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TREATMENT OF DISTAL RADIUS FRACTURES – CLINICAL OUTCOME, REGIONAL VARIATION AND HEALTH ECONOMICS

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Treatment of distal radius fractures – clinical outcome,
regional variation and health
economics

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my family

ABSTRACT

A distal radius fracture (DRF) remains the most common fracture encountered in health care. DRFs have traditionally been treated with a plaster or surgically with percutaneous methods. Since the end of the 20th century, when internal fixation with a volar locking plate (VLP) was introduced, the incidence of DRF surgery in general and of plating in particular have increased markedly. The change in practice took place despite the lack of evidence of the superiority of VLPs over percutaneous methods for adult patients and over non-operative treatment for elderly patients.

The aim of this thesis was to compare clinical outcome between treatment methods and to describe regional variation in surgical treatment of DRFs in Sweden.

Study I was a descriptive study using registry data from 22 378 individuals in the Swedish national patient registry from 2010 to 2013. There was a large variation in surgical treatment regimens for DRFs among the 21 health care regions, not explained by age or gender. Proportions of internal fixation varied from 41% to 95%, pin fixation varied from 2% to 44% and external fixation (EF) varied from 1% to 19%.

Study II and IV constituted a three-year follow-up of 118 and 113 patients respectively, 50-74 years old with an unstable dorsally displaced DRF, from a previously published randomized controlled trial of 140 patients, allocated to VLP or EF. Patient-reported outcome measures (PROMs) as well as grip-strength, range of motion, occurrence of osteoarthritis and complication rates presented in *Study II*, were similar in both groups. The VLP group displayed a higher mean total cost and less gained quality of life adjusted life-years (QALYs) compared with the EF group, indicating in *Study IV* that VLP is not cost-effective in comparison to EF.

Study III was a randomized controlled trial, allocating 140 patients, 70 years or older, with an unstable dorsally displaced DRF to VLP or non-operative treatment. At 12 months 119 patients were evaluated and PROMs, grip-strength, volar flexion and radiographs were significantly better for the VLP group. Complication rates were similar.

In conclusion, surgical treatment regimens for DRFs vary widely among health care regions in Sweden and when comparing treatment outcomes; for elderly patients VLP fixation seems to yield superior clinical results compared with non-operative treatment, but for patients aged 50-74 years, VLP fixation does not seem to yield superior clinical results and does not seem to be cost-effective as compared with EF in a three-year perspective.

LIST OF SCIENTIFIC PAPERS

The thesis is based on the following studies, which can be found at the end of this work and are indicated in the text by their Roman numerals (Studies I-IV):

I. Distal Radius Fractures – Regional Variation in Treatment Regimens

Saving J, Ponzer S, Enocson A, Mellstrand Navarro C

PLos One (13(11): e0207002; <https://doi.org/10.1371/journal.pone.0207702>

II. External Fixation versus Volar Locking Plate for Unstable Dorsally Displaced Distal Radius Fractures – A 3-year Follow-up of a Randomized Controlled Study

Saving J, Enocson A, Ponzer S, Mellstrand Navarro C

J Hand Surg Am 2018, doi: 10.1016/j.jhsa.2018.09.015

III. Non-operative Treatment versus Volar Locking Plate Fixation for Dorsally Displaced Distal Radius Fractures in the Elderly – A Randomized Controlled Trial

Saving J, Severin Wahlgren S, Olsson K, Enocson A, Ponzer S, Sköldenberg O, Wilcke M, Mellstrand Navarro C

Accepted for publication. J Bone Joint Surg Am.

IV. Volar Locking Plate versus External Fixation for Unstable Dorsally Displaced Distal Radius Fractures – A Cost-Effectiveness Analysis

Saving J, Heintz E, Enocson A, Järnbert-Pettersson H, Mellstrand Navarro C

In manuscript

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1 LIST OF ABBREVIATIONS

ASSH	American Society for Surgery of the Hand
CEAC	Cost-effectiveness acceptability curve
CI	Confidence interval
CRPS	Complex regional pain syndrome
CTS	Carpal tunnel syndrome
DASH	Disabilities of the arm, shoulder and hand
DDD	Daily defined dose
DH	Danderyd Hospital
DRF	Distal radius fracture
DRG	Diagnosis-related group
DRU	Distal radio-ulnar
EF	External fixation
EQ-5D	Euroqol-5 dimensions
FASS	Pharmaceutical Specialities in Sweden
ICD	International classification of diseases
ICER	Incremental cost-effectiveness ratio
IF	Internal fixation
HRQoL	Health-related quality of life
MCID	Minimal clinical important difference
NICE	National Institute for Health and Clinical Excellence
NOMESCO	Nordic Medico-Statistical Committee
NPR	National patient register
OA	Osteoarthritis
PA	Posteranterior
PDR	Prescribed drug register
PF	Pin fixation
PIN	Personal identification number
PROM	Patient-reported outcome measure
PRWE	Patient-rated wrist evaluation
QALYs	Quality-adjusted life-years
RCT	Randomised controlled trial
ROM	Range of motion
SCB	Statistics Sweden
SBU	Swedish Agency for Health Technology Assessment and Assessment of Social Services
SH	Södersjukhuset Hospital
WTP	Willingness to pay
VLP	Volar locking plate

2 INTRODUCTION

2.1 EPIDEMIOLOGY

A distal radius fracture (DRF) is the most common fracture to be treated in health care¹. The incidence is high among children but declines when individuals reach the age of puberty². For women it increases again from the age of 50 and for men from the age of 70, mainly due to osteopenia^{3,4} (Figure 1). Incidence for women and men over the age of 50 is 66-110 and 12-25 per 10 000 person-years, respectively⁵. The total incidence increased from the 1950s⁶ but has decreased since the turn of the century⁴.

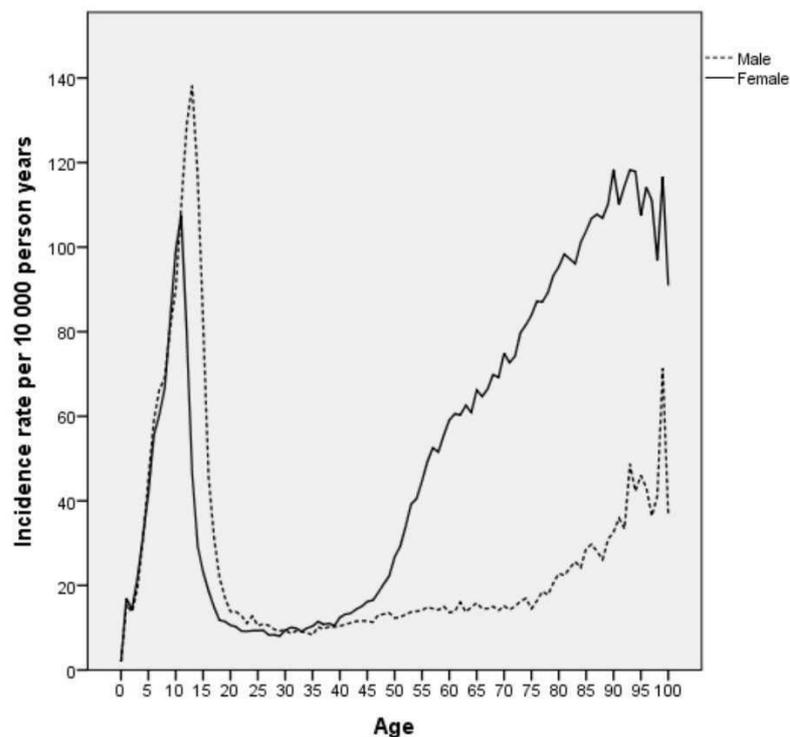


Figure 1. Incidence rates for DRFs in Sweden from 2005 to 2010³

2.2 ETIOLOGY

DRFs are caused by a combination of axial loading and bending forces through the carpus acting on the distal radius, commonly experienced when falling on an outstretched arm/hand.

Among young adults, the mechanism of injury is often high energy trauma, whereas among elderly persons with osteopenia the fractures are most often caused by low-energy trauma, such as a fall from a standing or walking position^{7,8}.

2.3 FRACTURE CLASSIFICATION

DRFs are traditionally divided into three main types; isolated intraarticular fracture with the rest of the metaphysis intact, i.e. Barton's fracture or Chauffeur's fracture, metaphyseal fracture with volar angulation of the distal fragment, i.e. Smith fracture, and metaphyseal fracture with dorsal angulation of the distal fragment, i.e. Colles' fracture, which constitutes the vast majority of all DRFs (Figure 2).



Figure 2. Radiograph of a dorsally displaced DRF (Colles' fracture), lateral and posteroanterior (PA) views

There are several classification systems for DRFs. For Colles' fractures, the Older classification⁹ is useful. It describes the degree of dorsal displacement of the distal fragment, the degree of radial shortening and the degree of comminution of the dorsal cortex close to the fracture, as predictors of fracture instability. A further development of the Older classification is the recently introduced Buttazoni classification¹⁰, which is simpler and includes comminution of the volar cortex as a predictor of instability. A commonly used classification is the universal AO/OTA system¹¹ which describes three main types of fractures: (A) extraarticular, (B) partial intraarticular and (C) complete intraarticular, with subgroups within each main type. Another common classification is the Frykman classification¹², which divides the DRFs into intra- or extraarticular fractures, with or without a concomitant fracture of the distal ulnae. The Fernandez classification¹³, which is based on the mechanisms of the injury, ranging from bending, shearing, compression, avulsion/fracture dislocation to combined/high velocity injury is also commonly used. However, all classification systems have more or less low intra- and interobserver reliability^{10,14,15}, which makes it difficult to choose a treatment strategy based on the fracture classifications.

2.4 TREATMENT METHODS

2.4.1 Non-operative treatment

Treatment with a cast or a splint is the oldest and most common treatment method¹⁶. It is applied dorso-radially from the distal third of the metacarpal bones to the proximal forearm and is maintained for four to five weeks. The method has few complications (limited to pressure/wounds from the cast/splint). If the fracture is displaced, casting is preceded by closed reduction under local, regional or general anaesthesia. For most fractures, non-operative treatment is sufficient¹⁶⁻¹⁸, but for unstable fractures a cast alone cannot prevent fracture re-displacement before healing, which renders malunion¹⁹.

In general, a malunited fracture results in an inferior clinical outcome^{20,21}. However, there are controversies whether this correlation exists for elderly patients²²⁻²⁹.

A fracture is considered unstable if it cannot be maintained in an adequate position in a cast until healing. Factors predicting DRF instability are high age, high degree of initial displacement and comminution of the cortex at the fracture site^{19,30-34}.

2.4.2 Surgical treatment

Surgical treatment aims to reduce unstable fractures and retain them in an adequate position until healing, thereby preventing malunion.

2.4.2.1 Pin fixation (PF)

During the 1960s, PF was introduced. It is a method where metal pins are inserted into the fractured bones to reduce and fix the fracture fragments³⁵ (Figure 3). Usually a cast is used as a complement to add further stability³⁶. The cast and the pins are removed when the fracture is healed. This method have been proven to yield good results, but may have worse outcomes in older patients with osteopenic bone, in which the pins can lose the grip and thereby be unable to retain the fracture reduction until healing occurs³⁷. Pins can also be used as a complement to other surgical treatment methods. Common complications to pinning are soft tissue infections at pin sites³⁸ and damage to nerves or tendons when inserting the pins³⁹.



