Complications and functional outcome
of distal radius fractures in elderly patients

PhD Thesis by Rikke Thorninger

"The art of medicine consists in amusing the patient while nature cures the disease" Voltaire

"The natural healing force within each of us is the greatest force in getting well" Hippocrates

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Rikke Thorninger
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Abbreviations

AAOS	The American Society of Orthopedic Surgery
AO	*Arbeitsgemeinschaft für Osteosynthesefragen* – AO Foundation
ASA	American Society of Anesthesiologists Classification (ASA class 1–6)
BSSH	The British Society of for Surgery of the Hand
CI	Confidence Interval
DRF	Distal Radius Fracture
EQ5D	European Quality of Life – 5 dimensions
GRADE	Grading of Recommendation, Assessment, Development and Evolution
IQR	Inter-Quartile Range
MCID	Minimal Clinically Important Difference
NCG	National Clinical Guidelines
NRS	Numeric Rating Scale
ORIF	Open Reduction and Internal Fixation
OTA	Orthopedic Trauma Association
PPI	Public and Patient Involvement
PROM	Patient-Related Outcome Measure
PRWHE	Patient-Rated Wrist and Hand Evaluation
QuickDASH	Quick Disabilities of the Arm, Shoulder and Hand
RCT	Randomised Controlled Trial
RoB	Risk of Bias tool for randomised trials
ROM	Range Of Motion
VLP	Volar Locking Plate

English Summary

Distal radius fractures (DRF) account for 18% of all fractures in the elderly ≥65 years of age. The incidence rate of DRF is around 200-280 per 100,000 person-years. With rising age of the general population, it is expected that DRF in the elderly will assume growing importance in the healthcare system. The primary aim of this thesis was to prospectively investigate the complication rate and functional outcome of displaced DRF after non-operative treatment vs. operative treatment with volar plating in patients 65 years of age or older. The secondary aim of this thesis was to report the complications, functional outcome and radiological evaluation of minimally or non-displaced DRF in the same age group. The tertiary aim was to evaluate the complications and functional outcome between non-operative treatment of minimally/non-displaced vs. displaced DRF.

This thesis is based on four papers including a randomised controlled trial and three prospective observational studies.

Paper I is the published study protocol of the randomised controlled trial.

Paper II evaluated the clinical outcome of minimally or non-displaced DRF in patients treated non-operatively according to the national clinical guidelines (NCG). The main purpose of this study was to provide reliable and up-to-date information about Danish patients with DRF before fracture and at 5 weeks, 6 months, and 12 months. The outcomes measured were complications and functional outcome. Furthermore, this cohort was meant to serve as reference group in Paper III.

Paper III investigated the potential superiority of non-operative treatment vs. surgical volar plating of displaced DRF in patients older than 65 years with regards to complications and functional outcome. Volar plating is currently the recommended treatment according to the NCG.

Paper IV compared the functional outcome at the time points 2 and 5 weeks and 12 months in between non-operatively treated minimally or non-displaced and displaced DRF with functional outcome and complications as endpoints.

Paper V investigated the clinical outcome of minimally or non-displaced DRF in patients treated non-operatively. The main purpose of this study was to provide data on patient outcome three years or more after DRF and compare the results with the 12-month results. Outcome measures in this study were complication, functional outcome, and post-traumatic articular arthrosis.

The findings of this thesis provide insight into the treatment of DRF in the elderly. Similar results in terms of complication rates and functional outcomes were found in all groups. No clinical signs of post-traumatic articular arthrosis were seen after more than 3 years of follow-up.
This thesis suggests that treatment of DRF in the elderly should rest on shared decision making where the patient is actively involved in choosing the treatment strategy.

Danish summary

Distale radiusfrakturer (DRF) udgør 18% af alle frakturer hos ældre over 65 år, og incidens-raten er cirka 200-280 pr. 100.000 person-år. Med den stigende alder forventes det, at DRF hos ældre vil få stor betydning for sundhedsvæsenets drift. Formålet med denne afhandling var at beskrive og sammenligne komplikationer og funktionelle resultater efter håndledsbrud hos patienter ældre end 65 år, der enten bliver behandlet operativt eller konservativt.
Denne ph.d.-afhandling er baseret på et randomiseret kontrolleret forsøg og observationelle studier.

Artikel I er den publicerede studieprotokol fra det randomiserede kliniske forsøg.

I artikel II, der var et prospektivt kohortestudie, evaluerede vi det kliniske resultat hos minimalt eller ikke-dislokerede DRF-patienter behandlet non-operativt i henhold til de nationale kliniske retningslinjer. Hovedformålet med denne undersøgelse var at indhente pålidelig og opdateret information om danske DRF-patienter før fraktur samt efter 5 uger og 6 og 12 måneder efter operationen. De målte resultater var komplikationer og funktionelt resultat. Desuden skulle indsamlede data fra denne kohorte fungere som referencegruppe i artikel IV.

I artikel III undersøgte vi ved hjælp af et randomiseret kontrolleret studie den potentielle overlegenhed af ikke-operativ behandling vs. kirurgisk volar plating af forskudt DRF hos patienter, som var ældre end 65 år, med hensyn til komplikationer og funktionelt resultat. Volar plating er i øjeblikket i henhold til de nationale kliniske retningslinjer den anbefalede behandling ved forskudte DRF.

I artikel IV sammenlignede vi det fundne funktionelle resultat på tidspunkterne 2 og 5 uger og 12 måneder mellem ikke-operativt behandlede minimalt eller ikke-displacerede og forskudte DRF i forhold til det funktionelle resultat og komplikationer.

I artikel V undersøgte vi det kliniske resultat af minimalt eller ikke-displacerede DRF hos ikke-operativt behandlede patienter. Hovedformålet med denne undersøgelse var at frembringe data om patientresultater tre år eller mere efter DRF og sammenligne resultaterne med 12 måneders-

resultaterne. Resultatmålene i denne undersøgelse var komplikationer, funktionelt resultat og posttraumatisk slidgigt.

Denne afhandling giver indsigt i behandlingen af DRF hos ældre. Vi fandt sammenlignelige resultater målt på komplikationsfrekvens og funktionelt resultat i alle grupperne. Der var ingen kliniske tegn på posttraumatisk slidgigt ved langtidsopfølgning.

Denne ph.d. peger på, at behandlingen af DRF hos ældre med fordel bør omfatte inddragelse af patienten, så patienten i samråd med kirurgen kan finde den rigtige behandlingsløsning. Behandlingen af DRF bør i fremtiden individualiseres.

Inspiration

This thesis was inspired by my clinical experience with the Danish national clinical guidelines from 2014 which were updated in 2017:

https://www.sst.dk/da/udgivelser/2014/nkr-behandling-af-haandledsnaere-brud

and my previous research in DRF:

Complications of volar locking plating of distal radius fractures in 576 patients with 3.2 years follow-up.

Thorninger R, Madsen M, Wæver D, Borris L, Rölfing J.

Injury. 2017 Jun;48(6):1104-1109. doi.org/10.1016/j.injury.2017.03.008.

Distal radius fractures are difficult to classify.

Wæver D, Madsen ML, Rölfing J, Borris L, Henriksen M, Nagel L, **Thorninger R.**

Injury. 2018 Jun;49 Suppl 1: S29-S32. doi.org/10.1016/S0020-1383(18)30299-7.

Volar plating of distal radius fractures does not restore the anatomy.

Madsen M, Wæver D, Borris L, Nagel L, Henriksen M, **Thorninger R**, Rölfing J.

Dan Med J. 2018 Aug;65(8):A5497.

List of studies

This PhD thesis is based on the following publications and manuscripts:

I   **A protocol for a single-center, single-blinded randomized-controlled trial investigating volar plating versus conservative treatment of unstable distal radius fractures in patients older than 65 years.**

Pedersen J, Mortensen S, Rölfing J, Thorninger R.
BMC Musculoskelet Disord. 2019; 20(1):309. doi.org/10.1186/s12891-019-2677-y
Impact factor (2021): 2.562

II   **Objective outcome measures continue to improve from 6 to 12 months after conservatively treated distal radius fractures in the elderly - a prospective evaluation of 50 patients.**

Thorninger R, Wæver D, Pedersen J, Tvedegaard-Christensen J,
Tjørnild M, Lind M, Rölfing J.
J Clin Med. 2021; 10(9):1831. doi.org/10.3390/jcm10091831
Impact factor (2021): 4.964

III   **VOLCON - a randomized controlled trial investigating complications and functional outcome of volar plating vs casting of unstable distal radius fractures in patients older than sixty-five years.**

Thorninger R, Wæver D, Tjørnild M, Lind M, Rölfing J.
J Orthop Traumatol. 2022; 23(1):54. doi.org/10.1186/s10195-022-00673-4
Impact factor (2021): 4.239

IV   **Prospective evaluation of two cohorts of non-operatively treated patients with displaced vs. minimally and non-displaced distal radius fractures**

Thorninger R, Wæver D, Tjørnild M, Lind M, Rölfing J.
J Clin Med. 2023; 12(5):2076. doi.org/10.3390/jcm12052076
Impact factor (2021): 4.964

Extension of the original protocol beyond 12 months of follow-up:

V   **Posttraumatic arthritis and functional outcomes after nonoperatively treated distal radius fractures: A prospective study with a minimum 3-year follow-up**

Thorninger R, Romme KL, Wæver D, Henriksen MB, Tjørnild M, Lind M, Rölfing J.
Submitted: 10th March 2023.

Figure 1 provides an overview / flow diagram of the studies and is also available

online: doi.org/10.5281/zenodo.7677689

Introduction

In the elderly ≥65 years of age, distal radius fractures (DRF) account for 18% of all fractures (1). The estimated lifetime risk for DRF is 15% for females and 2% for males (2). The incidence rate is approximately 200-280 per 100,000 person-years in Denmark (3-5). In Denmark, DRF is the most common fracture and currently accounting for 12,000-18,000 fractures per year (5, 6). Low-energy DRF are associated with osteoporosis, and among women, the age-related incidence rate of low-energy DRF increases almost 3-fold from the age of 60 to 99 (1, 7-9). In Europe, the burden of this disease is rising as the population is getting older (5, 10).

Classification of DRF

Traditionally, DRF have been described using eponyms (e.g. Colles', Barton's, Smith's fracture) based on the direction of displacement of the distal fragment. Even though these names are still commonly used in clinical practice in Denmark, several more detailed classification systems have been developed (11).

Older's classification subdivides DRF into four types with increasing degree of comminution and severity (12). Frykman's classification has been used in the literature and to some extend in Danish clinical practice. Frykman discriminates between intra- and extra-articular DRF and the presence or absence of an ulnar styloid fracture (13).

The AO classification system is frequently used for other fractures of long bones in terms of research and to some degree in clinically decision making. An AO classification for DRF has also been derived, here DRF are divided into three major types (extra-articular, partially articular, and completely articular), which are further subdivided into three subtypes describing the degree of comminution. It has also been shown that the classification of DRF is difficult, and a simple approach is thus advisable (14). Fernandez argues that a classification system in order to be clinically relevant, should have a high degree of intra- and inter-observer reliability, recommend treatment options, and have a prognostic value. Fernandez thus proposed his own classification system that classifies DRF according to the mechanism of injury and argues that it fulfils these demands (15). Nonetheless, classification systems are not frequently used in clinical practice, which is also reflected in the national clinical guidelines, where treatment recommendations are made

based on radiological measurements in the vast majority of these guidelines and in some of them by patient factors such as pre-injury status and age (see below).

Treatment options

In a historical perspective, the treatment of DRF has undergone a tremendous development and refinement over the years. Up to the middle of the 20th century, all DRF were treated non-operatively with or without a reduction attempt to improve the alignment of the radius (13). Cast immobilization is still the preferred treatment of non-displaced extraarticular DRF (i.e., AO type A) regardless of the patients age (16). Cast immobilization following closed reduction is also used for displaced fractures if the radiological measurements align with the clinical guidelines (see below).

Non-operative treatment, i.e., plaster immobilization is a non-invasive treatment that involves immobilizing the fracture and wrist joint, with or without prior reduction in a cast or a splint. Despite an increase of operative treatments, non-operative treatment is still the most frequent treatment choice for DRF (5, 17). Non-operative treatment is often used on well reduced distal radius fractures or for patient, who are not suitable for surgery. However, the optimal length of immobilization and cast material (plaster, splint, etc.) are a matter of scientific debate. Lucas et al. (18) argue for 4 weeks of immobilization. This conclusion is also supported by Olech et al. in a recent RCT comparing 4 to 6 weeks of immobilisation (19). A systematic review from 2019 by Delft et al (20) suggests an even shorter time of 3 weeks only. Notably, only Olech et al. study exclusively the elderly population, which is the target population of this PhD thesis. Throughout the history cast or splint have also taken different shapes and lengths. Interestingly, a recent prospective randomized study by Caruso found no outcome difference between above or below the elbow casting (21).

Before open reduction and internal fixation (ORIF) with volar plating became the surgical treatment of choice for distal radius fractures, other surgical methods were used. Most of these methods were based on closed reduction and percutaneous fixation with either Kirschner-wires and/or in combination with bridging of the DRF by means of external fixation (22)

Several studies comparing external to internal fixation of displaced DRF have been published over the recent years. In a meta-analysis, Margaliot et al. (23) draw the conclusion that there was no evidence proving the superiority of internal vs. external fixation. However, more recent meta-analyses including high quality randomized controlled trials favoured internal fixation over external fixation, also including functional outcome. Moreover, Cui et al. could show that external fixation posed a higher risk of complications (24, 25).

When ORIF is indicated, different types of internal implants are available. While intramedullary nails and combined methods are being developed, plates are predominantly used (5, 26, 27). Dorsal plates, radial plates, and angle-stable volar locking plates (VLP) are commercially available. The literature on this subject is not consistent. Wichlas et al. (28) recommend using a volar approach as, even though the post-surgery reduction is similar for dorsal and volar fixation, the complication rate and the operation time were significantly lower in the VLP group. In contrast, Yu et al. (29) found no significant difference in complication rates between the volar and dorsal plates when using newer low-profile dorsal plates except for a higher incidence of neuropathy in the volar group. In general, the advantage of volar plating is that the fracture is directly visualized, and the plate is covered under several layers of muscle mitigating the risk of infection.

The treatment method of choice varies among countries and surgeons (30). In Finland, surgery rates using VLP doubled from 2006 to 2008, whereas in Sweden a three-fold increase in the use of volar plating was noted from 2005 to 2010 (17, 31).

Volar plating appears to improve early functional recovery, but functional results after 1 year are found to be similar to those achieved with other treatment modalities such as non-operative treatment or with other surgical methods like Kirschner-wire or external fixation in patients of 65 years of age and older (32-34). On the other hand, some studies show that operative treatment with VLP in the elderly is superior to non-operative management when measuring PROMs (35, 36). Martinez-Mendez showed in a RCT from 2017 that at final follow-up after two years all mean functional and quality of life scores were better in the surgical group but this was accompanied by a higher complication rate as well (36). Savings et al. confirmed these findings in an RCT, reporting better functional outcome in the surgical group and a trend towards increased complication rate (35).

On the other hand, other studies report more complications after operative treatment, but with no clinically relevant difference in the functional outcome compared with non-operative treatment (32, 37). Furthermore, non-operatively treated patients with DRF may experience less pain and better or equal wrist function after a one-year follow-up (38). The scientific debate regarding the pros and cons of non-operative and operative treatment of DRF is thus lively. These findings also led to the conduction of the RCT of this PhD thesis exploring operative vs. non-operative treatment of displaced DRF in terms of complications and function.

Complications

Complications and long-term sequelae after DRF arise from either the injury itself or the performed treatment. And surgical treatment will always result in risks of complications. No matter how small, the risk of iatrogenic complications lays in the nature of surgical intervention and is unenviable.

The trauma leading to the fracture are also related to complications other than the facture itself. Examples of complications inflicted by the trauma include some degree of joint stiffness. In the literature, traumatic rupture of the extensor pollicis longus, acute compartment syndrome, carpal tunnel syndrome and complex regional pain syndrome have also been associated with the injury itself regardless of the treatment option (3).

Complications after DRF can be classified into minor and major complications. Minor complications may encompass sensory disturbances, pain, pressure wound from the plaster and decline in range of motion, while major complications include reoperation, due to deep infection, hardware failure, non-unions or malunions. Moreover, complex regional pain syndrome and tendon ruptures are classified as major complications (32, 37). However, to the best of my knowledge no internationally accepted consensus exists regarding the graduation of complications based on the severity (39).

Importantly, there are no reporting guidelines regarding complications. Authors thus tend to copy and modify complication classifications on previously published scientific reports. The lack of reporting guidelines may also partially explain the wide variation in complication rates after volar

plating. Previous studies report complication rates ranging from 4% to 36% after operative treatment of DRF (28, 32, 40-42). Our own estimation of the complication rate after volar plating of DRF was 14.6% [95% CI 11.8–17.7%] in a retrospective cohort of 595 patients with 3.2 years follow-up (3).

Given the fact that surgery imposes a risk itself, it is not surprising that recent studies report that operatively treated patients have more complications than non-operatively treated patients (3, 28, 32, 40, 43, 44). If complications occur, these may cause permanent sequelae and morbidity to the patient and increase the treatment cost for society (45).

Complications are thus an important outcome when evaluating difference in treatment options. Other important outcomes for evaluating differences in treatment options are functional and radiological outcome measures.

Patient-reported Outcome Measures (PROMs)

A systematic review from 2022 analysed the most frequently used outcome measures for DRF (46). More than 70% of the 119 studies used the PROM: Disability of the Arm, Shoulder and Hand (DASH) and range of motion (ROM). These were followed by the grip strength, pain and Patient-Rated Wrist Evaluation (PRWE).
With regards to PROMs, availability of a translated and culturally-adapted version in the native language of the patient is mandatory. There exist validated Danish versions of both the DASH, QuickDASH and PRWHE. In the current thesis, the abbreviated version of the DASH, i.e., QuickDASH and modified PRWHE PROMs were applied. Reasoning for this methodological choice is given in the methods section below.
Alternative PROMs are the Michigan Hand Outcomes Questionnaire, which is infrequently used, but has also been used in a randomized controlled trial: the WRIST trial (47).

The minimally clinically important difference (MCID) for PROMs is a matter of debate and no consensus has been reached (48-52). As an example, while some authors suggest a MCID for QuickDASH of 14 (95%CI: 9-20) points and 14 (95% CI: 8-20) points for PRW. But according to

the homepage of the DASH developers, a minimally clinically important difference (MCID) was defined as a 16-20-point difference in QuickDASH (50, 53, 54).

Grip strength and range of motion (ROM) are also commonly applied objective measurements of interest when evaluating the functional outcome after DRF. Here it is of paramount importance to use reliable and reproduceable evaluations. A calibrated dynamometer and repeated measurements should be used for grip strength measurements (55-57). More details regarding the applied methodology in the papers of this thesis are given below.

Radiological evaluation

As orthopedic surgeons we often base our decision making on radiographs, while radiographs themselves have little importance for patients if not functionally relevant. However, radiological evaluation can also be used to determine the severity and treatment effect of the fracture. Angulation both dorsal and volar, radial inclination and comminution as well as ulnar variance are all frequently evaluated radiological parameters (58).

Comminution is defined as one or more fragments of cortical bone and is of importance for the stability of the fracture. However, while some authors suggest a fragment size of 3 mm as clinically significant comminution, in clinical practice dorsal comminution is seldomly clearly defined and thus remains a subjective assessment of the treating physician (59-63).

Dorsal angulation of more than 10 degrees, radial inclination of less than 15 degrees and ulnar variance for more than 2 mm are all reported to affect the functional outcome negatively (64, 65).

Patients with intra-articular DRF that heal with an incongruent joint are reported to increase the risk of radiocarpal arthrosis (66-68). However, a gap in the joint surface does not pose the same arthrosis risk in all patients. The presence of posttraumatic arthrosis does not always lead to deterioration in patient-perceived function or pain (50, 66, 67, 69). Clinical consensus is, however, that a step off in the joint surface of more than 2 mm should be addressed in both the radiocarpal and the distal radioulnar joint (65, 70, 71). Posttraumatic arthritis (PA) may occur after fractures and even more so after intraarticular fractures. In 1986, Knirk and Jupiter published data on PA with an estimated prevalence of 65% after a mean follow-up of 6 years after intraarticular distal radius fractures (72).

National Clinical Guidelines

Attempting to unify the management of DRF, many countries have made an effort to develop national clinical guidelines (NCG). Interestingly, there are significant differences from country to country, and even guidelines that were developed in the same time period and thus base the recommendations on the same scientific evidence, come to different conclusions and recommendations.

The Danish Clinical Guidelines for displaced DRF from 2014 and reinstated in 2017 recommend volar locking plating regardless of the age of the patient, unless the patient has a low functional demand (43). However, the guidelines do not define the term low functional demand. This guideline is no longer mandatory to follow, as it has been marked as "outdated" in 2023. The Norwegian guidelines from 2015 have some similarity with the Danish guidelines (73). In contrast, quoting the same literature, which was available in 2015, the Finnish Medical Society states that there is no difference in functional outcome between operative and non-operative treatment wherefore non-operative treatment is recommended due to lower costs and to avoid complications (74).

More recent guidelines, as the British guidelines from 2018 and the American guidelines from 2020 focus mostly on radiographic parameters as a primary decisive factor for surgery. The American guidelines refer to the treatment of elderly above 65 years of age with strong evidence for non-operative treatment, and reserved radiographic indication for surgery for the younger population (75). The British guidelines also refers to treatment of the elderly above 65 years of age with non-operative treatment as primary treatment of displaced distal radius fractures but operative treatment can be discussed with the patient depending on pre-injured function, medical comorbidities and fracture characteristics (76).
Clinically applicable, the Swedish guidelines from 2021 divide functional demand of the patient into low, medium, and high. High demands patients are recommended surgically treatment according to radiographic parameters like the Danish guidelines. However non-operative treatment is recommended for low demand patients, describing patients whom are not able independently to take of activity of daily living (77).

The national clinical guidelines (NCG) by to the Danish Health Authority recommends treatment of low-energy DRF with VLP (6) according to the following radiologic criteria following attempted closed reduction:

> 10° dorsal tilt of the radius in relation to perpendicular to the longitudinal axis of the radius
> 2 mm articular step-off
> 2 mm ulnar variance
– incongruence of the distal radioulnar joint
– substantial dorsal comminution indicating gross instability

Regardless of the patient's age, ORIF utilising a VLP is recommended if one or more of these criteria are met. The guideline also highlights that non-operative management should be considered in patients with "low functional demands"; however, "low functional demands" is not defined in the guidelines.

NCG guidelines are based on evaluation of the existing literature using GRADE (Grading of Recommendation, Assessment, Development and Evolution) (78, 79). All recommendations are of low evidence and to be considered as "good clinical practice" guidelines. The decision for surgical treatment in the NCG rely on radiological and previous literature has shown that the reliability of the specific radiological parameters is low (80). Another issue with the NCG is that no recommendations are presented for high-energy, open fractures or grossly instable fractures such as volar displaced (Smith), radial styloid (Chauffeur) or volar / dorsal articular rim (Barton) fractures. Most of these fractures, however, are also treated with VLPs in Denmark.

This PhD thesis investigates complications and functional outcome after DRF in patients (≥ 65 years), where return to work and faster recovery may not be as important. It appears relevant to investigate these in the interest of patients and society alike (81, 82).

Aim

The primary aim of this thesis was to prospectively investigate the complication rate and functional outcome of displaced DRF after non-operative treatment vs. operative treatment with volar plating in patients 65 years of age or older.

The secondary aim of this thesis was to report the complications, functional outcome and radiological evaluation of minimally or non-displaced DRF in the same age group.

The tertiary aim was to evaluate the complications and functional outcome between non-operative treatment of minimally/non-displaced vs. displaced DRF.

Hypotheses

Paper II)   Treatment of minimally or non-displaced DRF according to the NCGs with closed reduction and cast immobilisation is associated with few complications and has a good functional outcome, e.g. changes in the patient-reported outcome measure (PROM) Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH) is below the minimal clinically important difference compared with the recalled pre-injuried level (ΔQuickDASH$_{12months-preinjury}$<16) (53, 83).

Paper III)   Non-operative treatment of displaced DRF is superior to ORIF with a VLP in terms of complications. However, both treatments have comparable functional outcome after 12 months (ΔQuickDASH<16).

Paper IV)   Non-operative treatment of minimally or non-displaced and displaced DRF has an acceptable functional outcome after 12 months (ΔQuickDASH$_{12months-preinjury}$<16) (53, 83). However, the early functional outcome at 2 and 5 weeks is poorer for displaced DRF than for minimal or non-displaced DRF (ΔQuickDASH$_{minimal/non-displaced-displaced}$).

Paper V)   Follow-up at minimun three years on non-operatively treated minimally or non-displaced DRF wil find no clinically or radiographically relevant symptoms of post-traumatic articular arthrosis and, secondarly, will be similar to results found after 1 year in terms of complications and PROM (Paper II). (Δcomplications$_{minimal/non-displaced\ 1\ year-minimal/non-displaced\ 3\ years,}$). ($\Delta$QuickDASH$_{minimal/non-displaced\ 1\ year-minimal/non-displaced\ 3\ years,}$).

Design

The primary aim is investigated in a single-center, single-blinded, randomised, controlled superiority trial.

The secondary and tertiary aim are investigated in observational studies, namely a prospective case series and a prospective cohort study.

The study was conducted at Regional Hospital Randers, Denmark, which has an estimated uptake area of 270,000 inhabitants.

Paper I - Protocol

Paper II - Prospective case series (aim 2)

Evaluation of clinical outcome in patients with minimally or non-displaced DRF (n_3=50) treated non-operatively according to the NCG (grey column, Fig.1). The main purpose of this study was to provide reliable, up-to-date information about Danish patients with DRF before fracture and at 5 weeks and 6 and 12 months. Furthermore, this cohort was meant to serve as a reference group in Paper IV.

Outcome: Complications, functional outcome (PROMs: QuickDASH, patient-rated wrist and hand evaluation (PRWE), European Quality of Life – 5 dimensions (EQ5D)) and objective measures (range of motion (ROM) and grip strength, pain, quality of life). Radiological evaluation measuring dorsal angulation at presentation, after potential closed reduction and after 5 weeks follow-up.

Paper III - Single-centre, single-blinded, randomised controlled trial (aim 1)

Investigation of the potential superiority of non-operative treatment (n_1=50) vs. surgical volar plating (n_2=50) of displaced DRF in patients older than 65 years with regards to complications. Volar plating is currently the recommended treatment according to the NCG.

Primary outcome: Complication rate

Secondary outcome: Same as stated as outcome in Paper II.

Follow-up: Day of injury, 2 weeks, 5 weeks, 6 months, and 12 months after the injury.

Paper IV - Prospective cohort study (aim 3)

Comparison of the functional outcome at the time points 2 and 5 weeks and 12 months between non-operatively treated minimally or non-displaced (n_3=50) and displaced DRF (n_1=50) in patients with DRF, i.e., green vs. grey column in Fig. 1.

Primary outcome: Functional outcome (QuickDASH)

Secondary outcome: Complications and primary outcome measures of Paper II-III.

Paper V - Prospective case series (aim 2)

Evaluation of clinical outcome of minimally / non-displaced DRF in patients (n_3=50) treated non-operatively (grey column, Fig.1). The main purpose of this study was to provide data on patient outcome 3 years or more after DRF and compare the results with those achieved at 12 months. Patients were seen in the outpatient clinic.

Primary outcome: Radiographs to evaluate potential post-traumatic and articular arthrosis.

Secondary outcome: Complications, functional outcome (PROMs: QuickDASH, PRWE, EQ5D) and objective measures (range of motion and grip strength, pain, quality of life).

Radiographs were taken to evaluate protentional post-traumatic articular arthrosis. Radiological evaluation measuring dorsal angulation at presentation, after potential closed reduction and after 5 weeks follow-up and latest follow-up after more than 3 years.
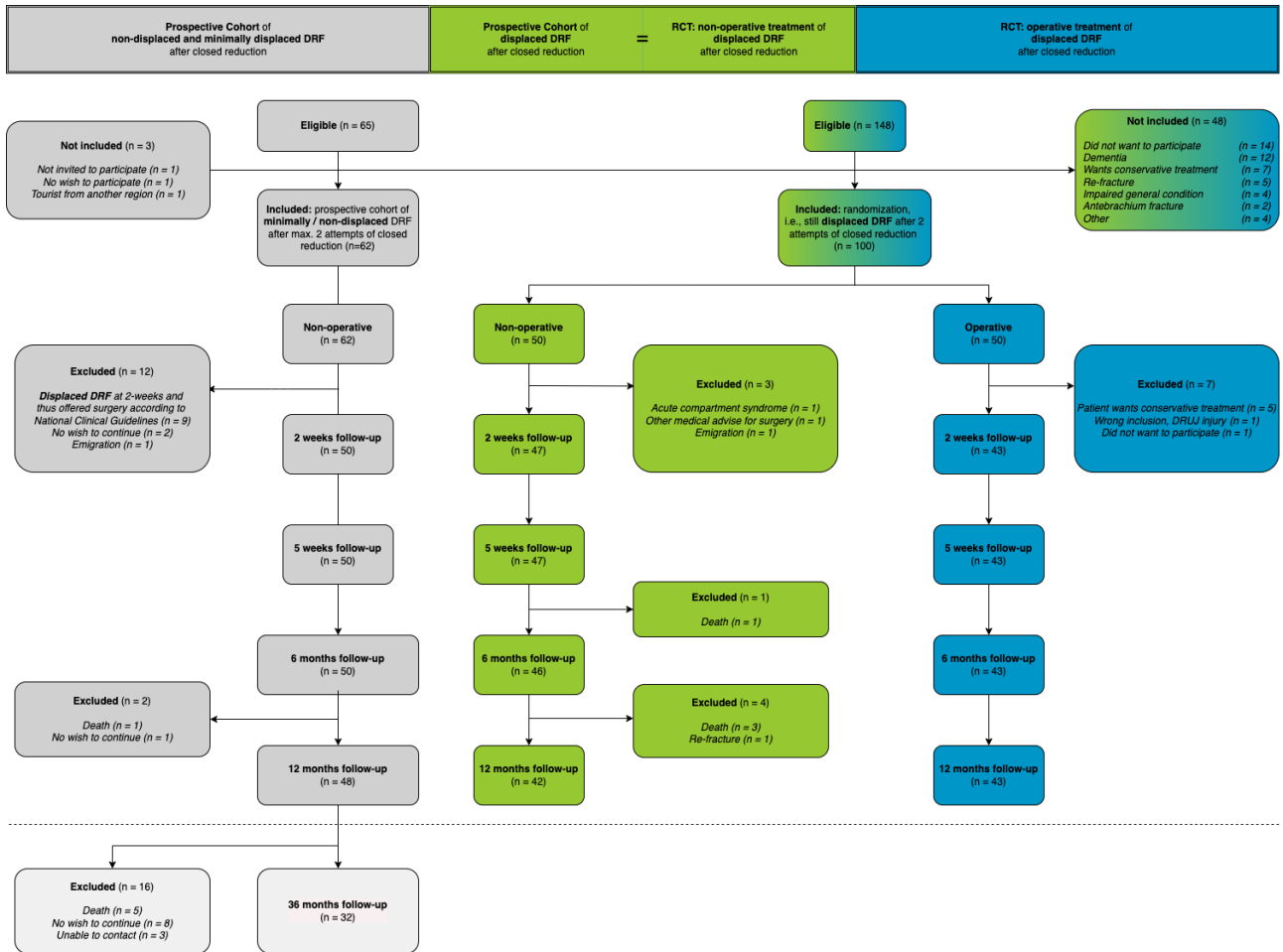
Figure 1. Consort flow diagram of all patients included in the present PhD thesis.

Paper II	grey column	with 1 year follow-up.
Paper III	green vs. blue columns	with 1 year follow-up.
Paper IV	grey vs. green columns	with 1 year follow-up.
Paper V	grey column	with >3 years follow up.

Figure 1 is also available online in full scale for the readers of the printed version of this PhD thesis, where the text might be too small and cannot be enlarged:

doi.org/10.5281/zenodo.7677689

Materials and methods

Eligibility criteria

All patients aged 65 years and above with a radiologically diagnosed DRF presenting at the Emergency Department of Regional Hospital Randers in the period from 1 November 2018 to 31 Marts 2021 were screened for eligibility (Paper III).

The eligibility of all participants had to be approved by one of the consultants in the research group or by the house physician who was on call on the day of inclusion. Patients were primarily recruited by direct contact in the emergency room on the day of the injury. On this occasion, they were informed about the study and asked to provide written consent; and they were given at least 1 hour to decide upon inclusion or not. The Danish standard consent form (Appendix 1) and patient information material were given to the patient in Danish (Appendix 2).

All radiographs of DRF at Regional Hospital Randers, Denmark were screened for eligibility by the main investigator (R.T.) on a daily basis. Radiographs from Friday, Saturday, and Sunday were either screened from home or the next working day. Before holidays R.T. instructed the surgeons on call (12 colleagues) to review the radiographs and contact her, if eligibility criteria were met or when in doubt. Moreover, posters with inclusion criteria were placed in the emergency department with direct contact details of R.T. After her holiday, the PhD student would review all DRF which presented during the vacation. This process aimed to ensure that all eligible patients were offered study enrolment either immediately while in the emergency room or the day after by telephone by one of the doctors from the research group. If recruited by telephone, written consent was obtained before surgery or, for the non-operatively treated patients, at the 2-week out-patient visit.

