal tunnel questionnaire), VAS (visual analogue scale), Levine´s FSS and SSS (Levine´s functional status score and symptom severity scale), LSUMC (Louisiana State University Medical Center classification system) etc]. Several have reported moderate to high responsiveness, independently for each PROM (85-87). However, some of these measures and scales are not diagnose-specific for UNE and others have not been tested in terms of validation or reproducibility in UNE patients. This lack of a specific outcome measure leads to some difficulties in clinical research on UNE (83). It is also known that response rates to surveys in general tend to be moderate, and even lower if extensive or multiple questionnaires are used (88, 89). Some smaller studies imply that a simple doctor-reported outcome measure (DROM) by the treating surgeon, based on postoperative patient-reported symptoms and satisfaction at the last follow-up consultation might correlate to improvement in the PROM QuickDASH at one year postoperatively (90-92). Since these studies are smaller in their design, there is a knowledge gap concerning the role of DROMs in UNE.

Aims of thesis

The overall aim of the present thesis is to advance in essential knowledge concerning UNE, and in this way to contribute to creating an evidence-based, standardized process in diagnostics, treatment indications and surgical treatment options for attaining the best possible clinical outcome for UNE patients. A unified global strategy may reduce the time between onset of UNE symptoms and treatment and thus contribute to easing affliction for patients on an individual level as well as to reducing costs for society from a socioeconomic perspective.

This subject is complex and multifaceted and hence the following specific aims were formulated:

- To evaluate outcome after primary simple decompression surgery and assess factors that may predict functional outcome (Paper I).

- To study outcome after primary and revision transposition surgeries and assess potential predictors of revision surgery (Paper II).

- To investigate diabetes as influencing factor on surgical outcome and evaluate potential sex differences (Paper III).

- To evaluate ulnar nerve dislocation as influencing factor on surgical outcome and to analyze relations between outcome measures instruments (i.e. patient-related and doctor-related outcome measures; PROMs and DROM, respectively) (Paper IV).

- To analyse the influence of preoperative electrophysiological grading on surgical outcome and assess the influence of patient factors and comorbidities on electrophysiological grading (Paper V).

Methods

Study design and data collection

The Skåne University Hospital population

Skåne University Hospital is the third largest hospital in Sweden. Patients with more severe hand injuries and conditions, according to a specific agreement with the Swedish Orthopaedic Society, are referred to the Department of Hand Surgery from the entire southern region of Sweden, with a total population of 1.8 million. The department, however, primarily treats patients with any kind of hand injury and condition, from the Malmö-Lund area, which has an ethnically mixed population.

In Papers I and II, all cases of UNE that were surgically treated between 2004 and 2008 at the Department of Hand Surgery, Skåne University Hospital, were studied retrospectively. A total of 343 surgically treated UNE cases (i.e. 281 patients) were found for which medical records were thoroughly reviewed. During the study period, postoperative outcome based on PROMs (i.e. validated, standardized questionnaires evaluating outcome e.g. the QuickDASH questionnaire) was not used on a standardized and regular basis and could therefore not be reproduced. Instead, postoperative outcome was based on a simple DROM grading (i.e. a patient-reported and surgeon-evaluated outcome registered in the patient files at the last out-patient visit and graded as cured, improved, unchanged or worsened). Six cases were excluded from the original 343 cases due to no outcome being registered in the patient files. Preoperative electrophysiological protocols were retrospectively revised, assessed and graded by a specialist in neurophysiology (see below under Electrophysiology).

In Paper I, the 242 primary cases that were surgically treated with simple decompression were included and analysed. In Paper II, all cases that were treated with subcutaneous and submuscular transposition surgery were studied (i.e. 43 primary transposition surgeries and 44 revision transposition surgeries).

The population from the National Quality Register for Hand Surgery (HAKIR)

HAKIR is the National Quality Register for Hand Surgery in Sweden (www.hakir.se) (93). The register was started on February 1st 2010 and collects data on all hand surgical procedures performed from all seven public departments of hand surgery in Sweden, as well as two private hand surgery units. Patients above 16 years of age, with a Swedish social security number, are asked to complete the Swedish version of the validated PROM questionnaire QuickDASH (94) and a HAKIR specific outcome questionnaire HQ-8 (95), preoperatively as well as at three and 12 months postoperatively. The overall response rate in the HAKIR register in 2016 was 43% at three months and 43% at 12 months postoperatively (96). The study population in Papers III, IV and V comprised surgically treated UNE cases registered in HAKIR between 2010 and 2016.

In Paper III, 1354 primary UNE cases (i.e. 1316 patients) were included out of the 1395 UNE surgeries registered in HAKIR with correct UNE coding. The 1354 cases were linked to the Swedish National Diabetes Register (NDR) and then analysed. The NDR register (www.ndr.nu) (97) was started in 1996 and collects data on diabetes diagnosis, treatment, complications and associated risk factors among approximately 90% of patients in Sweden with diabetes above 18 years of age. All primary clinics as well as secondary and tertiary referral clinics treating patients with diabetes report to the NDR register (98). Paper IV focused solely on the UNE cases surgically treated in two of the hand surgery departments reporting to the HAKIR register, Malmö and Linköping, Sweden. Additionally, all 548 UNE cases in HAKIR with correct UNE coding were retrospectively studied and data not specified in HAKIR were extracted from the patients' medical records (i.e. surgery being primary or revision, clinically verified pre- or intraoperative ulnar nerve dislocation and DROM grading) and then analysed. Paper V focused on the same study population as Paper IV. The 548 UNE cases were linked to the Swedish National Diabetes Register (NDR) and all preoperative electrophysiological protocols were additionally retrospectively revised, assessed and graded by a specialist in neurophysiology, as in Papers I and II (see below under Electrophysiology). These data were then analysed.

Electrophysiology

Preoperative electrophysiological examinations are, from an international perspective in some regions, mandatory as part of the clinical assessment and diagnostics of UNE. In our region, it is not standard practice for all patients to undergo electrophysiological testing. Electrophysiology might instead be used according to the treating surgeon's preference, to support UNE diagnosis or in cases of differential diagnostic reasoning. In a previous Swedish study, 91% of the included UNE patients were evaluated preoperatively using electrophysiology (90), indicating that in a number of cases, UNE diagnosis is based solely on patient symptoms and clinical signs.

At the Departments of Clinical Neurophysiology in Lund and Linköping, the ulnar nerves were stimulated at wrist level, then below and above the elbow, after which a response was recorded from the abductor digiti minimi muscle. Orthodromic sensory response of the ulnar nerve to stimulation and F-waves were recorded from the little finger. At the Department of Clinical Neurophysiology in Lund, the ulnar nerves were also examined using an inching technique with 2 cm segments across the cubital tunnel. In the included studies, preoperative electrophysiological protocols were retrospectively revised, assessed and graded by one of the authors (GS.A), a specialist in neurophysiology and blinded to both treatment and outcome. Grading was done based on reference values at the Departments of Clinical Neurophysiology in Lund and Linköping, Sweden, according to: (1) normal findings, (2) reduced conduction velocity across the elbow segment, (3) nerve conduction block (i.e. reduced amplitude when stimulating above, compared to stimulating below the elbow) or (4) axonal degeneration (i.e. reduced motor and/or sensory response amplitudes). If a nerve showed both reduced conduction velocity and axonal degeneration, it was graded according to its most pathological parameter.

Outcome measures

Patient-reported outcome measures - PROMs

Most recent studies use various PROMs to evaluate treatment outcome in UNE. These PROMs are validated, standardized questionnaires that evaluate treatment outcome and assess pre- and postoperative hand function, health status and patient satisfaction. The PROMs QuickDASH, DASH and HQ-8 were used in Papers III, IV and V. The diagnose-specific PROM for UNE (i.e. Patient-rated Ulnar Nerve Evaluation [PRUNE]) was not available in Swedish at the time the studies were carried out (87).

DASH

The Disability of Arm, Shoulder and Hand (DASH) outcome measure is a validated patient-reported questionnaire designed to assess upper extremity disability and used as an indicator of the impact of an impairment, based on both the level and type of disability (92, 99, 100). It comprises in total 30 questions, of which 21 items assess the difficulty in performing various physical activities; five items focus on the severity of symptoms (including weakness, tingling, stiffness, pain and activity-related pain) and four items inquire about the impact on activities of daily life (work, social functioning, sleep and self-image). Each question has five response options scored 1-5 on a Likert scale, with 1 representing no difficulty/ability and 5 representing extreme difficulty/disability. From these scores, a scale score ranging from 0-100 is calculated, with a higher score indicating more disability. Responsiveness to the DASH questionnaire is comparable to other joint and disease-specific measures (101). The DASH score is used in Paper IV and correlated with the QuickDASH score where, in a limited number of cases (n=15), the patients had completed both the full version of the DASH questionnaire (originally as part of another study) (102) and the QuickDASH questionnaire.

QuickDASH

The QuickDASH outcome measure is the validated, shortened version of the DASH. From the original 30 questions, 11 items were extracted for inclusion in the QuickDASH. As with the DASH, from the five response options scored 1-5, a total scale score of 0-100 is calculated, ranging from no to most severe disability. A reduction in the total score of 7-8 points between pre- and postoperative scores is considered to reflect the minimal clinically important difference (86). A postoperative total score of more than 10 is interpreted as the presence of persistent symptoms (103-106). The QuickDASH is commonly used as, being shorter, it is less time consuming, resulting in a slightly higher response rate than the original DASH outcome measure (100, 107). The QuickDASH score is used in Papers III, IV and V, as one of the validated PROMs used in the HAKIR register.

HQ-8

HQ-8 is a HAKIR specific outcome measure, which includes seven questions on perceived symptoms in the affected hand (i.e. pain on load, pain on motion without load, pain at rest, numbness, weakness, stiffness and cold sensitivity), and one question on the ability to perform activities of daily life. The HQ-8 questions are also reported on a Likert scale ranging from 0-100 with a higher score indicating more disability. The HAKIR group recommends that all HQ-8 questions are studied independently (95). The HQ-8 score is used in Paper III as it is used in the HAKIR register and is believed to complement the QuickDASH score.

Doctor-reported outcome measure - DROM

Pre- and postoperative evaluation using the QuickDASH questionnaire was first implemented in regular clinical praxis at the Department of Hand Surgery, Skåne University Hospital in 2009. During the study period of Papers I and II, between 2004 and 2008, no other PROM was used on a standardized basis. Since real-time data on treatment outcome cannot be reproduced, postoperative outcome was instead based on a created DROM grading. This simple doctor-reported outcome measure was assessed by the author of this thesis, a specialist in orthopaedic surgery, but not a treating surgeon in any of the cases. The DROM grading was based on the patient-reported and surgeon-evaluated outcome registered in the patient files at the last out-patient visit and was defined as: (1) cured, (2) improved, (3) unchanged and (4) worsened. In the analyses in the different papers, the DROM grading was dichotomized for statistical reasons into: (1) cured/improved and (2) unchanged/worsened. In Papers IV and V, DROM grading was assessed for comparison with the PROMs used as primary outcome measures, in accordance with a previous publication (90).

Data management and statistical analyses

Statistical analyses

SPSS Statistics, versions 25 and 26 (SPSS Inc., Chicago, IL) was used for statistical analyses in all calculations. Data were presented as median [interquartile range; IQR; Q25-Q75]. Nominal data were presented as numbers (%). For nominal data, a Chi-squared test was used to compare differences between groups. The non-parametric Kruskal-Wallis test was used to compare differences between groups for continuous data. When indicated, subsequent posthoc analyses were made using the Mann-Whitney U test or Chi-squared test. Correlations were assessed by Pearson correlation coefficient (r, with p-value) for continuous data and Point-Biserial correlation coefficient for dichotomous variables. An r-value of >0.30 was required for interpretation as a real correlation and to be presented (i.e. 0.30 – 0.50 = weak correlation; 0.50 - 0.7 = moderate correlation; >0.70 = strong correlation). Linear regression analyses were performed to study the effects of nominal factors on QuickDASH score (unstandardized B [95% CI]; p-value). A p-value <0.05 was considered statistically significant. Each treated arm was analysed as a separate case and statistical entity.