Figure 3. Radiograph after pin fixation of a DRF, PA view

2.4.2.2 External fixation (EF)

Treatment with EF, a metal construction worn outside the arm and attached to the bone on each side of the fracture via pins through the skin, was introduced during the 1970s^{40,41} (Figure 4). Two threaded pins are inserted into the diaphysis of the radius, via either stab incisions or a longer dorsolateral incision, and two pins are inserted into the second metacarpal bone of the hand via stab incisions. Under fluoroscopic control, traction is then applied over the wrist and the fracture is reduced as the traction force is transferred to the distal fragment through ligamentotaxis^{42,43}. Traction is maintained by a metal rod attached to the pins by metal blocks. The EF device is subsequently removed after five to six weeks, usually at an outpatient clinic visit. EF is a simple and fast surgical method. Percutaneous pinning can be used to further add stability to the construct^{44,45}. A common complication is soft tissue infection at the pin sites^{46,47}, which sometimes needs treatment by oral antibiotics. Daily cleaning of the pin sites is recommended to reduce the risk of infection⁴². Injury to the cutaneous branch of the radial nerve can occur when inserting the proximal pins into the forearm⁴⁶. This can be avoided by doing larger incisions so that nerves can be identified and respected. Due to elongation of the radiocarpal ligaments and capsule, loss of reduction can occur during the fixation time^{48,49}. The treatment method can be perceived as negative by the patient due to the bulky construct of the EF device, and because movement of the wrist joint during the fixation time is prevented.



Figure 4. External fixation of a DRF (Copyright: Cecilia Mellstrand Navarro)

2.4.2.3 *Internal fixation (IF) with a dorsal plate*

During the 1990s, the method of using open reduction and IF with screws through a dorsally applied plate close to the bone was introduced^{31,50,51}. The plate prevents dorsal displacement of the distal fragment but can often, due to the tight anatomy on the dorsal aspect of the wrist, cause extensor tendon synovitis and/or rupture^{50,51}. An advantage of this method is the possibility of early motion of the wrist, which is considered favourable for rehabilitation. However, plating requires superior surgical skills compared with percutaneous methods.

2.4.2.4 *IF with a volar locking plate (VLP)*

At the end of the 20th century, plates with angle stable screws were introduced⁵², and they have provided good clinical and radiological results⁵³⁻⁵⁵. The construct enables volar placement of the plate, which reduces the tendon attrition problems associated with the dorsal plate^{56,57}, without the risk of loosening the screws and plate when the dorsal displacement forces on the distal fragment exceeds the screw attachment in the bone⁵⁸. The skin incision is made over the flexor carpi radialis tendon and the flexor tendons, the median nerve and the radial artery are held aside with retractors. The pronator quadratus muscle is detached from its radial attachment and the plate is placed under the muscle on the volar aspect of the radial bone (Figure 5).



Figure 5. Volar locking plate during surgery of a DRF (Copyright: Cecilia Mellstrand Navarro)

Volar, as well as dorsal, plating requires superior surgical skills compared with percutaneous methods. The strength of the angle stable construction requires a subchondral placement of the distal row of the screws⁵⁹ (Figure 6). Too proximal a placement of the plate and the screws can lead to a loss of the entire construct from the bone and subsequent fracture displacement⁶⁰. Improper placement of the plate or inadequate fracture reduction can cause damage or irritation to tendons and/or nerves due to impingement caused by the plate⁶¹. Screws that are too long and protrude on the dorsal aspect of the radial bone can impact extensor tendons and cause tenosynovitis, or even tendon rupture⁶².

Thus, common complications are tenosynovitis and symptoms from the median nerve due to the plate and screws^{39,63}, and plate extraction is performed in 15-30% of the patients⁶⁴⁻⁶⁶.

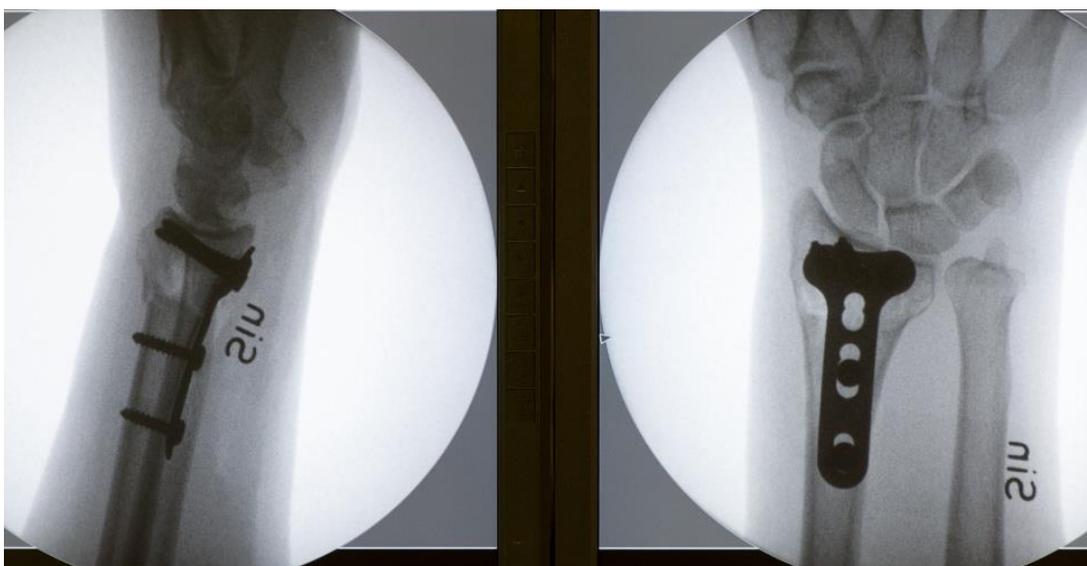


Figure 6. Radiographs after volar locking plate fixation of a DRF, lateral and PA views

2.4.3 General complications

Complex regional pain syndrome (CRPS) is a condition that presents with abnormal pain, swelling, hyper-sensibility, increased or decreased hydration and/or skin temperature after an injury¹². The pathogenesis is unclear. The risk of CRPS in the hand after a DRF is reduced by short surgical time, restricted use of a tourniquet, sufficient pain relief and accurate occupational therapy⁶⁷.

Carpal tunnel syndrome (CTS) is caused by impingement of the median nerve by sharp fracture edges, callus formation, hematoma or a volar plate. The risk is reduced by adequate fracture reduction/retainment and adequate placement of an eventual volar plate.

Rupture of the extensor pollicis longus tendon in the third dorsal tendon compartment can occur even after a non-displaced DRF⁶⁸. The pathogenesis is unclear.

2.4.4 Treatment decisions

There has been a shift in surgical treatment choices over the last 15 years, in Sweden^{3,4} as well as in other countries⁶⁹⁻⁷¹, from predominantly percutaneous methods to IF with a volar plate. This shift has taken place despite the lack of evidence for the superiority of plate fixation versus EF or PF. In a meta-analysis from 2005 based on 46 studies, the authors concluded that there was no evidence that VLP was better than EF for unstable DRFs regarding functional outcome⁷². Since then, many studies have been conducted that compared VLP with EF or PF. The results are diverse, and there is still no consensus regarding which method renders the best functional outcome⁷³⁻⁷⁶. However, many studies imply that there is an advantage for VLP in the early recovery period, up to three months, but not thereafter^{74,77}.

The total rate of complications is similar for the different surgical methods, but for percutaneous methods they generally occur early, such as fracture displacement requiring IF or minor complications such as pin site infections, whilst VLPs render more late secondary surgeries, such as plate extractions and tendon reconstructions^{74,78-81}.

Few studies compare results beyond one year after surgery. Since VLPs seem to be associated with secondary surgeries up to seven years after primary surgery, long term results are of value⁷⁹⁻⁸³.

2.5 MEASURING OUTCOMES

2.5.1 Objective measures

2.5.1.1 Range of motion (ROM)

ROM of the wrist is measured as degrees of dorsal extension, volar flexion, pronation, supination, radial deviation and ulnar deviation. There is a variation in ROM with respect to gender and age⁸⁴ and it can therefore be measured as a percentage of the contralateral side. Most normal activities do not require full ROM⁸⁵.

2.5.1.2 Grip strength

Grip strength is measured in kilograms or kilopascals, using a Martin vigorimeter (a ball) or a Jamar dynamometer (two handles). It is often reported as the mean of three attempts with maximal force. Grip strength varies with gender and age and it can therefore be expressed as a percentage of the contralateral side⁸⁶. Both instruments are valid for pathologic conditions of the wrist⁸⁷. A Martin vigorimeter is easier for elderly bedridden patients to use⁸⁸. The minimal clinically important difference (MCID) is considered to be 19.5% of the contralateral side, or six kilograms⁸⁹. In right-handed people the dominant hand is considered 10% stronger than the non-dominant hand, but in left-handed people both hands are considered equally strong⁹⁰.

2.5.1.3 Radiographs

Standard projections are PA and lateral. In the PA projection, the length of the radius is measured at its ulnar corner in relation to the distal end of the ulna at its radial corner. The radial length is normally -1 to +2 mm in relation to the ulna. When a fracture of the distal radius occurs, there is normally a shortening of the radius, which is measured in millimetres. The inclination of the articular surface of the radius in relation to the perpendicular plane of the vertical axis of the radius is also measured. It is normally 19-24 degrees⁹¹ and it often decreases when a fracture occurs. In the lateral projection, the articular surface of the radius in relation to the perpendicular plane of the vertical axis of the radius is measured. It normally has a volar angle of 10-12 degrees. In a Colles' fracture, a dorsal angulation occurs. A Colles' fracture is considered minimally displaced if the radius is shortened less than three mm and the dorsal angulation is less than 15 degrees⁹². Posttraumatic osteoarthritis (OA) in the radiocarpal joint can be measured and graded according to Knirk and Jupiter⁹³ on a scale of 0-3, where 0 is no loss of joint space, and 3 is a total loss of joint space.

2.5.2 Patient-reported outcome measures (PROMs)

For conditions in the musculoskeletal system, PROMs are suitable for measuring pain and functional impairment in daily life.

2.5.2.1 Organ-specific protocols

The Patient-Rated Wrist Evaluation (PRWE) score is a protocol designed and validated for wrist fractures^{94,95}, which is also translated to and validated in Swedish⁹⁶. Five questions

regarding pain and ten questions regarding function in daily life are answered on a scale of 0-10 points, where 0 represents no pain/discomfort and 10 represents maximum pain/discomfort. The sum of the questions regarding function is divided by two and is then added to the sum of the questions regarding pain. The total score ranges from 0-100 points, where 0 represents no pain/discomfort in daily life. The MCID is considered to be 6-14 points^{97,98}.