Inclusion criteria

The inclusion criteria were seperated in two groups. Those for the randomised controlled trial (RCT) and those for the prospective cohort (Figure 1). The following inclusion criteria had to be meet:

- ≥ 65 years old
- ability to give written informed consent.

To be included in the RCT study, one or more of the following radiological criteria had to be met:

- > 10° dorsal tilt of the radius in relation to perpendicular to the longitudinal axis of the radius
- > 2 mm ulnar variance
- > 2 mm articular step-off
- Incongruence of the distal radioulnar joint
- Substantial dorsal comminution
- < 20° radial inclination
- < 5 mm radial length

To be included in the prospective cohort study, the following criteria had to be met:

- ≤ 10° dorsal tilt of the radius in relation to perpendicular to the longitudinal axis of radius
- ≤ 2 mm ulnar variance
- ≤ 2 mm articular step-off
- No incongruence of the distal radioulnar joint
- ≥ 20° radial inclination
- ≥ 5 mm radial length

Exclusion criteria

- Patients < 65 years
- High-energy fracture
- Open fracture
- Concomitant injuries, e.g., multiple fractures on afflicted arm
- Previous DRF or forearm fracture on the same side
- Not able to provide written informed consent (due to dementia, inability to communicate in Danish (read / write / talk) or cognitive impairment)

Randomisation

Random drawing of sealed, completely opaque envelopes was used for randomisation. Moreover, the note including the randomisation was folded in the envelope to make sure that treatment assignment was truly randomised and non-transparent (84, 85). Fifty participants were allocated to each group. Thus, 100 identical A5 opaque envelopes were sealed – each containing a folded note with a written note saying "*operation*" or "*conservative*". For similarity in timewise enrolment and allocation concealment, the following measures were applied (Figure 2).

Block randomisation was used, and the 50 envelopes for operative and conservative treatment were packed into stacks of five envelopes. One stack from each group was mixed and the including doctor drew one of the ten envelopes; thus, randomly allocating the participant to either treatment arm 1 or 2. When only three envelopes were left, one stack from each group was mixed into the remaining three envelopes. By this measure, the including doctor could not predict the allocated treatment from the order of the previous, mixed treatment allocation from the mixed small envelope pool, and the allocation concealment was kept.
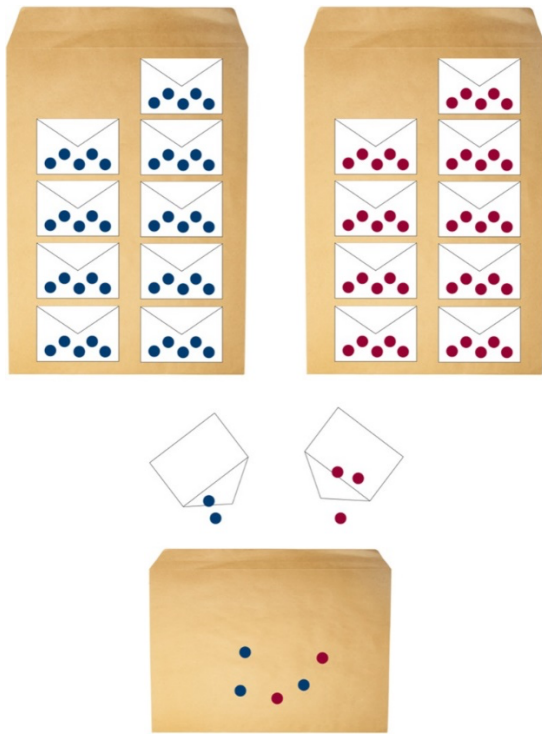
Figure 2. Illustration of the intervention group randomisation, e.g., treatment arm 1 and 2. Each dot represents a sealed, completely opaque envelope containing a note with the treatment arm allocation. The blue dots represent "conservative treatment"; the red dots, "operative" treatment. Whenever only three envelopes were left, five new "operative" and five new "conservative" treatment envelopes were mixed and added.

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Intervention

Prior to inclusion and randomisation, all patients who did not fulfil the NCG criteria for non-operative treatment (displaced DRF) underwent intervention in the emergency department. When diagnosing the DRF with a standardised wrist radiograph (anterior-posterior projection and lateral projection), closed reduction was performed by the doctor on call to achieve an acceptable position for conservative treatment according to the NCG. The reduction was done under local anaesthesia with a 20 mg/ml lidocaine haematoma block under x-ray guidance. A maximum of two reduction attempts were made per patient. After acceptable reduction, a cast was applied and standardised radiographs were obtained at the Department of Radiology. After reduction, the patient was offered to enter the PhD project either in the prospective cohort or the RCT depending on the inclusion criteria. The PhD project was divided into three arms, two intervention arms in the RCT and one prospective, non-operatively treated cohort as shown in Figure 1.

Intervention group 1: Blue column

Operative treatment consisted of ORIF and volar plate fixation using Acu-Loc® 2 wrist plating system from Acumed, Swemac Osmedic, Denmark or VariAx® Distal Radius Locking plate from Stryker, Denmark. The choice of volar locking plate, i.e., Acu-Loc or VariAx was at the descretion of the operating surgeon. Both of these plates were readily available at our institution.

In most patients, the surgery was performed in regional anaesthesia, and the remaining patients underwent surgery in general anaesthesia. The surgeon had the choice to use a tourniquet or not. During surgery, the surgeon used a standard Henry approach for distal radius and pronator quadratus repair if possible. The skin was closed at the discretion of the surgeon by either intra- or extracutaneous suture. After surgery, the patient was immobilised in a cast for two weeks. At two weeks, an outpatient clinic visit was made, sutures removed, and the patient was converted into a removable orthosis for another three weeks. At two weeks, a single-hand therapeutic instruction took place.

Intervention group 2: Green column

These patients were randomised to non-operative treatment consisting dorsal plaster cast immobilisation for 5 weeks. Only discomfort, neurologic deficit or sign of infection were indicators for changing the cast to another dorsal cast earlier than at 5 weeks. A single-hand therapeutic instruction was given after cast removal after 5 weeks.

Both intervention column 1 and 2 involved taking standardised wrist radiographs (anterior-posterior projection and lateral projection) after 2 and 5 weeks.

Prospective cohort of minimally or non-displaced DRF with or without closed reduction: Grey column

In conformity with the NCG, patients with minimally or non-displaced fractures before or after a closed reduction performed under local anaesthesia did not undergo surgery; intervention column two. At two weeks, a standardised wrist radiograph was obtained. If, after two weeks, the patient still fulfilled the NCG criteria for non-operative treatment, they would stay in the project. Opposite, if the fracture fulfilled the NCG criteria for surgery, surgery was offered, and the patient left the trial.

The investigators reserved the right to exclude a participant if it was considered clinically inappropriate to let them stay in the trial. Patients were at all times free to withdraw their consent. If patients withdrew consent, trial-related registration in the electronic patient records was discontinued. Consequently, the intention-to-treat principle for data analysis could not be met.

Sample size

Sample size calculation was based on a 20% difference in complication rate between the two treatment groups, a 5% alpha level and a power of 80%. Consequently, each group should include a minimum of 49 participants. It was decided that the prospective cohort of minimally / non-displaced DRF with/without closed reduction should have the same size as the intervention groups of the RCT (81).

The sample size of $50=n_1=n_2=n_3$ was based on the following assumptions: Δprimary outcome (complication rate of 0.06 vs. 0.26) = 0.2, power=0.8, alpha=0.05 (14, 28, 40-42, 86). It was decided to include 50 patients in each of the three groups.

Data collection and management

According to Good Clinical Practice, all data were stored and managed by the investigators. Data were collected on paper. Each patient's file was kept in a plastic cover with their name, social security number and project number. When not in use, files were kept in a locked drawer in the locked office of the principal investigator. All paper files were later entered into and managed in REDCap, an electronic data capture tool database hosted at Aarhus University, Denmark, for later statistical analyses (87). All patients were contacted by phone, email, or surface mail if they did not show up in the outpatient clinic for follow-up. Non-attendance contacts included an offer of another appointment to ensure retention and complete follow-up.

Outcome measures

Primary outcomes

Complications were used to estimate sample size and were the primary outcome in Paper II and III. The complication rate was assessed prospectively at the following time points: day 0, recalling the pre-injury state; 2 and 5 weeks; and 6 months and 12 months after the injury. Patients answered investigators' questions and were allowed to make additional comments if their complications were not on the predefined list. In addition, patients' medical journals were reviewed, checking for additional complications the patient might have forgotten or failed to report themselves. Complications were defined as the presence of one of the following:

– Sensory disturbance, including carpal tunnel syndrome and chronic regional pain syndrome

– Flexor tendon rupture and irritation

– Extensor tendon rupture and irritation

– Hardware failure, e.g., osteosynthesis loosening

– Infection: superficial (treated with antibiotics only) or deep (requiring surgical intervention)

– Reoperation with hardware replacement

– Reoperation with hardware removal (partial or total), which is not routinely performed in Denmark

– Vascular compromised (capillary refill ≥ 2 seconds)

In Paper II and IV, the Danish version of the QuickDASH (83) was used as primary outcome to assess the level of function prior to injury (patient were asked for their disabilities 2 weeks prior to the fracture), after 2 weeks, 5 weeks, 6 months and 12 months. The minimal clinically important difference (MCID) was defined as a 16-20-point difference in QuickDASH (50, 53, 54).

In Paper II, range of motion (ROM) was measured by a trained registered nurse using a goniometer and a pre-printed introduction with pictures so that the measurement was done in the same way by all the four different nurses. To ensure that the observer was blinded, the patient was instructed not to refer to the treatment methods. To make the blinding by the nurse more effective, all wrists were covered by a glove concealing potential scars. (Figure 3)

Observed ROM included wrist flexion, extension, pronation, supination, radial deviation, and ulnar deviation. The contralateral side was also evaluated as a reference, and history of injuries or operations of the contralateral side were recorded.

Figure 3. Assessor blinding by concealing potential scars.

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Secondary outcomes

A patient-related outcome measure, the Danish version of the Patient-rated Wrist Evaluation questionnaire (PRWHE) was used after 6 and 12 months and > 2 years (88). The MCID for PRWHE was set to 10 points (49).

Another PROM, the EQ5D (European Quality of life – 5 Dimensions), was used after 6 and 12 months and > 2 years. The EQ5D score was registered by an unblinded physician at the out-patient clinic visits (89).

The last PROM used was self-reported pain on a numerical rating scale (NRS). Pain experienced within the preceding 2 weeks before the injury and at 2 and 5 weeks, 6 and 12 months and >2 years of follow-up was stated on a 0–10-point NRS (90).

A dynamometer (EH101 Camry, by Camry scale) was used to assess grip strength on the left and the right hand both as the maximum and the average strength score of three repetitions of each hand after 6 and 12 months and > 2years. The MCID of grip strength was 6.5 kgs (55-57).

Objective measurement was performed by the investigators using a pinch gauge. If the participant could pinch a sheet of paper, both the left and the right hand were evaluated (yes/no). These measures were collected after 6 and 12 months and after > 2 years. Furthermore, a potential flexion deficit of the 1st finger towards the base of the 5th finger was measured by the distance in cm from the pulp of the 1st finger to the carpometacarpal joint of the 5th finger and the pulp-to-palm distance of the distal 2nd-5th finger and palmar surface of the side treated for DRF after 6 and 12 months and again after 2 years.

Radiological outcome measures include the degree of the dorsal / volar angulation and degree of arthrosis based on standardized lateral and anteroposterior radiographs of the injured wrist at the stipulated timepoints given in the papers (58, 72).

Baseline demographics were recorded as follows: gender, age, side of DRF, hand dominance (right-handed, left-handed, ambidextrous), working status, American Society of Anesthesiologists Classification (ASA class 1–6) (91, 92), smoking (cigarettes/day), alcohol consumption (units/week) and diabetes (yes/no). Finally, all use of medicine before, during and after surgery was recorded.

Statistical analysis

Discrete / categorical data (complications: yes / no) are presented as percentages and were compared using Fisher's exact test. Continuous data are presented as means with 95% confidence intervals (CI) if normally distributed; otherwise as medians with IQR or median with (min, IQR, max.) depending on the author guidelines of the respective journals.

In Paper II, Fisher's exact test and Mann Whitney U test were used for analysis. Odds ratio with Pearson's 95% confidence interval were calculated. Mixed effects analysis with correction for multiple comparisons was applied to analyse the longitudinal change of the different outcome measures, i.e., QuickDASH, VAS, dorsal angulation and ROM. Spearman's correlation was applied to QuickDASH vs. PRWHE. EQ5D-3L were presented as raw data and indices.

In Paper III, Fisher's exact test of the accumulated complication rate after 12 months was used to compare complication rates. Only one complication was accounted for per patient to avoid double counting in patients with multiple complications. Mixed-effects analysis with Sidak's multiple comparisons test were used to analyse data for secondary outcome measures. All available data were used without imputations for missing values. Continuous measures were presented as means with standard deviations and medians with IQR in tables for QuickDASH and NRS.

In Paper IV, the complication rate was analysed as in Paper III. Descriptive monographic data were presented using descriptive statistics and, as previously, continuous measures were presented as means with standard deviations and medians with IQR in tables for QuickDASH, ROM and NRS. Secondary outcome measures were analysed using mixed-effects analysis with Sidak's multiple comparison test, as in Paper III.

In Paper V, Fisher's exact test was used to compare PA after 5 weeks vs. 3 years as well as complication rates. One-way repeated measures ANOVA including Sidak's multiple comparison test was employed for the repeated QuickDASH values because analysis was restricted to the 32 patients with complete data, i.e., no missing data were used, which would have required a mixed-methods analysis instead of ANOVA.

All statistical tests were performed using Prism 9 for macOS (version 9.1.0, GraphPad Software, San Diego, CA, USA). Statistical significance was defined as $p \leq 0.05$.

Ethical considerations and permissions

Papers II-IV are registered at clinicaltrials.gov (NCT0371661) and have been approved by the Danish Scientific Ethical Committee (1-10-72-420-17). Paper V has also been approved by the Danish Scientific Ethical Committee as an appendix to the primary study (1-10-72-420-17 / 79290). All studies were registered at the Danish Data Protection Agency (1-16-02-609-18).

The studies were performed according to the ethical principles of the Helsinki Declaration. Patients could withdraw their written consent at any time during the study without any negative effect on their continued treatment.

Main results

Paper II

Please refer to the grey boxes of the CONSORT flow diagram. In total, 62 patients were included and 12 were excluded, mainly due to fracture dislocation after the first 2 weeks, leaving the study cohort with 50 patients. During the follow-up period, two patients died, resulting in 48 patients with complete data for analysis after 12 months of follow-up.

The main results from Paper II were the reported complications. Eight patients of 50 possible (16%) reported complications after 6 months, while 3/48 (6%) reported complications after 12 months. Complications after 12 months included two patients who complained about sensory disturbances and one patient who complained about swelling during activity and reduced strength.

For secondary outcomes, at week 2 and 5 after surgery, both the QuickDASH and the pain score were significantly worse than before surgery. Both outcome measures had returned to their

preinjury level after 6 and 12 months, and no statistically significant difference was seen between the three time points (93).
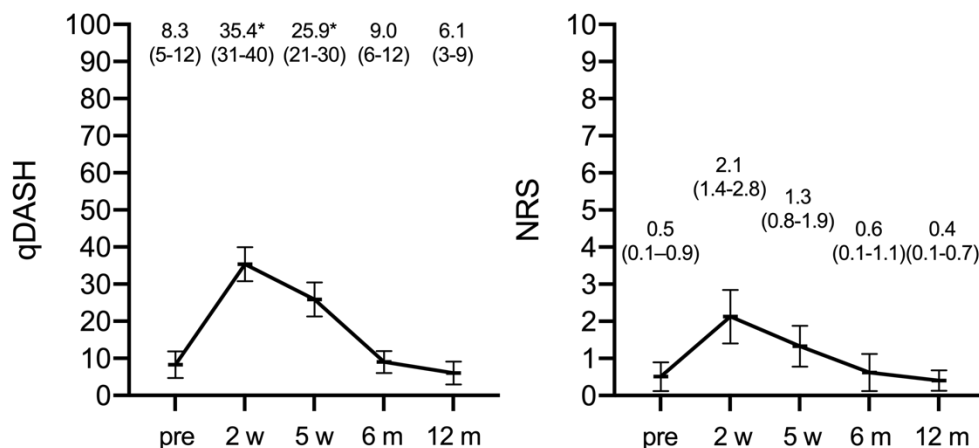

Figure 4. QuickDASH and NRS pain score, preinjury (pre), 2 weeks (w), 5 weeks (w), 6 and 12 months (m); * $p < 0.05$ compared with preoperative, i.e., recalled scores.
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A statistically significant (p = 0.05) change was seen in mean PRWHE scores from 13.5 (95% CI 9.0-18.0, IQR 0-19) after 6 months to 8.7 (95% CI 3.6-13.7, IQR 0-10) after 12 months.

Both patient-related outcome measure instruments showed a strong correlation at any given time point, as evidenced by Spearman's r(PRWHE-QuickDASH) = 0.74 (p<0.0001) after 6 months and r(PRWHE-QuickDASH) = 0.66 (p<0.0001) after 12 months. Furthermore, a strong correlation of the same instrument over time was seen over time, e.g. from 6 and 12 months: r (PRWE (6 months – 12 months)) = 0.50 (p<0.0004) and r(QuickDASH(6 months – 12 months)) = 0.56 (p<0.0001) (93).

Active ROM in Figure 5 improved over the entire period and was not significantly different from the uninjured side after 12 months.

In the injured wrist, grip strength increased significantly from 6 to 12 months after injury (mean diff. 1.6 (95% CI 2.8 – 0.4, p<0.01). However, it remained impaired compared with the uninjured side at 6 months (mean diff. -6.0 (95% CI -7.9 - -4.2), p<0.0001) and 12 months (mean diff. -4.1 (95% CI -6.3 - -1.9, p<0.0001).
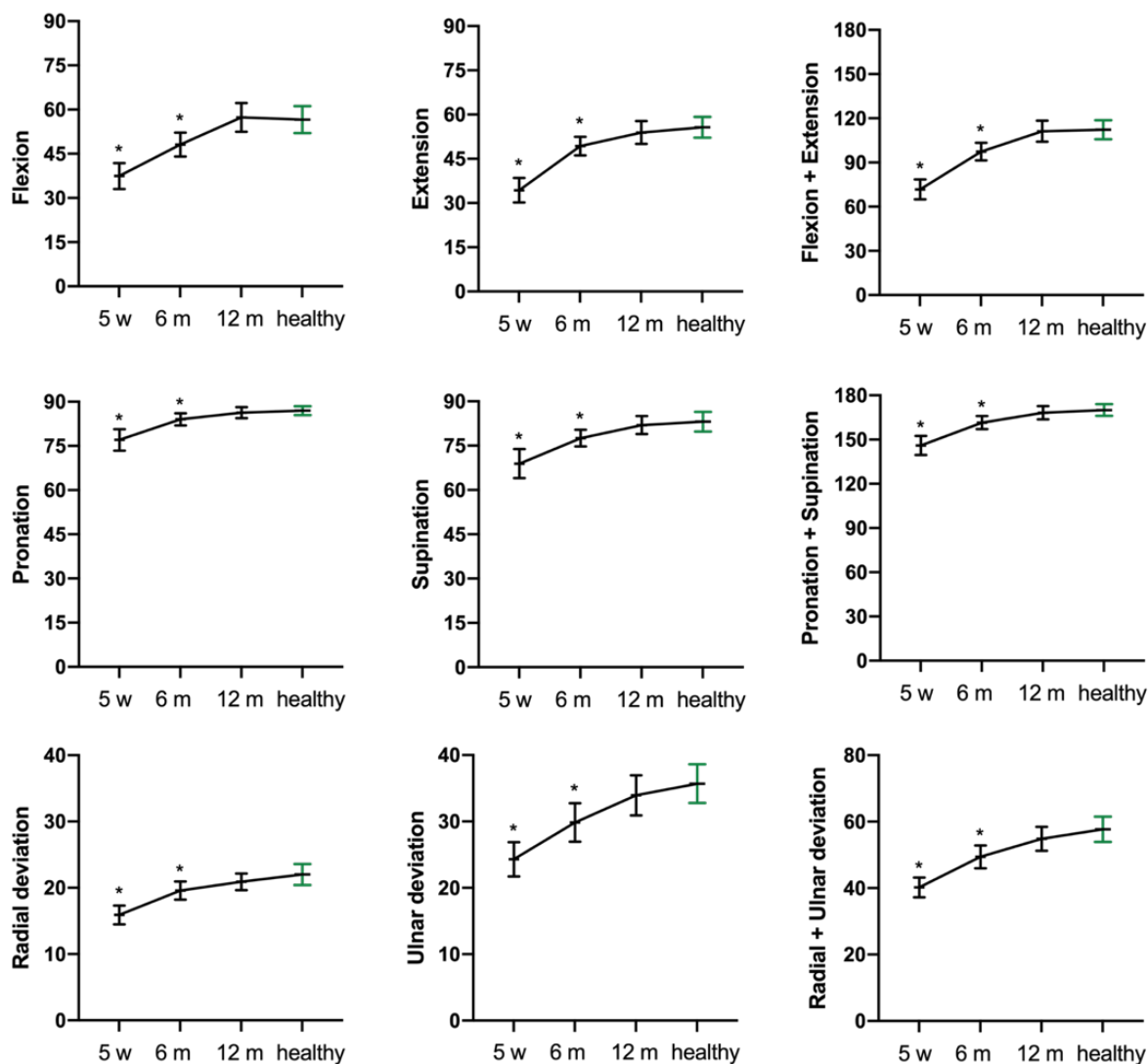

Figure 5. Temporal changes in active range of motion (degrees) after 5 weeks (w) and 6 and 12 months (m) compared with the healthy side at 12 months. * *p* < 0.05 compared with the healthy side (green).

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In total, 27 of the 50 patients included had their DRF reduced using a haematoma block, correcting the initial mean dorsal angulation of 14.8° (95% CI 9.0-20.5) (p<0.001) prior to reduction. The mean dorsal angulation after reduction was 1.8° (95% CI -0.2 - 3.7).

This correction was partially lost, 5.2° (95% CI 2.0-8.3; p=0.001), during the 5 weeks of conservative treatment with a dorsal plaster cast, both before and after the first 2 weeks.

In 23 patients conservatively treated without reposition, treatment maintained the mean dorsal angulation of 0.5° (-1.7-2.7) (mean difference: 2.4° (95% CI -0.2-4.9, p=0.066), Figure 6).

However, 9/27 reduced and 4/23 not-reduced fractures had a dorsal angulation of more than 10° on the latest radiographs after 5 weeks; still, 2 weeks after the injury, they had a dorsal angulation below 10° according to the radiographical control (Figure 5).
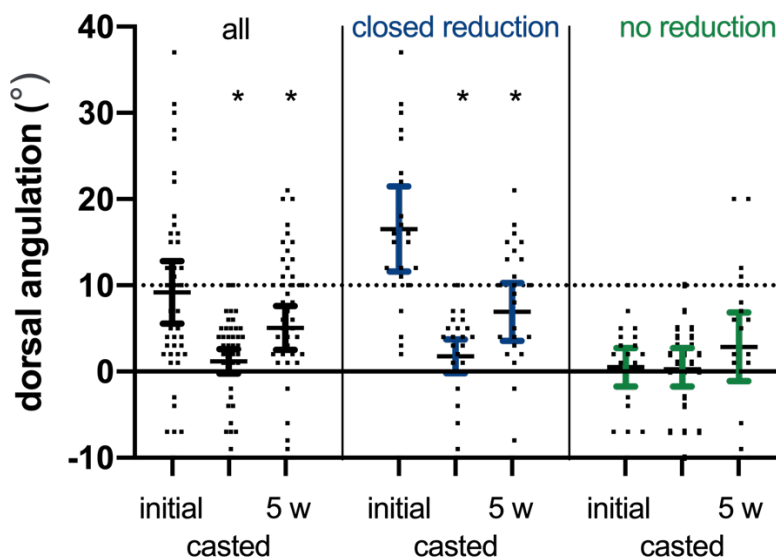

Figure 6. Dorsal angulation of the DRF at presentation, i.e., the initial radiograph, the casted radiograph, and the final radiograph after 5 weeks (5 w) for all DRF and subdivided based on closed reduction (yes; no). * $p < 0.05$ compared with the initial dorsal angulation. Reprinted from Thorninger et al., doi.org/10.3390/jcm10091831 according to (http://creativecommons.org/licenses/by/4.0/) (93)

Paper III

Of 148 patients assessed eligible for the study, 100 patients were enrolled and randomised to either surgery or conservative treatment. Figure 1 shows the inclusion process and patients available for 12-month follow-up. Exclusion was due to lack of consent due to refusal to participate, inability to write and refusal to undergo surgery.

Figure 1 shows loss to follow-up. A total of five patients were lost to follow-up, all of whom changed their mind after they had been randomised to surgery and refused to be operated. Four patients (4%) died before the 1-year follow-up, and 8 patients were excluded due to causes such as re-fracture, withdrawn consent and other reasons.

Baseline demographics of the population are shown in Table 1, showing no significant difference between the two groups (94).

	Non-operative (n=50)	Operative (n=50)
Female / Male	40 (80%) / 10 (20%)	41 (82%) / 9 (18%)
Median age (min., IQR, max.) [years]	74 (65, 69-82, 91)	75 (65, 70-80, 92)
Fractured side: R / L	24 (48%) / 26 (52%)	18 (36%) / 32 (64%)
Hand dominance: R / L / Ambidextrous / Missing data	46 (92%) / 1 (2%) / 1 (2%) / 2 (4%)	38 (76%) / 3 (6%) / 0 (0%) / 9 (18%)
Dominant side fractured	23 (46%)	16 (32%)
Retired / Working / Volunteer / Retired / Missing data	45 (90%) / 1 (2%) / 2 (4%) / 2 (4%)	42 (84%) / 0 (0%) / 0 (0%) / 8 (16%)
Smoking: Yes / No / Missing data	9 (18%) / 37 (74%) / 4 (8%)	2 (4%) / 36 (72%) / 12 (24%)
Alcohol overconsumption: Yes / No / missing data	8 (16%) / 38 (76%) / 4 (8%)	6 (12%) / 32 (64%) / 12 (24%)
ASA class 1 / 2	13 (26%) / 30 (60%)	14 (28%) / 29 (58%)
ASA class 3 / 4-6 / missing data	6 (12%) / 0 (0%) / 1 (2%)	4 (8%) / 0 (0%) / 3 (6%)
Comorbidities:		
Hypertension	23 (46%)	16 (32%)
Diabetes	6 (12%)	2 (4%)
Depression	4 (8%)	1 (2%)
Osteoporosis	3 (6%)	3 (6%)
Prescribed medications: None / 1-4 / $\geq$ 5	8 (16%) / 26 (52%) / 16 (32%)	19 (38%) / 21 (42%) / 10 (20%)

R = Right, L = Left

A fracture in an ambidextrous patient was not considered a fracture of the dominant side.

Alcohol overconsumption was defined as more than 7 units/week for females and 14 units/week for males.

Operative						
	day 0	2 weeks	5 weeks	6 months	12 months	TOTAL
N	50	42	43	43	43	9/43 (20.9%)
Carpal tunnel syndrome	0	0	0	0	1	1
Unspecific sensory disturbance	1*	3*	7*	8*	6	6
Flexor tendon rupture or irritation	0	0	0	0	0	0
Extensor tendon rupture or irritation	0	1	0	0	1	2
Vascular compromise (refill >2 s)	0	0	0	0	0	0
Osteosynthesis loosening / failure	0	0	0	0	0	0
Infection (deep or superficial)	0	0	0	0	0	0
Cast causing superficial wounds	NA	0	0	NA	NA	0
Reoperation	NA	0	0	0	2**	2**

Non-operative						
	day 0	2 weeks	5 weeks	6 months	12 months	TOTAL
N	50	47	47	45	42	7/42 (16.6%)
Carpal tunnel syndrome	0	0	1	0	1	2
Unspecific sensory disturbance	1*	1*	1*	7*	3	3
Flexor tendon rupture or irritation	0	0	0	0	0	0
Extensor tendon rupture or irritation	0	0	0	0	0	0
Vascular compromise (refill >2 s)	0	0	0	0	0	0
Osteosynthesis loosening / failure	NA	NA	NA	NA	NA	0
Infection (deep or superficial)	0	0	0	0	0	0
Cast causing superficial wounds	NA	0	2	NA	NA	2
Reoperation	NA	0	1**	0	1**	2**

NA = not applicable

* = Temporary change and therefore not counted in the row total.

** = Max. 1 complication per patient, i.e., only the reason for the reoperation is counted.

Complications in the two groups were described in Table 2 (94).

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Unspecific sensory disturbances at different time points over the follow-up period were reported by the participants. Most of these disturbances often had disappeared and were not reported at later follow-up visits. Therefore, only sensory disturbances at the 12-month visit were included in the stated complication rate. In addition, sensory disturbances the examiner did not related the

disturbance to a specific nerve, and reported disturbances were therefore subjective. However, two carpal tunnel syndromes were registered. Any complex regional pain syndromes were not observed. The seven events contributing to the complication rate of 16.6% in 42 non-operatively treated patients were: three unspecific sensory disturbances at 12 months of follow-up, two carpal tunnel syndromes causing "reoperations", i.e., decompression of the nerve after 5 weeks and 12 months, respectively; and two superficial scars without signs of infection at cast removal after 5 weeks; all highlighted in Table 2 in the green area and marked in bold.

In 43 operatively treated patients, the complication rate was 20.9% due to nine events, all highlighted in Table 2 in the blue area and marked in bold; six unspecific sensory disturbances at 12 months of follow-up, one carpal tunnel syndrome giving rise to a reoperation, i.e., plate removal and nerve decompression after 12 months; one extensor tendon irritation because of a protruding screw causing plate removal after 12 months and one extensor pollicis longus rupture which was not repaired. Thus, in the operative group, two re-operations were performed. In this group, a third patient fell again and sustained a new DRF / bending of the volar plate (Figure 7). The cause of the latter was a new trauma, and the case was therefore not counted as a complication or reoperation (94). Lastly, three trigger fingers after 5 weeks, 6 months and 12 months, respectively, were observed in the operative group but no trigger fingers were observed in the non-operative group. However, these observations were not classified as complications (94).

Furthermore, minor complications and observations were made. In the non-operative group these minor complications consisted of one cast changed due to loosening after the initial swelling had subsided. Moreover, one patient complained of ulnar wrist pain at final follow-up. In the operative group, three patients complained about a decrease in Rom that was bothersome.

These events or minor complains were not counted as complications. Still, the data were disclosed in the article in order ensure complete reporting of all complications and observations made.
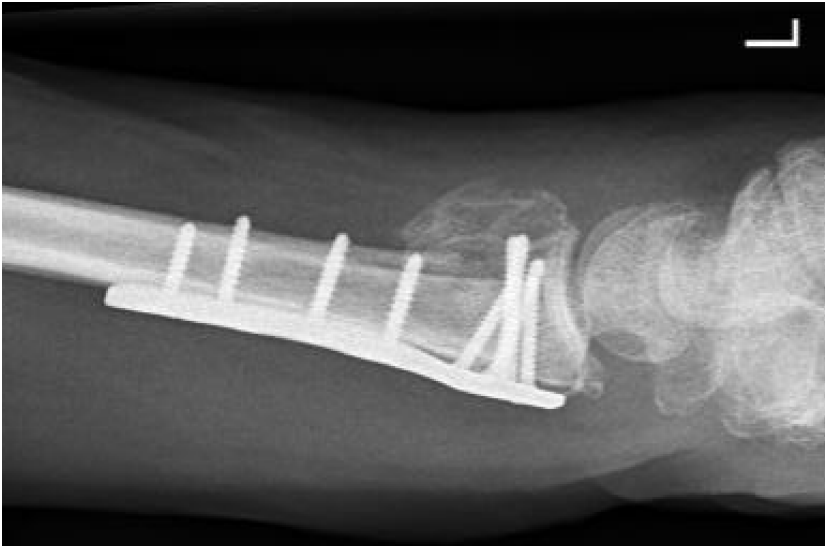
Figure 7. Bent volar locking plate. Lateral wrist radiograph of an operatively treated patient with DRF after a new fall causing a re-fracture and bending of the volar locking plate. This was a new trauma and therefore not accounted for as a complication.