Results

The results from each paper are summarized below. For details the reader is referred to the individual papers.

Paper I

In Paper I, the purpose was to evaluate outcome after primary simple decompression in UNE aiming to identify predictors for functional outcome.

Outcome after primary simple decompression

In the cohort, 78 % (189/242) of the primary UNE cases treated with SD reported an excellent or good outcome (measured by DROM grading), where patients perceived a complete or partial recovery, while 22% (53/242) had no change or experienced worsened symptoms compared to preoperatively. Sex, smoking, associated diseases and the presence of various clinical signs supporting UNE diagnosis did not affect surgical outcome. A tendency towards worse outcome was observed for cases with higher age, a manual occupation, presence of preoperative ulnar nerve dislocation and experiencing UNE with constant symptoms instead of intermittent. Similar outcome was found regardless of whether cases received initial conservative treatment with a night-splint or were directly treated surgically. Cases operated on by a specialist in hand surgery were found to have a better outcome than cases treated by an experienced resident surgeon.

Additional results - Electrophysiology

In the cohort, 81% (196/242) of all cases underwent electrophysiological examination, while in the remaining cases (19%) the treating surgeons based their UNE diagnosis purely on patient history and clinical examination. In 79% (155/196) of these cases, the electrophysiological examination showed signs of ulnar nerve affection supporting UNE diagnosis (36% reduced conduction velocity; 12% conduction block; 52% axonal degeneration), while 21% (41/196) had normal findings. No difference in outcome was noted between cases where UNE diagnosis was confirmed by electrophysiological findings and cases with UNE diagnosis based solely on patient history and clinical examination. Cases with nerve conduction block or axonal degeneration (i.e. electrophysiologically more severe pathology) showed worse outcome after SD.

Paper II

Paper II aimed to study surgical outcome after subcutaneous and submuscular ulnar nerve transposition in primary UNE and UNE relapse, with the aim of identifying predictors for revision surgery.

Outcome after transposition surgery

In the cohort, 93% (14/15) of SCT cases and 79% (22/28) of SMT cases reported an excellent or good outcome (measured with DROM grading) after transposition surgery due to primary UNE. Among revision surgery cases due to UNE relapse, 86% (6/7) in the SCT group and 73% (27/37) in the SMT group reported being cured or improved. There were no differences in outcome between primary and revision transposition surgeries, either when analysing all transposition cases or when analysing primary SMT alone compared to revision SMT.

Additional results

Revision transpositions had a higher frequency of concomitant systemic diseases, musculoskeletal conditions and CTS. No differences were found between primary and revision transposition cases concerning age, sex, profession or clinical signs of UNE. Both primary (79%) and revision SMT (76%) cases had a high frequency of ulnar nerve dislocation. A higher frequency of primary SMT (61%) cases had positive electrophysiological findings, supporting UNE diagnosis, compared to revision SMT cases (35%). Analysis of electrophysiological data showed that all primary transposition surgeries as well as primary SMT surgeries alone had a tendency to have nerve conduction block or axonal degeneration (i.e. a more severe pathology), while revision surgeries (all revision cases and revision SMT cases alone) had normal electrophysiological findings or reduced conduction velocity.

Paper III

In Paper III, the purpose was to evaluate patient-reported outcome after surgical treatment for primary UNE in patients with and without diabetes, as well as to assess whether sex influences outcome.

Diabetes and outcome

Preoperative QuickDASH scores did not differ between patients with and without diabetes. No differences were found in surgical outcome (measured using the PROM QuickDASH) between patients with and without diabetes at either three or 12 months postoperatively. In the linear regression analyses, diabetes did not predict a higher postoperative QuickDASH score at 12 months. The total-score change between preoperative and 12 months postoperative QuickDASH was, however, lower in cases with diabetes. Men with diabetes reported higher postoperative QuickDASH scores than men without diabetes, which was not seen in women.

Additional results

Diabetes was present in 12 % (160/1354) of the cases, of which 76% (111/160) were type 2 diabetes and 23% (33/160) were type 1 diabetes. Median HbA1c levels (mmol/mol) were 56 [IQR 44-71] and no differences in HbA1c levels were found between men and women. The patients had had a diabetes diagnosis for a median of 9 years [IQR 3-20]. The diabetes group comprised a majority men and was older compared to the group without diabetes. Patients with diabetes were surgically treated with SD more often than patients without diabetes and were also to a greater extent operated on simultaneously for another nerve compression. In the HAKIR specific HQ-8 questions, cases with diabetes reported preoperative cold sensitivity more often than cases without diabetes.

Women scored their disability based on QuickDASH higher than men on all occasions pre- and postoperatively, but showed larger improvement from preoperatively to 12 months postoperatively compared to men. However, men had better surgical outcome at both 3 and 12 months postoperatively. Additionally, women scored higher on all HQ-8 items (i.e. pain on load, pain on motion without load, pain at rest, weakness, numbness, cold sensitivity, ability to perform daily activities) preoperatively, except stiffness. Women also scored higher on items regarding pain and numbness postoperatively.

Patients operated with ulnar nerve transposition scored 10.8 points higher on QuickDASH at 12 months (95% CI 1.98-19.6). Ulnar nerve transposition resulted in more residual symptoms.

Paper IV

Paper IV aimed to assess ulnar nerve dislocation as an influencing factor on outcome after primary and revision surgeries for UNE, using both PROM and DROM.

Ulnar nerve dislocation and outcome

In the cohort, 20% of all cases had a documented pre- or intraoperative ulnar nerve dislocation and the majority were found among revision surgeries (47%) in comparison to primary surgeries (16%). No differences were found between cases with and without ulnar nerve dislocation preoperatively or at three months postoperatively. Cases with dislocation had higher QuickDASH scores at 12 months postoperatively than those without dislocation. At the same time, no correlation was found between ulnar nerve dislocation and QuickDASH scores at 12 months postoperatively. An adjusted regression model for age and sex did not predict higher QuickDASH scores at 12 months postoperatively.

Primary surgeries had better outcome compared to revision surgeries, according to DROM grading, but postoperative QuickDASH scores did not differ. In total, 73% of primary surgeries and 61% of revision surgeries were cured-improved at follow-up. Primary simple decompressions had better outcome at 12 months postoperatively, with respect to QuickDASH scores, compared to primary transposition surgeries.

Additional results - relation between PROM and DROM

Cases graded by DROM as cured-improved had lower QuickDASH scores than cases graded as unchanged-worsened at three and at 12 months postoperatively, while preoperative QuickDASH scores did not differ between the two DROM groups. A strong positive correlation was found between DASH and QuickDASH scores at 12 months postoperatively as well as a positive, but weak, correlation at three and 12 months postoperatively between DROM grading and QuickDASH score. A DROM grading of unchanged-worsened predicted higher QuickDASH scores at both three and 12 months postoperatively in the linear regression analysis adjusted for age and sex.

Paper V

In Paper V, the purpose was to evaluate impact of preoperative electrophysiology on surgical outcome for UNE and to analyse the relation between electrophysiology, age, sex and diabetes.

Electrophysiology and outcome

No differences in QuickDASH score were found either preoperatively or at three and 12 months postoperatively between the four electrophysiology groups (normal electrophysiology, reduced nerve conduction velocity, nerve conduction block or axonal degeneration), both when analysing all cases and primary UNE cases alone. With DROM grading, no differences were found in postoperative outcome in relation to the four electrophysiological grades of nerve affection. Dichotomizing electrophysiological grading into normal and pathologic electrophysiology respectively, cases with normal electrophysiology had worse preoperative QuickDASH score than cases with pathologic electrophysiology, while postoperative QuickDASH scores did not differ. When dichotomizing the electrophysiological grading into normal/reduced conduction velocity against nerve conduction block/axonal degeneration (i.e. more severe pathology), a worse postoperative outcome was noted in the latter group with DROM, but not with QuickDASH. No correlation was found between electrophysiology and outcome measures in the form of QuickDASH and DROM.

Additional results

Primary surgery cases had electrophysiologically more pronounced nerve pathology than revision surgeries. No differences were found in electrophysiological grading between primary simple decompressions and primary transposition surgeries. Men and older cases had more severe electrophysiological nerve affection in the form of nerve conduction block or axonal degeneration. A moderate positive correlation was found between age and electrophysiological grade of nerve pathology, where higher age increased severity of nerve affection. Cases with diabetes had more severe electrophysiological pathology, similar for men and women with diabetes, but no correlation between diabetes and electrophysiology was found. In the linear regression analysis, a higher age and diabetes were associated with a higher risk of a worse electrophysiological classification, while female sex was associated with better electrophysiological grading.

General discussion

Primary ulnar nerve entrapment

Outcome of surgical treatment

Surgical treatment of primary UNE includes simple decompression (open or endoscopic), ulnar nerve transposition (subcutaneous, intramuscular or sub-muscular) or medial epicondylectomy, where the latter procedure has not been a focus of the present thesis. A number of studies have been conducted over the years focusing on outcome after surgical treatment of primary UNE, where different types of surgical methods have been compared. In the present thesis, consisting of principally two different cohorts of 285 and 473 cases, I found excellent or good outcome (i.e. patients reporting being cured or improved), in 74-78% of the cases after SD (Papers I and IV) and in 78-84% of the cases after transposition surgery (93% in SCT and 79% in SMT) (Papers II and IV) measured using DROM grading. These data are similar to reports in multiple previous prospective RCT studies and retrospective studies (defined as excellent or good outcome in 61-84% cases after open SD and in 62-83% after SCT or SMT) (4, 67, 73).

I found no differences in outcome between SD and transposition surgeries measured using DROM grading (Paper IV), which is in line with what numerous previous studies have shown (4, 66, 67, 73, 108). When analysing the validated PROM QuickDASH, I found no differences in preoperative QuickDASH scores between cases treated with SD or transposition surgery, hence, all cases rated their symptoms as equally pronounced preoperatively. Interestingly, however, cases treated with SD were found to have a better outcome at 12 months postoperatively compared to transposition surgeries (Paper IV). These results were also reproducible when analysing the whole HAKIR register population of 1354 primary UNE cases; simple decompressions had a better outcome than ulnar nerve transpositions at 12 months postoperatively (Paper III). This finding is interesting since it contrasts with what previous studies have noted. The multiple studies showing no differences in outcome between SD and transposition surgeries have, on the other hand, included fewer UNE cases in their analyses; between

44-152 cases in contrast to the 473 and 1354 cases included in the present thesis (4, 67, 73, 82, 108-110). This leads me to speculate as to whether previously reported data may be slightly skewed due to fewer cases being analysed and that my findings may suggest a different view on surgical outcome in relation to chosen surgical method, than noted and accepted in the scientific community to date. To achieve a deeper knowledge about which surgical method actually offers best outcome, further studies on larger cohorts are still needed with a clear definition of the staging of UNE problems.

Simple decompression is commonly considered the gold standard in primary UNE cases since it is easier to perform, surgically less invasive with lower risk of postoperative complications (67, 72, 73) and is more cost effective (75). However, transposition surgery is commonly chosen as the primary surgical method, if partial or total ulnar nerve dislocation is present preoperatively, or in cases where ulnar nerve dislocation arises intraoperatively when performing primary SD. Interestingly, my findings concerning outcome, analysed using QuickDASH, does not agree with previous studies, which show similar outcome for SD and transposition surgeries (4, 66, 67, 72, 73, 82, 108, 109), which also alerted me to questions concerning predictors of outcome. For example, ulnar nerve dislocation in UNE and its potential influence on surgical outcome has not been sufficiently highlighted in previous studies (34, 35, 37-39). I also speculate whether my finding of a worse outcome among transpositions than SD might be explained by a high frequency of clinically relevant ulnar nerve dislocations in the primary ulnar nerve transposition group, the presence of nerve dislocation potentially being the reason for choosing primary ulnar nerve transposition over the gold standard simple decompression. I, therefore, decided to analyse this further.