The Disabilities of the Arm, Shoulder and Hand (DASH) score is a protocol designed and validated for measuring function in the upper extremity⁹⁹. It has been translated to and validated in Swedish¹⁰⁰. It consists of 30 questions on a scale of 1-5 regarding daily activities, where 1 represents no disabilities. Thirty is subtracted from the total sum, and the remaining sum is then divided by 1.2. The total score ranges from 0-100 points and 0 represents no disabilities/no pain in daily life. The MCID is considered to be 10 points¹⁰¹.

The Green O'Brien score¹⁰² was often used before the introduction of DASH and PRWE. It combines patient-reported pain and disabilities during daily activities with radiographs and ROM and renders a result within a four-grade score (excellent – good – fair – poor).

There are also several other commonly used outcome protocols, for example the Gartland and Werely score¹⁰³, the Mayo wrist score and the Michigan hand outcome score, but they are not reliable and valid for DRFs¹⁰⁴.

2.5.2.2 *Health-related quality of life (HRQoL) instruments*

To compare a broad spectrum of injuries and conditions, HRQoL-instruments are used as complements to organ-specific protocols.

The EuroQol 5 Dimensions (EQ-5D) index score is such an instrument^{105,106}. It consists of five questions where the responders classify their disabilities regarding mobility, self-care, usual activities, pain/discomfort and anxiety/depression at three levels; no problem, some problems or major problems. The combination of the answers leads to a five-digit health profile which is converted into a utility score using tariff values from a standard UK population¹⁰⁷. A value of 0.00 indicates the worst possible state of health, and a value of 1.00 indicates the best possible state of health. The score is translated into Swedish and is valid for DRFs¹⁰⁸. The MCID is considered to be 0.074 units¹⁰⁹.

The EQ-5D index score can be used as an HRQoL component when calculating quality-adjusted life years (QALYs), a measure used in cost-effectiveness analyses of healthcare treatments. QALYs constitute a composite of a state of HRQoL and the time in years spent in the state¹¹⁰. Thus, one QALY represents one year of perfect health.

2.6 ELDERLY PATIENTS

For elderly patients, the incidence of volar plating has increased to the detriment of non-operative treatment¹¹¹. When a person becomes elderly is not clearly defined but a commonly accepted age is 65 years¹¹². At that age many people retire and the demands on function decreases.

The association between a malunited DRF and an impaired function has not been proven in elderly patients, as it has been in younger patients²²⁻²⁹.

Surgical treatment of unstable fractures among the elderly has not proven superior to non-operative treatment regarding functional outcome^{64,113-116}. However, among an active and slightly younger population (61-80 years), one study has shown a better functional outcome after volar plating compared with non-surgical treatment¹¹⁷. Today's elderly individuals live a more active life than in the past, and up-to-date trials designed for this population are largely lacking.

Age is the single strongest predictor for instability in a DRF¹¹⁸, and unstable fractures among elderly patients tend to displace beyond the first two weeks¹⁹. Therefore, a radiologic examination up to two weeks to detect instability is not useful for elderly patients. In addition, for the oldest patients, closed reduction is of limited benefit as the fractures often re-displace to the initial position before healing¹¹⁹.

2.7 HEALTH ECONOMIC ASPECTS

In a setting with limited healthcare resources it is valuable to investigate health economic aspects of different treatment options. Because of the high incidence of DRFs and a growing preference for surgical treatments, in combination with the lack of evidence of the superiority of either surgical treatment method, there is a strong incentive to perform health economic evaluations of treatment options.

American studies based on costs for insurance reimbursements found that costs were twice as high for EF and almost three times as high for VLP, compared with non-operative treatment¹²⁰⁻¹²².

British studies have shown that VLP treatment is not cost-effective compared with PF up to one year after treatment of a DRF^{123,124}.

To the best of our knowledge, health economic assessments of surgery with VLP compared with EF for DRFs are lacking, and no study has investigated the cost-effectiveness of DRF surgery beyond a one-year perspective.

2.8 REGIONAL VARIATION

Studies in the US^{69,125,126} and in the Netherlands¹²⁷ found large regional variation in the incidence of treatment methods for DRFs. After adjusting for factors that possibly influence the choice of surgical method, such as proportion of hand surgeons, academic level of the clinic, age, gender and race, the region remained as a strong predictor for the choice of treatment¹²⁵.

Regional differences regarding treatment of ankle fractures, for which a consensus for treatment is also lacking, displayed the same pattern¹²⁸. Furthermore, for hip fractures for which there is a convincing consensus, regional differences have been reported to be small¹²⁹.

Possible explanations for these variations are: a large interest in novel techniques, access to subspecialists, local traditions and personal preferences of the surgeon¹²⁹.

Within areas where cost-effectiveness differs markedly among the different treatment options, there are good reasons to discourage regional variations by establishing clear guidelines and presenting information to patients and professionals¹³⁰.

As there are indications that VLP is not cost-effective compared with percutaneous methods^{120-122,124}, and as health care resources are limited, there is a need to investigate regional differences in Sweden and similar countries regarding surgical treatment of DRFs.

2.9 SWEDISH NATIONAL HEALTHCARE REGISTERS

The unique Swedish personal identification number (PIN) was introduced in 1947 and is used in all healthcare registers and all patient records.

The Swedish National Patient Register (NPR), maintained by the National Board of Health and Welfare, contains all inpatient and outpatient care, excluding primary healthcare. Data include patient data (PIN, gender, place of residence), caregiver's data (a code from which department, hospital, city and healthcare region can be derived), date of admission and discharge, and medical data including diagnoses according to the 10th version of the International Classification of Diseases (ICD) and surgical procedures according to the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures¹³¹. The accuracy of the data in the NPR has been approximated to be 90%¹³².

The Swedish Prescribed Drug Register (PDR)¹³³, maintained by the National Board of Health and Welfare, includes information on all drug prescriptions. Data include patient data (PIN), drug data (name of drug and type of drug (a generic code), dose, quantity and number of daily defined doses (DDD)) and prescriber data.

3 AIMS OF THE THESIS

The overall aim of this thesis was to compare outcomes between treatment methods and to describe regional variation in surgical treatment of DRFs in Sweden.

The specific aims of the individual studies were as follows:

Study I: To determine if the choice of surgical methods for treatment of DRFs differs among health care regions in Sweden.

Study II: To compare VLP fixation with EF three years after surgical treatment of patients aged 50-74 years with an unstable dorsally displaced DRF.

Study III: To compare VLP fixation with non-operative treatment in patients aged 70 years or older with an unstable dorsally displaced DRF.

Study IV: To assess the cost-effectiveness of VLP fixation compared with EF three years after surgical treatment of patients aged 50-74 years with an unstable dorsally displaced DRF.

4 PATIENTS AND METHODS

4.1 STUDY I

This was a registry study based on records from the NPR. All adult patients recorded with a DRF and a simultaneous code for surgical fracture treatment of the hand or forearm from 2010 to 2013 were included. Register variables included gender, age, type of surgical procedure and geographic location for the treatment according to the unique code for each of the 21 healthcare regions in Sweden.

Treatments were divided into four groups: IF (volar, radial, dorsal or combined plating), PF, EF or other treatments or combinations of methods (Other).

The total number and proportion (number in each group divided by the total number of operations) for each surgical treatment group was calculated for all regions together, and for each region separately.

Incidence rates were calculated as the number of surgeries divided by the population in each region each year on November 1st according to Statistics Sweden (SCB) (www.scb.se).

4.2 STUDY II

4.2.1 Patients

This was a three-year follow-up of a previously published randomized controlled trial⁸⁰ in which patients treated at Södersjukhuset Hospital, Stockholm, Sweden, from September 2009 to February 2013 for a DRF were included.

Inclusion criteria were 50-74 years of age for women and 60-74 years for men, fall from a standing height, wrist radiographs with >20 degrees of dorsal angulation in the lateral view and/or >5 mm of radial shortening in the PA view, fracture diagnosed within 72 hours of injury, adequate knowledge of written and spoken Swedish language and residency within the catchment area of the hospital. Exclusion criteria were former disability of either wrist, severe joint disorder, concomitant injuries, cognitive dysfunction (Pfeiffer¹³⁴ score <5), drug or alcohol abuse, psychiatric disorder, dependency in activities of daily life or a medical disorder preventing use of general anaesthesia.

4.2.2 Interventions

One hundred and forty patients were, after giving written consent, allocated to either VLP fixation (n = 70) or EF with or without additional pinning (n = 70). At the end-point after one year, 134 patients (EF n = 65, VLP n = 69) remained in the study. The early results have been reported previously and displayed no relevant differences after six weeks up to one year⁸⁰.

Before three years from surgery had passed, these 134 patients were contacted by telephone or mail and asked to participate in a three-year follow-up study.

4.2.3 Outcome measures

DASH score was the primary outcome. PRWE score, EQ-5D index score, grip strength, ROM, radiological signs of OA and complications were secondary outcomes. An occupational therapist investigated grip strength (using a Martin vigorimeter) and ROM in the injured and uninjured extremity and results were presented as percentage of the uninjured side. A radiologist investigated radiographs for signs of OA. For detection of complications, patients were examined and interviewed, and patient records were reviewed. Any complication remaining at the three-year follow-up and all reoperations (except for removal of the external fixator) were reported.

4.3 STUDY III

4.3.1 Patients

The study was a fusion of two separate prospective randomized controlled studies at Södersjukhuset Hospital (SH) and Danderyd Hospital (DH) in Stockholm, Sweden. The study population consisted of patients aged 70 years or older admitted to SH from April 2013 to February 2017 (n = 76) or to DH from December 2009 to January 2017 (n = 64), with an unstable dorsally displaced DRF. The studies were fused in December 2016 to reach the estimated sample size in an acceptable time period. Inclusion and exclusion criteria are presented in Table 1.

Table 1. Inclusion and exclusion criteria in a randomized controlled study comparing non-operative treatment with VLP fixation in patients 70 years or older, with a dorsally displaced DRF.

Inclusion criteria

- Patient age ≥ 75 years (from September 2015 ≥ 70 years at SH*)
- Wrist radiography with ≥ 20 degrees dorsal tilt (and/or ≥ 4 mm axial shortening at DH**)

Exclusion criteria

- Former disability of either wrist
- High-energy trauma (SH*)
- Associated ulna fracture proximal to the ulnar styloid
- Injury to the ipsilateral upper extremity
- Rheumatoid arthritis or other severe joint disorder
- Dementia or Pfeiffer score < 5 at SH* and < 8 at DH**
- Drug/alcohol abuse or psychiatric disorder
- Dependency in activities of daily living
- Patient not resident within the catchment area of the two centres
- Fracture diagnosed > 3 days from injury at SH* and > 6 days at DH**
- Patient not fit for surgery/ASA class 4

*Sodersjukhuset Hospital

**Danderyd Hospital

4.3.2 Interventions

All patients underwent closed reduction and immobilization in a dorsal or dorsoradial short-arm plaster splint in the emergency room. After written consent, patients were randomized to surgical treatment with a VLP or to non-operative treatment with continuation in the plaster splint. Surgery with VLP was performed within 14 days of the fracture date with a standard volar Henry's approach under fluoroscopic control. The wrist was then immobilized in a dorsal plaster splint for two weeks. For the non-operative treatment group, the plaster splint from the emergency department was maintained for four to five weeks. Thereafter all patients were referred to an occupational therapist. Follow-up took place at four to five weeks, three months and one year after initial treatment. At DH the three-month follow-up ceased in November 2011. Therefore, data were available for only 93 patients at three months.