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QuickDASH and NRS were also measured in the two groups. Mean QuickDASH and NRS with 95% CI as error bars were depicted before the injury (pre) and after 2 and 5 weeks (w) and 6 and 12 months (m). The mean difference (95% CI) between the operative group (blue) and the non-operative group (green) was given above the time points showed in Figure 8.
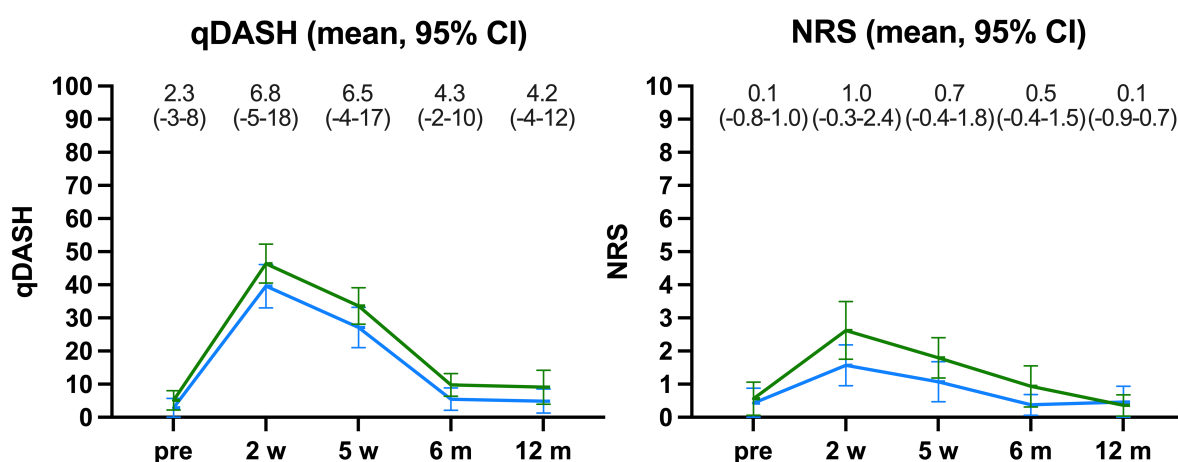
Figure 8. Functional outcome. Mean QuickDASH and NRS with 95% CIs as error bars are depicted pre-injury (*pre*) and after 2 and 5 weeks (*w*) and 6 and 12 months (*m*). The mean difference (95% CI interval) between the operative group (*blue*) and the non-operative group (*green*) is given above the timepoints,
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No significant difference in the two scores was recorded at any time. In addition, after 6 and 12 months, a statistically significant difference from the recalled pre-injury state was reported for neither of the two group.

The operative and non-operative groups had a similar mean PRWHE after 6 months: 9.6 (4.5-14.7) vs. 12.6 (8.7-16.5) and 12 months: 8.6 (2.5-14.7) vs. 8.0 (3.6-12.4). No statistically significant difference was observed between the two treatments at any timepoint. However, a slight overall improvement was observed from 6 to 12 months; mean difference 2.8 (0.1-5.5), p=0.04 (94).

The active ROM improved throughout the 12-month observation period. After 5 weeks and 6 months, some of the observed movements were statistically significantly reduced compared with the healthy side. Still, none of these ROM were statistically significantly different from those of the healthy side after 12 months. Comparing the two treatment groups, there was a statistically significant difference in combined flexion-extension ROM after 5 weeks: mean diff. 14.7° (5.5-23.8, p<0.0001); and 6 months: mean diff. 9.8° (0.3-19.3, p=0.037). After 12 months, the mean

difference was 6.8° (-3.2-16.7, p=0.61). At every measured time point, flexion-extension ROM slightly favoured the operative group.

At 12-month follow-up, the mean difference in grip strength was 1.4 (-2.6-5.5) kg. Mixed model analysis of grip strength taking all time points into account showed a significant time effect (p<0.0001) but no treatment effect (p=0.23) (94).

Paper IV

The two conservatively treated groups (green and grey column in Figure 1) were followed regarding primary outcomes as complications and regarding secondary outcomes as QuickDASH, PRWHE, ROM and grip strength measures. All outcomes were measured at day 0 and 2, 5 weeks and 6 and 12 months. Conservative treatment consisted of immobilisation with a dorsal splint cast for 5 weeks followed by occupational therapist instruction.

At 12 months, a complication rate of 16.6% was found in the displaced DRF group, consisting of three unspecific sensory disturbances at 12 months of follow-up and two carpal tunnel syndromes treated with surgical decompression after 5 weeks and 12 months, respectively.
In the minimal or non-displaced DRF group, the 12-month complication rate was 6.3 % (3/48) after 12 months. Two patients complained of unspecific sensory disturbances, whereas a single patient complained of swelling and lack of strength compared with the preoperative state. This difference between the complications rates in the non-operatively treated displaced and minimal or non-displaced DRF group of 7/42 vs. 3/48 patients was not statistically significant (p = 0.18, Fisher's exact test).

Secondary outcomes, i.e., QuickDASH and NRS, were compared at baseline (recalled pre-injured state) and at 6 and 12 months. The mean difference in QuickDASH between the two groups was statistically significant after 2 weeks (Figure 9) but of borderline clinical relevance as the minimal functional clinically important difference was 16-20 points.
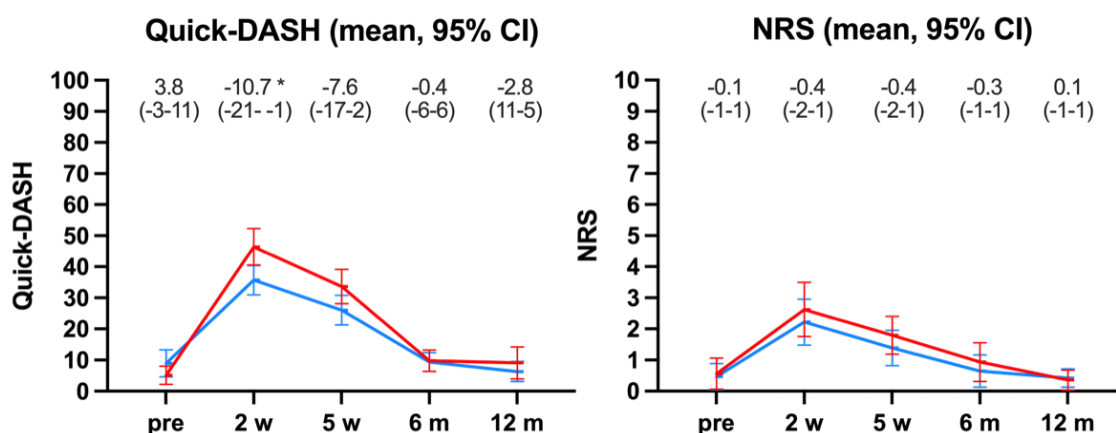
Figure 9. QuickDASH and NRS (pain) of the displaced (red) and minimally/non-displaced (blue) non-operatively treated DFRs. Mean differences (95% CI) between the groups at the different timepoints and statistical significance * p < 0.05.

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In patients with displaced DRF, mean PRWHE was 12.6 (8.7-16.5) after 6 months and 8.0 (3.6-12.4) after 12 months. In patients with minimal or non-displaced DRF, a mean PRWHE of 13.5 (9.0-18.0) was observed after 6 months and a mean PRWHE of 8.7 (3.6-13.7) was observed after 12 months. Hence, the mixed effects model showed a time (p=0.01) but not a fracture type dependency of PRWHE (p=0.79).

At 5 weeks and again at 6 months after inclusion, ROM was significantly impaired compared with the uninjured wrist in both groups (Figure 10; p<0.05). However, the overlaying graphs and statistical analyses highlight temporal improvements with similarity in both groups. Moreover, no statistically significant difference in ROM was observed compared with the uninjured side after 12 months; Figure 10 (p>>0.05).
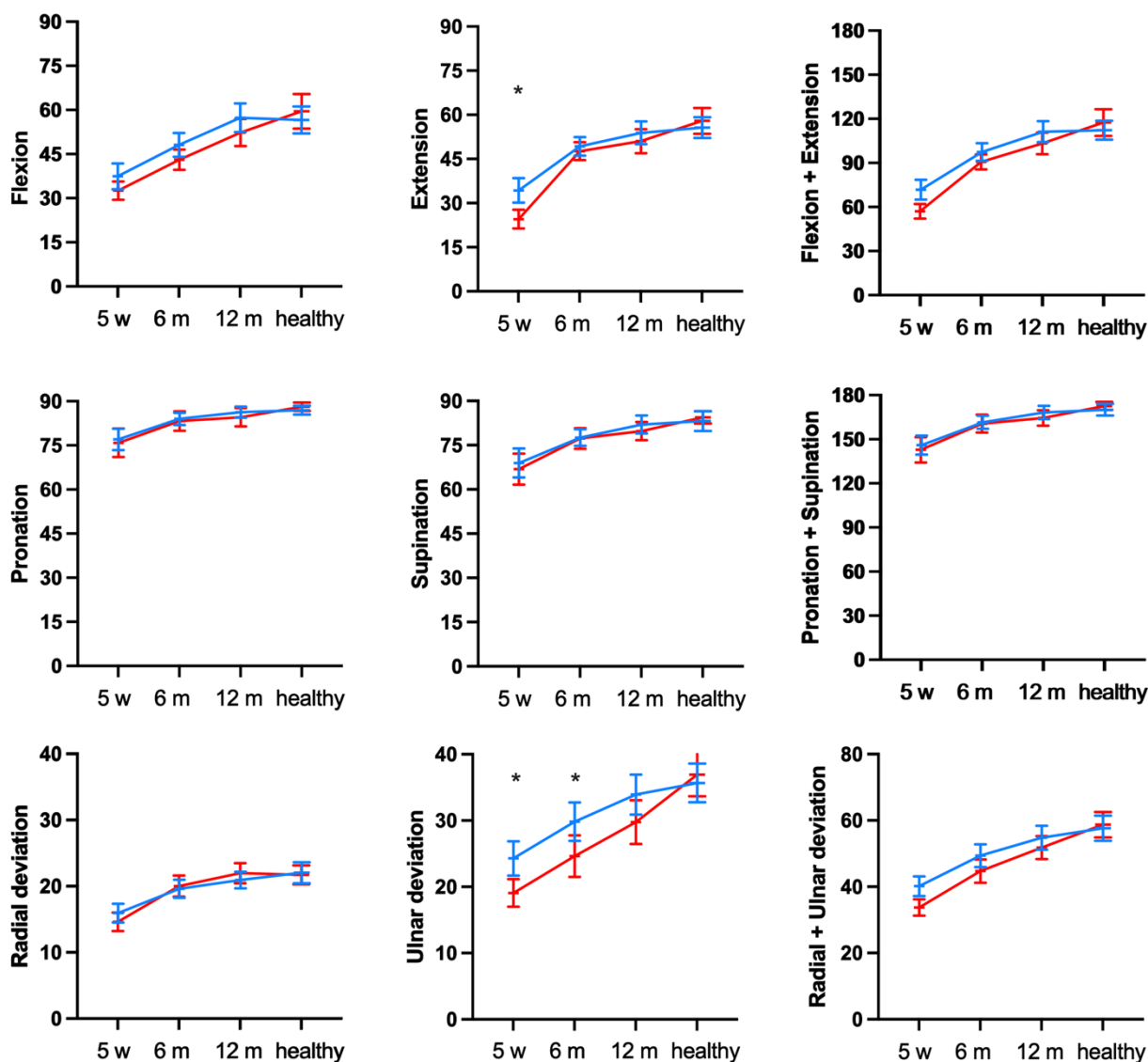
Figure 10. Mean range of motion of wrists with displaced (red) and minimally/non-displaced (blue) DRF at 5 weeks (w), 6 and 12 months (m) compared with the uninjured/healthy side. Error bars represent 95% CIs. * p < 0.05.

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The mean grip strength was measured and found to be low in both cohorts after 12 months, i.e., 18.8 kg (14.1-23.6) in the group with minimal or non-displaced DRF and 16.6 kg (11.8-21.4) in the group with displaced DRF. The between-group mean difference in grip strength was 0.5 (-2.2 – 3.2) after 6 months and 1.2 (-4.0 – 1.6) after 12 months, and of no clinical importance.

EQ5D-3L indices of patients with minimal or non-displaced DRF had improved at 12 months after injury; from 0.87 (95% CI 0.84–0.90, range 0.68–1.00) at 6 months to 0.93 (95% CI 0.90–0.96, range 0.71–1.00). The corresponding values were 0.79 (95% CI 0.72-0.86, range 0.28-1.00) and 0.84 (95% CI 0.76-0.93, range 0.14-1.00) in the displaced, non-operatively treated DRF group (95).

Paper V

Of the 48 patients who were eligible to remain in the study (Paper II), seven had died, three could not be reached and three withdrew their consent to participate in the 3-year follow-up. A total of 35 patients gave oral consent to attend; however, three patients did not show up, and they could not be reached again. The remaining 32 patients fulfilled the complete follow-up with radiographic control and examination for complications, PROMs, and ROM. Mean follow-up time of the 32 patients was 3.3 (95% CI: 3.1-3.4; min. 2.8; max. 4.1) years.

In total, 10 out of 32 wrists had signs of PA. Arthritis was not evident in any of the 32 wrists 5 weeks after injury (Figure 11). At the latest follow-up, seven wrists were rated as PA grade 1, two as PA grade 2 and one as PA grade 3. This change was statistically significant, i.e., radiological signs of wrist arthritis were seen in 0/32 patients after 5 weeks and in 10/32 patients after 3 years (Fisher's exact test, $p<0.001$).

The radiological evaluation after 3 years revealed a median dorsal angulation of 5 ° (range: 15-24°). Compared with the 5-week radiographs, the mean difference was -0.9 (95% CI: -5.6-3.8) degrees. The change from 5 weeks to 3 years was thus negligible for most fractures. However, 11 out of 32 fractures healed with a dorsal angulation of ≥ 10 °. Five of these fractures had radiological signs of PA on the latest radiographs. The 32 fractures were rated according to the AO/OTA classification: 12 were rated as A2, 11 were rated as A3, one was rated as B1, four were rated as B2 and four were rated as B3. There were no C-type fractures. AO type A fractures accounted for 72% of the fractures, whereas type B fractures accounted for 28%.
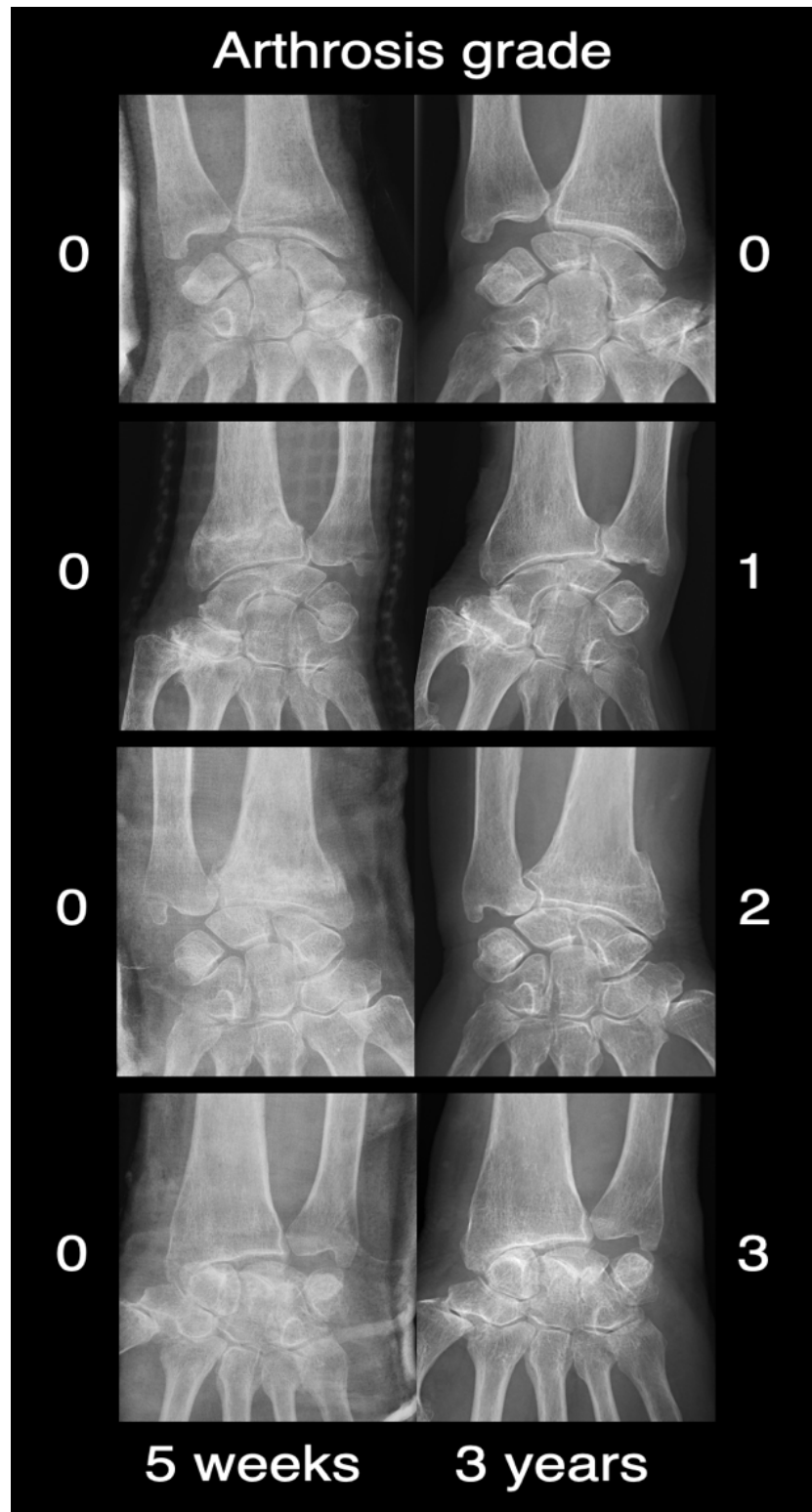
Figure 11. Examples of assessed anteroposterior radiographs with PA grades 0, 1, 2 and 3 after 5 weeks and a mean of 3.3 years after the injury.

The complication rate was 6/32 (19%). The complications reported were five patients with sensory disturbance in the fingertips and one patient with pain and a bothersome, decreased ROM. After 12 months, patients only reported complications in three of 48 cases (6%). The difference in complication rate between 1 year to final follow-up was not statistically significant (Fisher's exact test, p=0.15). All the complications were minor. Moreover, no secondary operations were associated with the DRF.

QuickDASH did not statistically significantly change from 12 months to latest follow-up. The mean QuickDASH values and 95% CI are given in Figure 12.

Moreover, one-way repeated-measures ANOVA showed that mean PRWHE was comparable after 6, 12 and 36 months, i.e., 12.9 (95% CI 7.2-18.6), 9.1 (95% CI 3.8-14.5), and 9.0 (95% CI 4.3-13.6), respectively (p=0.25).
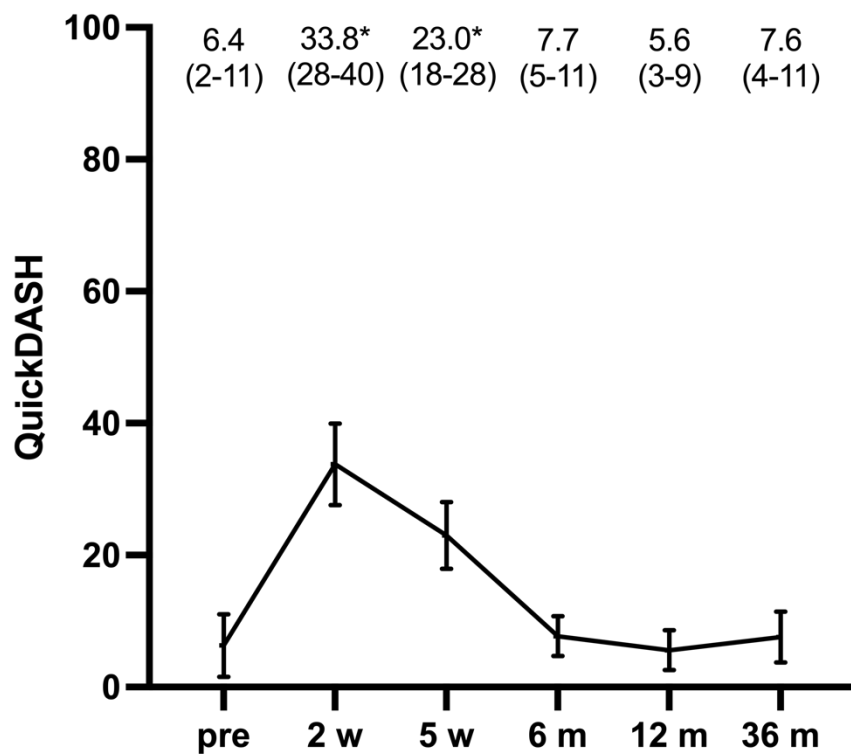

Figure 12. Mean QuickDASH and 95% CI as error bars are given before the injury (pre) and after the injury at 2 and 5 weeks (w) and 6, 12 and 36 months (m). * p<0.05 compared with the pre-injury state.

Discussion

Paper II

Non-operative treatment with plaster cast immobilisation for 5 weeks in 50 patients with DRF with minimally or non-displaced DRF (before or after reduction) was associated with a low complication rate of 6% (3/48 patients) after 12 months. These results agree with those of Saving et al. (35) who reported a complication rate of 11% encompassing of five cases of nerve numbness and two cases of CRPS in conservatively treated patients after 12 months. One of the cases presented with delayed extensor pollicis longus tendon rupture within 1 year which persisted up to 10 years after the fracture (96).

The Quick DASH score improved statistically significantly from 6 to 12 months, returning to pre-injury levels. Unlike us, Aparicio et al. (97) reported a significant increase in upper limb disability at 1 year after surgery, and Dewan et al. (66) reported that improvement in fracture-specific disability was completed after 6 months. We, on the contrary, noticed a trend towards further improvement from 6 to12 months (p>0.05). QuickDASH is highly recommended as a PROM for outcome measures in DRF (90) and may even be more sensitive and responsive to functional impairments than the DASH (98, 99). ROM also progressed from 6 to 12 months and normalised, which is corroborated in results reported by Hassellund et al. (67).

Paper II confirms that closed reduction and non-operative treatment is an acceptable treatment modality with a low complication rate and good subjective and objective outcomes. Only 9/62 (15%) of the included patients did not maintain the angle after 2 weeks. But in 9/27 (33%) of the reduced fractures and 4/23 (17%) of the non-reduced cases of DRF, dorsal angulation of the distal radius in the radiographic lateral view exceeded 10° at the latest 5-week radiographic follow-up. Nonetheless, in this group, functional recovery and the complication rate were not compromised despite the angulation. This and the supporting evidence regarding non-operative treatment suggest a need to reserve surgery for patients in need of fast recovery (32, 35, 36, 67-69, 100-103).

This also raises the question of the expediency of the NCR criterion for operative treatment, which is dorsal angulation of more than 10° (6). The included patients were reasonably healthy, had a low ASA score and good pre-injury function of the fractured arm and low QuickDASH scores, which indicates a high expectation for a good functional outcome. The AAOS and the BSSH have recently changed their guidelines to recommend conservative treatment for patient above 65 years of age with DRF (75, 76, 104).

Paper III

The most important finding of Paper III was that no statistically significant differences in complication rate, functional or PROMs were demonstrated between operatively or non-operatively treated dislocated DRF in patients ≥ 65 years after 12 months.

No statistically significant differences were seen in complication rates between the two groups. This finding is supported by other RCT studies and meta-analyses (4, 80, 81, 100, 105-107). In Paper III, the results in terms of complication rates after DRF are thus in line with those of previous studies on this subject. Literature definitions of complications are highly variable, and complication outcomes are therefore challenging to interpret and compare. Chen et al. divided complications into minor and major ones and reported a significantly higher major complication rate in the operative group (106). The definition of complications used in the present study adheres to an earlier published protocol, and complications were therefore not subdivided as suggested by Chen et al. (81).

For patient-reported outcome measures, i.e., the QuickDASH score, the existing literature reports similar results in operatively and non-operatively treated patients (102, 108). Still, a meta-analysis found a significantly lower QuickDASH score favouring the operative group in the first year (109). An effect size of -5.22 was found in the present study, and in the study the mean difference in QuickDASH was 4.2, both well below the threshold of the MCDI difference of 16-20 points. Likewise, the ROM was similar between groups; in addition, the statistically significant difference in flexion – extension ROM at 5 weeks and 6 months – was barely clinically relevant. Thus, after 12 months, the mean the difference was 6.8°.

Paper IV

One year after 5 weeks of dorsal below-elbow casting of low-energy DRF in ≥ 65-year-old patients, the complication rate was 6.3% (3/48) in minimally or non-displaced DRFs and 16.6% (7/42) in displaced DRFs; thus, no statistically significant difference was seen between the two. Similarly, no statistically significant difference was observed in functional outcome regarding QuickDASH score, pain, ROM, grip strength or EQ-5D score (95).

The definition of complications after DRF is not arbitrary; in both groups, the complications were overall mild and temporary. As reported previously, the unspecific post-DRF sensory disturbances over time and may thus not neither necessarily be lasting complications, nor do they follow an anatomical innervation pattern (93, 94).

Paper V

It is expected that fractures, especially intra-articular fractures, can lead to post-traumatic arthritis (PA) (72). Ten out of 32 patients had radiological signs of PA at latest follow-up, while none had arthritis after 5 weeks. In seven patients with grade 1 arthrosis, five had a B fracture according to the AO classification. Grade 2 PA was found in 2 patients with A2 fractures; grade 3 PA was found in one B2 fracture. The AO classification on B fractures contains intra-articular fractures; six out of nine fractures with signs of post-traumatic arthrosis were intra-articular fractures. In a systemic review, Lameijer et al. described that intra-articular fractures with articular incongruence were a predictor of PA, but also that older age at the time of fracture was a predictor (110). The review found no correlation between AO classification of the fracture and development of PA, and no prediction of PA and dorsal angulation, radial length, ulnar variance, and radial inclination.

Due to the unexpectedly low rate of PA and the limited number of patients, correlation analysis for PA and type of fracture was not performed.

A study from 2008 in younger patients supports the theory that despite mal-reduction and radiological signs of PA, the patients did not suffer from symptomatic arthritis even after 30 plus

years, which supports our results presented here (71). Van Leerdam et al. (38) also described that type A and B fractures with a mean follow-up of almost 4 years had better PROMs when treated conservatively than when treated with surgery in elderly patients. Our study and the stud by Marchewka et al. (111) confirmed that theory, as one-third of the patients healed in mal-union and with overall good functional outcome and pain. No statistically significant deterioration in functional outcome was found according to QuickDASH and PRWHE scores after 1 year compared with 3 years.

The complication rate increased from 6% to 19% over a time period of more than 3 years. All complications were minor and consisted mostly of sensory disturbances in all or few of the fingertips. None concerned specific nerves, and none of the patients were re-operated. It is expected that patients experience complications after DRF. The literature shows complication rates reaching almost 15% and a re-operation rate of 10% in surgically treated DRF at a 3.2-year follow-up has been reported (3). Our complication rates increased over time; yet, although the increase was significant, the rate was comparable to that of earlier published RCT studies (37).

Overall discussion

Like similar previous RCT studies and metanalyses, this RCT study showed that functional outcome was similar after 1 year in all groups. Complications rates in the groups were similar as well, which was not the case in all previous studies (32, 35, 52, 67, 69). A review from 2022 separated complications into major (loss to reduction, carpal tunnel syndrome, nerve injury, deep infection, tendon rupture, non-union, malunion and osteotomy) and minor complications (tendon irritation, superficial infection, finger stiffness, mal-positioning of implant, pain and CRPS) (52). In the present study, complications were not subdivided into major or minor, because all complications, subjective or objective, minor or major, might be of importance for the patient.

Fractures were not enrolled according to classification but according to surgical criteria. Fractures are difficult to classify, and no fracture classification was specific enough to determine choice of surgery according to the NCG (6, 14). The included fractures were classified according to the AO classification, and no differences were found between the groups. Paper II reported on 38 A fractures and 10 B fracture. Paper III, the randomised controlled trial on non-operative fractures,

reported on 27 A type, 17 B type and 4 C type of fractures; and in the operated group, 28 were A type fractures, 16 B type and 3 C type. Both intra- and extra-articular fractures were included.

The finding of this PhD thesis invites the question whether non-operative treatment is good and safe for all elderly and which type of treatment fits the demand the individual patient prefers. These questions are relevant. However, it was not the aim of the present PhD thesis to investigate these questions of optimal / preferred choice of the individual patient. However, several dropouts occured, where patients in the RCT randomized to surgical treatment denied surgery despite proper informed consent. This suggests a strong preference for non-operative treatment of these individuals.

In this study the non-operative treatment produced a good functional result with insignificant pain. At randomisation, several patients (10%) dropped out after having been randomised to surgery simply because they wished to undergo non-operative treatment. In another RCT conducted in 2020, the WRIST study, patients were asked to choose between surgery or conservative treatment. Out of 304 included patients 187 chose surgery. Randomisation was done between surgical methods (47). Future studies should include public and patient involvement (PPI) prior to constructing the protocols to attempt to fulfil the elderly's needs. Even when a choice of treatment is offered, a trade-off will always exist as surgery may be beneficial in securing adequate grip strength and ROM and casting may produce less pain and better functional outcomes as described by Yoon et al. (112).

In this thesis, the cut off age was 65 years which is close to the Danish retirement age, and therefore an age at which functional needs for many patients may be assumed to play a slightly lesser role for daily living than while people are still in gainful employment. Even though this methodological choice may be supported by other studies also applying a chronological age as an inclusion criteria, this choice is a matter of debate. People age very differently and a many individuals have still high functional demands and a need for rapid recovery. Moreover, the age of retirement increases in many countries, which may also provide an argument for assessing the individual patient's preoperative function and need for rapid recovery before choosing treatment strategy. As clinicians and researchers, we should be careful not to discriminate the patients based on chronological age, but instead we should council them with regards to their needs for rapid recovery, functional demands, and expectations. Nonetheless, to the best of my knowledge only the Swedish DRF

guidelines from 2021 clearly define the function demand as high, medium, and low. Moreover, examples are given, i.e., high: demanding physical activities at work, in leisure time, and activities of daily living; medium: living independently without any help for activities of daily living and without the need of heavy lifting or other high demanding tasks; low: requiring help for activities of daily living (64).

In this thesis, loss of fracture reduction was observed in terms of length and angulation in non-operatively treated DRF. However, despite this radiological malreduction or loss of reduction during non-operative treatment, the functional outcome was good. In 2015, Madsen et al. reported that volar plating did not restored the anatomy (80). Radiological thresholds for surgery should be researched further. In a systematic review from 2021, Esworthy et al. describe the origin of the threshold for recommending surgery (113), which dates back to 1986 (72) and recommendations issued by the British Society for Surgery of the hand (BSSH) and others. However, these criteria have later been questioned due to methodological flaws and lack of correlation between the radiological and clinical results. The positive predictive value of radiological parameters has been shown to be very low, as mentioned earlier. Anatomical reposition and functional outcome do not agree, nor do radiographic articular arthrosis and pain. Pain and functional outcome are essential to the patient, and further research should be done to identify a possible radiological predictor.

Considerations regarding study design

We chose a parallel group, randomized controlled superiority trial for the primary study (paper III). The sample size calculation was based on the assumption of a 20% difference in complication rate. The literature states complication rates ranging from 3% to 36% (14, 28, 40-42).

Blinding in a study comparing conservative with operative treatment is difficult. In the present study, sham surgery was not performed for several reasons. Firstly, sham surgery entails a complication risk for example infection but also because most of the operations were done under regional anaesthesia to which the patient could not be blinded. Secondly, it was found unethical to perform sham surgery. The purpose of blinding is to reduce risk of ascertainment and observational bias.

Randomised controlled trials are considered to be evidence level A1b according to the Oxford Centre of Evidence-based Medicine (114). To ensure that randomisation was done properly and in conformity with the Cochrane Risk of Bias Tool for Randomised Trials (RoB 2.0), all envelopes were sealed and non-translucent (85). To ensure that the block randomisation remained unbiased if previously included patient treatments were known, only the primary investigator knew their status.

The intention-to-treat principle was not followed. Patients were analysed only within the treatment group to which they were randomised. If they did not accept the randomised treatment and therefore withdrew consent, they were not followed. This decision was made in conformity with current legislation which bars investigators from following patients beyond the clinically relevant follow-up of 5 weeks. Unfortunately, this implies that a type 1 error risk exists which could lead to false positive results in randomised patients because they chose to be included and chose their randomisation.

Complications were defined as described earlier. Throughout the data collection period, it was obvious that the definition of complications was deficient. Both subjective and objective complications were reported, for example sensory disturbances. Some of the complications observed and recorded were relatively weak and not nerve specific but were recorded anyway.

Trigger finger was also recorded as a complication of the flexor tendon. It could be discussed if it would have occurred anyhow or even if it should be registered as a complication of the tendon where post-surgical complications were otherwise referred to only as rupture or irritation. In retrospect, complications could have been more clearly defined and divided into objective major and minor complications.

PROM used in this study were QuickDASH and PRWHE. Pre-injured PROM was obtained according to the patient's memory which could be inaccurate. Both PROMs are recommended for outcome measures in the DRF (90, 98, 115). The MCID varies in the literature from 8 to 26 points, but at study from 2016 described an MCID for musculoskeletal disorders of 16-26 (48-51, 53). In a metanalysis from 2022, QuickDASH was used as a primary outcome measure and was compared with PRWHE in eight out of 12 RCT studies (52). According to the official website of DASH and QuickDASH (dash.iwh.on.ca) these PROMs were developed to assess upper extremity disabilities in adults. While there was no specific age limit, the general guidelines were developed for 18-65-year-old patients. Moreover, the website states a MCID of QuickDASH ranging from 16 to 20 QuickDASH points (with a mean of 18) (54).