Notably, outcome after primary simple decompression surgery, as measured by the levels of postoperative QuickDASH scores [ranging between 34-38 points at 12 months postoperative (Papers III and IV)], is not impressive. Also, outcome after surgical treatment for UNE has been found to be less favourable compared to outcome after carpal tunnel release (4), another more common peripheral mononeuropathy. The reason for this is not fully understood. My interpretation of the findings is that they reflect some residual postoperative symptoms, being consistent with postoperative satisfaction rates of 74-78% as measured by DROM. My belief, however, is that these unfavourable outcomes may have a multifaceted cause, which might be explained by different prognostic factors.

Predictors of surgical outcome

A variety of patient-related factors are often studied in their role as risk factors for developing UNE, but not as often in their role as potential predictors influencing treatment outcome. Throughout the work on the different papers included in this thesis, I studied different patient-related factors in the role as predictors of surgical outcome.

Ulnar nerve dislocation

I found a total of 16% documented pre- or intraoperative, partial or total, clinically verified ulnar nerve dislocations among primary surgeries in both my smaller study group (Papers I and II; unpublished results) and in my larger study group from the HAKIR register (Paper IV). Among revision surgeries, I noted 47% pre- or intraoperative clinically verified ulnar nerve dislocations, which was significantly higher than among primary surgeries (Paper IV). In my smaller study population, the frequency of nerve dislocations among revision surgeries was even higher (63%; Papers I and II; unpublished results). In total, I found ulnar nerve dislocation to be present in 20-23% of all surgically treated cases (Papers I, II and IV). In previous studies among UNE patients, a similarly wide distribution of ulnar nerve dislocation, 18 - 46 %, has been reported, which is in accordance with my findings (38, 39, 111). These studies analyse the occurrence of partial dislocation (i.e. subluxation) and total nerve dislocation separately (found in 7-25% and 7-21% of the cases, respectively). However, they do not specify whether UNE was primary or recurrent. My hypothesis is that this wide range of ulnar nerve dislocations in previous studies may reflect the difference in ulnar nerve dislocations among primary and recurrent UNE cases, as noted in my present analyses. Commonly, when partial or total ulnar nerve dislocation is present preoperatively in primary UNE, when ulnar nerve dislocation arises intraoperatively when performing primary SD and in cases of recurrent UNE, transposition surgery is chosen as surgical method, which is a frequent clinical routine in Sweden.

I found that a majority of the primary cases with ulnar nerve dislocation were surgically treated with transposition surgery [67% of the cases in our smaller study population (Paper II) and 93% in our larger study population (Paper IV)]. When analysing revision surgeries, I noted that almost all the recurrent UNE cases with concomitant nerve dislocation were surgically treated with transposition surgery [97% of the cases in my smaller study population (Paper II) and 100% in my larger study population (Paper IV)]. These observations presumably reflect the mentioned surgical choices, with reference to both the presence of ulnar nerve dislocation and to recurrent UNE.

When analysing surgical outcome in all surgically treated UNE cases (including both primary and revision surgeries), I found that cases with dislocation had higher QuickDASH scores at 12 months postoperatively than those without dislocation, reflecting a worse outcome (Paper IV). No such difference could be found at 3 months postoperatively, but a tendency towards a worse outcome, measured using DROM, was also noted in my smaller retrospective study among primary simple decompressions with ulnar nerve dislocation (Paper I). At the same time, the presence of clinically relevant ulnar nerve dislocation did not predict higher QuickDASH scores, and no correlation was found between ulnar nerve dislocation and QuickDASH scores at 12 months postoperatively (Paper IV). Ulnar nerve dislocation and its effect on surgical outcome has previously not been sufficiently highlighted. A recently published study, in which no significant differences were found in surgical outcome among UNE cases with or without dislocation, also supports this notion (112). With reference to my findings, indicating that presence of nerve instability might influence postoperative outcome negatively, my belief is that more detailed studies are needed on the role of ulnar nerve dislocation in UNE.

Preoperative electrophysiology

It is not standard procedure in our region for all UNE patients to undergo electrophysiological examination prior to surgery, but it is regarded as a complement in clinical diagnostics. In my smaller study group, 81% of the primary SD cases (Paper I) and 58% of the primary transposition cases (Paper II) had a preoperative electrophysiological test. In my larger HAKIR register group, 75% (Paper V) of all primary surgery cases underwent electrophysiological examination. In the remaining cases, UNE diagnosis was based solely on patient history and clinical examination. Of the cases that had preoperative testing, I found that 79% of the primary cases surgically treated with simple decompression and 88% of primary transpositions had positive electrophysiological findings, supporting UNE diagnosis (Papers I and II). In addition, I found no difference in outcome, measured using DROM, after primary simple decompression between cases where UNE diagnosis was confirmed by electrophysiological findings and cases diagnosed by patient history and clinical examination alone (Paper I), giving support to the notion that clinical symptoms should weigh heavily in diagnostics and treatment decisions concerning UNE. I wonder whether electrophysiological examinations perhaps do not need to be assessed on a mandatory basis, but rather regarded as a complement in UNE diagnostics.

I found no differences in electrophysiological grading between primary simple decompressions and primary transposition surgeries (Paper V), but I noted electrophysiologically more pronounced nerve pathology (i.e. nerve conduction block or axonal degeneration) among primary surgeries compared to revision surgeries (i.e. normal findings or reduced conduction velocity) both in my smaller (Papers I and II) and larger (Paper V) study populations, which is in accordance with previous findings (76). My conjecture is that this might reflect the high frequency of concomitant ulnar nerve dislocation among revision surgeries, the dislocation itself being the main reason for needing revision surgery, rather than a UNE relapse due to increased nerve affection, which should have been demonstrated by worsened electrophysiological grading. Surgeons should, therefore, routinely assess the possible presence of intraoperative ulnar nerve dislocation when performing SD for primary UNE and, if dislocation is found, perform a transposition of the ulnar nerve in the same session, to minimize the risk of needing future revision surgery.

Further, I analysed the relation between the electrophysiological grade of ulnar nerve pathology and surgical outcome. In my smaller study, I noted worse outcome, measured using DROM, after primary SD among cases with electrophysiologically more severe pathology (Paper I). My reflection was that electrophysiological assessment and grading might be a good predictor of surgical outcome, as has also been indicated in some previous studies (113, 114). However, in my larger HAKIR register-based study (Paper V), I found no differences in postoperative outcome in relation to the electrophysiological grades of nerve affection, either when measured by QuickDASH score at 3 and 12 months postoperatively, or by DROM, which on the other hand is consistent with what has been shown previously in a systematic review (4). I found the same results when analysing solely primary UNE cases as well as all cases, including revision surgeries. Also, I found no correlation between electrophysiological grades and my used outcome measures (i.e. QuickDASH and DROM). Only when dichotomizing electrophysiological grading into normal findings/less severe nerve pathology against more severe nerve pathology, did I notice a worse postoperative outcome with DROM among cases with more pronounced nerve pathology, which was in accordance with my findings in Paper I.

I conclude from my studies that preoperative electrophysiological assessment and grading of ulnar nerve affection may influence surgical outcome, but is not a clear predictor of outcome. The relation between electrophysiology and surgical outcome is complex and may be skewed by other patient-related factors influencing surgical outcome, such as ulnar nerve dislocation and comorbidities. Nevertheless, electrophysiology provides treating surgeons with valuable information when discussing patient expectations preoperatively.

Diabetes

Diabetes is a disease that may affect the peripheral nervous system, amongst other organ systems, and is a known risk factor for both distal sensory polyneuropathy (115) and nerve compression neuropathies, most notably CTS (116), as well as UNE (3, 22, 27, 28). I found comorbidity with diabetes in 12% of all surgically treated UNE cases from the HAKIR register, the majority having type 2 diabetes (76%) (Paper III). The cases with diabetes were well regulated (as indicated by the HbA1c levels), older and the majority were men. I noted that UNE patients with diabetes were more frequently operated for concomitant nerve compression other than UNE, reported more preoperative cold sensitivity (Paper III) and had more severe electrophysiological pathology; the last-mentioned was similar in both men and women (Paper V). Further, I found concomitant diabetes to be associated with a higher risk of a worse electrophysiological grading (Paper V). Taken together, my interpretation is that these findings reflect the pathophysiology of diabetic neuropathy; i.e. the intraneural structural changes that diabetes is known to induce in peripheral nerves through systemic metabolic changes (117, 118), where it has also been shown that the small nerve fibres that are damaged first in the course of diabetic neuropathy are responsible for mediating thermal sensation (119).

In patients with diabetes, simple decompression was chosen over transposition of the ulnar nerve more often than in the group without diabetes (Paper III). One may wonder whether the treating surgeons are more prone to avoid more complex surgery in patients with diabetes, in order to minimize risk of postoperative complications. I found no differences in postoperative outcome between patients with or without diabetes (Paper III), which is consistent with results from previous studies (76, 78, 120-122). Neither did diabetes predict a higher postoperative QuickDASH score at 12 months. However, the cases in my study had well-regulated diabetes and one may consider whether a cohort with less well treated diabetes might present a worse outcome after surgery. Nevertheless, I noted that patients with diabetes reported a smaller improvement in the QuickDASH total score compared to patients without diabetes (Paper III), which may be related to the diabetic nerves having more pronounced changes, as I noted in Paper V where patients with diabetes had more severe electrophysiological pathology.

Further, I noted that men with diabetes had electrophysiologically more severe nerve pathology (Paper V) as well as worse surgical outcome after simple decompression (Paper III) compared to men without diabetes, and in contrast to women with diabetes. Previous studies have shown that men have a higher risk of developing UNE (21, 24, 123). Men are also affected by diabetic neuropathy earlier and to a greater extent than women (124, 125), and have a lower intraepidermal nerve fibre density (126). My interpretation is that this supports men having a more sensitive peripheral nervous system and less reserve capacity compared to women, which in turn influences regeneration and recovery after nerve compressions, resulting in a worse surgical outcome. Another, although less plausible, explanation for my findings may be that men tend to seek medical advice later than women.

Age and sex

UNE is a peripheral mononeuropathy that is mainly considered to be idiopathic, but several risk factors predispose for the development of nerve compression, including older age and male sex (21, 24, 123). I found that both men and older patients had more severe electrophysiological nerve affection compared to women and younger patients in the form of nerve conduction block or axonal degeneration. Further, I noted a positive correlation for age, indicating that increasing age may affect electrophysiological findings negatively and increase severity of nerve pathology (Paper V). I interpret these findings as reflecting the known higher risk of developing UNE both in men and with increasing age. Men have also been found to have a lower intraepidermal nerve fibre density (126), indicating a more sensitive peripheral nervous system, which I believe may correlate to our findings of men having more severe electrophysiological nerve affection.

Interestingly, in my larger HAKIR register-based study group, I found that men had better outcome after primary SD at both 3 and 12 months postoperatively compared to women (Paper III), regardless of men from part of the same cohort having more severe electrophysiological nerve pathology (Paper V). At the same time, neither sex nor age affected surgical outcome after primary simple decompression in my smaller study group, even though a tendency toward worse outcome was observed for older cases (Paper I). Intriguingly, I found that women scored their disability higher than men both pre- and postoperatively, indicating that women perceive their UNE symptoms as more pronounced than men. At the same time, women showed greater improvement, measured using QuickDASH at 12 months postoperatively, compared to men (Paper III). I also observed that female sex was associated with better electrophysiological grading and hence less pronounced nerve pathology compared to men (Paper V).