4.3.3 Outcome measures

PRWE score was the primary outcome at SH and a secondary outcome at DH. DASH score was the primary outcome at DH and a secondary outcome at SH. Other secondary outcomes at both sites were EQ-5D index score, grip strength, ROM, radiological parameters and complications. Grip strength and ROM were evaluated by an occupational therapist at each site. A 10% adjustment for hand dominance was performed for right-handed individuals as suggested by Crosby et al⁹⁰. All radiographs were evaluated by a radiologist at DH. Patients were interviewed and examined for complications and patients' records were reviewed. Life-threatening events or complications requiring surgical intervention were considered major complications. All other complications were considered minor.

4.4 STUDY IV

4.4.1 Patients

This study was a cost-effectiveness analysis based on the same patient cohort as in Study II. Of the 140 patients, 50-74 years old, with an unstable dorsally displaced DRF randomized to VLP or EF, 118 were available three years after the surgery.

4.4.2 Methods

The primary outcome was the incremental cost effectiveness ratio (ICER) for VLP compared with EF. The ICER was defined as the difference in mean total cost per patient divided by the difference in mean QALY per patient, expressed as the incremental cost per gained year of full health for VLP compared with EF. If the mean difference in total cost was positive and the mean difference in QALYs was negative (i.e. VLP cost more but gained less QALYs), no ICER was calculated, as VLP was then dominated by EF. If the mean difference in total cost was negative and the mean difference in QALYs was positive, no ICER was calculated, as VLP was then dominating EF.

Total cost per patient was calculated by combining resource use with resource unit costs and summing up indirect costs (i.e. sick leave) and direct costs (all other costs) up to one and three years after surgery, respectively. Only participants with complete data were analysed.

4.4.2.1 Resource use

All resources needed for each treatment method were identified by the research group. Resource use data of surgical time for the primary surgery were derived from prospectively inserted data in the surgery software system (Orbit) used at SH. Inpatient and outpatient visits were retrieved from the NPR. Drug usage (number of DDDs prescribed for antibiotics and analgesics) was collected from the PDR. Data regarding sick leave were collected from the Swedish Social Insurance Agency. Any reoperations were detected by searches of patient records and/or registry data from the NPR regarding surgical procedures related to any possible related complication. Estimations of resource use were performed by the study group for

occupational therapy and X-rays since no complete registry or study protocol source was available. The time frame for all resource use was set from the date of the injury to the date for the three-year follow-up.

4.4.2.2 Unit costs

Unit costs for the operating theatre, including staff, were derived from the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU)¹³⁵. Costs regarding in- and outpatient care including emergency ward visits were collected from the diagnosis-related group (DRG) financial reimbursement system used at SH. Costs for drug usage were calculated from prices defined in Pharmaceutical Specialities in Sweden (FASS), a compilation from the pharmaceutical industry with information about drugs used in Sweden, for one DDD as defined in the PDR. Unit costs for reoperations were calculated based on the study group's opinion regarding surgical time and material usage. The unit cost regarding production loss per day (sick leave) was derived from SCB, using the mean income for adults 20-74 years of age plus taxes and social service fees. All costs were presented in euros converted from Swedish krona (SEK) using an exchange rate of 0.0978.

4.4.2.3 Effectiveness

Effectiveness of treatment was defined as QALYs as calculated from prospectively collected data of EQ-5D index score reported by trial participants at baseline and at two weeks, six weeks, three months, one year and three years postoperatively. Individual QALYs for each time interval were calculated by taking the average EQ-5D index score at two adjacent time points multiplied with the time in years spent in each time interval. Total QALYs gained at one and three years were then calculated on an individual level using the area under the curve approach. In clinical trials EQ-5D index score at baseline is invariably imbalanced between trial arms even if not statistically significant. In cost-effectiveness analyses the difference needs to be adjusted for, as it will be conducted throughout the entire follow-up period and contribute to QALYs not as an effect of treatment¹³⁶. Therefore, the difference in mean QALYs between VLP and EF was adjusted for EQ-5D index score at baseline.

5 STATISTICAL METHODS

Data in all studies were analysed using SPSS version 23 or 24 (IBM, Armonk, NY USA).

5.1 STUDY I

As the study population consisted of the entire Swedish population (a descriptive study), no p-values or confidence intervals were needed for proportions of surgical treatments. Nevertheless, a multinomial logistic regression was performed controlling for age over 60 years and gender, choosing the region using IF most frequently as the reference. Significance was set at $p < 0.05$ in two-sided tests.

5.2 STUDIES II-IV

Normality was tested with the Shapiro-Wilks test for numerical variables. Student's t-test was used for normally distributed variables, and Mann-Whitney U test for variables with skewed distributions. Chi-square test or Fisher's exact test was used for comparisons of categorical variables. The level of significance was set at $p < 0.05$ in two-sided tests. In Study II linear regression was performed to detect any correlation between radiographic signs of OA and inferior DASH score.

In Study IV, multiple linear regression was used to adjust the mean difference in QALYs at one and three years for imbalance between groups in EQ-5D index score at baseline¹³⁶. Non-parametric bootstrapping¹³⁷ was used to determine the level of sampling uncertainty around the ICER. The bootstrap was performed as a resampling from the original sample, with replacement of each individual picked, to select 58 individuals from the VLP group and 55 individuals from the EF group in each sample (i.e. one individual could be picked several times in each sample). To adjust for baseline differences in EQ-5D index scores between groups¹³⁶, we calculated the adjusted differential QALYs (VLP = intervention, EF = control) in each sample. One thousand samples were generated, rendering 1 000 estimates of mean incremental cost and effect pairs. The bootstrap was presented on an incremental cost-effectiveness plane¹³⁷. This illustrated the uncertainty surrounding the estimates of expected incremental costs and QALYs associated with VLP compared with EF. From the bootstrap cost-effectiveness acceptability curves (CEACs) were derived to summarize the uncertainty in the scatterplots, i.e. express the probability that VLP is cost-effective in comparison with EF for a range of thresholds for willingness to pay (WTP) per gained QALY¹³⁷. A threshold of 35 000 euros was chosen as the maximum WTP per gained QALY, which approximates the 30 000 UK pounds sterling, considered a threshold for DRF treatment recommended by the National Institute for Health and Clinical Excellence (NICE) in Great Britain¹³⁸.

6 RESULTS

6.1 STUDY I

A total of 22 378 individuals were identified with a surgically treated DRF from 1 January 2010 to 31 December 2013. The proportions of surgical methods were: IF 72%, PF 15%, EF 10% and Other 3%. Among the 21 health care regions, the incidence rate of surgical treatment varied from 4.2 to 9.2 per 10 000 person-years. The proportion of IF varied from 41% to 95%, PF varied from 2.3% to 44% and EF varied from 0.6 to 19%. Differences were significant in all but six comparisons when controlled for gender and age. The regions with the highest IF frequencies were situated in the south of Sweden and regions reporting the lowest IF frequencies were, mainly situated in the northern parts of Sweden (Figure 7).

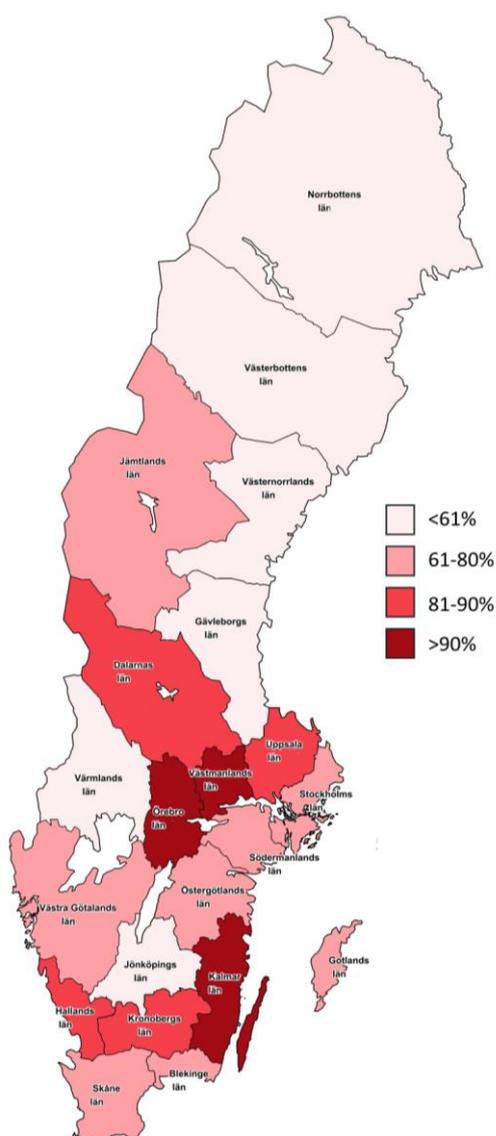


Figure 7. Proportions of internal fixation in surgically treated DRFs for each health care region in Sweden from 2010 to 2013

6.2 STUDY II

Of the 134 patients available for the one-year follow-up, 118 agreed to participate in the three-year follow-up (EF n = 56, VLP n = 62) and completed the PROM questionnaires. Three patients in each group did not take part in the clinical and radiological evaluations.

There were no clinically or statistically significant differences in PROMs, grip strength or ROM between groups (Table 2).

Table 2. Clinical results in patients aged 50-74 years, treated for an unstable dorsally displaced DRF with EF or VLP, available at the three-year follow-up

	EF (n=56)	VLP (n=62)	Mean Difference	95% CI
Mean DASH (SD)	7.0 (9.9)	5.4 (7.1)	1.6	-1.6 to 4.8
Mean PRWE (SD)	6.6 (12.0)	6.1 (9.2)	0.5	-3.4 to 4.4
Mean EQ-5D (SD)	0.92 (0.13)	0.92 (0.13)	0.00	-0.04 to 0.05
Mean grip strength as % of uninjured wrist (SD)	90 (16)	102 (59)	12	-4.5 to 28.7
Mean dorsal extension as % of uninjured wrist (SD)	94 (12)	97 (14)	3	-2.5 to 7.5
Mean volar flexion as % of uninjured wrist (SD)	89 (10)	93 (14)	4	-1.0 to 8.5
Mean radial deviation as % of uninjured wrist (SD)	94 (11)	100 (13)	6	0.9 to 10.0
Mean ulnar deviation as % of uninjured wrist (SD)	102 (15)	99 (13)	3	-2.6 to 7.9
Mean supination as % of uninjured wrist (SD)	96 (8)	95 (11)	1	-3.0 to 4.0
Mean pronation as % of uninjured wrist (SD)	100 (8)	99 (7)	1	-1.6 to 4.1

SD = Standard Deviation

There were radiographic signs of OA in 28% (15/53) of the EF patients and in 42% (25/59) of the VLP patients. There was no correlation between signs of OA and inferior DASH score. Reoperations were performed in 14% (8/56) of the EF patients and in 21% (13/62) of the VLP patients. The plate was removed in 11 of 62 patients in the VLP group. Five of these occurred later than one year after primary surgery. In the EF group, scar adherence was present in 60% (32/53) of the patients compared with 8% (5/59) in the VLP group, and minor nerve symptoms in 8% (4/53) of EF patients compared with 3% (2/59) in the VLP patients. The differences in signs of OA and complications were not statistically significant.