Bias considerations

RCTs are considered by researchers to produce high-level evidence. Even so, potential bias may still exist. The Cochrane Handbook therefore developed a tool for assessing risk of bias in RCTs called RoB 2 (85).
According to RoB 2, bias may arise in different domains of a study.
(1) the randomisation process;
(2) deviations from intended interventions;
(3) missing outcome data;
(4) outcome measurement;
(5) selection of the reported result.

AD 1: Bias arising from the randomisation process may occur when participating patients are accepted into the trial, their participation is rejected or during allocation to the intervention. Such

bias occurs when the investigator interferes, consciously or unconsciously, with the inclusion or allocation because of his or her knowledge of the allocation. Allocation sequence concealment was reduced by using block randomisation. When only three envelopes were left, another ten were added. This minimised the risk of allocation concealment bias. All envelopes were non-translucent and the paper in the envelopes was folded, also to reduce the risk of allocation concealment bias. Five patients randomised to surgery withdrew their written consent immediately after randomisation, arguing that they did not want surgery; mainly due to their age. That could represent selection bias because none of the participants allocated to non-surgical treatment withdrew their consent.

AD 2: Bias may also arise due to deviation from the intended interventions. In paper I, we planned for analysis of the RCT according to intention-to-treat principals. However, as stated above patients, who withdrew their consent, could not be followed. This study was only partially blinded and therefore bias may occur. Bias can arise because of the trial context, meaning that patient allocated to a treatment can feel "unlucky" because they wished for another treatment. Thus, five patients allocated to surgery withdrew their consent. If a large number of participants did not receive the intended intervention, this may involve potential over- or underestimation of the treatment results and, therefore, bias.

Also, only some of the investigators were blinded, which could potentially increase attention to a specific treatment group and thus create potential bias. To prevent bias due to deviation, clinical visits outside the study protocol were also taken into consideration when determining complications.

Sham surgery was not an option in this study, and therefore blinding of the participants was not done.

AD 3: Bias due to missing outcome may also occur. Such bias arises when participants withdraw from the study ('loss to follow-up' or 'dropout'), they do not attend the outpatient clinic, do not provide relevant data or they die before follow-up; and when data or records are lost or are unavailable. In the present study, not many were lost to follow-up in the first year. However, due to the patients' high median age, several patients lost the 3-year follow-up. Missing outcome data of less than 5% is accepted as a "small" loss (with corresponding implications for risk of bias), whereas loss exceeding 20% is considered to be a "large" loss (85).

Ad 4: Bias in measurement of the outcome may arise when the measured values do not equal the true or the underlying values, for example if the investigator or participants affect the outcome measure because of their knowledge of the allocation. The patients were not allowed to tell the examining nurse of the allocation to keep her blinded, which minimised the risk of this bias. The patient's outcome scores from the previous examination were not known to the patients or the investigator to prevent any effect of such knowledge on the measures.

AD 5: Bias in selection of the reported result is a risk that arises only when parts of the results of the study are published. To reduce this bias, the protocol was published before the study was implemented.

Limitations

In addition to the considerations regarding bias, mentioned above, the PhD thesis is limited by the small size of the study population. For sample size analysis, complication rates for operative treatment were estimated based on our own retrospective account of complication rates in 576 patients (14). In the non-operatively treated group, the posthoc observed complication rate was higher than anticipated and this has resulted in a reduced posthoc study power. The posthoc power of the present trial was therefore not sufficiently large to allow us to determine statistically significant differences, which could lead to both type 1 and 2 errors. This is a serious limitation of the PhD. However, the initial sample size calculation assuming a complication rate of 6% and 26% in the two groups of the RCT was reasonable at the time of planning the PhD project. Considering the results of recently published RCTs in the field as well as meta-analyses, the present study adds to the evidence that complications also should be expected in non-operatively treated patients with DRF.

Since the average age of the included patients was high, loss to follow-up due to death was high with four patients in one group and none in the other group. That taken in consideration, the overall loss to 12-month follow-up was 15 patients (15/100: 15%), which is comparable to the 10-30% drop-out rates reported in other RCT studies (116, 117).

The lack of double blinding is another limitation of the present study. No sham surgery was conducted because most patients with DRF at our institution are operated wide awake under regional anaesthesia. Moreover, it was considered unethical to operate under general anaesthesia only to ensure proper blinding of patients. Not performing sham surgery may have resulted in performance bias in paper III, likely to overestimate the effect of operative treatment (105). Finally, the statistician and the investigators conducting the analysis were not blinded.

Regarding paper V, limitations include the size of the patient cohort and loss to follow-up. Only 32 of 62 eligible patients could be analysed after 3 years of follow-up. This is certainly a point of caution and could potentially bias the findings and limit the generalizability of the results (see also paragraph AD 3: Bias due to missing outcome). Compared with the existing literature, the follow-up rate in our study is higher than the dropout rate of 65% (104), which is why this is also mentioned in the paragraph *Strengths*.

Secondly, arthritis was graded by 5-week radiographs while the wrist was still in a cast, i.e., standardised radiographs were taken to assess the healing of the fracture before cast removal. Theoretically, the artifact of the cast may thus have affected the PA rating. Evaluating arthritis with these radiographs may have obscured subtle signs of arthritis. Another limitation could be unawareness of the patients' comorbidities, such as rheumatoid arthritis or pain, and disability from basilar thumb arthritis. Assessment of the contralateral wrist by standardised PROMs and radiographs may partly have overcome this limitation.

Strengths

This single-centre RCT was performed by a relatively small research group which ensured a high level of control and consistency. The came consultant assessed all potential candidates for inclusion, which minimised the risk of selection bias. Data collection was also performed by only few persons, ensuring uniform data collection.

As mentioned, RCT studies are trials with high evidence levels. Another advantage of conducting a prospective study is the ability to study multiple outcomes for a given exposure and including baseline demographics. Also, providing 3-year data on the prospectively followed cohort of

minimally and non-displaced DRF patients is a strength of the thesis and rarely seen in the published DRF literature.

Another strength of this study was the low percentage of eligible patients who were not enrolled, i.e., inclusion of consecutive patients took place.

As paper V is not published at the time of writing, its limitations should be highlighted:

A strength of the present study is the 3-year long follow-up, which is longer than in most other DRF studies. Moreover, the study design was prospective and thus accounted for even minor and rather non-specific changes in, for example, complications such as sensory disturbances. Moreover, the loss to follow-up was low compared to figures reported in the literature. From the 1-year follow-up until the final follow-up, only 16 patients dropped out, and seven died. In comparison, loss to follow-up over a 3-year period was 65% in a recent study from 2022 (118).

Conclusions

Regarding the 3 aims of this PhD thesis, the following conclusions can be drawn:

AIM 1:

For patients 65 years of age or older treated with non-operative or operative treatment of displaced DRF a similar complication rate (16.6% vs. 20.9%) and functional outcome was found after 1 year observation time (Paper III).

AIM 2:

PROMS and objectively assessed functional outcome improved during the first year in minimally and non-displaced DRF. After 12 months the vast majority of patients had either returned to or close to the pre-fracture level (Paper II), but may lose some grip strength compared with the uninjured hand. These observations were made despite the partial loss of reduction of 5 degrees (95% CI 2-8) in the fractures that were initially reduced.

After 3-year follow-up of 32 of these patients, osteoarthritis was observed in 10 wrists, but with without clinical impact on the PROM (Paper V).

AIM 3:

The reported complication rate after non-operative treatment between the two cohorts was pronounced, i.e., 6.3% (3/48 patients) minimally/non-displaced DRF vs. vs. 16.6% (7/42 patients) in displaced DRF, respectively. However, this difference was not statistically significant, and many complications were sensory disturbances and thus of minor nature (Paper IV). Nonetheless, given the limited number of patients, no firm conclusions should be drawn.

Overall, regardless of fracture displacement, most elderly patients (>= 65 years of age) sustaining a DRF obtained a good functional outcome after 1 year. Moreover, the prospectively evaluated complications of this thesis may be used to inform clinicians and patients alike.

Perspectives and future research

Further research in this area is needed. Treatment of DRF has changed over the past three decades from mostly non-operative treatment towards mainly operative treatment despite lack of high-level evidence justifying these changes. Recently, several RCT and metanalyses have questioned the use of operative treatment as a first choice for the elderly.

Future research should focus on functional demands and patient involvement. For some elderly, early recovery is essential for activities of daily living. Some elderlies are dependent on their arms to maintain their daily living; arms to operate crutches or arms to move their body from chair to bed, etc. I personally believe that we should aim for shared decision making and not discriminate based on chronological age, but should take functional status and demand of the patient into account.

The long-term effects after operative and non-operative treatment should also be further investigated. One issue to consider in the longer perspective, e.g., with a 10-20-year follow-up, to detect post traumatic articular arthrosis with functional and pain-related symptoms.

Specifically for Denmark, the NCG from 2014/2017 have been marked as "outdated" in 2023 by the Danish Health Authority. This leaves a clinical as well as legal question regarding the treatment of DRF. A revision of the Danish NCG should be considered with reference to the increasing body of scientific evidence and in alignment with recently published NCG of other countries.

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APPENDIX
1 and 2

Appendix 1 – Written consent

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┌─────────────────────────────────┐
│  Patientlabel                   │
│  Stor label                     │
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Samtykkeerklæring og fuldmagt

Studie omkring håndledsnære brud

Jeg bekræfter hermed at have fået skriftlig og mundtlig information vedrørende ovenstående projekt, som jeg frivilligt deltager i.

Jeg er informeret om at deltagelse i projektet er frivillig og at jeg til enhver tid kan trække mit tilsagn om deltagelse tilbage, uden at dette vil påvirke min behandling.

Jeg er informeret om og giver min fuldmagt til (jf. lov om patienters retsstilling §20), at medarbejdere i studiet omkring håndledsnære brud kan få oplysninger i min patientjournal og fra Lands Patient Registret. Fuldmagten er gældende indtil udgangen af 2020.

Alle oplysninger bliver behandlet strengt fortroligt.

Udfyldes af patienten:

Dato:_____ Underskrift:_____

Information givet af:

Undertegnede bekræfter hermed, at ovenstående patient er mundtligt og skriftligt informeret om projektet. Patienten har fået udleveret kopi af patientinformationen og samtykkeerklæringen samt folderen "Forsøgspersoners rettigheder i et sundhedsvidenskabeligt forskningsprojekt".

Dato:_____ Underskrift:_____

Navn med blokbogstaver.

Appendix 2 – Patientinformation

Patientinformation
Studie omkring håndledsnære brud

Vi vil med denne skrivelse, anmode dig om at deltage i et videnskabeligt forskningsprojekt. Projektet har til formål at give os ny og bedre viden, så vi i fremtiden kan blive bedre til at forebygge komplikationer og skrædder-syg behandlingen af håndledsnære brud.
Alle patienter der indlægges på Regionshospitalet Randers med håndledsnære brud i perioden maj 2017 til maj 2019 vil blive spurgt om deltagelse i projektet.

Det er frivilligt at deltage
Du bedes læse denne skriftlige information, før du beslutter dig til at deltage i projektet. Endvidere vil du få mundtlig information om projektet af en læge.
Du skal underskrive vedlagte skriftlige samtykke, før du kan indgå i projektet.
Hvis du har behov for betænkningstid før du underskriver samtykket, kan du bede om dette.
Hvis du siger nej til at deltage i projektet får det ingen betydning/konsekvens for din behandling.
Du kan til enhver tid trække dit skriftlige samtykke tilbage uden at det vil få betydning for din behandling.

Baggrund

Omkring 15.000 personer pådrager sig hvert år et håndledsnært brud i Danmark, hvilket gør det til det hyppigst forekommende brud. På trods af den høje forekomst ved vi meget lidt om langtidskomplikationerne efter pådragelsen og behandlingen af disse brud. Specielt ved vi ikke så meget om hvilke patienter, der har en øget risiko for at få disse komplikationer og hvilke konsekvenser for ens daglige liv, de har.

Formål

Formålet med dette projekt er at skabe ny viden, så antallet af patienter, der udvikler komplikationer og livskvalitetsnedsættelse i forbindelse med behandling af håndledsnære brud, kan nedsættes. Projektets hovedformål er at opnå højere grad af individualisering i behandlingen.

Hvad beder vi dig om?
- Vi vil bede om din tilladelse til at vi indhenter oplysninger i Lands Patientregistret om dine tidligere sygdomme og dit medicinforbrug
- Vi vil bede dig komme til kontrol 6 og 12 måneder efter din behandling (dette ligger ud over det normale kontrolforløb)
- Vi vil bede dig udfylde spørgeskemaer i forbindelse med hver kontrol

Ulemper

Du vil blive bedt om at møde op til to ekstra kontroller, hvilket ligger ud over det sædvanlige kontrolprogram.

Fordele

Du vil blive fulgt endnu tættere i efterforløbet efter din behandling, og du har mulighed for at hjælpe fremtidige patienter med at få et endnu mere sikkert forløb.

Data behandles fortroligt

Alle oplysninger vil blive behandlet fortroligt. Dit CPR-nummer vil ikke blive offentliggjort nogen steder. Alle der arbejder med projektet har tavshedspligt.

Projektet er godkendt af den lokale videnskabsetiske komité, Datatilsynet og ledelsen på Ortopædkirurgisk Afdeling, Regionshospitalet Randers.

Konklusionen på undersøgelsen forventes at foreligge i 2019.

Venlig hilsen

Rikke Thorninger
Projektleder, overlæge, speciallæge i ortopædkirurgi
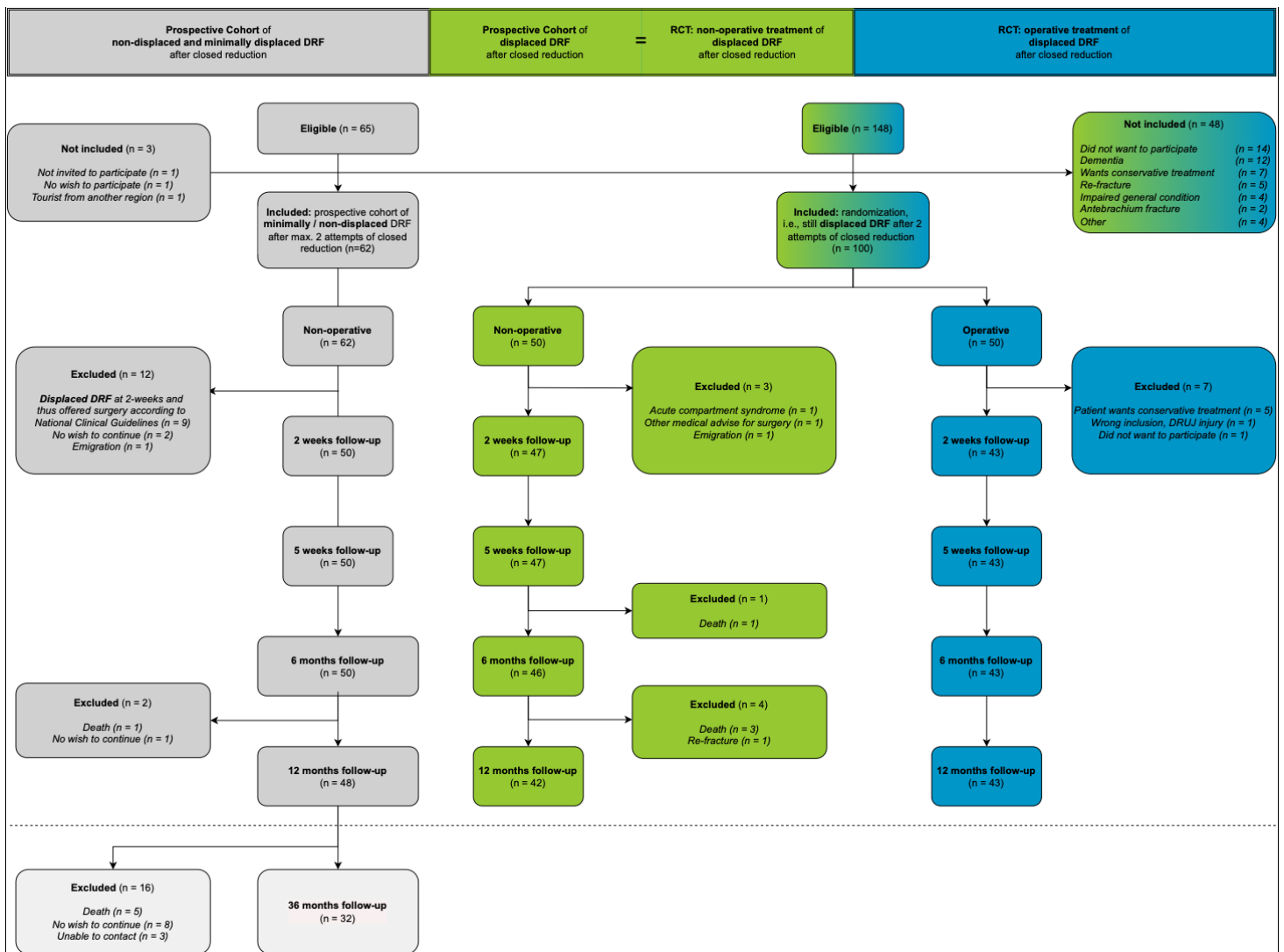
APPENDIX 3

List of studies

This PhD thesis is based on the following publications and manuscripts:

I   **A protocol for a single-center, single-blinded randomized-controlled trial investigating volar plating versus conservative treatment of unstable distal radius fractures in patients older than 65 years.**

Pedersen J, Mortensen S, Rölfing J, Thorninger R.
BMC Musculoskelet Disord. 2019; 20(1):309. doi.org/10.1186/s12891-019-2677-y
Impact factor (2021): 2.562

II   **Objective outcome measures continue to improve from 6 to 12 months after conservatively treated distal radius fractures in the elderly - a prospective evaluation of 50 patients.**

Thorninger R, Wæver D, Pedersen J, Tvedegaard-Christensen J, Tjørnild M, Lind M, Rölfing J.
J Clin Med. 2021; 10(9):1831. doi.org/10.3390/jcm10091831
Impact factor (2021): 4.964

III   **VOLCON - a randomized controlled trial investigating complications and functional outcome of volar plating vs casting of unstable distal radius fractures in patients older than sixty-five years.**

Thorninger R, Wæver D, Tjørnild M, Lind M, Rölfing J.
J Orthop Traumatol. 2022; 23(1):54. doi.org/10.1186/s10195-022-00673-4
Impact factor (2021): 4.239

IV   **Prospective evaluation of two cohorts of non-operatively treated patients with displaced vs. minimally and non-displaced distal radius fractures**

Thorninger R, Wæver D, Tjørnild M, Lind M, Rölfing J.
J Clin Med. 2023; 12(5):2076. doi.org/10.3390/jcm12052076
Impact factor (2021): 4.964

Extension of the original protocol beyond 12 months of follow-up:

V   **Posttraumatic arthritis and functional outcomes after nonoperatively treated distal radius fractures: A prospective study with a minimum 3-year follow-up**

Thorninger R, Romme KL, Wæver D, Henriksen MB, Tjørnild M, Lind M, Rölfing J.
Sci Rep. 2023; submitted: 10th March 2023.

An overview / flow diagram of the studies is available online:
doi.org/10.5281/zenodo.7677689

AARHUS UNIVERSITY

CONSORT FLOW DIAGRAM

| Prospective Cohort of non-displaced and minimally displaced DRF after closed reduction | Prospective Cohort of displaced DRF after closed reduction | RCT: non-operative treatment of displaced DRF after closed reduction | RCT: operative treatment of displaced DRF after closed reduction |

Not included (n = 3)

Not invited to participate (n = 1)
No wish to participate (n = 1)
Tourist from another region (n = 1)

Eligible (n = 65)

Eligible (n = 148)

Not included (n = 48)

Did not want to participate (n = 14)
Dementia (n = 12)
Wants conservative treatment (n = 7)
Re-fracture (n = 5)
Impaired general condition (n = 4)
Antebrachium fracture (n = 2)
Other (n = 4)

Included: prospective cohort of **minimally / non-displaced** DRF after max. 2 attempts of closed reduction (n=62)

Included: randomization, i.e., still **displaced DRF** after 2 attempts of closed reduction (n = 100)

Non-operative (n = 62)

Non-operative (n = 50)

Operative (n = 50)

Excluded (n = 12)

Displaced DRF *at 2-weeks and thus offered surgery according to National Clinical Guidelines (n = 9)*
No wish to continue (n = 2)
Emigration (n = 1)

Excluded (n = 3)

Acute compartment syndrome (n = 1)
Other medical advise for surgery (n = 1)
Emigration (n = 1)

Excluded (n = 7)

Patient wants conservative treatment (n = 5)
Wrong inclusion, DRUJ injury (n = 1)
Did not want to participate (n = 1)

2 weeks follow-up (n = 50)

2 weeks follow-up (n = 47)

2 weeks follow-up (n = 43)

5 weeks follow-up (n = 50)

5 weeks follow-up (n = 47)

5 weeks follow-up (n = 43)

Excluded (n = 1)

Death (n = 1)

6 months follow-up (n = 50)

6 months follow-up (n = 46)

6 months follow-up (n = 43)

Excluded (n = 2)

Death (n = 1)
No wish to continue (n = 1)

Excluded (n = 4)

Death (n = 3)
Re-fracture (n = 1)

12 months follow-up (n = 48)

12 months follow-up (n = 42)

12 months follow-up (n = 43)

Excluded (n = 16)

Death (n = 5)
No wish to continue (n = 8)
Unable to contact (n = 3)

36 months follow-up (n = 32)

I

A protocol for a single-center, single-blinded randomized-controlled trial investigating volar plating versus conservative treatment of unstable distal radius fractures in patients older than 65 years.

Pedersen J, Mortensen S, Rölfing J, Thorninger R.

STUDY PROTOCOL

Open Access

A protocol for a single-center, single-blinded randomized-controlled trial investigating volar plating versus conservative treatment of unstable distal radius fractures in patients older than 65 years

Jonas Pedersen[1,3], Simon Oksbjerre Mortensen[1], Jan Duedal Rölfing[2,3] and Rikke Thorninger[1*]

Abstract

Background: Distal radius fractures (DRF) are very common in elderly patients, who present at the Emergency Department. Surgical treatment with open reduction and internal fixation using volar locking plates is widely prevalent despite the lack of evidence proving its superiority to conservative treatment with closed reduction and plaster immobilization. The purpose of this study is to investigate whether conservative treatment is superior to volar plating in terms of number of complications and results in a comparable or superior functional outcome in patients ≥65 years.

Methods: In this single-center, single-blinded randomized-controlled trial, patients ≥65 years with distal radius fractures will be invited to participate. A total of 50 patients per treatment arm is required to provide 80% statistical power at a 5% alpha level assuming a difference of 20% in complication rate between operatively and conservatively treated patients. Primary outcome measures will be complication rate, Quick DASH score (Quick Disabilities of the Arm, Shoulder and Hand), PRWE (Patient rated Wrist evaluation), and range of motion of the wrist. Secondary outcome measures will be grip strength, pinch gauge, pain, use of pain medication EQ5D score (European Quality of life – 5 dimensions), standardized radiographs. One year of follow-up is planned with data collection at the day of injury, after 2 weeks, after 5 weeks, after 6 months, and after 12 months. An intention-totreat and per-protocol analysis will be performed.

Discussion: This prospective trial helps to clarify the best treatment strategy for displaced DRF patients ≥65 years.

Trial registration: This trial is approved by the Danish Scientific Ethical Committee (ID: 1–10–72-420-17) and registered at Clinicaltrials.gov (Trial registration number NCT03716661).

Keywords: Distal radius fractures, Volar plating, Conservative, Complications, Functional outcome, Elderly

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Background

Distal radius fractures (DRF) account for 18% of all fractures in the elderly ≥65 years of age [1]. The estimated lifetime risk for DRF is 15% for females and 2% for males [2]. The incidence rate is 190–200 per 100,000 person-years [3]. DRF is associated with osteoporosis, hence the age-related incidence rate increases almost 3-fold from the age of 60 to 99 in women [1, 4, 5]. In Europe, the proportion of the elderly population is estimated to increase by 56% in men and by 41% in women until 2035 [6, 7]. Consequently, the need to clarify the best treatment strategy for DRF in elderly is evident.

In recent years, there has been a trend to treat DRF patients that require surgical treatment with an open reduction and internal fixation (ORIF) using a volar locking plate. The Danish Health Authority stipulates in the National Clinical Guidelines (NCG) regarding the treatment of low-energy DRF [8] to volar plate fractures that fulfill the following radiologic criteria after attempted closed reduction:

– > 10° dorsal tilt of the radius in relation to perpendicular to the longitudinal axis of radius
– > 2 mm articular step-off
– > 2 mm ulnar variance
– incongruence of the distal radioulnar joint
– substantial dorsal comminution indicating gross instability

If one or more of these criteria are met, ORIF most often utilizing a volar locking plate is advised regardless of the patient's age. The guideline also highlights that conservative management should be considered in patients with low functional demands.

Notably, the guideline does not include recommendations for high-energy, open fractures nor grossly instable fractures: volarly displaced (Smith), radial styloid (Cheuffeur) or articular rim (Barton) fractures. However, most of these fractures are also treated with volar locking plates in Denmark.

The radiological NCG criteria rely on clinical observations only and have not been systematically evaluated prospectively. Furthermore, the reliability of the radiological criteria has been questioned [9]. Therefore, The Danish Health Authority evaluates that the recommendations for treating DRF primarily are based on low quality evidence and must be considered as "good practice"-guidelines.

Volar plating of DRF may harm patients. Complication rates of up to 33% have been reported in surgically treated DRF patients [10–14]. Our own estimation of the complication rate after volar plating of DRF is 14.6% [95% CI 11.8–17.7%] in a retrospective cohort of 595 patients with 3.2 years follow-up [3]. This high complication rate is not

insignificant for the patients. Neurologic disturbances, tendon irritation and rupture, infection, etc. often lead either to a re-operation or an increase in out-patient visits and may result in permanent morbidity and impaired function [15].

Furthermore, volar plating improves the early functional recovery, but long-term functional results are similar with other treatment modalities in patients ≥65 years [16]. However, volar plating is still the gold standard in the treatment of DRF in adults regardless of age.

An increase in complications with no clinically significant difference between the functional outcome of operatively and conservatively treated patients was demonstrated [16, 17]. Furthermore, the patients treated operatively had a higher complications rate than the conservatively treated patients [17]. In addition, patients with DRF treated nonoperatively have shown to have less pain and better or equal wrist function after a 1 year follow-up than those treated surgically [18]. A Danish review of operatively treated patients suggest a more restrictive choice of treatment for DRF amongst the elderly than the NCG stipulate [2]. All things considered, no existing evidence proves the benefit of treating DRF operatively in the elderly.

Here, we question whether the potential benefit of volar plating, namely an earlier functional recovery outweighs the risk of encountering a complication. Especially in the light of retired patients (≥ 65 years), where return to work is not a burning issue, it seems worthwhile to investigate this issue both in the interest of the patients and society.

Research hypothesis

Patients above 65 years of age, who sustain a DRF that fulfill the national radiologic criteria for operative treatment will experience fewer complications when treated with dorsal plaster cast immobilization only than when operated using a volar locking plate.

Meanwhile, the secondary outcome measures will be comparable and below the clinically relevant difference – e.g. a mean difference in the Danish version of the Quick Disabilities of the Arm, Shoulder and Hand (Quick DASH) below 16–20 point [19–22].

Methods/design

Study design

A prospective single-center, single-blinded randomized-controlled superiority trial with two parallel treatment arms and a third control arm (Fig. 1);

Arm 1: volar plating, 2-weeks dorsal plaster cast followed by 3-weeks orthosis immobilization with a single hand therapeutic instruction;
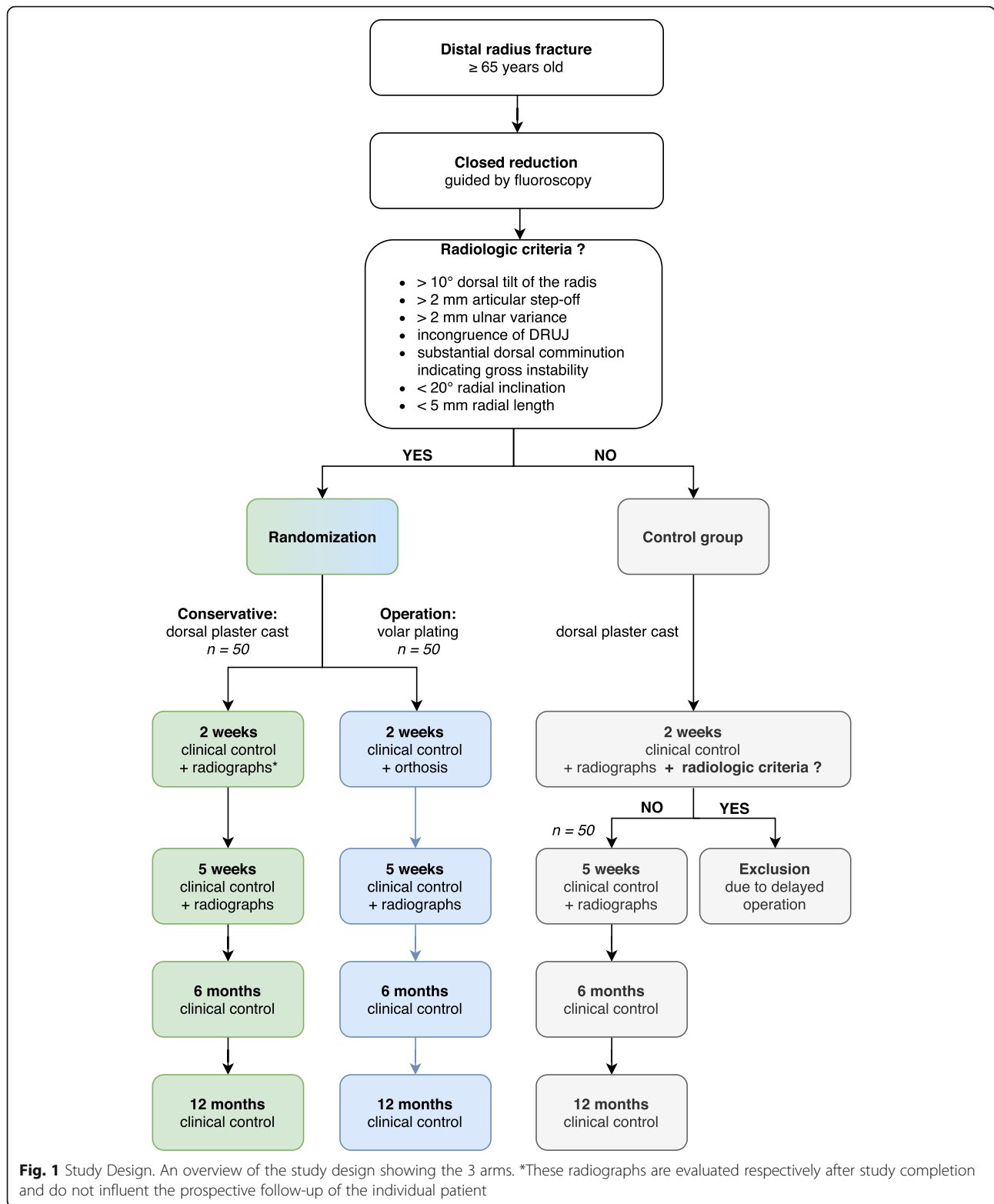
Fig. 1 Study Design. An overview of the study design showing the 3 arms. *These radiographs are evaluated respectively after study completion and do not influent the prospective follow-up of the individual patient

Arm 2: closed reduction and 5-weeks dorsal plaster cast immobilization with a single hand therapeutic instruction;
Arm 3: a control group of patients with minimally displaced DRF that do not fulfill the radiologic criteria.

Follow-up time is planned to be 1 year with out-patient visits at 2 weeks, 5 weeks, 6 months and 12 months after the injury. This trial is approved by the Danish Scientific Ethical Committee on the 3rd of September 2018. This study is carried out at the Regional Hospital Randers, Denmark with a coverage area of approximately 270,000 inhabitants.

Eligibility criteria
All patients with DRF diagnosed at the emergency department are screened for eligibility.

Intervention groups: (arm 1 and arm 2)
Eligibility criteria for participants who will be allocated to random treatment are:

– ≥ 65 years old
– low-energy distal radius fracture.

The distal radius fracture must fulfill at least *one* of the following radiological criteria after closed reduction in the emergency department in order to be randomized between treatment arm 1 and 2:

– > 10° dorsal tilt of the radius in relation to perpendicular to the longitudinal axis of radius
– > 2 mm Ulnar variance
– > 2 mm Articular step-off
– Incongruence of the distal radioulnar joint
– Substantial dorsal comminution
– < 20° Radial inclination
– < 5 mm Radial length

Control group: (arm 3)
Eligibility criteria for participants in the control group, arm 3:

– ≥ 65 years old
– low-energy distal radius fracture.