A recent study from our group, using the same HAKIR population as studied in Paper III, evaluated socioeconomic factors influencing outcome of surgical treatment for UNE and found that the UNE patients differed greatly from the general population in terms of having lower education levels and earnings as well as higher rates of unemployment and sick leave (26). It is known that socioeconomic status influences several musculoskeletal conditions (127) and that women with lower education levels exhibit a high prevalence of arm or hand pain with greater social gradient inequalities compare to men (128). I find it plausible that my findings, that women perceive their

UNE symptoms as more pronounced compared to men while having measurably less pronounced ulnar nerve pathology, and that male sex possibly predicts a better postoperative outcome, could be explained by differences in socioeconomic factors. Further analyses are needed to reach a deeper understanding of these relations.

Recurrent ulnar nerve entrapment

Outcome of surgical treatment

UNE relapse due to persistent or recurrent symptoms is usually treated with transposition surgery, as well as if ulnar nerve dislocation occurs postoperatively after primary SD. I found no difference in postoperative outcome when analysing QuickDASH scores between primary and revision surgeries due to UNE (Paper IV). Using DROM grading, my results were contradictory; showing the same results in my smaller study population (Paper II) as when the QuickDASH measure was used (i.e. no difference in outcome), while I noted a worse outcome among revision surgeries compared to primary surgeries in my larger study population from the HAKIR register (Paper IV). The latter is, however, consistent with findings in a previous study, showing significantly worse outcome after revision surgery (129).

I noted an excellent or good outcome (i.e. cases reporting being cured or improved) in 75% of the cases after revision transposition surgery (86% in SCT and 73% in SMT) (Paper II), measured by DROM grading in my smaller study population of 52 revision surgeries. In my larger study population from the HAKIR register of 75 revision cases, 62% reported excellent or good outcome after transposition surgery measured by DROM (Paper IV). There are fewer previous studies on recurrent UNE than on primary UNE, but they report satisfactory results in 73-82% cases (79, 80, 129-131), which is similar to the results from my smaller study. However, in my larger study population from the HAKIR register, I found a lower occurrence of postoperative satisfaction of 62%. Since the number of included cases in previous studies is 18-56, compared to the 75 cases included in my register study, I think that previously reported data may be slightly skewed by being based on too few cases. My findings might perhaps suggest that satisfaction after revision transposition surgery is actually lower than noted in the scientific community. However, newly published studies on modified surgical techniques in recurrent UNE, show higher satisfaction rates than previously reported. Reoperation with SCT and additional use of a protective collagen membrane to prevent postoperative adhesions showed an 80% satisfaction rate, while surgery with decompression and ulnar groove plasty found postoperative satisfaction as high as 95%

(132, 133), leading me to the conclusion that further studies on recurrent UNE are needed.

Predictors of revision surgery

I found that revision transpositions had a higher comorbidity with concomitant systemic diseases and other musculoskeletal conditions as well as concomitant CTS (Paper II). Of these risk factors predicting the need of revision surgery, concomitant CTS has also been highlighted in a previous study (77). Patients with CTS have a lower number of myelinated nerve fibres in the posterior interosseous nerve, a continuation of the deep branch of the radial nerve, which is an easily accessible nerve branch for biopsy studies and is located adjacent to the median nerve, but not compressed. These findings have been interpreted as an indicator that some patients, including those with diabetes, may be more prone to develop nerve compression lesions (134, 135). One may consider, in support of my findings, that patients with UNE might also have such microscopic intraneural changes.

I did not find other patient-related factors, such as age, sex, diabetes, profession, workload or severity of UNE, to predict the need of revision surgery (Paper II). These factors are often considered relevant for surgical outcome in peripheral nerve entrapments. However, previous studies have also been unable to show that these factors consistently increase the risk of UNE relapse needing surgical revision (76-78, 81); hence, their role in possible UNE relapse remains to be clarified.

I noted positive electrophysiological findings, supporting UNE diagnosis, in 35% of revision SMT cases (Paper II), which is a low frequency. At the same time, revision surgeries had either normal electrophysiological findings or less pronounced ulnar nerve pathology in the form of reduced conduction velocity (Paper II), which is in accordance with previous findings (76). Simultaneously, I noted a high frequency of preoperative ulnar nerve dislocation; 53% among revision transposition surgeries in my larger HAKIR register-based study group (Paper IV) and as high as 73% in my smaller study group (Paper II). I wonder whether this high frequency of ulnar nerve dislocation might possibly explain my electrophysiological findings, since it is contrary to what might be expected, i.e. an electrophysiologically more pronounced nerve pathology among cases with UNE relapse, with the higher degree of electrophysiological pathology being a possible predictor for revision surgery.

Taken together with my findings, that cases with a clinically relevant ulnar nerve dislocation have a significantly worse outcome at 12 months postoperative (Paper IV), lead me to speculate whether my findings concerning satisfaction rates after revision surgeries due to recurrent UNE also might be associated with the high frequency of preoperative ulnar nerve dislocation, the presence of dislocation possibly explaining the relatively low postoperative satisfaction rate of 62% among revision UNE surgeries (Paper IV). However, in my smaller study group, I noted 73% ulnar nerve dislocations among revision transposition surgeries in contrast to a postoperative satisfaction rate of 75% (Paper II). This in comparison with the 53% dislocations among revision surgeries and in contrast to a postoperative satisfaction rate of 62% in my larger study group (Paper IV). My conclusion is that the former reflects a better outcome regardless of a higher frequency of preoperative ulnar nerve dislocation. Previous studies on ulnar nerve dislocation in recurrent UNE are scarce and my present findings are assumed to be novel in this area. My belief is that the relation between ulnar nerve dislocation and recurrent UNE is more complex than previously noted, both regarding preoperative UNE symptoms and indications for revision surgery, as well as postoperative outcome. This relation needs to be studied more thoroughly in the future.

Outcome measures

One of the known challenges in scientific studies on hand surgical treatment evaluations is the application of validated outcome measures. Multiple types of diagnose-specific patient-reported outcome measures (PROMs) are used with variations in responsiveness (85-87), which in turn can lead to difficulties in clinical research on UNE due to selection bias (83). I used a simple doctor-reported outcome measure (DROM), based on information documented in the patient records at the last follow-up, to evaluate surgical outcome in Papers I and II, when the retrospective nature of these papers prohibited reproduction of outcome as measured by validated PROMs. The diagnosis-specific PRUNE was not available in Swedish, at the time of my studies, and was thus not used (87). A DROM grading is simple to use and, since it requires no patient participation in filling out the questionnaires, a 100% responsiveness is not impossible to achieve. Some previous studies have even found a DROM grading to be associated with improvement in the PROM QuickDASH at one year postoperatively (90-92).

In Paper IV, I analysed the relation between DROM and the clinically widely used PROM QuickDASH. I found that cases graded as cured-improved with DROM reported significantly lower QuickDASH scores at both three and at 12 months postoperatively. Further, I noted significant correlations between both DROM and postoperative QuickDASH scores as well as between postoperative DASH and QuickDASH scores. Additionally, in the linear regression analysis, adjusted for age and sex, I found that a DROM grading of unchanged-worsened predicted higher postoperative QuickDASH scores at both three and 12 months postoperatively. Taken together, my interpretation is that these results provide some support for a relationship between the DROM and the QuickDASH outcome measures. Hence, I conclude that a simple DROM may be used in clinical practice, either independently or as a complement to PROMs, such as QuickDASH and the diagnosis-specific PRUNE, once it has been translated and validated in the appropriate language, which is presently being done in Sweden (87, 136).

Strengths and Limitations

Limitations regarding the first two studies (Papers I and II) included in this thesis, are mainly related to their retrospective nature. Because of this factor, neither preoperative clinical examinations nor postoperative outcome could be assessed in the same structured and objective way as in a prospective study. Postoperative outcome was instead assessed by a simple doctor-reported outcome measure (DROM grading), which some studies have implied is related to improvement in the PROM Quick-DASH at one year postoperatively (90-92).

A limitation in my last three studies (Papers III, IV and V) was the low response rate for QuickDASH scores among the UNE cases included from the HAKIR register. This can never be as high as in a prospective cohort study, even if it was in accordance with response rates reported by similar previous studies (85-87). The HAKIR register was also a rather new register at the time of data collection, being introduced in 2010, and hence having some expected start-up problems. Among others, the coding system in HAKIR did not include data either on whether UNE surgery was primary or revision, if ulnar nerve dislocation existed preoperatively, if electrophysiological examination had been carried out, or on which type of transposition surgery was performed. Since these data were not specified in HAKIR, additional thorough retrospective research was done on each individual patient file (Papers IV and V) and added to the analyses. Further, data extraction from HAKIR included the years 2010-2016, and hence follow-up data were in some cases lacking for patients undergoing surgery for UNE during 2016, since this would have been introduced into the registry in 2017.

A strength of the first two studies (Papers I and II) is that the clinical routines for UNE diagnosis, treatment indications and surgical techniques, have essentially remained the same over the years. One strength of the last studies (Papers III, IV and V) included in this thesis is the use of national quality registries (HAKIR and NDR), which enables analyses to be made on detailed data concerning a nationwide population. I focused on only two hand surgery departments reporting to the Swedish national hand surgery quality registry HAKIR because of the additional retrospective research needed on each individual patient file. Another strength is the use of a validated and internationally accepted outcome measure (i.e. Quick-DASH) for assessing treatment outcomes.

Conclusions

The overall aim of the present thesis was to advance in essential knowledge concerning UNE, and in this way to contribute to creating an evidence-based, standardized process in diagnostics and surgical treatment options for attaining the best possible clinical outcome for UNE patients. Since this purpose is multifaceted and complex, specific aims were formulated in each paper. My overall conclusions from the papers included in this thesis are summarized below. For my conclusions on each specific aim presented in each paper, the reader is referred to the individual papers.

Surgical outcome in primary and revision ulnar nerve entrapment

- Outcome after primary simple decompression is better than after transposition surgeries, measured using QuickDASH (Papers III and IV). No difference in outcome is found with DROM grading (Paper IV). Satisfaction rate is 74-78% in primary simple decompression and 78-84% in primary transposition surgery (Papers I, II and IV).

- No difference in postoperative outcome is found between primary and revision surgeries, measured using QuickDASH (Paper IV). With DROM grading, revision surgeries have a worse outcome (Paper IV). Satisfaction rate is 62-75% after revision transposition surgery (Papers II and IV).

Predictors of surgical outcome

- Ulnar nerve dislocation in UNE is 16% in primary surgeries and 47-63% in revision surgeries (Papers I, II and IV). Ulnar nerve instability influences choices in surgical treatment approaches (papers I, II and IV) and may influence outcome negatively (Paper IV).

- Preoperative electrophysiological grading does not clearly predict surgical outcome measured using QuickDASH (Paper V) but may influence it negatively as measured by using DROM (Paper I). There were no differences in surgical outcome between primary UNE cases diagnosed by means of clinical or electrophysiological examination (Paper I).

- Concomitant diabetes in primary UNE is associated with a worse electrophysiological grading (Paper V) but does not influence surgical outcome (Paper III). However, men with diabetes have a worse outcome after primary simple decompression (Paper III) than men without diabetes, which is not seen in women with diabetes.

- Sex and age are not clear predictors of surgical outcome after primary simple decompression (Papers I and III). Men have better outcome than women measured using QuickDASH (Paper III), while neither sex nor age affects outcome measured using DROM (Paper I). Women score their disability higher than men, but show a greater postoperative improvement compared to men (Paper III). Female sex is associated with better electrophysiological grading. Male sex and increasing age affect electrophysiological findings negatively (Paper V).

- Concomitant systemic diseases, musculoskeletal conditions and CTS are predictors of revision surgery (Paper II). Revision surgeries have normal electrophysiological findings or less pronounced electrophysiological nerve pathology (Paper II) and a high frequency of preoperative ulnar nerve dislocations (Papers II and IV).