6.3 STUDY III

One hundred and forty patients were included in the study (VLP n = 68, non-operative n = 72). At three months 122 patients were still in the study (VLP n = 58, non-operative n = 64) and at one year 119 patients remained (VLP n = 56, non-operative n = 63). In the non-operatively treated group, there were 88% women (56/64) and the median age was 78 years (range 70-98). In the VLP group there were 95% women (55/58) and the median age was 80 years (range 70-90). The differences were not statistically significant. The dominant hand was injured in 36% of the non-operative patients compared with 47% in the VLP group ($p = 0.234$). The distribution of fracture types was similar in both groups.

PRWE, DASH, grip strength and volar flexion were statistically significantly better for the VLP group compared with the non-operative group at three and twelve months (Table 3). The differences for PRWE and DASH reached the MCID levels, but grip strength did not (MCID for volar flexion was not defined). Most other measurements were equal (Table 3). All radiographic measurements were better for the VLP group than for the non-operative group at three and twelve months (Table 4).

There were seven patients (11%) with major complications in the non-operative group compared with eight patients (14%) in the VLP group ($p=0.606$). Three of the non-operatively treated patients had a carpal tunnel release, but severe wrist pain persisted and after six months a corrective osteotomy was performed. Two patients in the non-operative group were cross-overs; one developed a severe carpal tunnel syndrome (CTS) the day after initial treatment and was treated with carpal tunnel release and VLP fixation, and one had a complete dorsal dislocation of the distal fracture fragment and carpus two weeks after initial treatment and was then treated with open reduction and VLP fixation. Minor complications occurred in seven patients (11%) in the non-operative group compared with eleven patients (20%) in the VLP group ($p = 0.197$).

Table 3. Clinical outcomes in patents aged 70 years or older, treated for an unstable dorsally displaced DRF with non-operative treatment or VLP fixation

	Non-operative (n=63)	Volar Locking Plate (n=56)	P-value*
3 months			
PRWE score	34.2 (21.3), 35.5 (36.8)	20.6 (20.3), 10.3 (29.8)	0.002
DASH score	30.2 (19.2), 29.2 (31.1)	21.2 (19.3), 14.4 (23.3)	0.016
EQ-5D score	0.758 (0.200), 0.796 (0.100)	0.805 (0.184), 0.796 (0.280)	0.306
Extension, degrees	50 (11), 50 (15)	47 (11), 50 (15)	0.111
Flexion, degrees	46 (15), 45 (23)	57 (15), 60 (20)	<0.001
Supination, degrees	90 (17), 95 (22)	95 (15), 92 (5)	0.485
Pronation, degrees	82 (11), 82 (16)	86 (8), 90 (5)	0.007
Ulnar deviation, degrees	24 (6), 24 (8)	25 (7), 25 (10)	0.254
Radial deviation, degrees	20 (6), 20 (10)	21 (5), 20 (5)	0.371
Grip strength, %	52.3 (29.3), 53.9 (30.0)	72.4 (18.6), 71.0 (23.0)	<0.001
12 months			
PRWE score	22.4 (21.4), 17.5 (34)	12.7 (15.0), 7.5 (18.3)	0.014
DASH score	23.1 (19.8), 19.9 (27.5)	15.6 (17.0), 8.3 (24.8)	0.028
EQ-5D score	0.765 (0.214), 0.796 (0.310)	0.794 (0.240), 0.796 (0.300)	0.215
Extension, degrees	56 (12), 57 (11)	55 (11), 55 (11)	0.574
Flexion, degrees	51 (14), 50 (20)	63 (13), 65 (24)	<0.001
Supination, degrees	92 (17), 90 (29)	96 (16), 95 (21)	0.214
Pronation, degrees	83 (10), 85 (12)	85 (9), 90 (10)	0.126
Ulnar deviation, degrees	26 (8), 25 (10)	30 (11), 30 (10)	0.030
Radial deviation, degrees	23 (7), 25 (5)	22 (4), 20 (5)	0.151
Grip strength, %	80.9 (23.6), 80.0 (22.0)	96.0 (23.7), 96.8 (32.0)	0.001

All values are presented as means (with standard deviations) and *medians (with interquartile ranges)*

*Mann-Whitney U test

Table 4. Radiographic outcomes in patients aged 70 years or older, treated for an unstable dorsally displaced DRF with non-operative treatment or VLP fixation

	Non-operative (n=58)	Volar Locking Plate (n=53)	P-value*
Dorsal tilt, degrees			
before treatment	27 (8), 27 (9)	31 (10), 30 (14)	0.019
after treatment	8 (8), 7 (10)	-1 (7), -1 (10)	<0.001
at 3 months	16 (12), 17(13)	-3 (8), -5 (11)	<0.001
at 12 months	14 (13), 17 (18)	1 (9), 0 (11)	<0.001
Radial inclination, degrees			
before treatment	14 (8), 14 (8)	14 (13), 13 (7)	0.901
after treatment	18 (6), 19 (7)	18 (8), 18 (9)	0.677
at 3 months	13 (4), 13 (6)	20 (6), 19 (9)	<0.001
at 12 months	14 (7), 15(7)	19 (8), 19 (6)	<0.001
Radial shortening, mm			
before treatment	2.3 (2.2), 2.3 (4)	2.4 (2.1), 2.0 (3.2)	0.758
after treatment	0.6 (1.6), 0.0 (1.7)	0.0 (0.3), 0.0 (0.0)	0.007
at 3 months	3.0 (2.0), 3.0 (3.3)	0.8 (1.6), 0.0 (0.0)	<0.001
at 12 months	2.7 (2.2), 2.5 (3.0)	0.5 (1.3), 0.0 (1.0)	<0.001

All values are presented as means (with standard deviations) and *medians (with interquartile ranges)*

*Mann-Whitney U-test

6.4 STUDY IV

Of the 118 patients evaluated at three years after injury, five who had not completed every EQ-5D questionnaire were excluded, leaving 113 patients (VLP n = 58, EF n = 55) for the cost-effectiveness analysis. In the VLP group 88% (51/58) were women and the mean age was 63 years. In the EF group 96% (53/55) were women and the mean age was also 63 years. The dominant hand was injured in 36% (21/58) of the VLP patients compared with 53% (29/55) of the EF patients. Differences in baseline characteristics were not statistically significant. The distribution of fracture types was similar in both groups.

During the first year mean direct costs were significantly higher for the VLP group compared with the EF group (mean difference (MD) 441 euros, $p < 0.001$) (Figure 8), mainly driven by higher costs for the primary surgery (MD 501 euros, $p < 0.001$). Most other costs were similar, but outpatient care was more expensive for the EF group (MD 93 euros, $p = 0.005$). Mean indirect costs (sick leave) were also higher for the VLP group (MD 436 euros), though not statistically significant. The mean total cost at one year was significantly higher for the VLP group compared with the EF group (MD 878 euros, $p = 0.006$).

At three years the mean difference in direct costs had increased to 554 euros ($p < 0.001$), mainly due to an increase in reoperation costs for VLP patients, from 195 euros during the first year, to 287 euros for the entire three-year period. The EF group did not display any more costs for reoperations beyond the first year. The mean indirect costs (sick leave) for VLP patients increased after the first year, but not for the EF patients, thereby increasing the mean difference to 535 euros ($p = 0.650$) at three years. The mean total cost had increased at three years after primary surgery and was 1 089 euros higher ($p = 0.012$) for the VLP group compared with the EF group (Figure 8).

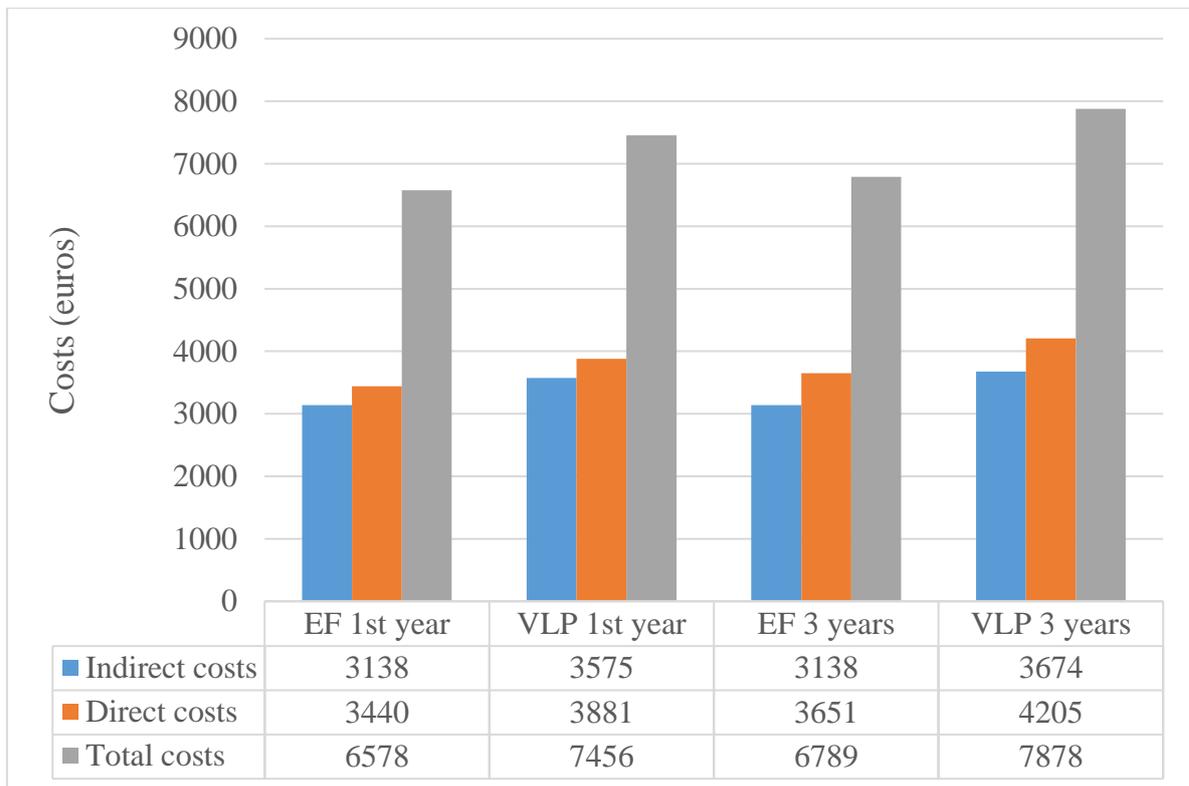


Figure 8. Mean costs, one and three years after surgery for patients 50-74 years old, treated with EF or VLP fixation due to a DRF.