This distal radius fracture had to fulfill *all* the following radiologic criteria:

– ≤ 10° Dorsal tilt of the radius in relation to perpendicular to the longitudinal axis of radius
– ≤ 2 mm Ulnar variance
– ≤ 2 mm Articular step-off
– No incongruence of the distal radioulnar joint

– ≥ 20° Radial inclination
– ≥ 5 mm Radial length

Exclusion criteria

– Patients < 65 years
– high-energy fracture
– open fracture
– concomitant injuries, e.g. multiple fractures on afflicted arm
– not capable of giving written consent
– previous DRF or forearm fracture on the same side

Recruitment
Any participant must be approved eligible for the study by either one of the consultants in the research group or the house physician on call. Patients are primarily recruited by directly contact in the emergency room on the day of primary contact, where they are informed about the study and asked for written consent. The Danish consent form and patient information material is given to the patient, a blank sample can be ordered from the corresponding author. Every patient who is treated in the emergency department during a shift is discussed the following day on a conference, where all radiographs also are reviewed. This additional control ensures that every potential participant is assed for eligibility and offered enrollment in the study either directly in the emergency room or the day after by telephone. When recruitment is done over the telephone, written consent is obtained before surgery or at the 2 week out-patient visit, if the participant should be randomly assigned to conservative treatment or if the patient is in the control group. The recruiting health care personnel randomly assigns participants to the interventions as described below.

Randomization
Randomization is executed by random drawing of sealed, opaque envelopes. According to the sample size calculation, 50 participants will be allocated to each group, hence 100 identical A5 envelopes have been sealed – each containing a folded note whereupon either *"operative"* or *"conservative"* is written. In order to assure similar time-wise enrolment the following measures will be applied (Fig. 2). The 50 envelopes for operative treatment will be packed into stacks of 5 envelopes. The same will be done with the 50 envelopes for conservative treatment. One stack of each treatment arm will be mixed resulting in an equal chance to draw either treatment or intervention among the ten envelopes. The including health care personnel will draw one of the 10 envelopes and hence allocate the participant randomly to either treatment arm 1 or 2. When there are only three envelopes left, one stack of each group will be opened and mixed into the

Fig. 2 Illustration of the randomisation process regarding intervention groups, e.g. treatment arm 1 and 2. Each dot represents a sealed, opaque envelope that contains a note with the treatment arm allocation. The blue and red dots represent "conservative" and "operative" treatment, respectively. Whenever only 3 envelopes are left, 5 new "operative" and 5 new "conservative" treatment envelopes are mixed and added

remaining. By this measure, the health care personnel cannot predict the allocated treatment based upon the order of previous mixed treatment allocation from the mixed pool of small envelopes.

Interventions
Interventions when a possible participant addresses the emergency room
After diagnosing the fracture on a standardized wrist radiograph (anterior-posterior projection and lateral projection) in the emergency room, the physician on call has two attempts to achieve an acceptable closed reduction under local analgesia with a 20 mg/ml Lidocaine hematoma block. While the effect of the hematoma block sets in, nurses measure the arm to be able to lay a proper dorsal plaster cast immobilization.

Fluoroscopy is readily available in the emergency room and guides the closed reduction and plaster immobilization. After reduction standardized radiographs are obtained at the department of radiology and the quality of the closed reduction is assessed by the physician on duty. If the radiologic eligibility criteria are fulfilled after closed reduction, the patient is informed about the study and offered enrollment. If the fracture is less severe, e.g. without any of the radiologic criteria warranting closed reduction or operation as mentioned above, the wrist is immobilized with a plaster cast without closed reduction.

Intervention group

Treatment arm 1:

Open reduction and volar plate fixation utilizing Acu-Loc®, Acumed or Variax®, Stryker with a standard Henry approach to the distal radius and pronator quadratus repair if possible. The vast majority of patients will be operated in regional anesthesia and the remaining patients in general anesthesia. It is the choice of the surgeon whether a tourniquet will be used. After surgery the wrist is immobilized in a dorsal plaster cast for 2 weeks followed by further 3 weeks of immobilization with a removable orthosis. A single hand therapeutic instruction will take place.

Treatment arm 2:

Conservative treatment consists of dorsal plaster cast immobilization for 5 weeks. Only discomfort, neurologic deficits or signs of infection warrant removal and replacement with another dorsal plaster cast. A single hand therapeutic instruction will take place.

Control group
Patients with less displaced fractures, before or after and eventual closed reduction will be:

Conservatively treated as described for treatment arm 2.
Patients in the control group that fulfill the radiologic criteria after 2 weeks due to loss of reduction, are offered operative treatment according to the NCG and hence will be excluded from the trial.
The investigators reserve the right to exclude a participant if it is considered clinically irresponsible to let them continue.

Outcomes
Summarized in Table 1.

Primary outcomes
The complication rate will be estimated at day 0, 2 weeks, 5 weeks, 6 months, and 12 months after the injury.
Complications are defined as the presence of:

- Sensory disturbance, including carpal tunnel syndrome and chronic regional pain syndrome
- Flexor tendon rupture and irritation
- Extensor tendon rupture and irritation
- Hardware failure, e.g. osteosynthesis loosening
- Infection: superficial
- Infection: deep
- Reoperation with hardware replacement
- Reoperation with hardware removal (partial or total), which is not routinely performed in Denmark
- Vascular compromised (capillary refill ≥2 s)

Patients will report complications at the given time-points by answering a questionnaire stating either yes / no and a free-text explanation. If the patient states any complications, a member of the research group will qualify the

Table 1 Illustration of timeline and outcome measures including baseline demographics

	DRF	2 weeks	5 weeks	6 months	12 months
Primary outcome complications					
Questionaire	x	x	x	x	x
Examination	x	x	x	x	x
Secondary outcome					
Patient reported outcome					
Quick DASH (DK)	x	x	x	x	x
PRWHE (DK)				x	x
EQ5D				x	x
Pain at rest (0–10)	x	x	x	x	x
Objective examination					
Wrist range of motion			x	x	x
Grip strength				x	x
Pinch gauge				x	x
Wrist radiographs	x	x	x		
Baseline demographics:					

Age, gender, hand dominance, working status, ASA class, diabetes, smoking, alcohol consumption

Illustration of timeline and outcome measures including baseline demographics Abbreviations: *Quick DASH (DK)* The quick disability of the arm, shoulder and hand outcome measure - validated Danish translation, *PRWHE (DK)* Patient-related wrist evaluation score - validated Danish translation, *ASA class* American Society of Anesthesiologists Classification

answer and fill in the free text. However, a YES can only be qualified and shall never be erased if the physician does not agree with the patient's opinion or explanation.

The Danish version of the Quick Disabilities of the Arm, Shoulder and Hand [22] will be used to assess the level of functionality prior to injury, after 2 weeks, 5 weeks, 6 months, and 12 months. The minimal clinically relevant difference is 16 to 20-point difference in Quick DASH [19–21].

Range of motion is measured by a registered nurse using a goniometer. To ensure the observer is blinded, the patient is instructed not to talk about the treatment. Furthermore, all wrists will be covered by a glove concealing potential scares (Fig. 3). The following data are thus collected in a blinded fashion wrist flexion, extension, pronation, supination, radial deviation, ulnar deviation. The contralateral side will serve as a reference and history of injuries or operations of the contralateral side will be recorded.

Secondary outcomes

The patient reported outcome measure Quick DASH will be supported by the following secondary outcome measures:

- A Danish version of the Patient rated Wrist Evaluation questionnaire (PRWE) will be evaluated after 6 month and 12 months [23].
- Grip strength of both left and right hand will be estimated as the maximum and average of score of three repetitions of each hand with alternating hands between attempts after 6 months and 12 months using a dynamometer.
- A pinch gauge where both left and right hand are evaluated (yes/no) if the participant can pinch a sheet of paper. This is collected after

6 months and 12 months by an unblinded physician or research year student.

- The potential flexion deficit of the 1st finger towards the base of the 5th finger measured as the distance (cm) from the pulp of the 1st finger to the carpometacarpal joint of the 5th finger after 6 and 12 months.
- The pulp-to-palm distance of the distal 2nd-5th finger and palmar surface of the side treated for DRF after 6 and 12 months.
- The experienced pain during activity within the preceding 14 days before the injury and at 6- and 12-months follow-up stated on a 0–10 Numeric Rating Scale (NRS).
- The pain at rest after 2 and 5 weeks given NRS.
- EQ5D (European Quality of life – 5 Dimensions) after 6 months and 12 months. This is registered by an unblinded physician or research year student [24].
- The self-reported use of pain medication at day 0, after 2 weeks, 5 weeks, 6 months, and 12 months.
- The prescribed use of pain medication compared 12 months before with 3 and 12 months after the injury.
- Standardized radiographs of the injured wrist at day 0 before and after closed reduction (all groups), week 2 (conservative treatment group, not reviewed before completion of the follow-up period), week 5 (all groups).

The following baseline demographics will be recorded: gender, age, side of DRF, hand dominance (right-handed, left-handed, ambidextrous), working status, American Society of Anesthesiologists Classification (ASA class 1–6), smoking (cigarettes/day), alcohol consumption (units/week) and diabetes (yes/no).

Blinding

The study is single blinded, as all measurements will be performed with a glove masking a potential scare. Hence,

Fig. 3 A demonstration of the blinding of treatment using a glove

the observer will be blinded when examining the participant. Furthermore, before each visit the patient is instructed, not to talk about the received treatment with the observer.

During the planning of the study, sham-operations were taken in consideration in order to blind the participants. However, most DRF are operated wide-awake under regional anesthesia only. The research group considered performing a skin incision and writing a manuscript simulating all the noises and communication, that usually take place during an operation. However, the efficacy of this potential blinding of participants during wide-awake surgery was deemed questionable. General anesthesia would have been a viable option, but it would vary too much from the current practice to be feasible at our hospital.

Surgeon experience and type of plates

Our previous retrospective follow-up study concluded, that neither surgeon experience nor type of volar locking plate was associated with the complication rate [3]. Therefore, we consider surgeon experience and type of plate of no to minor clinical importance for the outcomes of this study. Hence, all physicians that usually treat DRF conservatively and operatively at our hospital will treat patients. No selection, nor restrictions regarding treating physician and fracture type will be imposed and operating physicians range from residents to consultants.

Statistical plan and analysis
Sample size

The sample size was calculated based on a 20% difference in complication rate between the two treatment groups, an alpha level of 5% and a power of 80%. Consequently, each group shall at least consist of 49 participants. The control group was decided to be of equal size.

Data management

All data will be managed in accordance with Good Clinical Practice. Papers containing patient identifiable data along with informed consent are physically stored in a locked room. Study data will be collected and managed using REDCap electronic data capture tools hosted at Aarhus University, Denmark [25]. The Data Steering Committee (RT, JDR, JP) will review included and excluded patients every 14th day. If patients do not show up for follow-up in the outpatient clinic, The Data Steering Committee will contact the patient by phone and/or mail in order to ensure participant retention and complete follow-up. Only the Data Steering Committee will have access to the final trial data set. No publication of the data is planned; however data will be stored according to national legislation.

Statistical analysis plan

That data will be analyzed using Fisher's exact test and Mann Whitney U test. The desired applied statistic is odds ratio with Pearson's 95% confidence interval. Should any data be lost in the follow-up, the Last Observation Carried Forward concept will be used. Treatment arm 3 will be analyzed after 6 months follow-up and published separately.

All test will be two-tailed and assessed at the 5% alpha level. Categorical measures will be presented as percentages. An intention-to treat and per-protocol analysis will be considered. Continuous measures will be presented as means with standard deviations and medians with inter-quartile range. Treatment effects over time will be assessed using linear mixed effect models with patient treated as random factor. A normal distribution with an identity link function will be assumed for continuous measures, while a multinomial distribution and cumulative logit function will be applied to ordinal outcomes.

Discussion

This prospective trial helps to clarify the best treatment strategy for displaced DRF patients ≥65 years. Practical limitations prevent the conduction of a double-blinded data collection, as no sham operations will be performed.

To the best of our knowledge, only one similar randomized controlled trial investigating volar locking plates versus conservative treatment in patients ≥65 years with DRF has been conducted [8, 16]. In 2011, Arora and co-workers reported similar results in terms of patient-reported outcome measures DASH and PRWE, pain level and range of motion between 36 operatively and 37 non-operatively treated patients [16], while the complication rate was 36 and 14% in the two groups, respectively. However, this trial did not have a significant clinical impact on the treatment of this patient group in Denmark. In the light of these promising initial report limiting the need of surgical intervention, there is a need to verify its results. Thus, the current trial will help to clarify the best treatment strategy for displaced DRF in patients ≥65 years in terms of complication rate and expected comparable functional outcome. If the results of the study indicate one treatment superior to the other, clinical guidelines are likely to be influenced by the current study.

Furthermore, cost effectiveness calculations can be performed on the basis of results of the current study and unnecessary operations may be prevented in order to live up to the Hippocratic oath, 'primum non nocere - first do no harm'.

Abbreviations
ASA class: American Society of Anesthesiologists Classification; DRF: Distal radius fractures; EQ5D: European Quality of life – 5 dimensions;

NCG: National Clinical Guidelines; NRS: Numeric Rating Scale; ORIF: Open reduction internal fixation; PRWE: Patient rated Wrist evaluation; Quick DASH: Quick Disabilities of the Arm, Shoulder and Hand

Availability of data and materials
Not applicable.

Ethics approval and consent to participate
This study has been approved by the Danish Scientific Ethical Committee (ID: 1–10–72-420-17) and has been registered at the Danish Data Protection Agency. Protocol modifications are prohibited. Furthermore, this study is registered at Clinicaltrials.gov (ID: NCT03716661). Participation is based on written consent after the possible participant is carefully informed about participation by the including physician or research year student. Only information regarding the therapeutic process of the wrist and associated hospitalizations within the 1 year of follow-up will be extracted from the participants electronic medical journals. The surgical treatment is covered by The Danish Patient Compensation Association.
We do not expect that participants experience more and severe complications than those associated to the standard operative treatment. Plaster immobilization may lead to complications e.g. skin irritation, pain, and at rare occasions ulcer due to poorly applied plaster. All patients are given instructions for cast complications. Normally, this can be fixed by replacing the plaster cast. As previously stated, the investigators reserve the right to exclude participants at any time if it is considered clinically irresponsible to let them continue in the study. An interim analysis of the 6 months follow-up data will be performed when half of the patients has reached that milestone. The study will be terminated if treatment arm 2 should be inferior to treatment arm 1 in terms of complication rate. The patient can anytime withdraw their written consent.

Consent for publication
Written consent for publishing has been obtained by the individual in the images for Fig. 3.

Competing interests
RT is consultant for Acumed. The other authors have no conflict of interest.

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Publisher's Note

II

Objective outcome measures continue to improve from 6 to 12 months after conservatively treated distal radius fractures in the elderly - a prospective evaluation of 50 patients

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Article

Objective Outcome Measures Continue to Improve from 6 to 12 Months after Conservatively Treated Distal Radius Fractures in the Elderly—A Prospective Evaluation of 50 Patients

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Abstract: Distal radius fractures (DRF) in the elderly population above 65 years represent 18% of all fractures and are thereby the second most frequent fracture in the elderly. Fracture dislocation and comminution are often used to determine whether non-operative or operative treatment is indicated. The purpose of this prospective case series of minimally displaced DRF treated with a dorsal cast was to assess the complication rate and patient-reported outcome measures. This single-centre, single-blinded, prospective case series followed 50 conservatively treated DRF patients for one year. Primary outcomes were complications and Quick Disability of Arm Shoulder and Hand (qDASH) score. Secondary outcomes were range of motion (ROM), grip strength and pain, and Patient-Rated Wrist/Hand Evaluation (PRWHE). Results showed only minor complications with a return to prior ROM, qDASH, and pain after 12 months and improvement in outcomes after 6–12 months. In conclusion, the majority of DRF patients who were treated non-operatively with five-week dorsal casting recover fully after minimally displaced DRF. This standard approach is thus considered safe, and the present results provide a reference for other studies.

1. Introduction

Distal radius fractures (DRF) account for 18% of all fractures in the elderly $\geq$65 years of age and constitute the second most frequent fracture in the elderly next to hip fractures (37%) [1]. DRF are often low-energy fractures, predominantly occurring in females with an estimated life-time risk of DRF of 15% in contrast to a life-time risk of 2% in males [2]. The elderly population in Europe is estimated to increase by 56% in men and 41% in women within fifteen years, and therefore an increased incidence of DRF may be expected [3].

In the last two decades there has been a trend towards surgical intervention using volar locking plating (VLP). In Denmark, the treatment of a DRF is based on the National Clinical Guidelines (NCG) stipulated by The Danish Health Authority [4]. According to the NCG, a low-energy DRF, regardless of age, should be operatively treated when the fracture fulfills at least one of the following radiologic criteria after attempted closed reduction:

- >10° dorsal angulation of the radial joint surface;
- >2 mm articular step-off;
- >2 mm ulnar variance;

- Incongruence of the distal radioulnar joint;
- Substantial dorsal comminution indicating cross instability.

The reliability of these specific radiologic criteria has been questioned [5]. Internationally, different measurable radiological parameters have been reported to be of use in clinical decisions in predicting the functional outcome after a DRF, but the fundamental evidence verifying these parameters is varied and inconsistent [6,7].

Complications after DRF are not clearly defined, making it difficult to compare different complication rates in the literature. However, the literature points out that more complications may follow using VLP compared with conservative treatment [8].

This raises an interest in clarifying the complication rate and functional outcome of DRF—especially in the elderly who may not benefit from surgery in the long term [9].

The aim of this study was to investigate the complication rate, functional outcomes and patient-reported outcomes after conservatively treated, minimally displaced DRF that do not fulfil the criteria for operative treatment according to the NCG.

2. Materials and Methods

2.1. Study Design

A prospective case series of 50 DRF patients ($\geq$65 years old) not fulfilling the NCG radiologic criteria for surgical treatment. The follow-up time was 12 months from the day of injury with out-patient visits after two weeks, five weeks, and six and 12 months. The study was conducted at Regional Hospital Randers, Denmark, with an estimated coverage area of 270,000 inhabitants. Recruitment took place from 1 November 2018 until 31 July 2019.

Inclusion and exclusion criteria are stated in the published study protocol [9]. In brief, all patients were 65 years old or older and had sustained a minimally displaced DRF that does not fullfill the NCG criteria for operative treatment (please refer to the introduction).

2.2. Recruitment

All participants' eligibility was approved by a consultant of the research group or the house physician on call. Primarily, contact with patients was established in the emergency department (ED). The patients were informed orally and in writing about the study and invited to enroll by giving written consent. Each patient treated in the ED was discussed the following day, and all radiographs were evaluated at an ED conference. This ensured that every potential participant was assessed for eligibility and offered enrollment either directly in the ED or the following day by telephone.

2.3. Interventions

When a displaced DRF was diagnosed using standardized wrist radiographs with an anterior-posterior and lateral/axial projection, a 20 mg/mL Lidocaine hematoma block was induced. The physician on call had two attempts to perform closed reduction in order to achieve an acceptable radiologic reduction according to the NCG. The closed reduction and plaster immobilization were guided by fluoroscopy. The assessment of the closed reduction was based on new standardized radiographs in two projections obtained at the Department of Radiology. If the inclusion criteria were met, the patient was offered enrollment.

Furthermore, undisplaced and minimally displaced DRF fulfilling the NCG criteria for non-operative treatment were enrolled. The cast was removed after five weeks.

If reduction was lost at the two-week follow-up in the outpatient clinic and thus no longer fulfilled the radiologic NCG criteria for non-operative treatment, the participant was offered surgery and excluded from the present study.

2.3.1. Primary Outcomes

Complications were reported by the patient on a standardized form. The treating physician furthermore examined the patient and qualified the patients' responses and added additional observations. Thus, both patient-reported and objective complications were reported and registered. Complications were defined as one of the following:

- Sensory disturbance including carpal tunnel syndrome and chronic regional pain syndrome (CRPS);
- Flexor tendon rupture and irritation;
- Extensor tendon rupture and irritation;
- Infection: superficial or deep;
- Hardware failure and hardware loosening;
- Reoperation including hardware removal or replacement.

Furthermore, vascular compromise with a capillary refill of more than two seconds and a free text field was available on the form for reporting other complications or qualifying the complications mentioned above.

2.3.2. Secondary Outcomes

The validated Danish version of the Quick Disabilities of the Arm, Shoulder, and Hand (qDASH) was used to assess the patient-reported level of functionality [10–12]. The minimally clinical important difference (MCID) was a 16 to 20-point difference in qDASH [10,13,14].

Active range of motion (ROM) of the wrist, i.e., wrist flexion, extension, pronation, supination, radial deviation, and ulnar deviation was measured with a goniometer by an independent, blinded observer. Furthermore, patients wore stockings on their wrists in order to conceal minor deformities, etc. The ROM of the contralateral wrist served as a reference.

Grip strength was measured using an electronic hand dynamometer (EH101 CAMRY, by Camry scale). Grip strength is given as the mean of three measurements on each side [15,16]. The MCID of grip strength is 6.5 kg [17].

The EuroQol 5 dimensions—3 levels questionnaire (EQ5D-3L) was reported at six and 12 months. It contains five items (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) ranging from level 1–3 in each item [18].

Fracture-specific pain at rest was reported on a numeric rating scale (NRS) ranging from 0 to 10 [12].

The validated Danish version of the Patient-Rated Wrist/Hand Evaluation (PRWHE) was applied as a self-reported assessment of five items on pain, 10 items on function, and two optional items on appearance of the hand [19].

The following baseline demographics were recorded: gender, age, side of DRF, hand dominance (right-handed, left-handed, ambidextrous), working status, American Society of Anesthesiologists Classification (ASA class 1–6 ranging from 1 healthy, 2 mild systemic disease, 3 severe systemic disease, 4 severe systemic disease that is a constant threat to life, 5 moribund, 6 brain-dead), smoking (cigarettes/day), alcohol consumption (units/week), and diabetes (yes/no).

The preinjured state of qDASH, pain, and complications questionnaire were administered based upon recall of the patient at the time of injury.

2.4. Data Management and Statistical Analysis

Data were managed in accordance with Good Clinical Practice guidelines. Physical material with patient-identifiable data and informed consent were physically stored in a locked room according to national legislation. Data were collected physically on paper and subsequently registered in a database using REDCap (vers. 10.0.2, Vanderbilt University, Nashville, TN, USA, 2021) [20]. If a participant did not show up for follow-up in the out-patient clinic, the data steering committee established contact by telephone and/or

mail in order to ensure participant retention in the study and to complete follow-up. The data were only accessible for the data steering committee.

The complication rate is presented in % (n/50). qDASH was presented in score points with a mean difference and 95% confidence intervals (CI). ROM of the wrist is presented as mean degree of motion for each movement with range and mean difference between injured and contralateral side with 95% CI. Grip strength is presented as difference in kilograms with 95% CI. Pain is reported as mean NRS with 95% confidence intervals.

Mixed effects analysis with correction for multiple comparisons was applied to analyse the longitudinal change of the different outcome measures, e.g., qDASH, VAS, angulation, and ROM. Spearman's correlation was applied to qDASH vs. PRWHE. EQ5D-3L are given as raw data and indices.

Statistical significance was declared when $p \leq 0.05$. All tests were performed using Prism 9 for macOS (vers. 9.1.0, GraphPad Software, San Diego, CA, USA, 2021).

3. Results

Figure 1 depicts the CONSORT flow diagram regarding eligibility, inclusion, and exclusion. In total, 50 patients were available for data analysis after six months follow-up and 48 patients after 12 months. Baseline demographics of the cohort are given in Table 1.
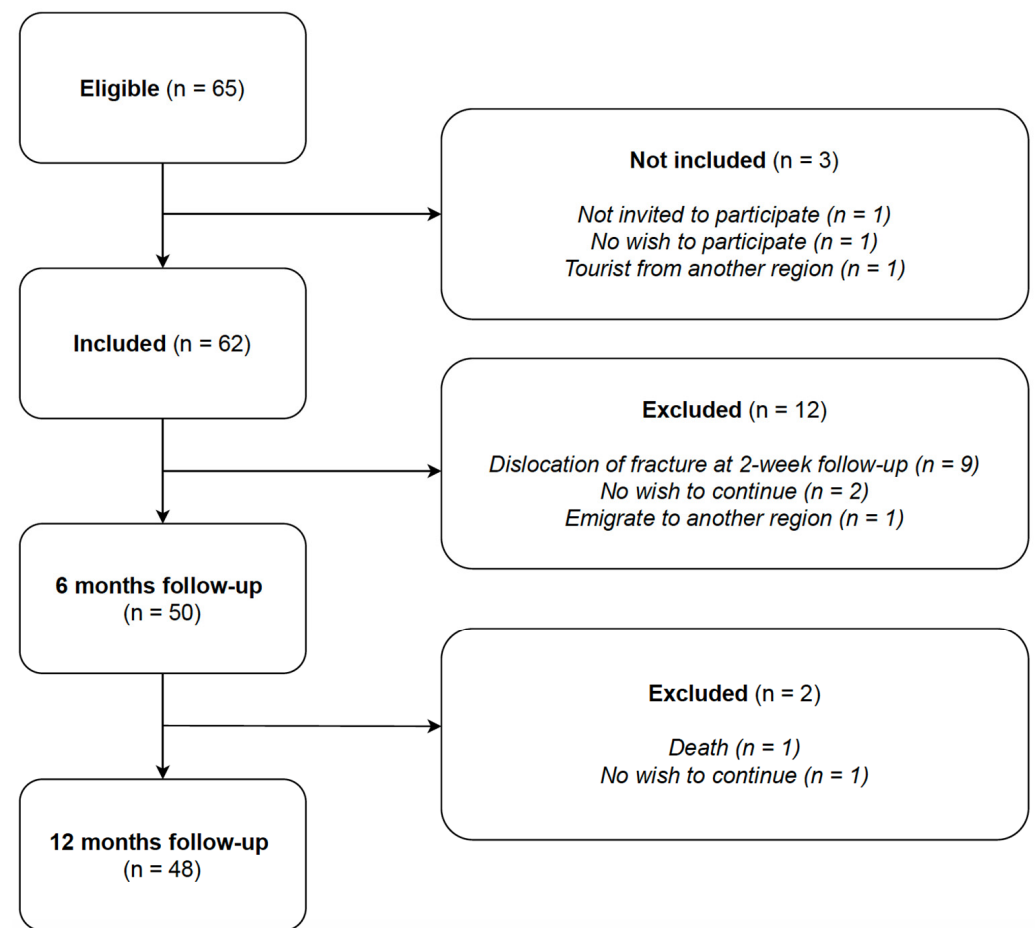
Figure 1. CONSORT Flowchart.

Table 1. Baseline Demographics.

		n (%)
Sex	Female	41 (82)
	Male	9 (18)
Age (years)	Median age	73.5
	Range	65–100
	IQR	70–78
Fractured side	Right	18 (36)
	Left	32 (64)
Hand dominance	Right	43 (86)
	Left	4 (8)
	Ambidextrous	3 (6)
	Dominant side fractured *	20 (40)
Working status	Full-time/part-time work	0 (0)
	Volunteer work	3 (6)
	Retired	47 (94)
Smoking status	Non-smoker	41 (82)
	Smoker	9 (18)
Alcohol consumption **	<7/14 units/week	44 (88)
	>7/14 units/week	6 (12)
ASA class	ASA class 1	16 (32)
	ASA class 2	25 (50)
	ASA class 3	9 (18)
	ASA class 4–5	0 (0)
Comorbidities	Osteoporosis	7 (14)
	Diabetes	3 (6)
	Hypertension	22 (44)
	Depression	9 (18)
Medications	No medications	5 (10)
	1–4 medications	38 (76)
	≥5 medications (polypharmacy)	7 (14)

* A fracture in an ambidextrous patient was not considered a fracture of the dominant side. ** Threshold defined as 7 units/week for females and 14 units/week for males.

3.1. Primary Outcome Measure: Complications

8/50 (16%) reported complications after six months, while only 3/48 (6%) reported complications after 12 months. Here, two patients complained about sensory disturbances, and one patient complained about swelling during activity and lack of strength (Table 2). Table 2 also highlights the time dependency of sensory disturbances with six patients (12%) complaining about sensory disturbances after six months. However, none of these cases were motorically compromised, and no atrophy was observed. Thus, all sensory disturbances were classified as nerve irritation instead of, for instance, carpal tunnel syndrome. The complications registered as others were two cases of pain during activity.

Table 2. Complications.

Complications	Day 0 (n = 50)	2 Weeks (n = 50)	5 Weeks (n = 50)	6 Months (n = 50)	12 Months (n = 48)
Sensory disturbance	1	1	0	6 (12%) *	2
Flexor tendon rupture and irritation	0	0	0	0	0
Extensor tendon rupture and irritation	0	0	0	0	0
Vascular compromised (capillary refill $\geq$ 2 s)	0	0	0	0	0
Other	0	2 **	0	2 (4%) ***	1 ****
Total:	1	3	0	8 (16%)	3

* Five patients reported unspecific dysaesthesia of single digits, one hyperalgesia of the dorsal aspect of the wrist (4 × 10 cm); ** two patients had an exchange of dorsal plaster cast; *** two patients reported ulnar pain and pain during activity as complications; **** swelling during cycling and lack of strength.

3.2. Secondary Outcome Measures: Patient-Related Outcome Measures (qDASH and Their Correlation to PRWHE) and Pain Score (NRS)

Both qDASH and pain score were statistically significantly worse at post-injury week two and five compared with the patient "recalled" scores before the injury (Figure 2). After six and 12 months, both outcome measures had returned to their preinjury level with no statistically significant difference between the three time points.
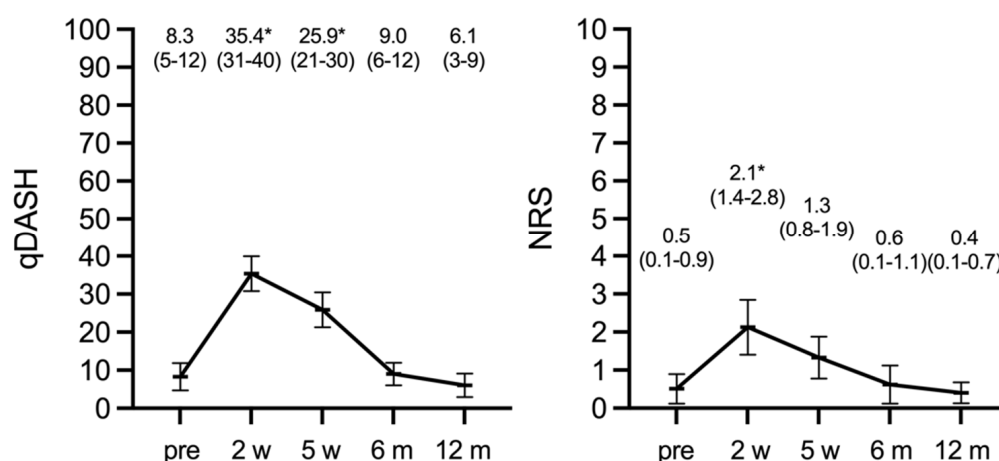
Figure 2. qDASH and NRS pain score, preinjury (pre), two weeks (w), five weeks (w), six and 12 months (m); * $p < 0.05$ compared with preoperative, i.e., recalled scores.

The change of mean PRWHE scores from 13.5 (95% CI 9.0–18.0, IQR 0–19) after six months to 8.7 (95% CI 3.6–13.7, IQR 0–10) after 12 months approached statistical significance ($p = 0.05$). To the PRWHE aesthetic item: "How important is the appearance of your hand to you?", 41/50 patients responded not important, three patients somewhat important, and only one patient very important (five patients did not answer this question). Only the latter stated that the appearance of the wrist/hand bothered the patient significantly during the last week: 8 on a 0–10 Likert scale (not at all—worst possible).

Both patient-related outcome measure instruments had a strong correlation at any given time point: Spearmans r(PRWHE-qDASH) = 0.74 ($p < 0.0001$) after six months, and r(PRWHE-qDASH) = 0.66 ($p < 0.0001$) after 12 months. Furthermore, the correlation of the same instrument over time, e.g., from six and 12 months was also strong: r(PRWE(6 months–12 months)) = 0.50 ($p < 0.0004$), and r(qDASH(6 months–12 months)) = 0.56 ($p < 0.0001$).