Relations between outcome measures

- There are correlations between postoperative DROM and QuickDASH as well as between postoperative DASH and QuickDASH, providing some support for a relationship between DROM and QuickDASH measures (Paper IV). DROM grading may be useful in clinical practice.

Future research perspectives

Several studies over the years have conducted analyses and found no differences in outcome after different types of surgical treatments in primary UNE (4, 65-67, 72, 73, 108, 109). However, outcome after primary surgery is not impressive as measured by different PROMs, such as QuickDASH. The more recent diagnose-specific PROM for UNE, i.e. PRUNE (patient-rated ulnar nerve evaluation) (87), is still not widely used and at the time of the work on this thesis was not available in Swedish. At the same time, some studies have shown an approximately 90% satisfaction rate in mild UNE with conservative treatment only (59-61). A recent review study concludes that it is not known when conservative treatment may be superior to surgical treatment and vice versa (4). My conclusion is that further studies on treatment options in UNE would be valuable, most notably RTCs comparing conservative with surgical treatment. However, such studies should be put in perspective and include specific criteria for diagnosis of UNE with grading of severity, presentation of findings from clinical examinations and preoperative electrophysiology as well as follow-up time.

For anatomical reasons, the ulnar nerve may in some patients be unstable, i.e. with risk of partial or complete dislocation, leading to pain and UNE symptoms. Ulnar nerve dislocation may also arise intraoperatively in primary simple decompression or as a postoperative complication after primary surgery, then requiring revision surgery. Previously, ulnar nerve dislocation and its role in UNE has not been sufficiently highlighted, particularly in recurrent UNE. However, recently, ulnar nerve dislocation has started to come more into focus in both the clinical and scientific communities (112). My studies included in this thesis indicate that ulnar nerve dislocation not only influences choices in surgical treatment approaches but may also influence surgical outcome. I therefore conclude that more studies are needed on the subject, which should preferably analyse primary and revision surgeries separately.

Electrophysiological examination in UNE is useful in supporting UNE diagnosis and estimating the severity of entrapment. In some regions of the world, it is also mandatory in UNE diagnostics, both in clinical practice preoperatively and in scientific studies on UNE. However, the role of electrophysiology in UNE is debated, as some studies have found electrophysiological assessments to be possible predictors of surgical outcome

(50, 113, 114), whereas a recent review study found no differences in surgical outcome based on electrophysiological protocols (4). My included studies in this thesis found that preoperative electrophysiological assessment and grading of ulnar nerve affection is not a clear predictor of surgical outcome but may influence it. Further, I noted no differences in surgical outcome in UNE cases diagnosed using electrophysiology or clinical examination alone. Taken together, my interpretation is that the relationship between electrophysiology and surgical outcome in UNE is complex, and may also be influenced by other patient-related factors (such as sex, age and systemic disease e.g. diabetes) and hence needs to be studied more thoroughly. In addition, it may perhaps not be necessary to assess electrophysiological examinations on a mandatory basis, but regard them rather as a complement in UNE diagnostics.

Studies on data from National Quality Registers are believed to be helpful since the registers can collect data on all patients treated at the affiliated clinics. In our region, similar National Quality Registers exist among both the different subspecialties in orthopaedic surgery and in other medical specialties, from which many valuable and internationally notable studies arise. One known limitation of studies based on data from National Quality Registers is that generally the response rates are lower than desired, and, as not all private clinics are affiliated and report to the registers, study results may be skewed. Our HAKIR register at present lacks coding concerning important factors in UNE which is the reason for additional retrospective research being made on the HAKIR population in two of the studies included in the thesis. My conclusion is that National Quality Registers have an important role in delivering well-founded scientific studies from which relevant medical conclusions may be drawn. However, they are at the same time dynamic, and improvements can be made in their data collection, for example our HAKIR register needs to include essential information on hand surgical treatments.

The application of validated outcome measures is a challenge for scientific studies on hand surgical treatment evaluations. The lack of a specific outcome measure to follow up and evaluate surgical treatment in UNE (83) at the time when the present studies were initiated led to several different patient-reported outcome measures (PROMs) being used (83, 84), out of which the DASH and its shortened version, the QuickDASH are common. However, responsiveness to outcome measures have been found to be lower than desired (85-87), possibly affecting not only research on UNE due to selection bias, but also choices in diagnostics and treatments of UNE in everyday clinical practice. I evaluated a simple doctor-reported outcome measure (DROM) in this thesis, which by previous studies has been implied to correlate to improvement in Quick-DASH at one year postoperatively (90-92) and I found some support for such a relationship. I conclude that a DROM grading may be useful independently or as a complement to PROMs in clinical practice, but further studies are required to strengthen this theory. It is also believed that the diagnose-specific outcome measure, PRUNE, could have a valuable role in contribution to future studies on UNE and needs to be incorporated into clinical follow-up on a regular basis. Translation and validation of PRUNE in the appropriate language is presently being carried out in Sweden (87, 136).

"It always seems impossible -
Until it's done"

Nelson Mandela

龍

Acknowledgements

I wish to give my deepest gratitude to everyone who has supported me throughout the work of this thesis, and especially to:

Lars B. Dahlin - my supervisor. Thank you for your mentorship, guidance and for sharing your knowledge in the field of hand surgery and research. Thank you for believing in me, pushing me and for always being available for questions and feedback, regardless of am or pm, latitude or longitude. This thesis would not have been possible without your support.

Malin Zimmerman – my co-supervisor, for our interesting discussions, your statistical support and valuable scientific advice. Thank you for these productive collaborations.

Erika Nyman – my co-supervisor, for your continuous encouragement, valuable feedback and support. Thank you for our great collaborations.

Gert S. Andersson – for valuable collaborations throughout the work of this thesis, for all the time you have put into the work on electrophysiological gradings and your guidance in the world of electrophysiology.

Göran Lundborg – a legend in the field of hand surgery. Thank you for introducing me to Lars and hence starting it all.

Tina Folker – for being the administrative spider in the web. Your help along the way has been invaluable to me.

Helene Wilhelmsson - for administrative assistance juggling all my different employments through the years.

Helene Jacobsson, **Marianne Arner, Katarina Eeg-Olofsson**, **Anna Karlsson and Ann-Marie Svensson** - for great collaborations.

Sandra Lindstedt Ingemansson - my friend and unofficial co-supervisor, for sharing your experience in the world of medical science and all our late-night discussions on the topic, which have been truly invaluable to me.

Misha Bhat and Sasha Koul – for being not only childhood friends, but also medical stars with great advice to give in science and Sasha also being a rock in the jungle that is statistics.

Olga Göransson - my friend, for helpful discussions and guidance on my portfolio work.

Roland van Veen – my friend, for sharing your beautiful anatomical artistry.

David Wisinger, Johan Nilsson, Magnus Tägil, Anders Kjellin, Carl-Fredrik Carlson, Thomas Anderson, Mara Barisic, Eva-Lotta Guldberg, Annika Rahm Andersson and Per Jonsson - for being my clinical supervisors and career inspirers through the years.

Annie Lantto and Cecilia Fränngård - my friends since medical school, for countless conversations, for your honest feedback and guidance and for all our amazing times together. Nothing is more important than friends who will be by your side no matter what.

All my friends – none mentioned, and none forgotten. Thank each and every one of you for your friendship and support, for all the laughs and discussions, for all wonderful memories and for creating new ones together as time passes us by.

Elisabeth Renney and Phil Renney - my parents. Thank you for your endless and unconditional love and continuous, immense support throughout life. I hope I can return at least some of that to you. I love you.

Elisabeth Ambrus, Ferenc Ambrus, Magdalena Kiss and Ferenc Kiss - my grandparents. Thank you for always being there for me ever since my childhood, supporting me in every possible way you could. I love you and I miss you.

Christian Anker-Hansen - my husband, best friend and colleague. Thank you for sharing your knowledge in orthopedic surgery and inspiring me to be a better doctor, for choosing our family first, and above all, thank you for being my partner in life, supporting me in all more or less crazy and challenging paths I embark myself and our family on. We have had amazing adventures together and I look forward to the upcoming ones. I love you always.

Sienna Anker, Dante Anker and Tristan Anker - my children. Thank you for giving true meaning to my life. I really look forward to following your chosen roads and hope to be allowed to tag along on the way. I love you most of all in the whole world, unconditionally and always.

References

1. Lee EY, Lim AYT. Nerve Compression in the Upper Limb. Clin Plast Surg. 2019;46(3):285-93.
2. Descatha A, Leclerc A, Chastang JF, Roquelaure Y, Study Group on Repetitive W. Incidence of ulnar nerve entrapment at the elbow in repetitive work. Scand J Work Environ Health. 2004;30(3):234-40.
3. Rydberg M, Zimmerman M, Gottsater A, Nilsson PM, Melander O, Dahlin LB. Diabetes mellitus as a risk factor for compression neuropathy: a longitudinal cohort study from southern Sweden. BMJ Open Diabetes Res Care. 2020;8(1):e001298.
4. Caliandro P, La Torre G, Padua R, Giannini F, Padua L. Treatment for ulnar neuropathy at the elbow. Cochrane Database Syst Rev. 2016;11:CD006839.
5. VanPutte C, Regan J, Russo A. Seelys Anatomy and Physiology. 12th ed. New York, USA: McGraw-Hill Education; 2019.
6. Catala M, Kubis N. Gross anatomy and development of the peripheral nervous system. Handb Clin Neurol. 2013;115:29-41.
7. Gibbons CH. Basics of autonomic nervous system function. Handb Clin Neurol. 2019;160:407-18.
8. Chalazonitis A, Rao M. Enteric nervous system manifestations of neurodegenerative disease. Brain Res. 2018;1693(Pt B):207-13.
9. Sunderland S. The intraneural topography of the radial, median and ulnar nerves. Brain. 1945;68:243-99.
10. Mukherji SK, Castillo M, Wagle AG. The brachial plexus. Semin Ultrasound CT MR. 1996;17(6):519-38.
11. Polatsch DB, Melone CP, Jr., Beldner S, Incorvaia A. Ulnar nerve anatomy. Hand Clin. 2007;23(3):283-9, v.
12. Stojkovic T. Hereditary neuropathies: An update. Rev Neurol (Paris). 2016;172(12):775-8.
13. Chalk CH. Acquired peripheral neuropathy. Neurol Clin. 1997;15(3):501-28.
14. Rubin R, Strayer D. Rubin's Phatology: clinicopathologic foundations of medicine. 6th ed. Philadelphia, USA: Lippincott Williams & Wilkins; 2011.
15. Staples JR, Calfee R. Cubital Tunnel Syndrome: Current Concepts. J Am Acad Orthop Surg. 2017;25(10):e215-e24.