At two and six weeks the VLP group had statistically significantly better mean EQ-5D index scores than the EF group, but differences did not remain at later follow-up time points (Figure 9). The mean total of QALYs during the first year was 0.814 in the VLP group and 0.787 in the EF group ($p = 0.236$) (table 5). After adjustments for baseline (before surgery) differences between the groups, the difference in the mean total of QALYs was 0.020 ($p = 0.344$) in favour of the VLP group. At three years, mean total QALYs was 2.6081 in the VLP group and 2.5967 in the EF group ($p = 0.865$) and the adjusted mean difference was 0.006 ($p = 0.921$) in favour of the EF group (table 5).

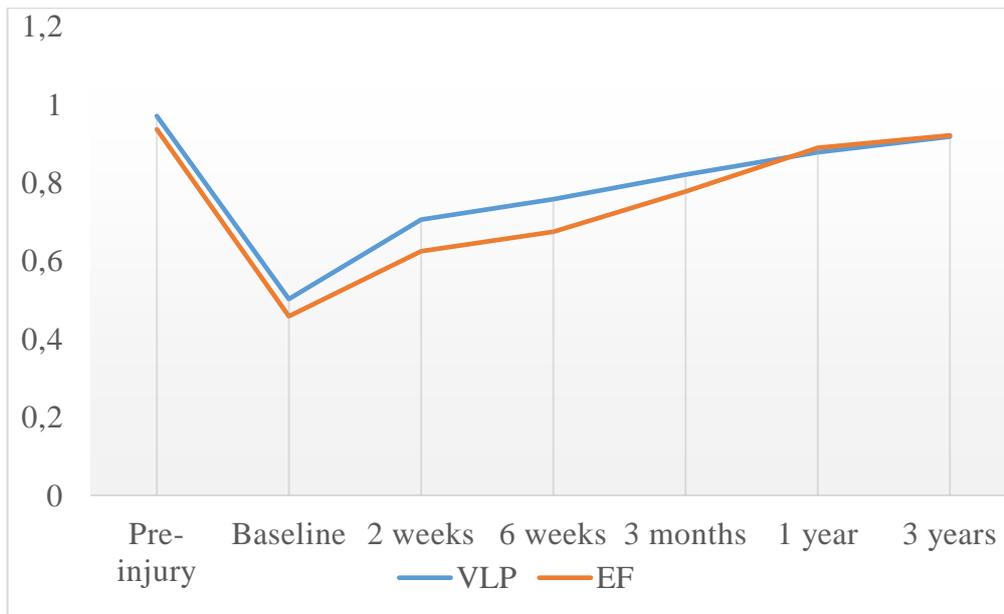


Figure 9. Mean EQ-5D index scores at pre-injury, baseline (before surgery) and follow-up points after surgery for patients 50-74 years old, treated with EF or VLP fixation due to a DRF.

At one year, VLP fixation had an ICER of 31 377 euros per QALY gained compared with EF. At three years, the mean total cost was higher for VLP fixation compared with EF, and less mean adjusted QALYs were gained, which means that VLP was dominated by EF (Table 5).

Table 5. Cost-effectiveness analysis for VLP fixation compared with EF after DRF surgery for patients 50-74 years old.

	Costs (euro) 1 st year	QALYs 1 st year	Cost per QALY gained 1 st year	Costs (euro) 3 years	QALYs at 3 years	Cost per QALY gained at 3 years
VLP	7 456	0.814	31 377	7 878	2.6081	Dominated
EF	6 578	0.787		6 789	2.5967	
Difference	878	0.020*		1 089	-0.006*	

*Adjusted for baseline differences

The bootstrap analyses of these estimates are presented in cost-effectiveness planes (Figure 10). The scatterplots cover all four quadrants indicating uncertainty about whether or not VLP was cost-effective and at what value it was cost-effective, compared with EF. The CEACs in Figures 11 and 12 summarizes the uncertainty; at a WTP threshold of 35 000 euros, the probability of VLP being cost-effective compared with EF was around 50 % at one year and 40% at three years. Moreover, at three years the probability of VLP being cost-effective compared with EF did not exceed 50% independent of the WTP.

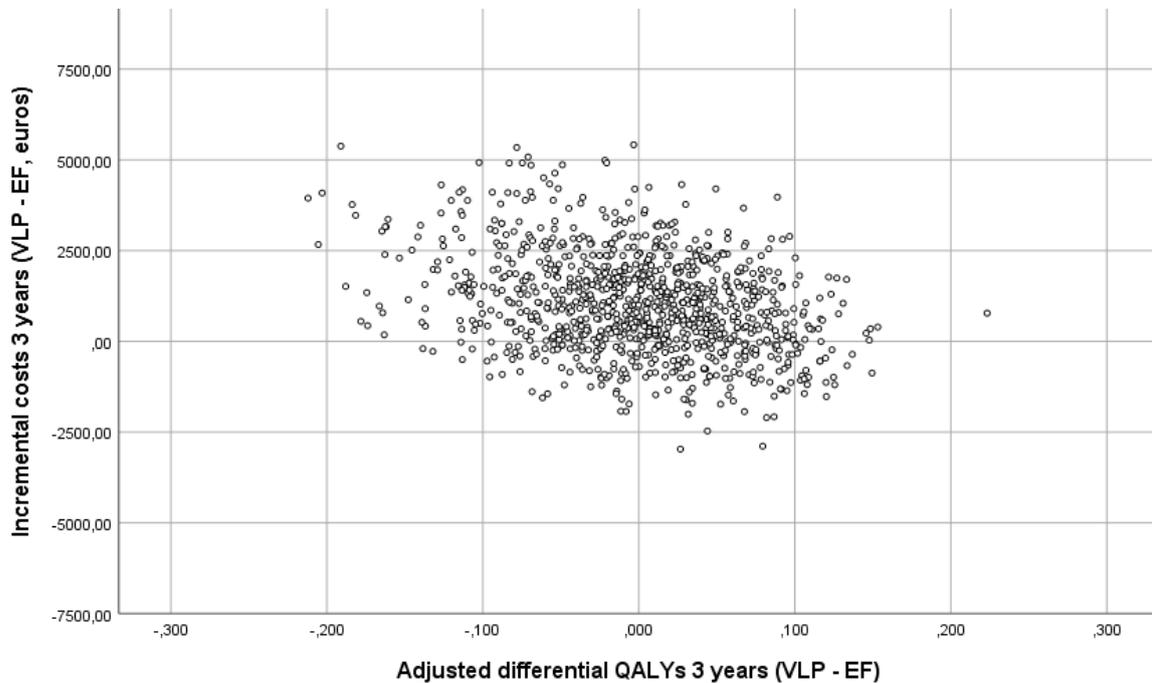
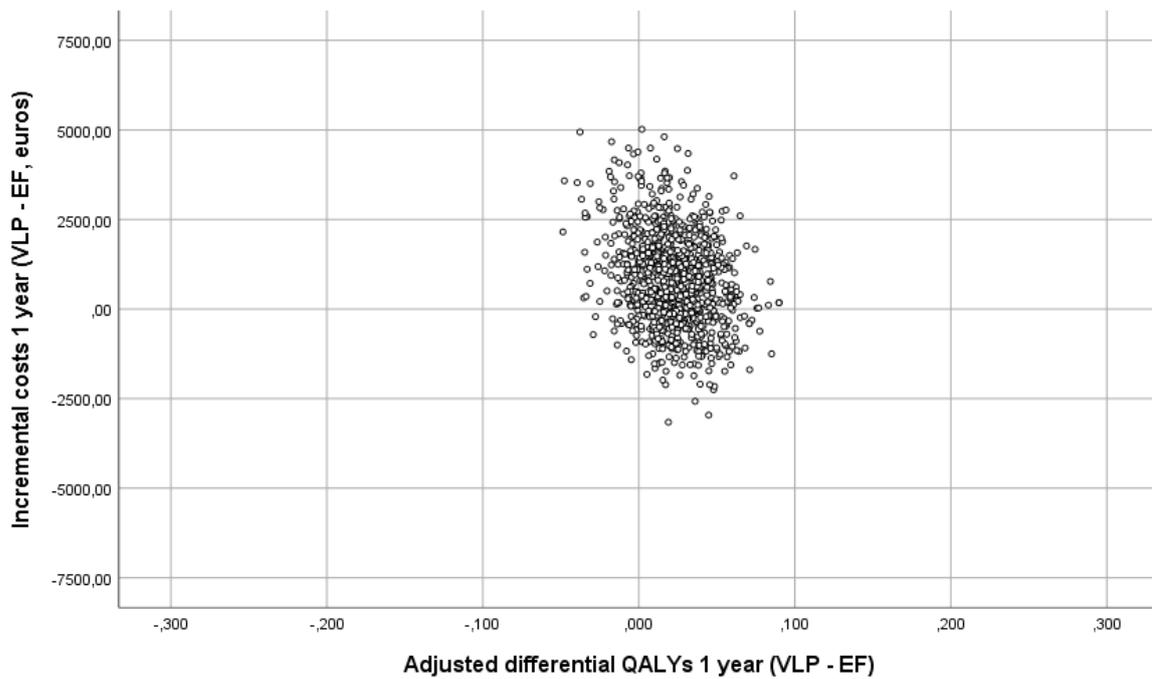


Figure 10. Scatterplots of 1 000 samples of bootstrapped mean total cost and QALY (adjusted for baseline differences in EQ-5D index scores) differences over one and three years after VLP fixation compared with EF, in cost-effectiveness planes

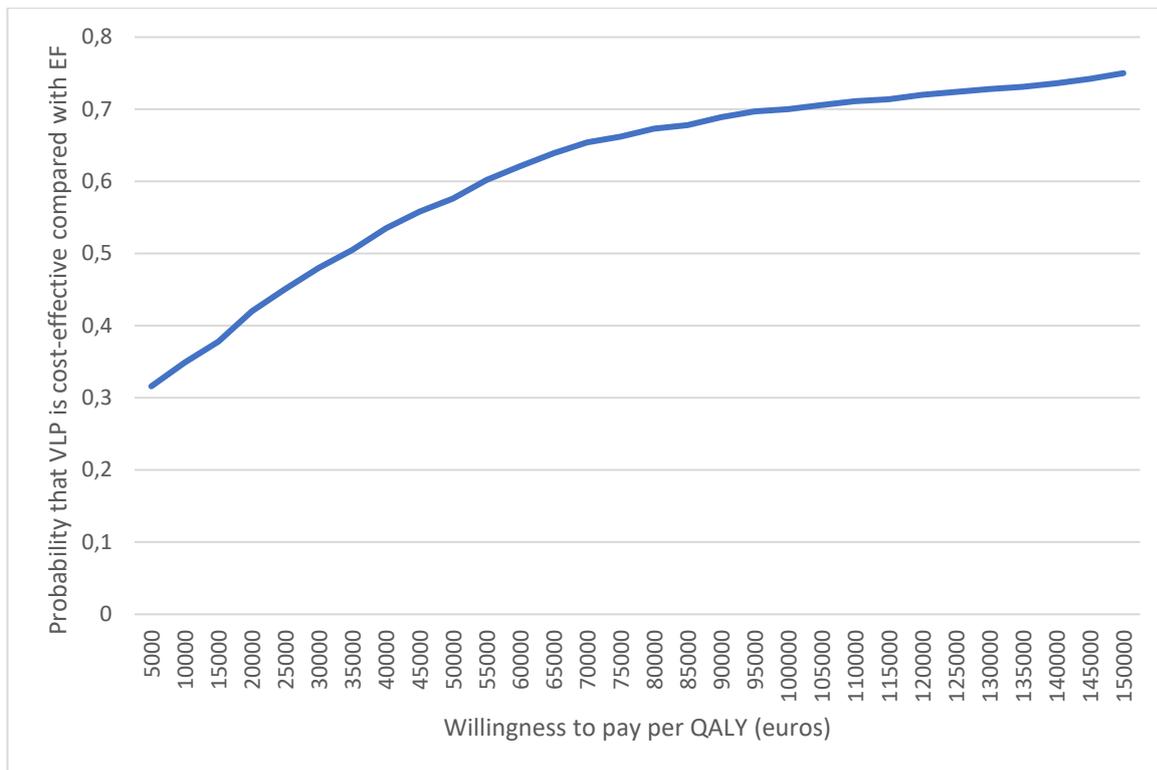


Figure 11. CEAC representing the probability of the cost-effectiveness of treatment using a VLP compared with EF at different WTP thresholds at one-year follow-up