Active ROM was still improving after six months and reached normal, i.e., contralateral ROM, after 12 months (Figure 3).
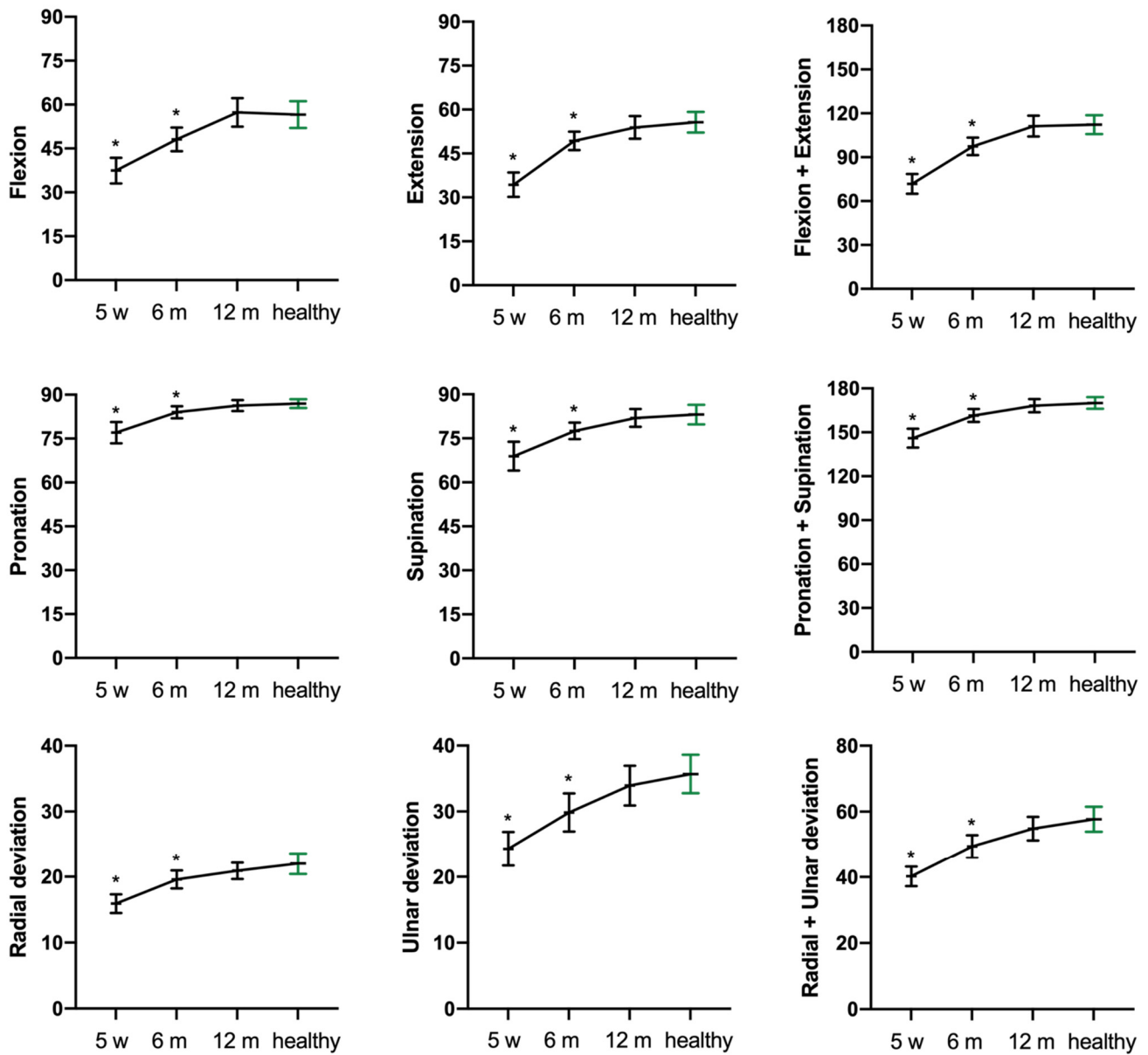
Figure 3. Temporal changes in active range of motion (degrees) after five weeks (w) and six and 12 months (m) compared with the healthy side at 12 months. * *p* < 0.05 compared with the healthy side (green).

3.3. Grip Strength

The grip strength of the injured wrist increased statistically significantly from six to 12 months post injury (mean diff. 1.6 (95% CI 2.8–0.4, *p* < 0.01)). However, the grip strength of the injured side remained impaired compared with the uninjured side both at six months (mean diff. −6.0 (95% CI −7.9−−4.2), *p* < 0.0001) and 12 months (mean diff. −4.1 (95% CI −6.3−−1.9, *p* < 0.0001).

3.4. Quality of Life (EQ5D)

EQ5D-3L indices after six and 12 months were 0.87 (95% CI 0.84–0.90, range 0.68–1.00) and 0.93 (95% CI 0.90–0.96, range 0.71–1.00), respectively (*p* < 0.001). EQ-5D-3L frequency results reported by dimension (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) are presented in Table 3.

Table 3. EQ-5D-3L frequencies reported by dimension and level after 6 month and 12 months, n (%).

Parameter	6 Months	12 Months
Mobility:		
Level 1	45 (90%)	39 (81%)
Level 2	5 (10%)	9 (19%)
Level 3	0 (0%)	0 (0%)
Total	50 (100%)	48 (100%)
Self-care:		
Level 1	45 (90%)	46 (96%)
Level 2	5 (10%)	2 (4%)
Level 3	0 (0%)	0 (0%)
Total	50 (100%)	48 (100%)
Usual activities:		
Level 1	43 (86%)	44 (92%)
Level 2	6 (12%)	4 (8%)
Level 3	1 (2%)	0 (0%)
Total	50 (100%)	48 (100%)
Pain/discomfort:		
Level 1	24 (48%)	39 (81%)
Level 2	26 (52%)	9 (19%)
Level 3	0 (0%)	0 (0%)
Total	50 (100%)	48 (100%)
Anxiety/depression:		
Level 1	46 (92%)	45 (94%)
Level 2	4 (8%)	3 (6%)
Level 3	0 (0%)	0 (0%)
Total	50 (100%)	48 (100%)

3.5. Dorsal Angulation

The DRF of 27 patients was reduced using a hematoma block, correcting the mean angulation of 14.8° (95% CI 9.0–20.5) (*p* < 0.001). The mean dorsal angulation after reduction was 1.8° (95% CI −0.2–3.7). This correction was partially lost, i.e., 5.2° (95% CI 2.0–8.3; *p* = 0.001) during the five weeks of conservative treatment with a dorsal plaster cast.

In the 23 patients without reposition, the mean dorsal angulation of 0.5° (−1.7–2.7) was maintained during treatment (mean difference: 2.4° (95% CI −0.2–4.9, *p* = 0.066), Figure 4). However, 9/27 reduced and 4/23 not-reduced fractures had a dorsal angulation of more than 10° on the latest radiographs after five weeks but had a dorsal angulation of less than 10° after the radiographical control two weeks post injury (Figure 4).
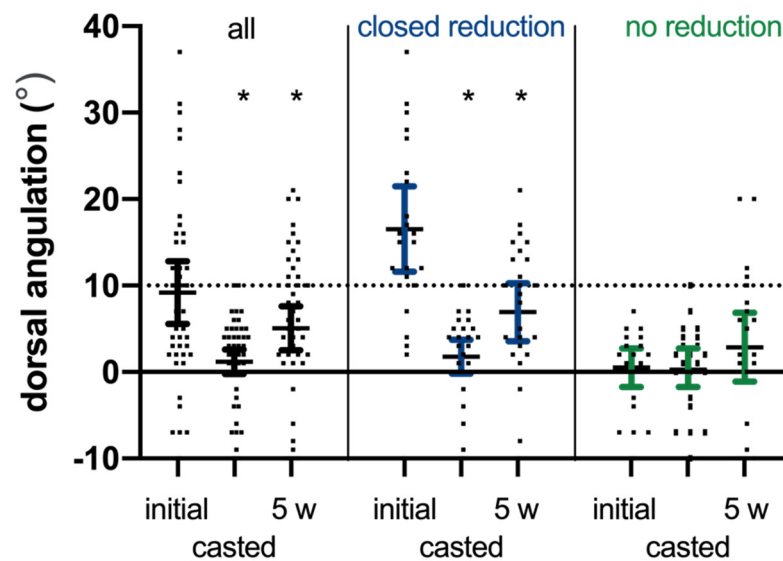
Figure 4. Dorsal angulation of the DRF at presentation, i.e., initial radiograph, the casted radiograph, and the final radiograph after five weeks (5 w) for all DRF and subdivided based on closed reduction (yes; no). * $p < 0.05$ compared with the initial dorsal angulation.

4. Discussion

The primary findings of the present study of 50 DRF patients with minimally displaced DRF treated conservatively with or without closed reduction and plaster immobilization was a low complication rate of 6% (3/48 patients) after 12 months. The complication types were sensory disturbances and activity-related wrist swelling. Interestingly, the reported complications were not consistent over time. After six months, 16% (8/50) of patients reported complications. However, the ulnar pain reported by two patients and the majority of sensory disturbances disappeared after 12 months. Please refer to Table 2 for details.

In agreement with these results, Saving et al. [15] investigated conservatively treated displaced DRFs after 12 months in elderly patients and found a complication rate of 11% consisting of five cases of nerve numbness and two cases of CRPS. Delayed extensor pollicis longus tendon rupture occurred in one of the cases within one year and up till 10 years after the fracture [21].

Subjective clinical outcomes based on the qDASH score improved statistical significantly from six to 12 months returning to preinjury levels. Contrary to our results, Aparicio et al. [22] found a significant increase in upper limb disability one year after the acquisition of conservatively treated DRF measured using the qDASH score. Dewan et al. [23] report that improvement in fracture-specific disability was completed after six months. This is in line with our results. However, we noticed a trend towards further improvement from six to 12 months ($p > 0.05$). qDASH as a tool is highly recommended for outcome measures in DRF [12]. In addition, the qDASH may even be more sensitive and responsive to functional impairments than the DASH (Disabilities of Shoulder and Hand) [24,25]. In our study, ROM also progressed from six until 12 months and normalized, which is corroborated by Hassellund et al. [26].

The findings of the present study confirms that closed reduction using a hematoma block is an acceptable and good treatment. Only 9/62 (15%) of the included patients did not maintain the reduction after two weeks and were thus excluded (Figure 1). However, mean change in dorsal angulation was 5.2 degrees (95% CI 2.0–8.3; $p = 0.001$) after the five weeks follow-up. Notably, 9/27 (33%) reduced and 4/23 (17%) non-reduced DRF had a dorsal angulation of more than 10° at the latest five-week radiographic follow-up. Nonetheless, the functional recovery and complication rate were not compromised in this group. Additionally, in this group there is a growing body of evidence in support of

non-operative treatment in the long-term and a suggestion to reserve surgery for patients in need of fast recovery [15,26–36].

The included patients were relatively healthy (low ASA score) and had good preinjury function of the arm (low qDASH scores), thereby indicating a high demand for a good functional outcome. It is therefore encouraging that this was achieved despite 13/48 patients healed with a radiographic configuration normally mandating surgery according to the NCG [4].

Strengths and Limitations

During the enrolment period only one potential study candidate missed inclusion; selection bias was therefore minimal. We only had few missing data: one patient died and one patient did not wish to participate; however, all patients had complete six-months data. The data collection of ROM was blinded, and the patients were instructed not to speak during the measurement. Limitations were the lack of a control group and the low ASA score in the study. Despite these strengths and limitations, we find that conservative treatment of DRF as described is to be considered a safe and reliable treatment for this group of patients.

5. Conclusions

In conclusion, in patients 65 years and older with conservatively treated non-displaced or minimally displaced DRFs, functional and patient-reported outcomes continue to improve from injury to six months and from six to 12 months. At the latest follow-up, the mean differences in qDASH, PRWHE, and ROM did not statistically significantly differ from the recalled preinjury or measured contralateral side.

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III

VOLCON - a randomized controlled trial investigating complications and functional outcome of volar plating vs casting of unstable distal radius fractures in patients older than sixty-five years.

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ORIGINAL ARTICLE

VOLCON: a randomized controlled trial investigating complications and functional outcome of volar plating vs casting of unstable distal radius fractures in patients older than 65 years

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Abstract

Background: Primary aim: to compare complications of operative vs non-operative treatment of unstable distal radius fractures (DRF) fulfilling national clinical guidelines for operative treatment. Secondary aim: to compare the functional outcomes.

Materials and methods: A single-centre randomized controlled trial of unstable DRF. 50 patients: volar locking plate, 2 weeks casting + 3 weeks orthosis. 50 patients: 5 weeks casting. Primary outcome: complications assessed after 2 and 5 weeks and 6 and 12 months. Secondary outcomes: Quick-DASH, PRWHE, range of motion, grip strength, EQ-5D-3L.

Results: 148 patients were screened from November 2019 to March 2021. 48 patients did not want to participate or were unable to participate in the follow-up. 100 patients were randomized and 85 patients were available for full analysis due to there being 4 deaths, 6 withdrawals, 1 wrong inclusion, 1 emigration, 1 refracture, 1 patient with compartment syndrome, and 1 who was advised to undergo surgery after being randomized to non-operative treatment. Median age was 74 years (range 65–92), 81 women/19 men, 42 right/58 left side, 87 retired, 11 smokers, 86 ASA class 1 or 2. Complication rates did not statistical significantly vary between the operative and non-operative group: 20.9% (9/43) vs 16.6% (7/42), $p = 0.78$ (Fisher's exact test). Complications were driven by sensory disturbances. Four reoperations were performed: two in the non-operative group: carpal tunnel syndrome; two in the operative group: one carpal tunnel syndrome, one protruding screw causing extensor tendon irritation. Mean difference in Quick-DASH varied from 2.3 (95% CI − 3 to 8) pre-injury to 4.2 (− 4 to 12) at 12 months. Quick-DASH and PRWHE were neither statistically nor clinically-relevant different between groups.

Conclusions: Complication rates after operative and non-operative treatment of DRF were similar. Volar plating did not improve the functional outcome after 5 weeks, 6 months, and 12 months. These findings are in line with recent RCTs and mandate a revision of guidelines towards more conservative treatment. Take home messages: (1) consider non-operative treatment in elderly patients sustaining unstable DRFs; (2) choosing operative treatment in patients

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older than 65 years should not be the gold standard; (3) however, non-operative treatment still carries a risk for complications.

Level of evidence: II.

Background

Distal radius fractures (DRF) account for 18% of all fractures in the elderly ≥ 65 years of age [1].

The incidence rate of DRF is approximately 190–200 per 100,000 person years and likely to increase in the future [1, 2]. Operative treatment with open reduction and internal fixation (ORIF) using volar locking plates is the recommended standard treatment of unstable DRF according to the National Clinical Guidelines (NCG) [3] issued by the Danish Health Authorities, similar to the American Academy of Orthopedic Surgeons [4].

The NCG recommend operative treatment of DRF that fulfils the following radiologic criteria after attempted closed reduction:

- > 10° dorsal tilt of the radius
- > 2 mm articular step-off
- > 3 mm ulnar variance
- Incongruence of the distal radioulnar joint,
- Substantial dorsal comminution indicating gross instability.

If one or more of these criteria are met, the advice is to use ORIF most often with a volar locking plate regardless of the patient's age.

However, according to the NCG, the scientific evidence is "very weak" for this recommendation compared to that of closed reduction and cast immobilization. Nonetheless, in 2021, the vast majority of unstable DRF were treated by volar plating according to guidelines. Furthermore, volar plating surgery is associated with a significant complication rate of up to 30% [5, 6].

Recent evidence indicates that non-operative treatment may deserve the role of gold standard in the elderly population [7–10].

This randomized controlled trial (RCT) aims to compare unstable DRF treated with plaster cast immobilization for 5 weeks with ORIF with a volar locking plate in terms of complication rate, functional outcome and patient-reported outcome in patients ≥ 65 years.

We hypothesized that treatment of unstable DRF with non-operative treatment would be superior to ORIF with a volar locking plate in terms of complication rate. However, both treatments are expected to have comparable functional and patient-reported outcomes after 12 months (mean difference in QuickDASH < 16).

Materials and methods

We conducted a prospective, single-centre, assessor-blinded, randomized, controlled superiority trial comparing non-operative treatment ($n1 = 50$) vs volar plating ($n2 = 50$) of unstable DRF in patients ≥ 65 years with regards to complications and functional outcome. The detailed study protocol has been published with open access [11]. The study was conducted from November 2019 to March 2022.

Interventions and randomization

All patients with DRF diagnosed at our emergency department (ED) were screened for eligibility. Exclusion criteria were age < 65 years, high energy fracture, open fracture, concomitant injuries, previous fracture on the same arm, and inability to give written consent (Fig. 1).

After diagnosing the DRF on standardized wrist radiographs (anterior–posterior and lateral projections) in the ED, the physician on call had two attempts to achieve an acceptable closed reduction under local analgesia with a 20 mg/ml lidocaine haematoma block. The radiological NCG criteria were assessed on new radiographs. According to the sample size calculation, 50 participants were allocated to each group; hence, 100 identical A5 envelopes were sealed, each containing a folded note whereupon either "operative" or "non-operative" were written. The concealment strategy was tested and light could not shine through the envelopes. Concealment of allocation was thus effective.

ORIF with volar plate fixation utilized Acu-Loc®, Acumed or Variax®, Stryker, depending on the surgeon's preference. A standard Henry approach to the distal radius and pronator quadratus repair, if possible, was performed in the operative group. The vast majority of patients were operated under regional anaesthesia, and the remaining patients were operated under general anaesthesia.

After surgery, the wrist was immobilized in a dorsal plaster cast for 2 weeks, followed by a further 3 weeks of
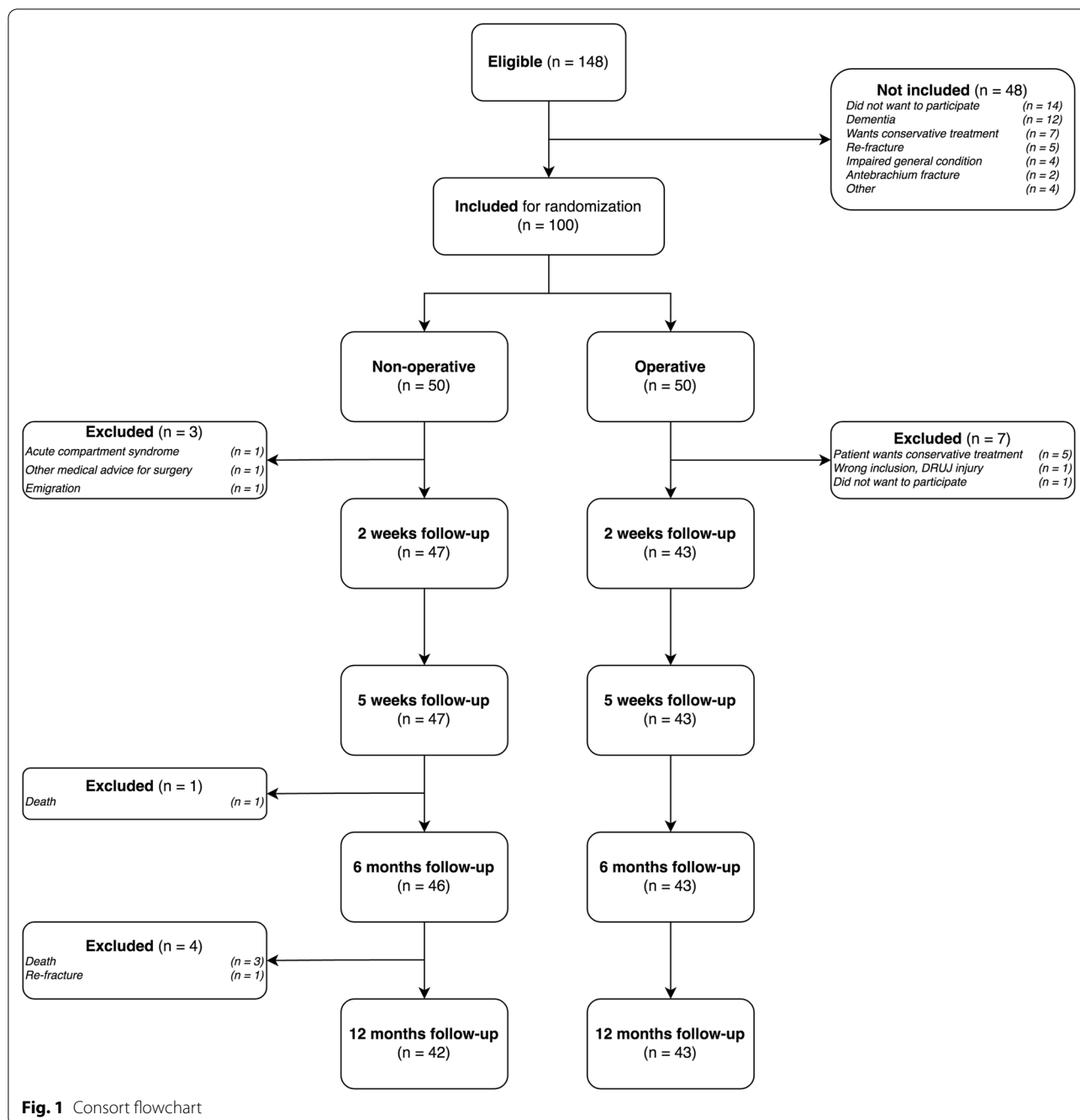
Fig. 1 Consort flowchart

immobilization with a removable orthosis. A single hand therapeutic instruction took place.

Non-operative treatment consisted of a dorsal plaster cast immobilization for 5 weeks. Only discomfort, neurologic deficits or signs of infection warranted removal and replacement with another dorsal plaster cast. A single hand therapeutic instruction took place in this group after removal of the cast. No radiological evaluation was performed before 5 weeks after the injury.

Outcomes

The primary outcome was the complication rate after 12 months. Complications were prospectively recorded at day 0 (baseline), 2 weeks, 5 weeks, 6 months and 12 months after injury. The patient answered standardized questions from the investigators at the given timepoints.

Complications were defined as the presence of:

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- Sensory disturbance, including carpal tunnel syndrome and chronic regional pain syndrome
- Flexor tendon rupture and irritation
- Extensor tendon rupture and irritation
- Hardware failure, e.g. osteosynthesis loosening
- Infection: superficial (treated with antibiotics only) or deep (requiring surgical intervention)
- Reoperation with hardware replacement
- Reoperation with hardware removal (partial or total), which is not routinely performed in our country
- Vascular compromise (capillary refill ≥ 2 s).

Secondary outcomes were obtained at the same time-points as the primary outcomes.

Patient-reported outcome measures included the Danish version of the Quick Disabilities of the Arm, Shoulder and Hand (Quick-DASH), which was used to assess the level of functionality prior to injury and after 2 weeks, 5 weeks, 6 months and 12 months. The minimal clinically relevant difference was defined as a 16- to 20-point difference in Quick-DASH [12–14]. The pain experienced during activity within the preceding 14 days before the injury and at 2 weeks, 5 weeks, 6 and 12 months of follow-up was recorded using the 0–10 Numeric Rating Scale (NRS). A validated Danish version of the Patient-Rated Wrist/Hand Evaluation (PRWHE) was also applied [15].

Range of motion (ROM) was measured by a registered nurse using a goniometer. To ensure the observer was blinded, the patient was instructed not to talk about the treatment. Furthermore, all wrists were covered by a glove concealing potential scars.

The grip strengths of both left and right hand were estimated as the mean score of three repetitions of each hand, alternating hands between attempts, after 6 months and 12 months using a calibrated dynamometer (EH101 CAMRY, by the Camry scale). Quality of life was assessed with European Quality of Life 5 Dimensions 3 Levels (EQ-5D-3L).

Baseline demographics were reported as age, gender, side of DRF, dominant hand, working status, ASA class 1–6 (American Society of Anaesthesiologists Classification), smoking, alcohol consumption and diabetes.

Statistical methods

The primary outcome, complication rate, was compared using Fisher's exact test of the accumulated complication rate after 12 months. In order to prevent double counting, in patients with multiple complications, only one complication was accounted for in this calculation (bold numbers in Table 2).

All secondary outcome measures were analysed for all obtained data using mixed-effects analysis with Sidak's multiple comparisons test. All available data were used without imputations for missing values.

According to our sample size calculation, 50 patients per treatment arm provide 80% statistical power at a 5% alpha level assuming a difference of 20% in complication rate between operatively and conservatively treated patients.

Statistical analyses were performed with Prism 9 for macOS.

The present trial was approved by the Danish Scientific Ethical Committee (ID: 1-10-72-420-17) and registered at Clinicaltrials.gov (ID: NCT03716661) [7].

Results

A total of 148 patients were screened for eligibility between November 2019 and March 2021. Due to the COVID-19 pandemic and the lower incidence of fractures during the pandemic, the inclusion period was longer than expected [16–18].

Of those 148 patients, 48 were excluded mainly because they did not want to participate or were excluded due to the stipulated exclusion criteria. 100 patients were randomized to either operative or non-operative treatment. A total of 85 patients were available for complete data analysis after 12 months. All patients stayed in their randomized group and none were allowed to cross over (Fig. 1).

Baseline demographics are given in Table 1. The vast majority of patients in both groups were healthy, active retired individuals with low ASA class scores.

Primary outcomes

The primary outcome complication rate after 12 months was 16.6% (7/42) in the non-operative group and 20.9% (9/43) in the operative group ($p = 0.78$, Fisher's exact test, Table 2). Patients with multiple complications were only accounted for once.

Many patients reported sensory disturbances at given time points; however, most often, these disappeared in follow-up visits. Consequently, only sensory disturbances at the 12-months visit contributed to the stated complication rate. Furthermore, sensory disturbances were not nerve specific. However, some carpal tunnel syndromes were registered. We did not observe any complex regional pain syndromes.

In 42 non-operatively treated patients, the complication rate was 16.6% due to 7 events: 2 carpal tunnel syndromes causing "reoperations", i.e., median nerve decompression after 5 weeks and 12 months; 3 unspecific sensory disturbances at 12-months follow-up; and 2 superficial wounds without infection at cast removal after 5 weeks.

Table 1 Baseline demographics

	Non-operative (n=50)	Operative (n=50)
Female / Male	40 (80%) / 10 (20%)	41 (82%) / 9 (18%)
Median age (min., IQR, max.) [years]	74 (65, 69-82, 91)	75 (65, 70-80, 92)
Fractured side: R / L	24 (48%) / 26 (52%)	18 (36%) / 32 (64%)
Hand dominance: R / L / Ambidextrous / Missing data	46 (92%) / 1 (2%) / 1 (2%) / 2 (4%)	38 (76%) / 3 (6%) / 0 (0%) / 9 (18%)
Dominant side fractured	23 (46%)	16 (32%)
Retired / Working / Volunteer / Retired / Missing data	45 (90%) / 1 (2%) / 2 (4%) / 2 (4%)	42 (84%) / 0 (0%) / 0 (0%) / 8 (16%)
Smoking: Yes / No / Missing data	9 (18%) / 37 (74%) / 4 (8%)	2 (4%) / 36 (72%) / 12 (24%)
Alcohol overconsumption: Yes / No / missing data	8 (16%) / 38 (76%) / 4 (8%)	6 (12%) / 32 (64%) / 12 (24%)
ASA class 1 / 2	13 (26%) / 30 (60%)	14 (28%) / 29 (58%)
ASA class 3 / 4-6 / missing data	6 (12%) / 0 (0%) / 1 (2%)	4 (8%) / 0 (0%) / 3 (6%)
Comorbidities:		
Hypertension	23 (46%)	16 (32%)
Diabetes	6 (12%)	2 (4%)
Depression	4 (8%)	1 (2%)
Osteoporosis	3 (6%)	3 (6%)
Prescribed medications: None / 1-4 / ≥ 5	8 (16%) / 26 (52%) / 16 (32%)	19 (38%) / 21 (42%) / 10 (20%)

R = Right, L = Left

A fracture in an ambidextrous patient was not considered a fracture of the dominant side.

Alcohol overconsumption was defined as more than 7 units/week for females and 14 units/week for males.

In 43 operatively treated patients, the complication rate was 20.9% due to 9 events: 1 carpal tunnel syndrome causing a reoperation, i.e., plate removal and nerve decompression after 11 months; 6 unspecific sensory disturbances at 12 months follow-up; 1 extensor tendon irritation due to a protruding screw that caused plate removal after 12 months; and 1 extensor pollicis longus rupture that was not repaired. Thus, two reoperations were performed in the operative group. Another patient in the operated group fell again and sustained a new DRF and bending of the volar plate (Fig. 2). This new trauma was not accounted for as a complication/reoperation. Lastly, 3 trigger fingers after 5 weeks, 6 months, and 12 months were observed in the operative group and none were observed in the non-operative group. However, these were not classified as complications.

Furthermore, in the non-operative group, one cast was changed due to loosening after the initial swelling had subsided, and one patient complained about ulnar wrist pain at final follow-up. In the operative group, three patients complained about a bothersome decrease in ROM. These events/complaints were not accounted for as complications, but were disclosed in order to report all data.

Secondary outcomes

According to Fig. 3, Quick-DASH and NRS did not statistically significantly differ between the operative and non-operative group at any timepoint. Furthermore, after 6 months and 12 months there was no statistically significant difference compared with the recalled pre-injury state in either group.

Mean PRWHE was similar in the operative and non-operative groups after 6 months: 9.6 (4.5–14.7) vs. 12.6 (8.7–16.5) and after 12 months: 8.6 (2.5–14.7) vs. 8.0 (3.6–12.4). There was no statistically significant difference between the two different treatments at any timepoint, but there was a slight overall improvement from 6 to 12 months: mean difference 2.8 (0.1–5.5), $p = 0.04$.

The active ROM improved throughout the observation period of 12 months. Many movements were statistically significantly reduced compared with the healthy side after 5 weeks and 6 months, but none was statistically significantly different from the healthy side after 12 months. Comparisons between the two treatment groups revealed a statistically significant difference in combined flexion–extension ROM after 5 weeks: mean diff. 14.7° (5.5–23.8°, $p < 0.0001$) and 6 months: mean diff. 9.8° (0.3–19.3°, $p = 0.037$). The mean difference after 12 months was 6.8° (− 3.2 to 16.7°, $p = 0.61$). At all time points, flexion–extension ROM slightly favoured the operative group.

Table 2 Complications

	Non-operative						Operative					
	day 0	2 weeks	5 weeks	6 months	12 months	TOTAL	day 0	2 weeks	5 weeks	6 months	12 months	TOTAL
N	*50*	*47*	*47*	*45*	*42*	**7/42 (16.6%)**	*50*	*42*	*43*	*43*	*43*	**9/43 (20.9%)**
Carpal tunnel syndrome	0	0	1	0	1	2	*0*	*0*	*0*	*0*	1	1
Unspecific sensory disturbance	1*	1*	1*	7*	3	3	1*	3*	7*	8*	6	6
Flexor tendon rupture or irritation	0	0	0	0	0	0	0	0	0	0	0	0
Extensor tendon rupture or irritation	0	0	0	0	0	0	0	1	0	0	1	2
Vascular compromise (refill >2 s)	0	0	0	0	0	0	0	0	0	0	0	0
Osteosynthesis loosening / failure	NA	NA	NA	NA	NA	0	0	0	0	0	0	0
Infection (deep or superficial)	0	0	0	0	0	0	0	0	0	0	0	0
Cast causing superficial wounds	NA	0	2	NA	NA	2	NA	0	0	NA	NA	0
Reoperation	NA	0	1**	0	1**	2**	NA	0	0	0	2**	2**

NA = not applicable

* = Temporary change and therefore not counted in the row total.

** = Max. 1 complication per patient, i.e., only the reason for the reoperation is counted.

The grip strength after 12 months was: mean (injured side, operative): 16.2 (14.0–18.5) kg; mean (uninjured side, operative): 17.1 (14.9–19.4); mean (injured side, non-operative): 14.8 (12.5–17.1); and mean (uninjured side, non-operative): 18.1 (15.0–21.3) kg. At 12 months follow-up, the mean difference in grip strength was 1.4 (− 2.6 to 5.5) kg. Mixed model analysis of the grip strength revealed a significant time effect ($p < 0.0001$), but no treatment effect ($p = 0.23$). Median EQ-5D-3L indices did not statistically significantly differ between the operative and non-operative group after 12 months (1.0 (range 0.36-1.0) vs. 1.0 (range 0.14-1.0)).