16. Apfelberg DB, Larson SJ. Dynamic anatomy of the ulnar nerve at the elbow. Plast Reconstr Surg. 1973;51(1):76-81.
17. Jones RE, Gauntt C. Medial epicondylectomy for ulnar nerve compression syndrome at the elbow. Clin Orthop Relat Res. 1979(139):174-8.
18. Lundborg G. Surgical treatment for ulnar nerve entrapment at the elbow [editorial; comment] [see comments]. J Hand Surg. 1992;17B(3):245-7.
19. Macnicol MF. Extraneural pressures affecting the ulnar nerve at the elbow. Hand. 1982;14(1):5-11.
20. Mondelli M, Giannini F, Ballerini M, Ginanneschi F, Martorelli E. Incidence of ulnar neuropathy at the elbow in the province of Siena (Italy). J Neurol Sci. 2005;234(1-2):5-10.
21. Osei DA, Groves AP, Bommarito K, Ray WZ. Cubital Tunnel Syndrome: Incidence and Demographics in a National Administrative Database. Neurosurgery. 2017;80(3):417-20.
22. Bartels RH, Verbeek AL. Risk factors for ulnar nerve compression at the elbow: a case control study. Acta Neurochir (Wien). 2007;149(7):669-74; discussion 74.
23. Kakosy T. Tunnel syndromes of the upper extremities in workers using hand-operated vibrating tools. Med Lav. 1994;85(6):474-80.
24. Omejec G, Podnar S. What causes ulnar neuropathy at the elbow? Clin Neurophysiol. 2016;127(1):919-24.
25. Hulkkonen S, Auvinen J, Miettunen J, Karppinen J, Ryhanen J. Smoking is associated with ulnar nerve entrapment: a birth cohort study. Sci Rep. 2019;9(1):9450.
26. Zimmerman M, Nyman E, Steen Carlsson K, Dahlin LB. Socioeconomic Factors in Patients with Ulnar Nerve Compression at the Elbow: A National Registry-Based Study. Biomed Res Int. 2020;2020:5928649.
27. Mondelli M, Aretini A, Rossi S. Ulnar neuropathy at the elbow in diabetes. Am J Phys Med Rehabil. 2009;88(4):278-85.
28. Rota E, Zavaroni D, Parietti L, Iafelice I, De Mitri P, Terlizzi E, et al. Ulnar entrapment neuropathy in patients with type 2 diabetes mellitus: an electrodiagnostic study. Diabetes Res Clin Pract. 2014;104(1):73-8.
29. Richardson JK, Green DF, Jamieson SC, Valentin FC. Gender, body mass and age as risk factors for ulnar mononeuropathy at the elbow. Muscle Nerve. 2001;24(4):551-4.
30. MacKinnon S, al e. Green´s operative hand surgery. In: Green DP, Kozin SH, Hotchkiss RN, Wolfe SW, Pederson WC, editors. Green´s operative hand surgery. 5th ed: Elsevier - Health Sciences Division; 2005.
31. Novak CB, Lee GW, Mackinnon SE, Lay L. Provocative testing for cubital tunnel syndrome. J Hand Surg Am. 1994;19(5):817-20.

32. Beekman R, Schreuder AH, Rozeman CA, Koehler PJ, Uitdehaag BM. The diagnostic value of provocative clinical tests in ulnar neuropathy at the elbow is marginal. J Neurol Neurosurg Psychiatry. 2009;80(12):1369-74.
33. Ochi K, Horiuchi Y, Tanabe A, Waseda M, Kaneko Y, Koyanagi T. Shoulder internal rotation elbow flexion test for diagnosing cubital tunnel syndrome. J Shoulder Elbow Surg. 2012;21(6):777-81.
34. Calfee RP, Manske PR, Gelberman RH, Van Steyn MO, Steffen J, Goldfarb CA. Clinical assessment of the ulnar nerve at the elbow: reliability of instability testing and the association of hypermobility with clinical symptoms. J Bone Joint Surg Am. 2010;92(17):2801-8.
35. Ozturk E, Sonmez G, Colak A, Sildiroglu HO, Mutlu H, Senol MG, et al. Sonographic appearances of the normal ulnar nerve in the cubital tunnel. J Clin Ultrasound. 2008;36(6):325-9.
36. Kim BJ, Date ES, Lee SH, Yoon JS, Hur SY, Kim SJ. Distance measure error induced by displacement of the ulnar nerve when the elbow is flexed. Arch Phys Med Rehabil. 2005;86(4):809-12.
37. Okamoto M, Abe M, Shirai H, Ueda N. Morphology and dynamics of the ulnar nerve in the cubital tunnel. Observation by ultrasonography. The Journal of Hand Surgery British Volume. 2000;25(1):85-9.
38. Kang S, Yoon JS, Yang SN, Choi HS. Retrospective study on the impact of ulnar nerve dislocation on the pathophysiology of ulnar neuropathy at the elbow. PeerJ. 2019;7:e6972.
39. Van Den Berg PJ, Pompe SM, Beekman R, Visser LH. Sonographic incidence of ulnar nerve (sub)luxation and its associated clinical and electrodiagnostic characteristics. Muscle Nerve. 2013;47(6):849-55.
40. McGowan AJ. The results of transposition of the ulnar nerve for traumatic ulnar neuritis. J Bone Joint Surg Br. 1950;32-B(3):293-301.
41. Nakashian MN, Ireland D, Kane PM. Cubital Tunnel Syndrome: Current Concepts. Curr Rev Musculoskelet Med. 2020;13(4):520-4.
42. Mallik A, Weir AI. Nerve conduction studies: essentials and pitfalls in practice. J Neurol Neurosurg Psychiatry. 2005;76 Suppl 2:ii23-31.
43. Todnem K, Michler RP, Wader TE, Engstrom M, Sand T. The impact of extended electrodiagnostic studies in ulnar neuropathy at the elbow. BMC Neurol. 2009;9:52.
44. Yuksel G, Karlikaya G, Tutkavul K, Akpinar A, Orken C, Tireli H. Electrodiagnosis of ulnar nerve entrapment at the elbow. Neurosciences (Riyadh). 2009;14(3):249-53.
45. van Dijk JG, Meulstee J, Zwarts MJ, Spaans F. What is the best way to assess focal slowing of the ulnar nerve? Clin Neurophysiol. 2001;112(2):286-93.

46. Tapadia M, Mozaffar T, Gupta R. Compressive neuropathies of the upper extremity: update on pathophysiology, classification, and electrodiagnostic findings. J Hand Surg Am. 2010;35(4):668-77.
47. Practice parameter for electrodiagnostic studies in ulnar neuropathy at the elbow: summary statement. American Association of Electrodiagnostic Medicine, American Academy of Neurology, American Academy of Physical Medicine and Rehabilitation. Muscle Nerve. 1999;22(3):408-11.
48. Padua L, Aprile I, Mazza O, Padua R, Pietracci E, Caliandro P, et al. Neurophysiological classification of ulnar entrapment across the elbow. Neurol Sci. 2001;22(1):11-6.
49. Visser LH, Beekman R, Franssen H. Short-segment nerve conduction studies in ulnar neuropathy at the elbow. Muscle Nerve. 2005;31(3):331-8.
50. Osterman AL, Davis CA. Subcutaneous transposition of the ulnar nerve for treatment of cubital tunnel syndrome. Hand Clin. 1996;12(2):421-33.
51. Beekman R, Schoemaker MC, Van Der Plas JP, Van Den Berg LH, Franssen H, Wokke JH, et al. Diagnostic value of high-resolution sonography in ulnar neuropathy at the elbow. Neurology. 2004;62(5):767-73.
52. Terlemez R, Yilmaz F, Dogu B, Kuran B. Comparison of Ultrasonography and Short-Segment Nerve Conduction Study in Ulnar Neuropathy at the Elbow. Arch Phys Med Rehabil. 2018;99(1):116-20.
53. Pelosi L, Mulroy E. Diagnostic sensitivity of electrophysiology and ultrasonography in ulnar neuropathies of different severity. Clin Neurophysiol. 2019;130(2):297-302.
54. Kutlay M, Colak A, Simsek H, Ozturk E, Senol MG, Topuz K, et al. Use of ultrasonography in ulnar nerve entrapment surgery--a prospective study. Neurosurg Rev. 2009;32(2):225-32; discussion 32.
55. La Torre D, Raffa G, Pino MA, Fodale V, Rizzo V, Visalli C, et al. A Novel Diagnostic and Prognostic Tool for Simple Decompression of Ulnar Nerve in Cubital Tunnel Syndrome. World Neurosurg. 2018;118:e964-e73.
56. Yoon JS, Walker FO, Cartwright MS. Ulnar neuropathy with normal electrodiagnosis and abnormal nerve ultrasound. Arch Phys Med Rehabil. 2010;91(2):318-20.
57. Vucic S, Cordato DJ, Yiannikas C, Schwartz RS, Shnier RC. Utility of magnetic resonance imaging in diagnosing ulnar neuropathy at the elbow. Clin Neurophysiol. 2006;117(3):590-5.
58. Baumer P, Dombert T, Staub F, Kaestel T, Bartsch AJ, Heiland S, et al. Ulnar neuropathy at the elbow: MR neurography--nerve T2 signal increase and caliber. Radiology. 2011;260(1):199-206.
59. Dellon AL, Hament W, Gittelshon A. Nonoperative management of cubital tunnel syndrome: an 8-year prospective study. Neurology. 1993;43(9):1673-7.

60. Svernlov B, Larsson M, Rehn K, Adolfsson L. Conservative treatment of the cubital tunnel syndrome. J Hand Surg Eur Vol. 2009;34(2):201-7.
61. Shah CM, Calfee RP, Gelberman RH, Goldfarb CA. Outcomes of rigid night splinting and activity modification in the treatment of cubital tunnel syndrome. J Hand Surg Am. 2013;38(6):1125-30 e1.
62. vanVeen KE, Alblas KC, Alons IM, Kerklaan JP, Siegersma MC, Wesstein M, et al. Corticosteroid injection in patients with ulnar neuropathy at the elbow: A randomized, double-blind, placebo-controlled trial. Muscle Nerve. 2015;52(3):380-5.
63. Cho YJ, Cho SM, Sheen SH, Choi JH, Huh DH, Song JH. Simple decompression of the ulnar nerve for cubital tunnel syndrome. J Korean Neurosurg Soc. 2007;42(5):382-7.
64. Osei DA, Padegimas EM, Calfee RP, Gelberman RH. Outcomes following modified oblique medial epicondylectomy for treatment of cubital tunnel syndrome. J Hand Surg Am. 2013;38(2):336-43.
65. Byvaltsev VA, Stepanov IA, Kerimbayev TT. A systematic review and meta-analysis comparing open versus endoscopic in situ decompression for the treatment of cubital tunnel syndrome. Acta Neurol Belg. 2020;120(1):1-8.
66. Nabhan A, Ahlhelm F, Kelm J, Reith W, Schwerdtfeger K, Steudel WI. Simple decompression or subcutaneous anterior transposition of the ulnar nerve for cubital tunnel syndrome. The Journal of Hand Surgery British Volume. 2005;30(5):521-4.
67. Biggs M, Curtis JA. Randomized, prospective study comparing ulnar neurolysis in situ with sub-muscular transposition. Neurosurgery. 2006;58(2):296-304; discussion 296-304.
68. Toirac A, Giugale JM, Fowler JR. Open Versus Endoscopic Cubital Tunnel In Situ Decompression: A Systematic Review of Outcomes and Complications. Hand (N Y). 2017;12(3):229-35.
69. Efstathopoulos DG, Themistocleous GS, Papagelopoulos PJ, Chloros GD, Gerostathopoulos NE, Soucacos PN. Outcome of partial medial epicondylectomy for cubital tunnel syndrome. Clin Orthop Relat Res. 2006;444:134-9.
70. O'Grady EE, Vanat Q, Power DM, Tan S. A systematic review of medial epicondylectomy as a surgical treatment for cubital tunnel syndrome. J Hand Surg Eur Vol. 2017;42(9):941-5.
71. Sahin O, Haberal B, Sahin MS, Demirors H, Kuru I, Tuncay IC. Is simple decompression enough for the treatment of idiopathic cubital tunnel syndrome: A prospective comparative study analyzing the outcomes of simple decompression versus partial medial epicondylectomy. Jt Dis Relat Surg. 2020;31(3):523-31.
72. Said J, Van Nest D, Foltz C, Ilyas AM. Ulnar Nerve In Situ Decompression versus Transposition for Idiopathic Cubital Tunnel Syndrome: An Updated Meta-Analysis. J Hand Microsurg. 2019;11(1):18-27.