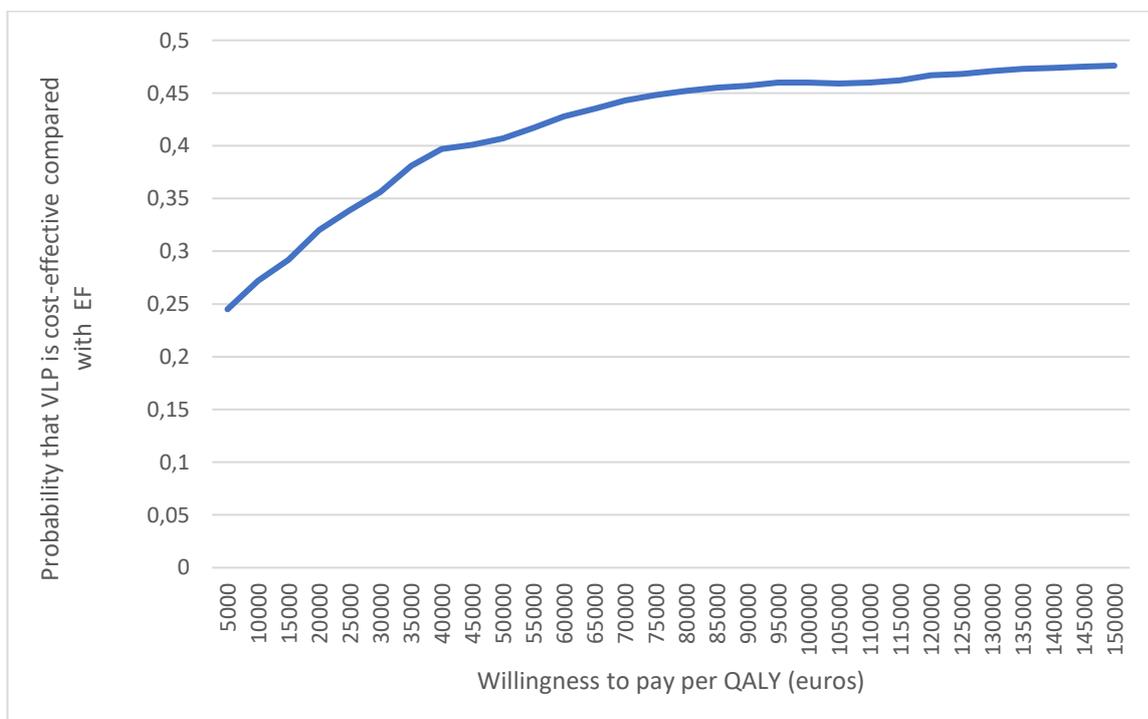


Figure 12. CEAC representing the probability of the cost-effectiveness of treatment using a VLP compared with EF different WTP thresholds at three-year follow-up

7 DISCUSSION

DRFs are very common, and the incidence of surgical treatment is rising. Moreover, the incidence of treatment with VLP is increasing to the detriment of percutaneous methods despite the lack of evidence of the superiority of VLP compared with PF or EF. Late complications are more common among plated patients, but long-term evaluations are largely lacking. The incidence of VLP is also rising among the elderly, but to the detriment of non-operative treatment. There are controversies regarding the best treatment for the elderly. From a societal perspective it is important that health care providers use cost-effective treatments whenever possible. For DRFs, VLP has not been proven to be cost-effective compared with percutaneous methods, but studies are few and none has been performed from a perspective of more than one year. There is evidence of large regional variation in treatment traditions for DRFs in the US and in the Netherlands, but knowledge of similar variations in Sweden is lacking. In regions with limited health care resources, knowledge of high incidence of a treatment that is not cost-effective could be of value.

The aim of this thesis was to compare treatment outcomes of DRFs; VLP compared with EF three years after surgery for patients 50-74 years old regarding functional outcome and cost-effectiveness, VLP compared with non-operative treatment one year after injury for patients 70 years or older regarding functional outcome and finally to describe the regional variation in treatment regimens in Sweden.

7.1 STUDY I

Our finding of a large regional variation (adjusted for age and gender) in surgical treatment care of DRFs are supported by several authors. Walenkamp et al.¹²⁷ reported that operative and non-operative treatment proportions differed largely among regions in the Netherlands. In the US, Fanuele et al.⁶⁹ and Chung et al.¹²⁵ found evidence of large regional differences regarding surgical treatment methods as well as surgical rates.

It is possible that some of the variation can be explained by different case mixes, as the register data do not include information on fracture classification, but it does not seem likely. Variation can also, to some extent, be explained by surgeon specialization – younger age of the surgeon and membership in the American Society for Surgery of the Hand (ASSH) are correlated to a preference for IF^{129,139,140}. In our study there was no information about the surgeons. However, regions including hand surgery clinics did display deviant patterns of surgical treatment rates.

Plausible explanations for regional variation are personal preferences among surgeons and local treatment traditions^{111,129,141}. Regional differences in surgical treatment are common in conditions with relative indications for surgery or lack of consistency regarding the best surgical option, such as ankle fractures¹²⁸ and proximal humeral fractures¹⁴², and rare in

conditions with strict indications for surgery, such as hip fractures¹²⁹. In the case of DRFs, there is a lack of national consensus regarding treatment recommendations, which might be reflected by our findings of large regional differences in treatment traditions.

Other explanations for regional differences may be technology diffusion and financial incentives. The more densely populated regions in the south of Sweden had the highest use of IF. Also, marketing may influence the choice of treatment when strict guidelines for a treatment-decision are lacking.

To reduce unmotivated variation, treatment decisions regarding DRFs should be based on the best available scientific evidence, patient preferences and health economic considerations.

7.2 STUDY II

7.2.1 PROM results

Our findings of equivalent results regarding PROMs for VLP and EF three years after surgery are supported by several authors. Williksen et al.⁸¹ reported similar DASH score for VLP and EF after five years, Landgren et al.⁷⁹ found no difference in DASH scores between plating and EF after five years and Kreder et al.¹⁴³ reported similar Musculoskeletal Functional Assessment scores¹⁴⁴ for plating and EF after two years. In contrast to our findings, Leung et al.¹⁴⁵ reported a better Gartland and Werley score for volar or dorsal plating compared with EF after two years, but they included only intraarticular fractures and the patients were relatively young (mean age = 42 years). Moreover, dorsal plates were routinely removed after six months to avoid discomfort due to tendon attrition.

7.2.2 Reoperations

When functional results are equivalent, it is important to consider the burden of complications. Complications in general are diversely classified in the literature, but reoperation rates are commonly reported. In our study there were 21% reoperations for VLP patients compared with 14% for EF patients after three years. Williksen et al.⁸¹ reported 31% reoperations for VLP and 17% for EF up to five years after primary surgery. Landgren et al.⁷⁹ reported 54% reoperations for plated patients and 41% for EF patients five years after initial surgery. Most of the reoperations in our study consisted of plate extractions; 18% of the VLP patients had their plate removed and nearly half of the plate removals occurred later than one year after the primary surgery. In Williksen and Landgren's studies mentioned above, they reported 21% and 46% plate removals, respectively. Esenwein et al.⁶⁵ reported plate extraction rates of 35% two years after VLP but as they removed plates on patients' demand they did not consider it as a complication.

Since reoperations occur relatively infrequently, larger studies are needed to detect statistically significant differences between groups. A large register study, based on 36 618 patients, found significantly more reoperations for plated patients than for EF patients³⁹. For EF patients they

occurred early, consisting mainly of secondary plate fixation due to fracture displacement and for VLP patients they occurred late, consisting mainly of hardware removal.

7.2.3 OA

There were more patients with radiographic signs of OA in the VLP group (42%) compared with the EF group (28%). In contrast to our findings, Leung et al.¹⁴⁵ reported more OA among EF patients than plated patients two years after surgery. Jupiter et al.⁵⁴ reported radiographic signs of OA in 27% of the patients in a cohort of VLP patients. Our results are slightly higher which may be due to the fact that we reported OA in both the radiocarpal joint and the distal radioulnar (DRU) joint. However, our study was not designed to detect significant differences in OA.

7.3 STUDY III

DASH score, PRWE score and grip strength were clinically significantly better in the VLP group compared with the EF group for unstable dorsally displaced DRFs in patients 70 years or older three months after injury. Differences remained at one year but did not reach the MCID for grip strength. Our findings are supported by Martinez-Mendez et al.¹¹⁷ who reported significantly better DASH and PRWE scores for VLP patients compared with non-operatively treated patients in a randomized controlled trial (RCT) with 97 patients who were 60 years or older with a dorsally displaced intraarticular DRF at two years after injury. In contrast to our findings Arora et al.⁶⁴ reported better DASH and PRWE scores for VLP patients compared with non-operatively treated patients in an RCT with 73 patients who were 65 years or older with dorsally displaced DRFs, at three months, but not thereafter. Grip strength was statistically better for the VLP patients at three and twelve months, but the differences were not clinically significant. A multicentre RCT by Bartl et al.¹¹³ with 149 patients, 65 years or older, randomized to VLP or non-operative treatment for an intraarticular dorsally displaced DRF also reported results contradicting our findings. There were no differences in PROMs between the groups at any time. However, 42% of the patients in the non-operative group were converted to surgical treatment with a VLP within two weeks due to loss of reduction, but were still analysed as non-operatives, which probably diminished the differences in outcomes between the treatments. In our study there were only two conversions to VLP in the non-operative group. Therefore, we believe that our findings for the non-operative group represents a realistic outcome.