Discussion

The most important finding of the present study was that there was no statistically significant difference in complication rate or in functional or patient-reported outcome measures between operatively or non-operatively treated unstable DRF in patients ≥ 65 years after 12 months.
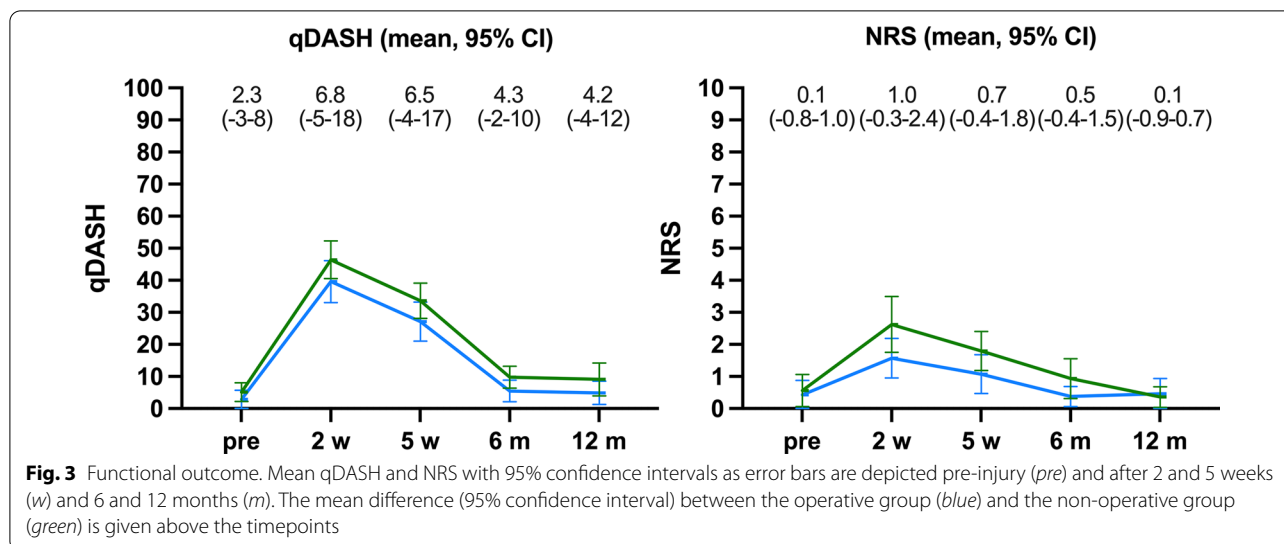
The similar complication rates between the operative and non-operative groups are supported by meta-analyses combining RCTs on non-operatively versus operatively managed DRFs [5, 7, 9, 10, 19–21]. Our results regarding complication rates after DRF are thus in line with previous studies on the subject. However, the definition of complications varies in the literature, and these results are therefore challenging to interpret. One meta-analysis divided complications into minor and major and found a significant higher rate of major complications in the operative group [21]. We report complications adhering to the published protocol and therefore did not subdivided them into major and minor complications [11]. Moreover, we observed 3 trigger fingers in the operative group and none in the non-operative group. However, these observations were not counted as complications, because these events were associated with operative treatment but were not necessarily caused by it.

Regarding patient-reported outcome measures, i.e., the Quick-DASH score, similar results for operatively

Fig. 2 Bent volar locking plate. Lateral wrist radiograph of an operatively treated distal radius fracture patient after a new fall causing a re-fracture and bending of the volar locking plate. This was a new trauma and therefore not accounted for as a complication
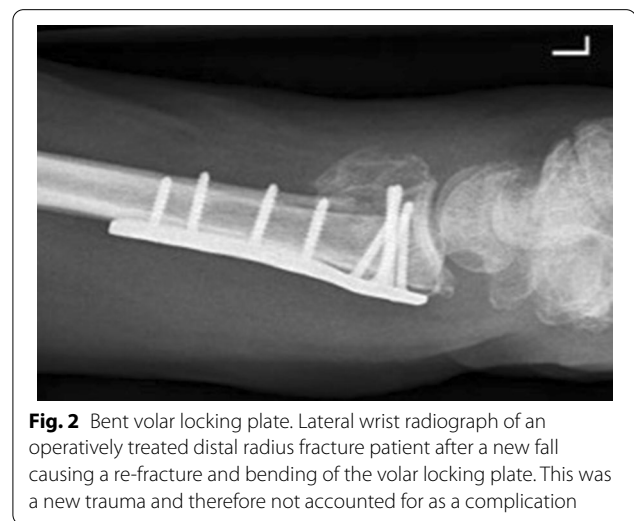
and non-operatively treated patients were reported in the existing literature [10, 20]. However, a meta-analysis that included not only RCTs but also prospective studies found a significantly lower Quick-DASH score favouring the operative group in the first year [19]. That meta-analysis found an effect size of − 5.22 (95% CI − 8.87 to − 1.57). In the present study, the mean difference in Quick-DASH was 4.2 (95% CI − 4 to 12), which was also well below the threshold for a minimal clinically relevant difference, 16–20 points. Likewise, the ROM was similar between groups, and the statistically significant difference in flexion–extension ROM at 5 weeks and 6 months was barely clinically relevant, i.e., the mean difference after 12 months was 6.8° (− 3.2 to 16.7°, $p = 0.61$).

Not all patients are ideal for non-operative treatment. The NCG recommend operative treatment in older patients with unstable DRF unless they have a low functional demand [3]. The same holds true in Norway [22]. In contrast, based on the same literature that was

Fig. 3 Functional outcome. Mean qDASH and NRS with 95% confidence intervals as error bars are depicted pre-injury (*pre*) and after 2 and 5 weeks (*w*) and 6 and 12 months (*m*). The mean difference (95% confidence interval) between the operative group (*blue*) and the non-operative group (*green*) is given above the timepoints

available in 2015, the Finnish Medical Society highlights that there is no difference in functional outcome and therefore recommends non-operative treatment to avoid costs and complications [23]. Furthermore, the latest British guidelines from 2018 state: "In patients 65 years of age or older, non-operative treatment can be considered as a primary treatment for dorsally displaced DRF unless there is significant deformity or neurological compromise" [24, 25]. It should be noted that both the Danish and British guidelines are more than 5 years old, and the majority of RCTs on this topic were published afterwards. These trials call for revisions of the guidelines towards a non-operative approach for the vast majority of patients.

So far, no long-term results of high-quality RCTs have become available. Theoretically, the functional outcome may decline over time in the non-operative group due to early onset of post-traumatic osteoarthritis, stiffness and pain.

The size of the study population is a limitation of our study. Performing the sample size analysis, we estimated complication rates for operative treatment based on our own retrospective complication rate in 576 patients [6]. The observed complication rate in the non-operatively treated group was higher than anticipated in the sample size calculation. Consequently, the power of the present trial was not sufficient to find statistically significant differences. However, considering the results of the meta-analyses discussed above, the present study adds to the evidence that complications are also to be expected in non-operatively treated DRF patients.

Another limitation of the present study is that it was not double blinded. We refrained from sham surgery due to the fact that most DRF patients at our institution are wide awake during surgery. We found it unethical to operate under general anaesthesia in order to ensure proper blinding of the patients. Lawson et al. state that people are more likely to rate their treatment as successful when they have had surgery [9]. However, we did perform assessor blinding of three trained nurses as described above and depicted in the published protocol [11].

Performing a single-centre RCT with a relatively small research group ensured a high level of control and consistency. All patients potentially eligible for inclusion were assessed by the same consultant and the risk of selection bias was minimized. Data collection was also performed by only a few persons, ensuring uniform data collection.

Conclusions
Complication rates after operative and non-operative treatment of DRF were similar. Volar plating did not improve the functional outcome after 5 weeks, 6 months, and 12 months. These findings are in line with recent RCTs and mandate a revision of guidelines towards more conservative treatment. Take home messages: (1) consider non-operative treatment in elderly patients sustaining unstable DRFs; (2) choosing operative treatment in patients older than 65 years should not be the gold standard; (3) however, non-operative treatment still carries a risk for complications.

Evaluation; Quick-DASH: Quick Disabilities of the Arm, Shoulder and Hand; RCT : Randomized controlled trial.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. The present trial was approved by the Danish Scientific Ethical Committee (ID: 1-10-72-420-17) and registered at Clinicaltrials.gov (ID: NCT03716661).

Competing interests
All authors declare no relevant financial or non-financial interests.

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IV

Prospective evaluation of two cohorts of non-operatively treated patients with displaced vs. minimally and non-displaced distal radius fractures

Thorninger R, Wæver D, Tjørnild M, Lind M, Rölfing J.

Article

Prospective Evaluation of Two Cohorts of Non-Operatively Treated Patients with Displaced vs. Minimally and Non-Displaced Distal Radius Fractures

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Abstract: Background: Distal radius fractures (DRFs) in the elderly are common. Recently, the efficacy of operative treatment of displaced DRFs in patients above 65 years of age has been questioned and it has been suggested that non-operative treatment should be the gold standard. However, the complications and functional outcome of displaced vs. minimally and non-displaced DRFs in the elderly has not been evaluated yet. The aim of the present study was to compare non-operatively treated displaced DRFs vs. minimally and non-displaced DRFs in terms of complications, PROMs, grip strength and range of motion (ROM) after 2 weeks, 5 weeks, 6 months and 12 months. Methods: We used a prospective cohort study that compared patients with displaced DRFs (n = 50), i.e., >10 degrees of dorsal angulation after two reduction attempts, with patients with minimally or non-displaced DRFs after reduction. Both cohorts received the same treatment of 5 weeks of dorsal plaster casting. Complications and functional outcomes (quick disabilities of the arm, shoulder and hand (QuickDASH), patient-rated wrist/hand evaluation (PRWHE), grip strength and EQ-5D scores) were assessed after 5 weeks, 6 months and 12 months post-injury. The protocol of the VOLCON RCT and present observational study has been published (PMC6599306; clinicaltrials.gov: NCT03716661). Results: One year after 5 weeks of dorsal below-elbow casting of low-energy DRFs in patients ≥ 65 years old, we found a complication rate of 6.3% (3/48) in minimally or non-displaced DRFs and 16.6% (7/42) in displaced DRFs (p = 0.18). However, no statistically significant difference was observed in functional outcomes in terms of QuickDASH, pain, ROM, grip strength or EQ-5D scores. Discussion: In patients above 65 years of age, non-operative treatment, i.e., closed reduction and dorsal casting for 5 weeks, yielded similar complication rates and functional outcomes after 1 year regardless of whether the initial fracture was non-displaced/minimally displaced or still displaced after closed reduction. While the initial closed reduction should still be attempted in order to restore the anatomy, failure to achieve the stipulated radiological criteria may not be as important as we thought in terms of complications and functional outcome.

Keywords: distal radius fracture; fracture; non-operative treatment; conservative treatment; complications; patient-reported outcome measures; QuickDASH; PRWHE; NRS; osteoporosis; aging

1. Introduction

Distal radius fractures (DRFs) have a bimodal distribution with high-energy fractures in the young and low-energy fractures in the elderly and post-menopausal women in particular [1]. Due to the growing elderly population, the socio-economic burden of DRFs is increasing [2].

Over the last two decades, there has been a trend towards open reduction and internal fixation (ORIF) with volar locking plates (VLP) of displaced DRFs. Indications for surgery

are stipulated in the clinical guidelines [3]. Minimally or non-displaced DRFs are commonly treated non-operatively with a cast.

Recent evidence questions the benefit of surgical treatment of DRFs in the elderly [4–9]. At 12 months follow-up there was no difference in patient-related outcome measures (PROM), i.e., QuickDASH (quick disabilities of the arm, shoulder and hand) and PRWHE (patient-rated wrist/hand evaluation). Consequently, the latest guidelines from the American Academy of Orthopedic Surgery have adopted this evidence [10]. However, the British guidelines state that "In patients 65 years of age or older, non-operative treatment can be considered as a primary treatment for dorsally displaced DRF unless there is significant deformity or neurological compromise" [11]. Counselling of patients regarding the expected rehabilitation, complications and functional outcome of non-operative treatment of displaced as well as minimally and non-displaced DRFs lacks evidence.

The aim of the present study was to compare non-operatively treated displaced DRFs vs. minimally/non-displaced DRFs (Figure 1) in terms of complications, PROMs, grip strength and range of motion (ROM) after 2 and 5 weeks, as well as after 6 and 12 months. To the best of our knowledge, no studies have investigated this relationship before.

Figure 1. Examples of radiographs of the two non-operatively treated cohorts: minimally displaced distal radius fracture (DRF) and displaced DRF after two attempts of fluoroscopic guided closed reduction. Pre-reduction, post-reduction and 5 week follow up.

2. Materials and Methods

In this prospective observational study, we evaluated two cohorts of displaced DRFs vs. minimally/non-displaced DRFs in patients above 65 years of age treated with a dorsal cast for 5 weeks. The study protocol for both the VOLCON randomized controlled trial (RCT)

and the present observational prospective cohort study has been published (PMC6599306; clinicaltrials.gov: NCT03716661) [12]. All patients gave written consent to participate in the study and could withdraw their consent at any time. STROBE reporting guidelines for observational studies were followed.

2.1. Cohorts

All ≥ 65-year-old patients presenting with a low-energy DRF at the emergency department (ED), Regional Hospital Randers, Denmark were eligible (Figure 2). Physicians had a maximum of two attempts of closed reduction and casting under fluoroscopic guidance using a hematoma block in order to achieve an acceptable reduction according to the radiological criteria of the National Clinical Guideline [3]. After each reduction attempt under fluoroscopic guidance, standard radiographs were taken at the Department of Radiology. These radiographs were assessed for acceptable reduction. If the radiological measurements were not acceptable, another attempt of reduction was performed. Patients were chosen above the age of 65 as it reflects the retirement age in Denmark. The Danish National Clinical Guidelines for surgery in displaced DRFs reflect the guidelines of the American Academy of Orthopedic Surgeons (AAOS) and British Society for Surgery of the Hand (BSSH) [10,11].
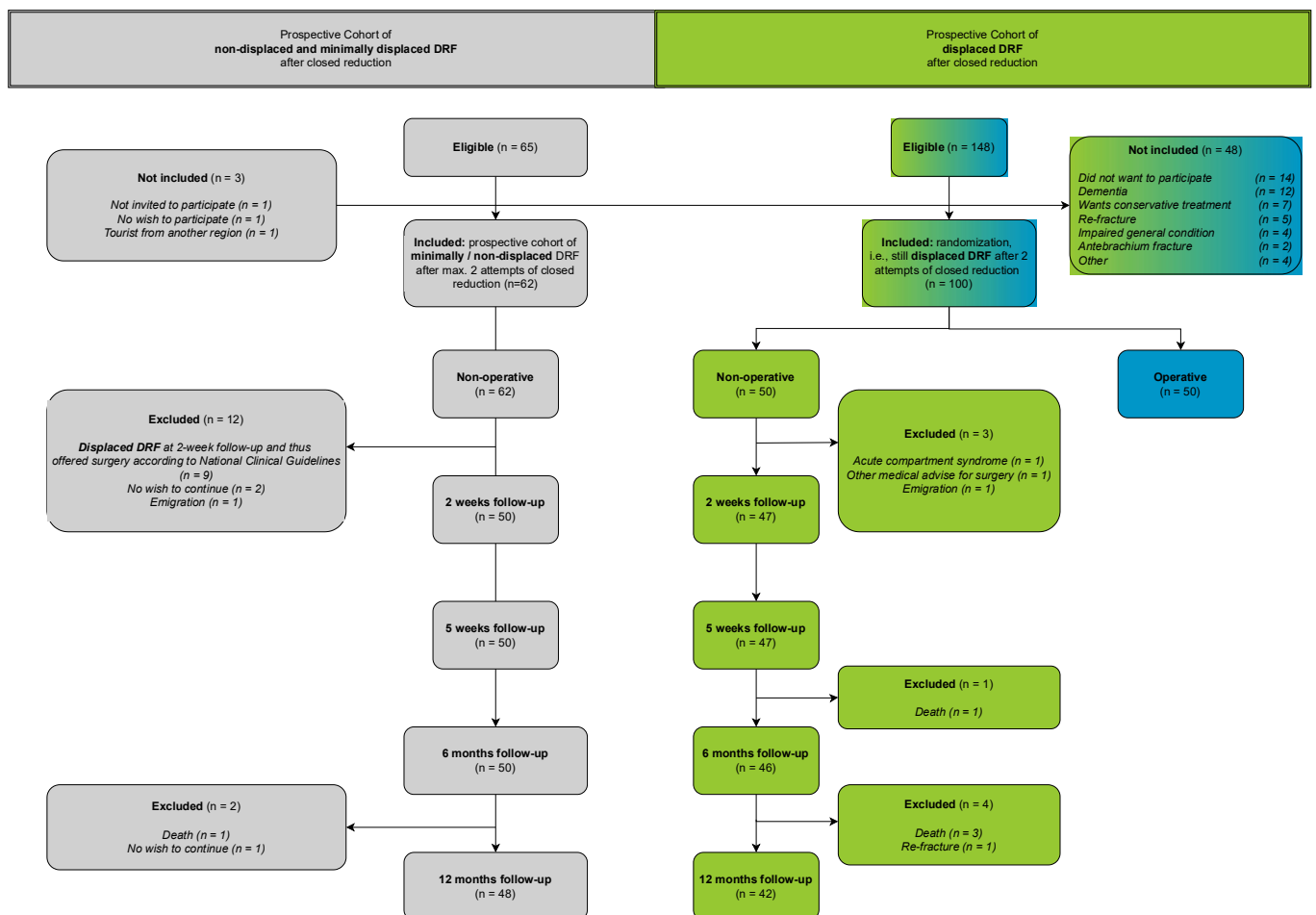

Figure 2. CONSORT flow diagram of the study including cohort 1 (minimally and non-displaced distal radius fractures) and cohort 2 ("non-operative" arm of the VOLCON randomized controlled trial). Numbers of eligible, included and excluded patients, as well as reasons for exclusion, are given. The eligible patients of the non-operative arm of the RCT had to consent to participate in the RCT in order to be included in the present study (green).

Cohort 1: defined as minimally or non-displaced or displaced DRF with acceptable reduction according to the radiological criteria of the national clinical guideline (n1 = 50) (Figure 2).

Cohort 2: defined as a displaced DRF with unacceptable reduction according to the National Clinical Guidelines after 2 attempts of closed reduction (n2 = 50). In the published RCT, patients from cohort 2 were randomized to either operative or non-operative treatment, i.e., the same treatment as cohort 1 comprised of 5 weeks of a dorsal, below-elbow cast and a single instruction by a hand therapist at the time of cast removal.

The two cohorts were prospectively evaluated regarding primary and secondary outcomes as described below at day 0 recalling the pre-injury state, 2 weeks, 5 weeks, 6 months and 12 months. Patients with high-energy fractures, open fractures, former ipsilateral fractures, concomitant fractures and patients unable to provide written consent were excluded.

2.2. Primary Outcome Measure

The primary outcome was the number of patients suffering from one or more of the complications listed below compared between the two cohorts.

The complication rate was prospectively assessed at day 0 recalling the pre-injury state and after 2 weeks, 5 weeks, 6 months and 12 months after the injury. The patient answered standardized questions from the investigators (R.T. and D.W.) who were aware of the purpose of the study and the group allocation as they also included the patient on the same day. In order to assess the day 0 complication rate correctly, we took the following measures as stated in the published protocol: "Patients will report complications at the given timepoints by answering a questionnaire stating either yes/no and a free-text explanation. If the patient states any complications, a member of the research group will qualify the answer and fill in the free text. However, a "yes" can only be qualified and shall never be erased if the physician does not agree with the patient's opinion or explanation" [12]. Patients were able to state additional comments, if the complication was not on the predefined list. Moreover, we reviewed the patients' medical journal in order to check for additional complications, which the patient may have forgotten/failed to self-report. Complications were defined according to the published protocol [12]:

- Carpal tunnel syndrome and chronic regional pain syndrome;
- Unspecific sensory disturbances;
- Flexor tendon rupture and irritation;
- Extensor tendon rupture and irritation;
- Infection: superficial/deep;
- Vascular compromised (capillary refill ≥2 s).

Regarding infection, superficial infection may occur due to pressure ulcers of the cast. Deep infection in closed, non-operatively treated DRFs is extremely rare, but it may arise from a hematogenous spread of bacteria.

2.3. Secondary Outcome Measures

Quick disabilities of the arm, shoulder and hand (QuickDASH) questionnaire was used to assess the patient-reported functional outcome [13–15]. The minimally functional clinical important difference (MCID) is a 16 to 20-point QuickDASH difference in accordance with the recommendations of the developers [13,16,17].

The patient-rated wrist/hand evaluation (PRWHE) was also applied and constitutes a self-reported assessment of 5 items on pain, 10 items on function and 2 optional items on appearance [18]. The MCID for PRWHE was set to 10 points [19].

Active range of motion (ROM) of the wrist (flexion, extension, pronation, supination, radial deviation, and ulnar deviation) was measured with a goniometer by an independent, blinded observer during the follow-up period. Blinding consisted of wearing stockings on the wrists in order to conceal scars and deformities. The primary reason for concealing the distal radius with a stocking was to blind the trained nurses, who performed the

ROM assessment because the stocking may mask a mild deformity. Secondly, the nurses evaluated both non-operatively treated patients of the present study in the same time period as operatively treated patients of the VOLCON RCT (blue boxes of the CONSORT flow diagram, Figure 2) [9]. The nurses were, thus, completely unaware of the group allocation and performed treatment. The ROM of the contralateral uninjured wrist served as reference. Only healthy contralateral wrists were included in the analysis.

Grip strength was measured using an electronic hand dynamometer (EH101 CAMRY). Grip strength is given as the mean of three measurements on each side [20,21]. The MCID of grip strength was 6.5 kg [22].

EuroQol-5D (EQ-5D-3L) was used to estimate quality of life using national population weights.

2.4. Statistical Analysis

The complication rate was analyzed using Fisher's exact test of the accumulated complication rate after 12 months. Double counting was avoided in patients with multiple complications as only one complication was accounted for per patient.

Secondary outcome measures were analyzed using mixed-effects analysis with Sidak's multiple-comparison test. According to our sample size calculation of the RCT, 50 patients per treatment arm provide 80% statistical power at a 5% alpha level, assuming a difference of 20% in complication rate between operatively and non-operatively treated patients. Prism 9 for macOS was used for statistical analysis and graphs.

The study was performed in accordance with the Declaration of Helsinki, prospectively registered at clinicaltrials.gov (NCT03716661) and approved by the Danish Scientific Ethical Committee (1–10–72-420-17) [12].

3. Results

Figure 2 presents the number of eligible, included and excluded patients. The baseline demographics of the two cohorts and the AO/OTA fracture classification are given in Table 1.

Table 1. Demographics.

	Displaced	**Minimally/Non-Displaced**
	n = 50	**n = 50**
Sex		
Female	40 (80%)	41 (82%)
Male	10 (20%)	9 (18%)
Age (years)		
Median (Min., IQR, Max.)	74 (65, 69–81, 91)	73 (65, 70–78, 100)
AO/OTA classification		
A1/A2/A3	0/22/16	0/17/15
B1/B2/B3	0/6/6	2/4/4
C1/C2/C3	0/5/1	0/2/0
Fractured side		
Right	24 (48%)	18 (36%)
Left	26 (52%)	32 (64%)
Hand dominance		
Right	46 (92%)	43 (86%)
Left	1 (2%)	4 (8%)
Ambidextrous	1 (2%)	3 (6%)
Missing data	2 (4%)	0 (0%)
Dominant side fractured *	23 (46%)	20 (40%)
Working status		
Full-time/part-time work	1 (2%)	0 (0%)
Volunteer work	2 (4%)	3 (6%)
Retired	45 (90%)	47 (94%)
Missing data	2 (4%)	0 (0%)

Table 1. *Cont.*

	Displaced	Minimally/Non-Displaced
	n = 50	n = 50
Smoking status		
Non-smoker	37 (74%)	41 (82%)
Smoker	9 (18%)	9 (18%)
Missing data	4 (8%)	0 (0%)
Alcohol consumption **		
<7/14 units/week	38 (76%)	44 (88%)
>7/14 units/week	8 (16%)	6 (12%)
Missing data	4 (8%)	0 (0%)
ASA		
ASA class 1	13 (26%)	16 (32%)
ASA class 2	30 (60%)	25 (50%)
ASA class 3	6 (12%)	9 (18%)
ASA class 4–5	0 (0%)	0 (0%)
Missing data	1 (2%)	0 (0%)
Comorbidities		
Hypertension	23 (46%)	22 (44%)
Diabetes	6 (12%)	3 (6%)
Osteoporosis	3 (6%)	7 (14%)
Depression	4 (8%)	9 (18%)
Medications		
0	8 (16%)	5 (10%)
1–4	26 (52%)	38 (76%)
≥5	16 (32%)	7 (14%)

* A fracture in an ambidextrous patient was not considered a fracture of the dominant side. ** Threshold defined as 7 units/week for females and 14 units/week for males.

3.1. Primary Outcome: Complications

In the minimally or non-displaced DRF group, 3 out of 48 patients experienced complications within the first year. The complication rate was, thus, 6.3% after 12 months; two patients complained about unspecific sensory disturbances and one patient complained about a lack of strength compared with the preoperative state as well as swelling. These complaints could be objectively qualified with a low grip strength measurement and were, thus, rated as complications. Moreover, two patients complained about pain during activity after 12 months. The latter two subjective statements were not rated as complications. The complication rate was 16.6% (7 out of 42 patients) in the displaced DRF group consisting of two superficial wounds without signs of infection at cast removal after 5 weeks, two carpal tunnel syndromes treated with surgical decompression after 5 weeks and 11 months, respectively, and three unspecific sensory disturbances at 12-month follow-up. This difference of 3/48 vs. 7/42 patients was not statistically significant (p = 0.18, Fisher's exact test).

3.2. Secondary Outcomes: Functional Outcome

QuickDASH and NRS were comparable at baseline (recalled pre-injury state), 6 and 12 months. The mean difference in QuickDASH of -10.7 (from -21 to -1) between displaced vs. minimally/non-displaced DRF was statistically significant after 2 weeks (Figure 3), but of borderline clinical relevance as the MCID was 16–20 points [17].

The mean PRWHE of displaced DRF patients was 12.6 (8.7–16.5) after 6 months and 8.0 (3.6–12.4) after 12 months, while for minimally or non-displaced DRF patients it was 13.5 (9.0–18.0) after 6 months and 8.7 (3.6–13.7) after 12 months. Accordingly, the mixed-effects model showed a time dependency (p = 0.01) but not a treatment dependency of PRWHE (p = 0.79).

The ROM of both groups was significantly impaired after cast removal at 5 weeks and after 6 months compared with the uninjured wrist (Figure 4; $p < 0.05$). The ulnar deviation

(Figure 4, lower-middle panel) was the only direction of movement where the graphs did not align, and statistical analysis revealed impairment in the displaced compared with the minimally or non-displaced group after both 5 weeks and 6 months (Figure 4, lower middle panel).
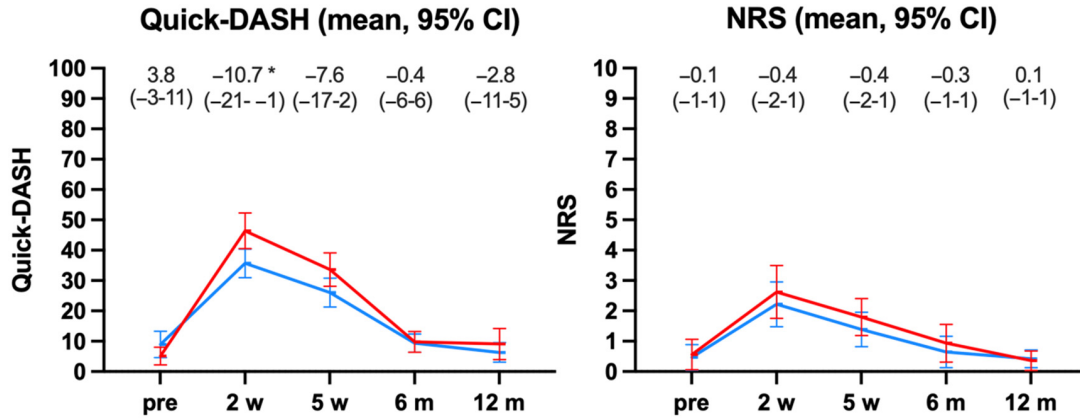

Figure 3. QuickDASH and NRS (pain) of the displaced (red) and minimally/non-displaced (blue). non-operatively treated DRFs. Mean differences (95% CI) between the groups at the different timepoints and statistical significance * $p < 0.05$.
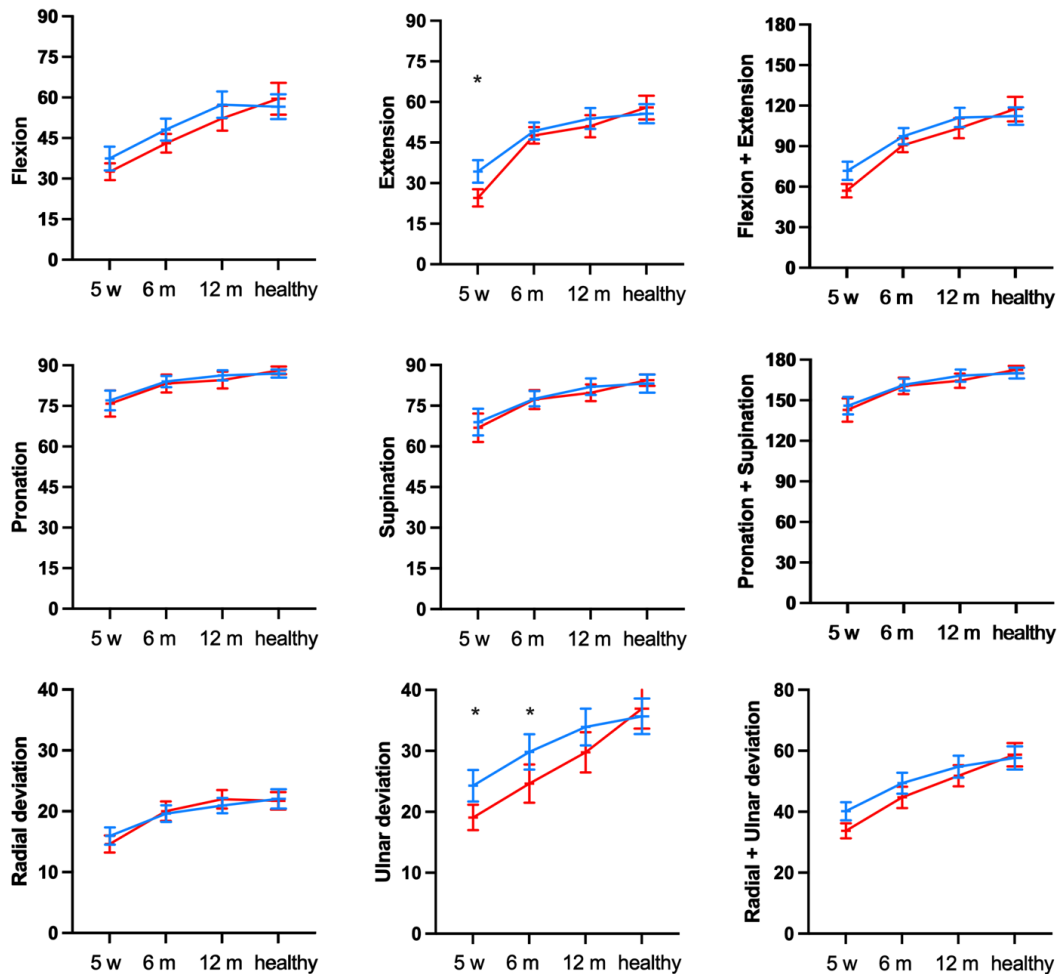
Figure 4. Mean range of motion of wrists with displaced (red) and minimally/non-displaced (blue) DRF at 5 weeks (w), 6 and 12 months (m) compared with the uninjured/healthy side. Error bars represent 95% confidence intervals. * $p < 0.05$.

For the remaining directions of movement, the overlaying graphs and statistical analyses highlighted that the improvements over time were similar in both cohorts and no statistically significant differences were observed compared with the uninjured side after 12 months ($p > 0.05$).

The mean grip strength was low in both cohorts, i.e., 18.8 kg (14.1–23.6) for minimally or non-displaced DRFs and 16.6 kg (11.8–21.4) for displaced DRFs after 12 months. The mean difference in grip strength between the groups was 0.5 (−2.2–3.2) after 6 months and 1.2 (−4.0–1.6) after 12 months.

EQ5D-3L indices of patients with minimally or non-displaced DRF improved from 0.87 (95% CI 0.84–0.90, range 0.68–1.00) at 6 months to 0.93 (95% CI 0.90–0.96, range 0.71–1.00 after 12 months post-injury. In the displaced DRF group the corresponding values were 0.79 (95% CI 0.72–0.86, range 0.28–1.00) and 0.84 (95% CI 0.76–0.93, range 0.14–1.00).

4. Discussion

One year after 5 weeks of dorsal below-elbow casting of low-energy DRFs in patients $\geq$ 65 years old, we found a complication rate of 6.3% (3/48) in minimally or non-displaced DRFs and 16.6% (7/42) in displaced DRFs ($p = 0.18$). However, no statistically significant difference was observed in the functional outcome in terms of the QuickDASH, pain, ROM, grip strength, or EQ-5D scores.

Complications of the present study were pre-defined according to the published RCT protocol. While making an effort to streamline the interpretation of complications, we did not grade the severity. Notably, the two carpal tunnel syndromes occurred in the displaced group leading to decompression surgery of the medial nerve, which resolved the symptoms at the latest follow-up. Our finding of 2/90 (2.2%) patients with carpal tunnel syndrome within the first 12 months was low/comparable with reports in the literature, stating an incidence of 6.3% in the first 6 months in 1198 out of 18,766 non-operatively treated DRF patients [23]. While hypothetical, it seems logical that the displacement of bony fragments in a displaced DRF may cause swelling and compression of the median nerve. In corroboration with this statement, we did not observe classic symptoms of carpal tunnel syndrome in any minimally or non-displaced DRFs, in which the bony anatomy was better restored during closed reduction. The increased swelling may also hypothetically have led to the two cases of superficial wounds noted upon cast removal at 5 weeks. Moreover, one patient returned to the ED for a cast exchange after swelling had subsided. This event was not accounted for as a complication.