73. Bartels RH, Verhagen WI, van der Wilt GJ, Meulstee J, van Rossum LG, Grotenhuis JA. Prospective randomized controlled study comparing simple decompression versus anterior subcutaneous transposition for idiopathic neuropathy of the ulnar nerve at the elbow: Part 1. Neurosurgery. 2005;56(3):522-30; discussion -30.
74. Giöstad A, Nyman E. Patient Characteristics in Ulnar Nerve Compression at the Elbow at a Tertiary Referral Hospital and Predictive Factors for Outcomes of Simple Decompression versus Subcutaneous Transposition of the Ulnar Nerve. Hindawi BioMed Research International Volume. 2019:Article ID 5302462, 9 pages
75. Bartels RH, Termeer EH, van der Wilt GJ, van Rossum LG, Meulstee J, Verhagen WI, et al. Simple decompression or anterior subcutaneous transposition for ulnar neuropathy at the elbow: a cost-minimization analysis--Part 2. Neurosurgery. 2005;56(3):531-6; discussion -6.
76. Krogue JD, Aleem AW, Osei DA, Goldfarb CA, Calfee RP. Predictors of surgical revision after in situ decompression of the ulnar nerve. J Shoulder Elbow Surg. 2015;24(4):634-9.
77. Seradge H, Owen W. Cubital tunnel release with medial epicondylectomy factors influencing the outcome. J Hand Surg Am. 1998;23(3):483-91.
78. Gaspar MP, Kane PM, Putthiwara D, Jacoby SM, Osterman AL. Predicting Revision Following In Situ Ulnar Nerve Decompression for Patients With Idiopathic Cubital Tunnel Syndrome. J Hand Surg Am. 2016;41(3):427-35.
79. Filippi R, Charalampaki P, Reisch R, Koch D, Grunert P. Recurrent cubital tunnel syndrome. Etiology and treatment. Minim Invasive Neurosurg. 2001;44(4):197-201.
80. Vogel RB, Nossaman BC, Rayan GM. Revision anterior sub-muscular transposition of the ulnar nerve for failed subcutaneous transposition. Br J Plast Surg. 2004;57(4):311-6.
81. Camp CL, Ryan CB, Degen RM, Dines JS, Altchek DW, Werner BC. Risk factors for revision surgery following isolated ulnar nerve release at the cubital tunnel: a study of 25,977 cases. J Shoulder Elbow Surg. 2017;26(4):710-5.
82. Lauretti L, D'Alessandris QG, De Simone C, Legninda Sop FY, Remore LM, Izzo A, et al. Ulnar nerve entrapment at the elbow. A surgical series and a systematic review of the literature. J Clin Neurosci. 2017;46:99-108.
83. Macadam SA, Bezuhly M, Lefaivre KA. Outcomes measures used to assess results after surgery for cubital tunnel syndrome: a systematic review of the literature. J Hand Surg Am. 2009;34(8):1482-91 e5.
84. Rodrigues JN, Neblett C. How to use patient-reported outcome measures with other clinical measurements in clinical reports. J Hand Surg Eur Vol. 2018;43(9):1007-9.
85. Ebersole GC, Davidge K, Damiano M, Mackinnon SE. Validity and responsiveness of the DASH questionnaire as an outcome measure following ulnar nerve transposition for cubital tunnel syndrome. Plast Reconstr Surg. 2013;132(1):81e-90e.

86. Malay S, Group SUNS, Chung KC. The minimal clinically important difference after simple decompression for ulnar neuropathy at the elbow. J Hand Surg Am. 2013;38(4):652-9.

87. MacDermid JC, Grewal R. Development and validation of the patient-rated ulnar nerve evaluation. BMC Musculoskelet Disord. 2013;14:146.

88. Asch DA, Jedrziewski MK, Christakis NA. Response rates to mail surveys published in medical journals. J Clin Epidemiol. 1997;50(10):1129-36.

89. Schwartzenberger J, Presson A, Lyle A, O'Farrell A, Tyser AR. Remote Collection of Patient-Reported Outcomes Following Outpatient Hand Surgery: A Randomized Trial of Telephone, Mail, and E-Mail. J Hand Surg Am. 2017;42(9):693-9.

90. Dahlin E, Dahlin E, Andersson GS, Thomsen NO, Bjorkman A, Dahlin LB. Outcome of simple decompression of the compressed ulnar nerve at the elbow - influence of smoking, gender, and electrophysiologicalal findings. J Plast Surg Hand Surg. 2017;51(2):149-55.

91. Zimmerman M, Dahlin E, Thomsen NOB, Andersson GS, Bjorkman A, Dahlin LB. Outcome after carpal tunnel release: impact of factors related to metabolic syndrome. J Plast Surg Hand Surg. 2017;51(3):165-71.

92. Atroshi I, Gummesson C, Andersson B, Dahlgren E, Johansson A. The disabilities of the arm, shoulder and hand (DASH) outcome questionnaire: reliability and validity of the Swedish version evaluated in 176 patients. Acta Orthop Scand. 2000;71(6):613-8.

93. Arner M. Developing a national quality registry for hand surgery: challenges and opportunities. EFORT Open Rev. 2016;1(4):100-6.

94. The Swedish translated version of QuickDASH. Available from: http://www.dash.iwo.on.ca/assets/images/pdfs/OuickDASH_Swedish.pdf [2019-01-15]

95. Carlsson IKE, Åström M, Stihl K, Arner M. Psychometric evaluation of the eight-item HAKIR questionnaire for reporting Patient Reported Outcomes in the Swedish national healthcare quality registry for hand surgery. J Hand Therapy. 2021; In press.

96. HAKIR. Annual report 2016. Available from https://hakir.se/wp-content/uploads/2018/05/Årsrapport_2016_PRINT_LR.pdf.

97. Gudbjörnsdottir S, Svensson AM, Eliasson B, Eeg-Olofsson K, Samuelsson P, Linder E, et al. Årsrapport 2016 års resultat. Göteborg, Sweden; 2016.

98. Eliasson B, Gudbjornsdottir S. Diabetes care--improvement through measurement. Diabetes Res Clin Pract. 2014;106 Suppl 2:S291-4.

99. Williams N. Dash. Occup Med (Lond). 2014;64(1):67-8.

100. 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.

101. Beaton DE, Katz JN, Fossel AH, Wright JG, Tarasuk V, Bombardier C. Measuring the whole or the parts? Validity, reliability, and responsiveness of the Disabilities of the Arm,

Shoulder and Hand outcome measure in different regions of the upper extremity. J Hand Ther. 2001;14(2):128-46.

102. Giostad A, Nyman E. Patient Characteristics in Ulnar Nerve Compression at the Elbow at a Tertiary Referral Hospital and Predictive Factors for Outcomes of Simple Decompression versus Subcutaneous Transposition of the Ulnar Nerve. Biomed Res Int. 2019;2019:5302462.

103. Mintken PE, Glynn P, Cleland JA. Psychometric properties of the shortened disabilities of the Arm, Shoulder, and Hand Questionnaire (QuickDASH) and Numeric Pain Rating Scale in patients with shoulder pain. J Shoulder Elbow Surg. 2009;18(6):920-6.

104. Hunsaker FG, Cioffi DA, Amadio PC, Wright JG, Caughlin B. The American academy of orthopaedic surgeons outcomes instruments: normative values from the general population. J Bone Joint Surg Am. 2002;84-A(2):208-15.

105. Marks M, Rodrigues JN. Correct reporting and interpretation of clinical data. J Hand Surg Eur Vol. 2017;42(9):977-9.

106. Bernstein DN, Houck JR, Mahmood B, Hammert WC. Minimal Clinically Important Differences for PROMIS Physical Function, Upper Extremity, and Pain Interference in Carpal Tunnel Release Using Region- and Condition-Specific PROM Tools. J Hand Surg Am. 2019;44(8):635-40.

107. Beaton DE, Wright JG, Katz JN, Upper Extremity Collaborative G. Development of the QuickDASH: comparison of three item-reduction approaches. J Bone Joint Surg Am. 2005;87(5):1038-46.

108. Gervasio O, Gambardella G, Zaccone C, Branca D. Simple decompression versus anterior sub-muscular transposition of the ulnar nerve in severe cubital tunnel syndrome: a prospective randomized study. Neurosurgery. 2005;56(1):108-17; discussion 17.

109. Keiner D, Gaab MR, Schroeder HW, Oertel J. Comparison of the long-term results of anterior transposition of the ulnar nerve or simple decompression in the treatment of cubital tunnel syndrome--a prospective study. Acta Neurochir (Wien). 2009;151(4):311-5; discussion 6.

110. Mitsionis GI, Manoudis GN, Paschos NK, Korompilias AV, Beris AE. Comparative study of surgical treatment of ulnar nerve compression at the elbow. J Shoulder Elbow Surg. 2010;19(4):513-9.

111. Omejec G, Podnar S. Does ulnar nerve dislocation at the elbow cause neuropathy? Muscle Nerve. 2016;53(2):255-9.

112. Clark DM, Piscoya AS, Dunn JC, Nesti LJ. The impact of pre-existing ulnar nerve instability on the surgical treatment of cubital tunnel syndrome: a systematic review. J Shoulder Elbow Surg. 2020;29(11):2339-46.

113. Beekman R, Wokke JH, Schoemaker MC, Lee ML, Visser LH. Ulnar neuropathy at the elbow: follow-up and prognostic factors determining outcome. Neurology. 2004;63(9):1675-80.

114. Shi Q, MacDermid J, Grewal R, King GJ, Faber K, Miller TA. Predictors of functional outcome change 18 months after anterior ulnar nerve transposition. Arch Phys Med Rehabil. 2012;93(2):307-12.

115. Barrell K, Smith AG. Peripheral Neuropathy. Med Clin North Am. 2019;103(2):383-97.

116. Tseng CH, Liao CC, Kuo CM, Sung FC, Hsieh DP, Tsai CH. Medical and non-medical correlates of carpal tunnel syndrome in a Taiwan cohort of one million. Eur J Neurol. 2012;19(1):91-7.

117. Dahlin LB, Rix KR, Dahl VA, Dahl AB, Jensen JN, Cloetens P, et al. Three-dimensional architecture of human diabetic peripheral nerves revealed by X-ray phase contrast holographic nanotomography. Sci Rep. 2020;10(1):7592.

118. Rota E, Morelli N. Entrapment neuropathies in diabetes mellitus. World J Diabetes. 2016;7(17):342-53.

119. Vinik AI, Holland MT, Le Beau JM, Liuzzi FJ, Stansberry KB, Colen LB. Diabetic neuropathies. Diabetes Care. 1992;15(12):1926-75.

120. Kong L, Bai J, Yu K, Zhang B, Zhang J, Tian D. Predictors of surgical outcomes after in situ ulnar nerve decompression for cubital tunnel syndrome. Ther Clin Risk Manag. 2018;14:69-74.

121. Suzuki T, Iwamoto T, Shizu K, Suzuki K, Yamada H, Sato K. Predictors of postoperative outcomes of cubital tunnel syndrome treatments using multiple logistic regression analysis. J Orthop Sci. 2017;22(3):453-6.

122. Tong J, Dong Z, Xu B, Zhang C, Gu Y. Predictors of surgical outcomes for severe cubital tunnel syndrome: a review of 146 patients. Acta Neurochir (Wien). 2018;160(3):645-50.

123. Uzunkulaoglu A, Ikbali Afsar S, Karatas M. Association Between Gender, Body Mass Index, and Ulnar Nerve Entrapment at the Elbow: A Retrospective Study. J Clin Neurophysiol. 2016;33(6):545-8.

124. Ennis SL, Galea MP, O'Neal DN, Dodson MJ. Peripheral neuropathy in the hands of people with diabetes mellitus. Diabetes Res Clin Pract. 2016;119:23-31.

125. Aaberg ML, Burch DM, Hud ZR, Zacharias MP. Gender differences in the onset of diabetic neuropathy. J Diabetes Complications. 2008;22(2):83-7.

126. Thomsen NO, Englund E, Thrainsdottir S, Rosen I, Dahlin LB. Intraepidermal nerve fibre density at wrist level in diabetic and non-diabetic patients. Diabet Med. 2009;26(11):1120-6.