7.4 STUDY IV

At one year the incremental total cost per gained QALY was just below the threshold recommended by NICE. At three years, the mean total cost was higher and less QALYs were gained for VLP patients compared with EF patients, indicating that VLP is not cost-effective compared with EF. However, the statistical analysis displayed a high level of uncertainty

surrounding our estimates, which implies that further studies are needed to support our findings.

To the best of our knowledge there are no previous cost-effectiveness studies comparing VLP with EF, but there are some studies comparing VLP with PF. Tubeuf et al.¹²⁴ found, at one year, an incremental cost of 815 euros (converted from UK pounds sterling) for VLP patients compared with PF patients. As VLP patients had a smaller gain in QALYs (0.008) than in our study, the resulting ICER was higher (100 295 euros per QALY). However, they did not investigate patients beyond the first year. Karantana et al.¹²³ presented a study comparing VLP with PF and optional EF and reported a statistically significant incremental cost of 801 euros (converted from UK pounds sterling) after one year. They also presented a smaller gain in QALYs (0.0178) for VLP patients than our study, resulting in an ICER of 44 990 euros per QALY for the VLP group in comparison with the PF group. Differences in EQ-5D index scores and resulting QALYs were very small in the studies of Tubeuf and Karantana, which is in accordance with the findings in our study. Even small differences in total costs render large differences in ICER due to small differences in QALYs. It is questionable whether the EQ-5D index score is sensitive enough to be used for health economic evaluations in upper extremity injuries. No other studies have compared VLP with percutaneous surgical methods for DRFs beyond one year and our results indicate that between one and three years after DRF surgery, VLP patients increase their costs more than EF patients and EF patients improve their EQ-5D index scores more than VLP patients.

7.5 LIMITATIONS AND STRENGTHS

The major strength of Study I is its size, with a large unselected population of DRF patients within a well-defined time-period. The main limitations of Study I are the lack of information regarding fracture severity, co-morbidities and surgeon characteristics that could affect treatment choices.

The strengths of Study II are its prospective randomized design, its size and the long follow-up period. A major limitation is that we had a 12% loss to follow-up from year one to year three, and as a consequence we did not reach the sample size from the power estimation.

The major strength of Study III is that the sample size was large enough to reach statistical significance for the primary outcomes. A major limitation is the fusion of two separate studies, introducing the risk of bias. However, the study protocols were similar, and an analysis of variance did not show any significant differences in outcomes between the two study centres.

The major strength of Study IV is the long follow-up period as treatment-related costs occur after the first year and HRQoL continues to improve. Another strength is the nature of the randomized design, which decreased the impact of potential biases. The use of national register data enabled us to capture any costs outside the study hospital's setting. The use of register data is also a limitation as we searched for DRG codes and drug prescriptions that we assumed could

be associated with the DRF, possibly rendering an overestimation of outpatient visits, sick leave and drug usage. Another limitation is that we in the retrospective perspective had to estimate the resource use of occupational therapy and X-rays

8 CONCLUSIONS

Surgical treatment regimens for DRFs vary widely among health care regions in Sweden and when comparing treatment outcomes; for elderly patients VLP fixation seems to yield superior clinical results compared with non-operative treatment, but for patients aged 50-74 years, VLP fixation does not seem to yield superior clinical results and does not seem to be cost-effective as compared with EF in a three-year perspective.

Study I: There was a large variation in surgical treatment regimens for DRFs among different health care regions in Sweden during the period of 2010 to 2013. Differences were not explained by age or gender. Future studies are needed to investigate whether differences in fracture pattern exist among regions. There is no support in the literature to motivate the differences in treatment traditions that we found.

Study II: The clinical and radiological results were comparable for VLP fixation and EF three years after surgical treatment of patients 50-74 years old with an unstable dorsally displaced DRF caused by low-energy trauma. There might be more reoperations after VLP fixation compared with EF. This study shows that modern fracture surgery, with more advanced technology and a more difficult surgical procedure did not yield a better clinical result than a traditional fracture surgery procedure.

Study III: Contrary to findings described in previous publications, this study showed that VLP fixation was superior to non-operative treatment regarding clinical and radiological results for patients 70 years or older with an unstable dorsally displaced DRF caused by low-energy trauma. The complication rates were similar. The current notion that elderly patients do not benefit from fracture surgery of DRFs is challenged by our findings.

Study IV: VLP fixation of a DRF was not cost-effective compared with EF three years after surgical treatment of patients 50-74 years old with an unstable dorsally displaced DRF caused by low-energy trauma. However, there was a high level of uncertainty surrounding our estimates. The fact that modern fracture surgery methods involve high costs and low gain in quality of life compared with traditional methods, represents an important field for future evaluation of fracture surgery.

9 CLINICAL IMPLICATIONS

Based on the results from the studies conducted for this thesis, it is reasonable to suggest that patients aged 50-74 years, who sustain an unstable DRF, should be supplied with full information about the different surgical treatment options available including their respective advantages and drawbacks. The informed patient should be offered the opportunity to take part in treatment decisions in cooperation with the fracture surgeon. From a societal perspective, future treatment recommendations should convey the knowledge that percutaneous methods are preferred instead of VLP if considered equally suitable for the patient, as VLP does not seem to be a cost-effective alternative. National treatment recommendations based on findings in the current literature might reduce unmotivated regional differences in treatment traditions. Elderly patients, who are living independently and sustain an unstable DRF should be offered surgery with VLP as an option to non-operative treatment. Complications to treatment should be explained, and if choosing non-operative treatment, patients should be informed about the possibility of corrective osteotomy later on.

10 FUTURE PERSPECTIVES

There are in general very small differences in the results from the PROMs that we commonly use, and the questions in the PROMs do not consider whether the dominant hand is injured or not. Clearly, there is a need for a new outcome tool that is more sensitive and can compensate for handedness. The outcome tool should be designed to reflect presently performed daily activities, such as handling a mobile phone and typing at a computer, and it should also enable weighing the questions differently according to the importance for the respondent.

There is also, in the absence of evidence of the best surgical option, a place for new perspectives on how to measure and interpret the current outcomes. To the best of our knowledge, no study regarding qualitative matter in fracture surgery has been published. Such information regarding patients' own experiences could add more information for better understanding of this issue.

The mounting pressure on health care budgets increases the demand for information concerning cost-effectiveness of treatment options to avoid allocating resources to treatments that are not cost-effective. Therefore, more well-designed health economic evaluations of DRF treatments as well as other orthopaedic treatments are needed. Measuring effect in cost-effectiveness analyses is challenging as the commonly used EQ-5D index score is possibly not sensitive enough to capture small but still clinically important effects regarding upper arm injuries. There is need for development of new methods for cost-effectiveness analyses to be able to compare DRF treatments.

A phenomenon discovered during the work for this thesis is that after a DRF, no matter which treatment is received, patients restore most of their function, but a small subset of patients have much worse results. It is, to our knowledge, unclear why their outcomes are inferior compared with the others. To thoroughly investigate this patient group would bring more clarification to this issue.

Finally, national recommendations for treatment of DRFs, based on the best available scientific evidence, needs to be developed in Sweden as well as in other countries, to minimize unmotivated regional variations and optimize the use of health care resources.

11 SAMMANFATTNING PÅ SVENSKA

Handledsfaktur, eller distal radiusfraktur, är den vanligaste frakturen som behandlas inom hälso- och sjukvården. Traditionellt har dessa frakturer behandlats med gips om de bedömts stabila eller med perkutan kirurgi om de bedömts instabila. Perkutan kirurgi innebär antingen temporära stift fästa i skelettet genom huden eller en temporär utanpåliggande extern fixation, fäst i skelettet via stift genom huden. Sen 1990-talet, när skelettnära fixation (intern fixation) på handledens insida med en så kallad vinkelstabil volar platta introducerades, har incidensen för operation av distal radiusfraktur i allmänhet och operation med volar platta i synnerhet ökat markant, på bekostnad av gipsbehandling och perkutan kirurgi. Förändringen i behandlingspraxis har skett utan att det finns vetenskapliga bevis för att volar platta är bättre än perkutan kirurgi för vuxna patienter i allmänhet eller bättre än gipsbehandling för de äldre patienterna. Kostnadsstudier från andra länder tyder på att volar platta inte är en kostnadseffektiv behandling i jämförelse med perkutana metoder.

Syftet med denna avhandling var att jämföra patientupplevt behandlingsresultat och kostnadseffektivitet mellan behandlingsmetoder samt att beskriva skillnader i förekomst av kirurgiska behandlingsmetoder för distala radiusfrakturer mellan olika landsting i Sverige.

Studie I var en beskrivande studie där data från Svenska Patientregistret användes. 22 378 vuxna individer var registrerade med en kirurgiskt behandlad distal radiusfraktur mellan åren 2010 och 2013 i Sverige. Andelen ingrepp med intern fixation var 72% för hela landet. Det förelåg stora skillnader i den procentuella fördelningen av de kirurgiska behandlingsmetoderna mellan de 21 landstingen. Andelen ingrepp med intern fixation varierade mellan 41% och 95%, andelen perkutan stiftning varierade mellan 2% och 44% och andelen extern fixation varierade mellan 1% och 19%. Incidensen för kirurgiskt behandlade distal radiusfrakturer varierade mellan 4.2 och 9.2 per 10 000 person-år mellan landstingen.

Studie II och IV bestod av en treårsuppföljning efter en tidigare publicerad randomiserad studie av 140 patienter, 50-74 år, med en instabil bakåtvinklad distal radiusfraktur som lottades mellan operation med volar platta och extern fixation. 118 patienter deltog i treårsuppföljningen. I *Studie II* undersöktes patientupplevt behandlingsresultat, greppstyrka, rörelseomfång, förekomst av tecken på artros på röntgenbilder samt komplikationer. Det förelåg ingen skillnad mellan grupperna. I *Studie IV* analyserades kostnader och livskvalitetsjusterade levnadsår (QALYs) (summan av den patientupplevda hälsorelaterade livskvaliteten upplevd under en viss tidsperiod) under de tre första åren efter operationen. Gruppen som behandlats med volar platta hade i medeltal högre totalkostnad och lägre QALYs i jämförelse med gruppen som behandlats med extern fixation, vilket antyder att volar platta inte är en kostnadseffektiv behandling av en instabil bakåtvinklad distal radiusfraktur sett över tre års tid.

Studie III var en randomiserad studie där 140 patienter, 70 år eller äldre, med en instabil bakåtvinklad distal radiusfraktur lottades mellan gipsbehandling och operation med volar platta. Efter ett år utvärderades 119 patienter och patientupplevt behandlingsresultat,

greppstyrka och röntgenologiskt utseende var signifikant bättre för gruppen som behandlats med volar platta. Andelen komplikationer var lika mellan grupperna.

De viktigaste slutsatserna av denna avhandling är att kirurgiska behandlingsval för distala radiusfrakturer skiljer sig stort mellan landstingen i Sverige och gällande jämförelser av behandlingsmetoder så verkar operation med volar platta ge ett bättre patientupplevt resultat än gipsbehandling för de äldre patienterna, medan för patienter i åldern 50-74 år så verkar operation med volar platta inte vara sig ge ett bättre patientupplevt resultat eller vara kostnadseffektivt i jämförelse med extern fixation.

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