127. Li X, Galvin JW, Li C, Agrawal R, Curry EJ. The Impact of Socioeconomic Status on Outcomes in Orthopaedic Surgery. J Bone Joint Surg Am. 2020;102(5):428-44.

128. McNamara CL, Balaj M, Thomson KH, Eikemo TA, Solheim EF, Bambra C. The socioeconomic distribution of non-communicable diseases in Europe: findings from the

European Social Survey (2014) special module on the social determinants of health. Eur J Public Health. 2017;27(suppl_1):22-6.

129. Aleem AW, Krogue JD, Calfee RP. Outcomes of revision surgery for cubital tunnel syndrome. J Hand Surg Am. 2014;39(11):2141-9.

130. Caputo AE, Watson HK. Subcutaneous anterior transposition of the ulnar nerve for failed decompression of cubital tunnel syndrome. J Hand Surg Am. 2000;25(3):544-51.

131. Gabel GT, Amadio PC. Reoperation for failed decompression of the ulnar nerve in the region of the elbow. J Bone Joint Surg Am. 1990;72(2):213-9.

132. Yushan M, Abula A, Ren P, Alike Y, Chen E, Ma C, et al. Outcomes of revision neurolysis of the ulnar nerve and ulnar groove plasty for persistent and recurrent cubital tunnel syndrome-A retrospective study of 21 cases. Injury. 2020;51(2):329-33.

133. Nicot C, Cesari B, Saint-Cast Y, Raimbeau G, Rabarin F. Benefits of a collagen membrane for recurrent ulnar nerve entrapment at the elbow: A series of 40 cases. Hand Surg Rehabil. 2021;40(2):145-9.

134. Thomsen NO, Mojaddidi M, Malik RA, Dahlin LB. Reduced myelinated nerve fibre and endoneurial capillary densities in the forearm of diabetic and non-diabetic patients with carpal tunnel syndrome. Acta Neuropathol. 2009;118(6):785-91.

135. Mojaddidi MA, Ahmed MS, Ali R, Jeziorska M, Al-Sunni A, Thomsen NO, et al. Molecular and pathological studies in the posterior interosseous nerve of diabetic and non-diabetic patients with carpal tunnel syndrome. Diabetologia. 2014;57(8):1711-9.

136. Koziej M, Trybus M, Mydlowska A, Piatek K, Banach M, Holda M. Polish version of the Patient-Rated Ulnar Nerve Evaluation in preoperative patients: Translation and psychometric testing. J Hand Ther. 2019;32(1):86-92.

Appendix

The QuickDASH questionnaire. Swedish version.

☒ **Före operation**

HAKIR
HANDKIRURGISKT KVALITETSREGISTER

Personnummer (ååååmmdd-nnnn): ☐☐☐☐☐☐☐☐–☐☐☐☐

Datum för ifyllande av enkät (åååå-mm-dd): ☐☐☐☐-☐☐-☐☐

Hälsoenkät (arm/axel/hand) QuickDASH

Denna enkät berör Dina symtom och Din förmåga att utföra vissa aktiviteter. Svara på **varje fråga**, baserat på hur Du har mått **den senaste veckan**, genom att kryssa för ett svarsalternativ för varje fråga. Om det är någon aktivitet Du inte har utfört den senaste veckan får Du kryssa för det svar som Du bedömer **stämmer bäst** om Du hade utfört aktiviteten. Det har ingen betydelse vilken arm eller hand Du använder för att utföra aktiviteten. Svara baserat på Din förmåga oavsett hur Du utför uppgiften.

	Ingen svårighet	**Viss svårighet**	**Måttlig svårighet**	**Stor svårighet**	**Omöjligt att göra**
1. Öppna en ny burk eller hårt sittande lock	☐	☐	☐	☐	☐
2. Utföra tunga hushållssysslor (t ex tvätta golv, putsa fönster, hänga tvätt)	☐	☐	☐	☐	☐
3. Bära matkassar eller portfölj	☐	☐	☐	☐	☐
4. Tvätta Din rygg	☐	☐	☐	☐	☐
5. Använda en kniv för att skära upp maten	☐	☐	☐	☐	☐
6. Fritidsaktiviteter som tar upp viss kraft eller stöt genom arm, axel eller hand (t ex spela golf, använda hammare, spela tennis, skytte, bowling)	☐	☐	☐	☐	☐

7. Under **den senaste veckan**, i vilken utsträckning har Dina arm-, axel- eller handproblem stört Ditt vanliga umgänge med anhöriga, vänner, grannar eller andra?

☐ Inte alls ☐ Lite ☐ Måttligt ☐ Mycket ☐ Väldigt mycket

8. Under **den senaste veckan**, i vilken utsträckning har Dina arm-, axel- eller handproblem stört Ditt vanliga arbete eller andra dagliga aktiviteter?

☐ Inte alls ☐ Lite ☐ Måttligt ☐ Mycket ☐ Väldigt mycket

Ange svårighetsgraden på Dina symtom **den senaste veckan:**

	Ingen	**Lätt**	**Måttlig**	**Svår**	**Mycket svår**
9. Värk/smärta i arm, axel eller hand	☐	☐	☐	☐	☐
10. Stickningar (sockerdrickskänsla) i arm, axel eller hand	☐	☐	☐	☐	☐

11. Har Du haft svårt att sova, under **den senaste veckan**, på grund av värk/smärta i arm, axel eller hand?

☐ Inte alls ☐ Viss svårighet ☐ Måttlig svårighet ☐ Stor svårighet ☐ Mycket stor svårighet

Fylls i av personal

☐ **3 månader** ☐ **12 månader** ☐ **Annat** **(ange antal månader)** ☐☐

Personnummer (ååååmmdd-nnnn): ☐☐☐☐☐☐☐☐–☐☐☐☐

Datum för ifyllande av enkät (åååå-mm-dd): ☐☐☐☐-☐☐-☐☐

Hälsoenkät (arm/axel/hand) QuickDASH

Denna enkät berör Dina symtom och Din förmåga att utföra vissa aktiviteter. *Svara på* ***varje fråga****, baserat på hur* Du har mått **den senaste veckan**, genom att kryssa för ett svarsalternativ för varje fråga. Om det är någon aktivitet Du inte har utfört den senaste veckan får Du kryssa för det svar som Du bedömer **stämmer bäst** om Du hade utfört aktiviteten. Det har ingen betydelse vilken arm eller hand Du använder för att utföra aktiviteten. Svara baserat på Din förmåga oavsett hur Du utför uppgiften.

	Ingen svårighet	**Viss svårighet**	**Måttlig svårighet**	**Stor svårighet**	**Omöjligt att göra**
1. Öppna en ny burk eller hårt sittande lock	☐	☐	☐	☐	☐
2. Utföra tunga hushållssysslor (t ex tvätta golv, putsa fönster, hänga tvätt)	☐	☐	☐	☐	☐
3. Bära matkassar eller portfölj	☐	☐	☐	☐	☐
4. Tvätta Din rygg	☐	☐	☐	☐	☐
5. Använda en kniv för att skära upp maten	☐	☐	☐	☐	☐
6. Fritidsaktiviteter som tar upp viss kraft eller stöt genom arm, axel eller hand (t ex spela golf, använda hammare, spela tennis, skytte, bowling)	☐	☐	☐	☐	☐

7. Under **den senaste veckan**, i vilken utsträckning har Dina arm-, axel- eller handproblem stört Ditt vanliga umgänge med anhöriga, vänner, grannar eller andra?

☐ Inte alls ☐ Lite ☐ Måttligt ☐ Mycket ☐ Väldigt mycket

8. Under **den senaste veckan**, i vilken utsträckning har Dina arm-, axel- eller handproblem stört Ditt vanliga arbete eller andra dagliga aktiviteter?

☐ Inte alls ☐ Lite ☐ Måttligt ☐ Mycket ☐ Väldigt mycket

Ange svårighetsgraden på Dina symtom **den senaste veckan:**

	Ingen	**Lätt**	**Måttlig**	**Svår**	**Mycket svår**
9. Värk/smärta i arm, axel eller hand	☐	☐	☐	☐	☐
10. Stickningar (sockerdrickskänsla) i arm, axel eller hand	☐	☐	☐	☐	☐

11. Har Du haft svårt att sova, under **den senaste veckan**, på grund av värk/smärta i arm, axel eller hand?

☐ Inte alls ☐ Viss svårighet ☐ Måttlig svårighet ☐ Stor svårighet ☐ Mycket stor svårighet

The HQ-8 questionnaire from HAKIR

☒ **Före operation**

HAKIR
HANDKIRURGISKT KVALITETSREGISTER

Personnummer (ååååmmdd-nnnn): ☐☐☐☐☐☐☐☐–☐☐☐☐

PATIENTENKÄT (arm/hand) HAKIR-8 (HQ-8)

Namn (texta):

Postnummer (t ex 123 45):

Gatuadress:

Ort:

Datum för ifyllande av enkät (åååå-mm-dd) ☐☐☐☐-☐☐-☐☐

Jag är (ange den hand du skriver med): ☐ Vänsterhänt ☐ Högerhänt ☐ Tvåhänt

Arm/hand som ska opereras: ☐ Vänster ☐ Höger

Röker du?
- ☐ Aldrig varit rökare
- ☐ Före detta rökare
- ☐ Röker, ej dagligen
- ☐ Dagligrökare

Enkäten gäller de besvär som du har haft **den senaste veckan**, i den **arm/hand** som ska opereras. Om du ska opereras för en akut skada så är det viktigt att du anger de eventuella besvär som du hade före den aktuella skadan. Kryssa för det svarsalternativ som stämmer bäst överens med dina ev. besvär.

1. Smärta vid belastning

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

2. Smärta vid rörelser utan belastning

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

3. Vilovärk

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

4. Stelhet

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

5. Svaghet

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

6. Domningar/stickningar i fingrarna ("sockerdrickskänsla")

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

7. Köldkänslighet (obehag/besvär när du utsätts för kyla)

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

8. Förmåga att utföra dagliga aktiviteter

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

1/2 Vänd!

Version 11 (2021-08)

HAKIR
HANDKIRURGISKT KVALITETSREGISTER

Fylls i av personal
☐ **3 månader** ☐ **12 månader** ☐ **Annat** (ange antal månader) ☐☐

Personnummer (ååååmmdd-nnnn): ☐☐☐☐☐☐☐☐—☐☐☐☐

PATIENTENKÄT (arm/hand) HAKIR-8 (HQ-8)

Datum för ifyllande av enkät (åååå-mm-dd) ☐☐☐☐-☐☐-☐☐

Jag är (ange den hand du skriver med): ☐ Vänsterhänt ☐ Högerhänt ☐ Tvåhänt

Arm/hand som har opererats: ☐ Vänster ☐ Höger

Röker du?
☐ Aldrig varit rökare
☐ Före detta rökare
☐ Röker, ej dagligen
☐ Dagligrökare

Enkäten gäller de besvär du har haft **den senaste veckan,** i den **arm/hand** som har opererats. Kryssa för det svarsalternativ som stämmer bäst överens med dina ev. besvär.

1. Smärta vid belastning

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

2. Smärta vid rörelser utan belastning

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

3. Vilovärk

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

4. Stelhet

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

5. Svaghet

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

6. Domningar/stickningar i fingrarna (”sockerdrickskänsla”)

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

7. Köldkänslighet (obehag/besvär när du utsätts för kyla)

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

8. Förmåga att utföra dagliga aktiviteter

	0	10	20	30	40	50	60	70	80	90	100	
Inga problem	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Värsta tänkbara problem

9. Hur upplever Du resultatet av operationen?

	0	10	20	30	40	50	60	70	80	90	100	
☺ Helt nöjd	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Helt missnöjd ☹

10. Hur upplever Du bemötandet på kliniken under behandlingstiden?

	0	10	20	30	40	50	60	70	80	90	100	
☺ Helt nöjd	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Helt missnöjd ☹