The definition of complications after a DRF is not arbitrary; taken together, the complications in both groups were mild and temporary. We have previously reported that the unspecific sensory disturbances after a DRF change over time and may, thus, not necessarily be a lasting complication and at final follow-up there was no motoric compromise and the sensory disturbance did not follow an anatomical innervation pattern [9,24]. However, all of these patients were informed about the symptoms and findings of medial and ulnar nerve compression as a precautious measure at the latest follow-up. Moreover, one patient mentioned diminished grip strength as a complication. It may be a matter of debate if this is a true complication, but we chose to adhere to the protocol, where we stated: "If the patient states any complications, a member of the research group will qualify the answer and fill in the free text. However, a YES can only be qualified and shall never be erased if the physician does not agree with the patient's opinion or explanation".

Regarding grip strength, one may speculate if the difference between the cohorts may be related to the frailty of the patients, for example, due to osteoporosis and sarcopenia [25,26]. Contrary to our a priori expectations, in the present study 3/50 displaced DRF patients vs. 7/50 minimally/non-displaced DRF patients suffered from osteoporosis at baseline. The diagnosis of osteoporosis was based on the past medical history of the patient including the list of medications (Table 1). Thus, osteoporosis present at baseline does not offer an explanation for the observed differences. Olech et al. reported increased grip strength and range of motion when casting DRFs in elderly patients for 6 weeks

compared with 4 weeks. In the present study, we followed the Danish standard of 5 weeks of casting [27]. The optimal duration of casting DRFs in the elderly population remains to be investigated.

The functional status and individual demands of patients should always be taken into consideration when counseling patients about treatment options. Based on our own VOL-CON RCT, other RCTs for displaced DRFs in this age group and the results of the present study, we think that non-operative treatment should be the gold standard [6,9,28–31]. Conversely to the current practice in Denmark, surgeons should clearly state the reasons for opting for surgical treatment of a displaced DRF specifically for patients who are 65 years old or more. For instance, patients depending on walking aids may benefit from operative treatment as the increased stability may allow earlier mobilization and use of walking aids, while casting for 5 weeks may cause not only an immobilization of the wrist, but may also restrict walking. Likewise, patients with bilateral injuries or contralateral functional impairments may be considered for operative treatment in order to facilitate an earlier return to self-care and daily activities [4,7,9]. In such cases, early mobilization may counteract the temporary or permanent loss of independence [32].

When opting for surgery of a displaced DRF in the elderly, one should remember to inform the patients that surgery entails risks besides the surgical complications. Many patients with DRFs are considered frail, which has been found to be a predictor of postoperative morbidity and mortality in patients undergoing surgery in general anesthesia [33]. Furthermore, cognitive impairment is not rare after surgery in the elderly. Steinmetz et al. suggested that inadequate recovery increases the risk of post-operative delirium, which increases the risk of long-term cognitive dysfunctions such as dementia [34].

Another important aspect concerning whether to undergo surgery or not is the patient's own involvement in the decision making of the treatment. We experienced that a large number of patients who asked to be a part of our primary RCT study did not want to participate due to the fact that they did not want surgery at any cost. The literature shows that public and patient involvement is of great value and importance [35]. For future studies, public and patient involvement should be mandatory in setting up a study such as this.

A limitation of the present study was that the patients ideally should have been blinded. As both groups were non-operatively treated, this would have been feasible if the study was not part of the VOLCON RCT [9,12]. Here, patients in the displaced DRF group had been informed about the radiological severity/displacement of the fracture—blinding of both groups was, thus, not possible in the present study.

Moreover, the number of patients in the two study cohorts limited the study power and the possibility to design the study based on a power analysis. This meant that the difference in complications rates found of 10% might be clinically relevant but more included patients would be needed to demonstrate a statistically significant difference. Furthermore, the external validity, i.e., generalizability, may have been hampered by the fact that more than 90% of the patients were retired. One should, therefore, be careful to draw conclusions for elderly people who are still working.

5. Conclusions

In conclusion, in patients above 65 years of age, non-operative treatment, i.e., closed reduction and dorsal casting for 5 weeks, yielded similar complication rates and functional outcomes after 1 year regardless of whether the initial fracture was non-displaced/minimally displaced or still displaced after closed reduction. While initially a closed reduction should still be attempted in order to restore the anatomy, failure to achieve the stipulated radiological criteria may not be as important as we thought in terms of complications and functional outcome. A non-operative treatment strategy for displaced DRFs appears to be a safe and reliable treatment option. The results of our study can inform patients about the expected complications and functional outcomes after dorsal plaster casting for 5 weeks of non-displaced as well as still-displaced DRFs after closed reduction.

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Extension of the original protocol beyond 12 months of follow-up:

Posttraumatic arthritis and functional outcomes after nonoperatively treated distal radius fractures: A prospective study with a minimum 3-year follow-up

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Posttraumatic arthritis and functional outcomes after nonoperatively treated distal radius fractures: A prospective study with a minimum 3-year follow-up

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Abstract:

Recent studies have shown that distal radius fractures (DRFs) in elderly patients can be treated nonoperatively with good functional results after 1 year. However, scientific evidence regarding longer follow-up to assess posttraumatic arthritis (PA), complications, and functional outcomes is scarce. This prospective case series aimed to evaluate these outcomes in a cohort of 50 patients ($\geq$ 65 years old) with nonoperatively treated DRFs after a minimum of 3 years. The primary outcome was PA. Secondary outcomes were complications, Quick Disabilities of the Arm, Shoulder and Hand Outcome Measure (QuickDASH), Patient-Rated Wrist/Hand Evaluation (PRWHE), pain, range of motion and grip strength. The full data of 32 patients with a mean follow-up of 3.3 years were available: 10/32 patients had radiological signs of PA, but only 3 of these patients reported pain. A total of 11/32 fractures healed in malunion (> 10° dorsal angulation). There was no significant difference in QuickDASH or PRWHE from 1 year to the latest follow-up. This study thus adds to the literature stating that radiological signs, including PA and malunion, do not necessarily result in symptoms. Moreover, it underpins that nonoperative treatment of these patients results in good functional outcomes after 1 and 3 years.

Word count (max 200): 198

Introduction

Distal radius fractures (DRFs) account for 18% of all fractures in elderly individuals ≥65 years of age [1,2]. The estimated lifetime risk for having a DRF is 15% for females and 2% for males [3]. The incidence rate is approximately 200 per 100,000 person-years [4,5]. Low-energy DRFs are associated with osteoporosis, and there is an age-related incidence rate that increases almost 3-fold from the age of 60 to 99 among women [1,4,6,7].

The standard treatment in Denmark for displaced DRFs is surgery with open reduction and internal fixation (ORIF) to obtain anatomic reduction, but that treatment has been debated [8-10]. Studies have shown that elderly patients might not benefit from surgery, despite displacement of the fracture and indication for surgery based on Danish National Clinical Guidelines (NCGs) [11].

Recent randomized controlled trials (RCTs) and metanalyses have shown no difference between operative and nonoperative treatment in terms of pain, patient-related outcome measures (PROMs), range of motion (ROM) or complications, but most of these studies only had a follow-up of 12 months, and PROM data after a longer follow-up are lacking [12-14].

Posttraumatic arthritis (PA) may occur after fractures and even more so after intraarticular fractures. In 1986, Knirk and Jupiter published data on PA with an estimated prevalence of 65% after a mean follow-up of 6 years [15]. However, these fractures were high-energy fractures in a relatively young population of 25–52-year-olds. Knirk and Jupiter also described radiological predictors for PA as signs of articular incongruity, articular step-off in millimeters and lack of anatomical repositioning, which have informed clinical guidelines aiming to minimize these changes by either closed reduction or operative treatment. Among patients treated with ORIF, PA has been shown to be associated with pain and limited ROM, especially flexion and radial deviation [15,16]. Notably, no previous studies have described PA or predictors of PA among elderly patients with low-energy DRFs.

The aim of this study was to assess PA after a minimum observation period of 3 years among elderly patients after nonoperative treatment of low-energy DRFs. The secondary aims were to estimate complications and functional outcomes; the former was thought to increase and the latter decrease due to PA impairing activities of daily living.

Materials and Methods

Setting. Health care in Denmark is fully tax funded and allows free and equal access for the country's 5.7 million inhabitants. The Danish NCGs for DRFs advocate operative treatment if one of the following radiological parameters is met after closed reduction: (1) > 10° dorsal tilt of the radius perpendicular to the longitudinal axis of the radius; (2) > 2-mm articular step-off; (3) > 2-mm ulnar variance; (4) incongruence of the distal radioulnar joint; or (5) substantial dorsal comminution indicating gross instability.

Design. This was a prospective case series of 50 patients with a minimum 3-year follow-up. The complication rate and functional outcomes of this cohort after 1 year have previously been published [17].

Patients older than 65 years of age with DRF who did not fulfill the radiologic criteria for surgical treatment according to the NCGs admitted to Randers Regional Hospital between November 2018 and July 2019 were included after providing written consent. If necessary, according to the NCGs, closed reduction/manipulation was performed under local anesthesia, i.e., a hematoma block using 5-10 mL of 20 mg/mL lidocaine without epinephrine injected at the fracture site. After 5-15 minutes the treating physician had a maximum of two attempts of closed reduction under fluoroscopic guidance. The patient was approved as eligible for this study by a member of the investigation group.

Recruitment and intervention. A minimum of three years after inclusion, the patients were contacted by telephone and invited to a follow-up in the outpatient clinic. Standardized radiographs (anterior-posterior and lateral projections) of the distal radius were acquired.

The following PROMs were evaluated: Quick Disabilities of the Arm, Shoulder and Hand Outcome Measure (QuickDASH) score, Patient-Rated Wrist/Hand Evaluation (PRWHE) score, and pain assessed on a numeric rating scale (NRS) of 0-10. ROM was assessed blinded as described in the published protocol. The complications form was filled out by a physician and nurse together with the patient.

This study complied with the Declaration of Helsinki and was approved by the Danish Scientific Ethical Committee as an extension of the study protocol (number: 1-10-72-420-17/79290, approved on 7th June 2021) [18]. Accordingly, all patients gave their informed consent.

Primary outcomes. PA was the primary outcome. Standardized radiographs in two projections (anterior-posterior and lateral) were assessed by two consultants, one trauma surgeon and one hand surgeon. PA was rated according to Knirk and Jupiter [15], where 0 equaled "none", 1 equaled "slight joint space narrowing", 2 equaled "marked joint space narrowing", and 3 equaled "bone on bone contact" [6].

The change in PA was assessed over time, i.e., radiographs taken 5 weeks after the fracture and the latest radiographs with a minimum of 3 years of follow-up.

Secondary outcomes. On the radiographs, dorsal tilt and radial length were measured as previously described. The fractures were classified according to the AO Foundation/Orthopaedic Trauma Association (AO/OTA) fracture classification.

Complications were assessed at the 3-year follow-up in the outpatient clinic. Complications were defined as flexor or extensor tendon rupture or irritations, vascular compromise or sensory disturbance, including carpal tunnel syndrome and chronic regional pain syndrome, any associated operation during follow-up, and infection (superficial or deep). All subjective and objective complications were recorded. Medical journals were also assessed to obtain potentially missed complications.

ROM, i.e., wrist flexion, extension, pronation, supination, radial deviation, and ulnar deviation, was measured with a goniometer. The ROM of the contralateral wrist served as a reference.

Grip strength was measured using an electronic hand dynamometer (EH101 CAMRY). Grip strength was given as the mean of three measurements on each side. The minimal clinically important difference (MCID) of grip strength was set to 6.5 kg [19-21].

Pain related to the fracture was reported on an NRS from 0-10. 0 was equal to "no pain", and 10 was equal to "the worst pain one could imagine". Pain was defined as the pain at the time of the examination.

The validated version of the Danish QuickDASH was used to assess the level of functionality and was self-reported by the patient. The MCID was a 16-point difference in QuickDASH [22-24].

The validated Danish version of the PRWHE was employed as a self-reported assessment of five items on pain, 10 items on function and two optional items on appearance of the hand [23,25,26]. The MCID for the PRWHE was set to 10 points [25].

Statistical analysis. The mean and 95% confidence interval (95% CI) are given. Fisher's exact test was used to compare the primary outcome after 5 weeks vs. 3 years. The secondary outcome measure, complication rates, was also assessed with Fisher's exact test. One-way repeated measures ANOVA including Sidak's multiple comparison test was employed for the repeated QuickDASH and PRWHE values of the 32 patients with a complete follow-up. The statistical significance level was set to 0.05. GraphPad Prism version 9.5.0 for macOS was used for statistical analysis.

Results

A total of 62 patients were included; 12 were excluded mainly due to fracture dislocation and operation after the first two weeks, leaving 50 patients in the study cohort. During the follow-up period from 6 to 12 months, another 2 patients were excluded due to death, leaving 48 for the follow-up visit.

Of these 48 patients at the 1-year follow-up, 7 had died, 3 could not be reached, and 3 withdrew their consent to participate in the 3-year follow-up. Thirty-five patients gave consent on the telephone; however, 3 patients did not show up and further attempts to reach the patients by telephone were unsuccessful. The full data of the remaining 32 patients with at least 3 years of follow-up were available (Figure 1). Demographic information is available in Table 1.

Primary outcome. In total, 10 out of 32 wrists had signs of PA after a mean follow-up time of 3.3 years (95% CI: 3.1-3.4; min. 3.0; max. 4.1). Arthritis was not evident in any of the 32 wrists 5 weeks post-injury (Figure 2). At the latest follow-up, 7 wrists were rated as PA grade 1, 2 as PA grade 2, and 1 as PA grade 3. This change was statistically significant, i.e., 0/32 patients after 5 weeks and 10/32 patients after 3 years had radiological signs of wrist arthritis (Fisher's exact test, p<0.001).

Secondary outcomes. Pain was reported by 5/32 patients at the latest follow-up. Among these patients, pain ranged from 1 to 4 on the NRS. Of these 5 patients, 3 had no radiological signs of PA but reported pain (NRS) as 4, 3 and 1 (3/7). Conversely, of the seven patients with PA, one with grade 1 arthritis reported a score of 1 on the NRS, one with grade 2 arthritis reported a score of 2 on the NRS, and the remaining five reported a score of 0 on the NRS.

The radiological evaluation after 3 years revealed a median dorsal angulation of 5 degrees (range: 15-24 degrees). Compared with the 5-week radiographs, the mean difference was -0.9 (95% CI: -5.6-3.8) degrees. The change from 5 weeks to 2 years was thus negatable for the vast majority of fractures. However, 11 out of 32 fractures healed with a dorsal angulation of ≥ 10 degrees. Five of these had radiological signs of PA on the latest radiographs. The 32 fractures were rated according to the AO/OTA classification: 12 were rated as A2, 11 were rated as A3, 1 was rated as B1, 4 were rated as B2 and 4 were rated as B3. There were no C-type fractures. AO type A fractures accounted for 72% of the fractures, whereas type B fractures accounted for 28%.

Complications after 12 months of follow-up were reported by 3/48 (6%) patients, while 6/32 (19%) experienced a complication at the latest follow-up: 5 patients reported nonspecific sensory disturbances, and 1 patient complained about limited function due to decreased ROM. The observed difference in the complication rate between the 12-month and 36-month follow-ups was not statistically significant (Fisher's exact test, p=0.15). Moreover, there were no associated operations during the follow-up time.

The mean QuickDASH values are given in Figure 3 and did not significantly change from the 1-year follow-up to the 3-year follow-up. Moreover, one-way repeated measures ANOVA also showed that mean PRWHE values were comparable after 6, 12, and 36 months, i.e., 12.9 (95% CI 7.2-18.6), 9.1 (95% CI 3.8-14.5), and 9.0 (95% CI 4.3-13.6), respectively (p=0.25).

Discussion

In the present study, 10/32 patients had radiological signs of PA after 3 years of observation of nonoperatively treated low-energy DRFs among elderly patients. Notably, none of the patients had PA on the radiographs taken 5 weeks after the injury. Based on the PA classification by Knirk and Jupiter, one can expect that DRFs, especially intraarticular fractures and high-energy fractures, lead to PA in the majority of these fractured wrists [15].

In the present study, 7 of the patients developed grade 1 arthritis, 2 of whom had an extraarticular fracture (type A) and 5 of whom had partially intraarticular fractures (type B) according to the AO/OTA fracture classification. Grade 2 arthritis was found in A2 and A3 fractures, and grade 3 arthritis was found in B2 fractures. In total, 6 out of 10 cases of PA were observed in partially intraarticular fractures, while there were no C fractures in the cohort.

In agreement with our observation, Lameijer et al. described that intraarticular fractures with articular incongruence and older age were predictors of PA [27]. However, the systematic review found no correlation between AO/OTA classification of the fracture and development of PA and no prediction of PA or dorsal angulation, radial length, ulnar variance or radial inclination. Due to the unexpectedly low rate of PA and limited number of patients, we did not attempt to correlate PA grade and type of fracture.

The clinical impact of PA after low-energy DRFs in elderly people may be limited. In our study, only 3/10 patients with radiological PA reported pain. Van Leerdam et al. [28] also described that type A and B fractures with a mean follow-up of almost 4 years had better PROMs when treated nonoperatively compared to operation among elderly patients. Our study and the study by Marchewka et al. [29] align with this hypothesis, as approximately one-third of the wrists healed in malunion but with a good functional outcome and almost no pain. However, the role of malunion is a matter of debate, as other authors have found an association between radiological parameters and functional outcome [30-32]. We also found no statistically significant deterioration in functional outcome, i.e., QuickDASH and PRWHE scores, after 1 year compared with 3 years.

To our knowledge, there are only a few studies with a follow-up of more than 3 years for DRFs treated with or without surgery in elderly patients. Previous publications have had only a 1-year

follow-up and showed good results in terms of PROMs and few complications [12,13,17]. It may be argued that the follow-up period should be even longer than 3 years before PA becomes symptomatic. However, a study from 2008 among younger patients supports the theory that malunion and radiological signs of PA do not necessarily result in symptoms even after more than 30 years [33].

We noticed a nonsignificant increase in the complication rate from 3/48 (6%) patients after 12 months to 6/32 (19%) patients after 36 months. All complications were minor, consisting mostly of sensory disturbances. None of these applied to specific nerves, and none of the patients with sensory disturbances required secondary surgery. In comparison, we reported a complication rate of 15% in operatively treated DRFs with a 3.2-year follow-up. However, that study was retrospective, and almost 10% of DRFs required reoperation due to major complications [4]. The complication rate in the present study is comparable to that in earlier published studies with a shorter follow-up [14,34,35].

Limitations of the present study include the size of the patient cohort. However, this study was an extension of a well-designed study with the primary aim of assessing complications after 12 months. Second, arthritis was graded by 5-week radiographs while the wrist was still in a cast, i.e., standardized radiographs taken to assess the healing of the fracture before cast removal. Evaluating arthritis with these radiographs may have obscured subtle signs of arthritis. Another limitation could be the unawareness of the patients' comorbidities, such as rheumatoid arthritis or pain and disability from basilar thumb arthritis. Assessment of the contralateral wrist by standardized PROMs and radiographs may partly have overcome this limitation. However, PROMs such as QuickDASH score are not side specific but assess the patient's ability to perform activities of daily living regardless of whether these activities are performed with the healthy or injured side [36].

A strength of the present study is its follow-up time of 3 years, which is long compared with the majority of other DRF studies. Moreover, the study design was prospective and thus accounted for even minor and rather nonspecific changes in, for example, complications such as sensory disturbances. Moreover, the loss to follow-up was low compared to the literature. From the 1-year follow-up until the final follow-up, only 16 patients dropped out, and 7 died. In comparison, the loss to follow-up over a 3-year period was 65% in a recent study from 2022 [28].

Conclusion

PA was observed in 10/32 (31%) wrists after low-energy, nonoperatively treated DRFs in patients older than 65 years of age after a minimum follow-up of 3 years. None of the patients had arthritis based on the 5-week postinjury radiographs. Notably, only 3 of the 10 patients with PA complained about any, i.e., mild pain and good functional outcomes (QuickDASH and PRWHE scores) after 1 year did not deteriorate over time. This study thus adds to the literature stating that radiological signs, including PA and malunion, do not necessarily result in symptoms. Moreover, it underpins that nonoperative treatment of these patients results in good functional outcomes after 1 and 3 years.

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Acknowledgements

Author contributions

R.T.: Methodology, investigation, data curation, formal analysis, writing–original draft, K.L.R.: Investigation, writing – review and editing, D.W.: Investigation, data curation, writing-review and editing, M.B.H.: Investigation, writing – review and editing, M.T.: Funding, supervision, writing – review and editing, M.L.: Supervision, writing – review and editing, JDR: Methodology, data curation, formal analysis, supervision, writing – review and editing. All authors approved the final manuscript.

Data availability statement

Anonymized data may be requested from the corresponding authors R.T. and J.D.R.

Additional Information

Figures and figure legends

Figure 1. CONSORT flowchart.

Prospective Cohort of
non-displaced and minimally displaced DRF
after closed reduction

Eligible (n = 65)

Not included (n = 3)

Not invited to participate (n = 1)
No wish to participate (n = 1)
Tourist from another region (n = 1)

Included: prospective cohort of
minimally / non-displaced DRF
after max. 2 attempts of closed
reduction (n=62)

Non-operative
(n = 62)

Excluded (n = 12)

Displaced DRF *at 2-weeks and*
thus offered surgery according to
National Clinical Guidelines (n = 9)
No wish to continue (n = 2)
Emigration (n = 1)

2 weeks follow-up
(n = 50)

5 weeks follow-up
(n = 50)

6 months follow-up
(n = 50)

Excluded (n = 2)

Death (n = 1)
No wish to continue (n = 1)

12 months follow-up
(n = 48)

Excluded (n = 16)

Death (n = 5)
No wish to continue (n = 8)
Unable to contact (n = 3)

36 months follow-up
(n = 32)

Figure 2. Examples of assessed anteroposterior radiographs with posttraumatic arthritis (PA) grades 0, 1, 2, and 3 after 5 weeks and a mean of 3.3 years after the injury.
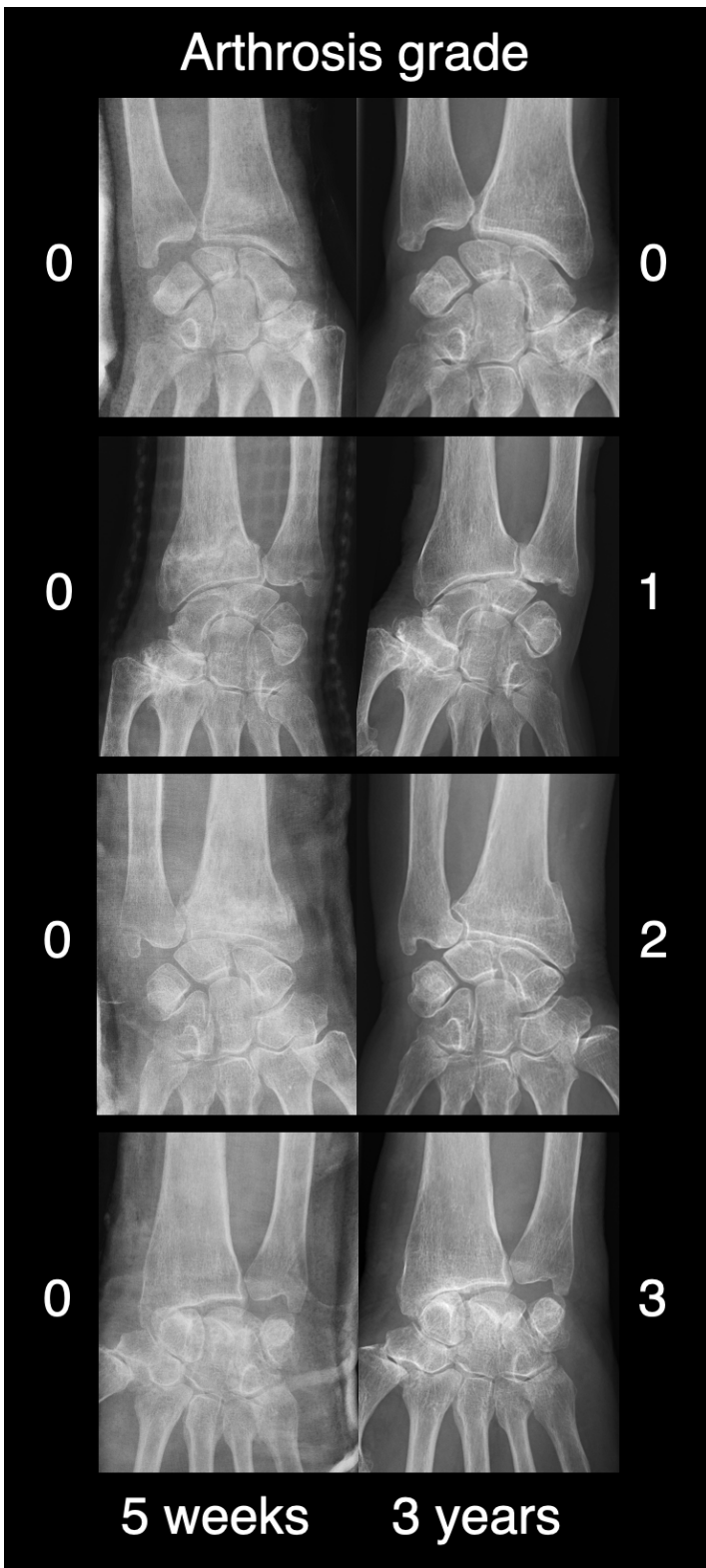
Figure 3. Mean QuickDASH score and 95% CI as error bars are given before the injury (pre) and after the injury at 2 and 5 weeks (w) and at 6, 12, and 36 months (m). * $p<0.05$ compared with the preinjury state.
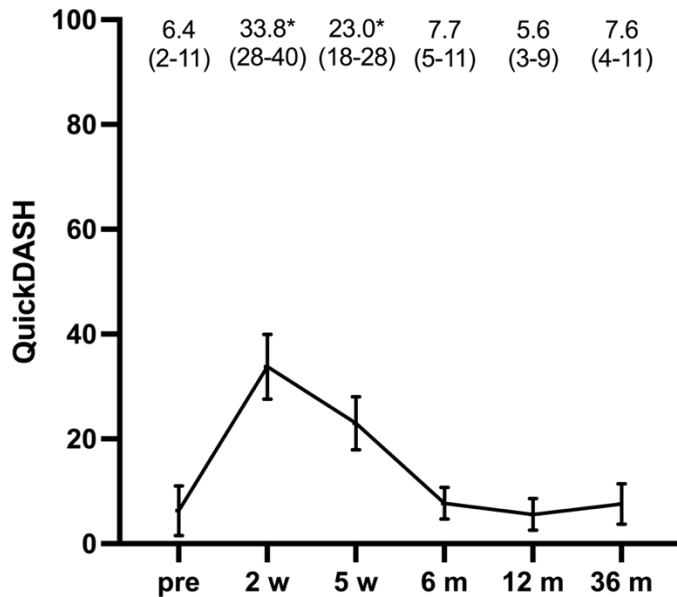
Tables

Table 1. Basic demographics. American Society of Anesthesiologists' Physical Status Classification (ASA).

Median age (min-max)	73 (66-86)
Female / Male	26 / 6
ASA: 1 / 2 / 3 / 4 / 5 / 6	11 / 18 / 3 / 0 / 0 / 0
Injured side: Right / Left	12 / 20
Working status: Retired / working	30 / 2
Smoker: Yes / No	4 / 28
Alcohol above limits: Yes / No	3 / 29

APPENDIX 4

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Rikke Thorninger

This declaration concerns the following article/manuscript:

Title:	A protocol for a single-center, singleblinded randomized-controlled trial investigating volar plating versus conservative treatment of unstable distal radius fractures in patients older than 65 years
Authors:	Jonas Pedersen, Simon Oksbjerre Mortensen, Jan Duedal Rölfing, Rikke Thorninger*

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preperation ☐

If published, state full reference: BMC Musculoskeletal Disorders, 2019, 20:309, https://doi.org/10.1186/s12891-019-2677-y

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

Your contribution

Please rate (A-F) your contribution to the elements of this article/manuscript, **and** elaborate on your rating in the free text section below.

- A. Has essentially done all the work (>90%)
- B. Has done most of the work (67-90 %)
- C. Has contributed considerably (34-66 %)
- D. Has contributed (10-33 %)
- E. No or little contribution (<10%)
- F. N/A

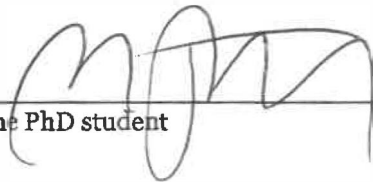| Category of contribution	Extent (A-F)
The conception or design of the work:	C
Free text description of PhD student's contribution (mandatory) RT has designed the study together with JDR. RT has registered the trial at clinicaltrials.gov	
The acquisition, analysis, or interpretation of data:	B
Free text description of PhD student's contribution (mandatory) Not applicable, i.e., published protocol	
Drafting the manuscript:	B
Free text description of PhD student's contribution (mandatory) JP and RT have drafted the manuscript.	
Submission process including revisions:	A

Free text description of PhD student's contribution **(mandatory)**
RT has managed the submission process.

Signatures of first- and last author, and main supervisor

Date	Name	Signature
20/2-2023	Rikke Thorninger (last + corresponding author)	
20/2-2023	Jonas Pedersen (first author)	
20/2-2023	Jan Duedal Rölfing (main supervisor)	

Date: 10.03.23

Signature of the PhD student

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Rikke Thorninger

This declaration concerns the following article/manuscript:

Title:	Objective outcome measures continue to improve from 6 to 12 months after conservatively treated distal radius fractures in the elderly - a prospective evaluation of 50 patients
Authors:	Rikke Thorninger *, Daniel Wæver, Jonas Pedersen, Jens Tvedegaard-Christensen, Michael Tjørnild, Martin Lind, Jan Duedal Rölfing

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preperation ☐

If published, state full reference: J. Clin. Med. 2021, 10, 1831.
https://doi.org/10.3390/jcm10091831

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:
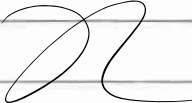
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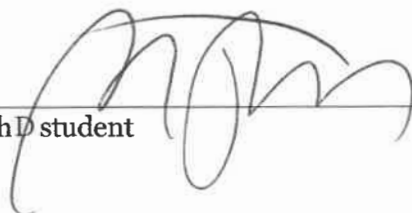| Category of contribution	Extent (A-F)
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The acquisition, analysis, or interpretation of data:	B
Free text description of PhD student's contribution (mandatory) Data acquisition was performed by RT, DW, JP. Analysis was performed by RT, JDR. Interpretation was drafted by RT; all authors contributed.	
Drafting the manuscript:	B
Free text description of PhD student's contribution (mandatory) RT drafted the manuscript.	
Submission process including revisions:	A

*Free text description of PhD student's contribution (**mandatory**)*
RT has helped during the submission and revision process

Signatures of first- and last author, and main supervisor

Date	Name	Signature
6/3-2023	Rikke Thorninger	
20/2-2023	Jan D. Rölfing (last author + main supervisor)	

Date: 10.03.23

_____
Signature of the PhD student

Declaration of co-authorship concerning <u>article for PhD dissertations</u>

Full name of the PhD student: Rikke Thorninger

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Title:	VOLCON: a randomized controlled trial investigating complications and functional outcome of volar plating vs casting of unstable distal radius fractures in patients older than 65 years
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The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preperation ☐

If published, state full reference: Journal of Orthopaedics and Traumatology, 2022, 23:54. https://doi.org/10.1186/s10195-022-00673-4

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The acquisition, analysis, or interpretation of data:	B
Free text description of PhD student's contribution (mandatory) Data acquisition was performed by RT, DW. Analysis was performed by RT, DW, JDR. Interpretation was drafted by RT; all authors contributed.	
Drafting the manuscript:	B
Free text description of PhD student's contribution (mandatory) RT drafted the manuscript.	
Submission process including revisions:	A

*Free text description of PhD student's contribution (**mandatory**)*
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Signatures of first- and last author, and main supervisor

Date	Name	Signature
20/2-2023	Rikke Thorninger (first + corresponding author)	
20/2-2023	Jan Duedal Rölfing (last author + main supervisor)	

Date: 10.03.23

_____

Signature of the PhD student

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Rikke Thorninger

This declaration concerns the following article/manuscript:

Title:	Prospective evaluation of two cohorts of non-operatively treated patients with displaced vs. minimally and non-displaced distal radius fractures
Authors:	Rikke Thorninger *, Daniel Wæver, Michael Tjørnild, Martin Lind, Jan Duedal Rölfing

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preperation ☐

If published, state full reference: J Clin Med. 2023; 12(5):2076. doi.org/10.3390/jcm12052076

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

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Your contribution

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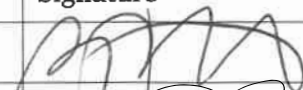
Category of contribution	Extent (A-F)
The conception or design of the work:	A
Free text description of PhD student's contribution (mandatory) RT has concipated the study and applied for extension of the ethical approval.	
The acquisition, analysis, or interpretation of data:	B
Free text description of PhD student's contribution (mandatory) RT was granted approval to radiological examination and outpatient visit / followup. RT has significantly contributed to the analysis, data and the interpretation.	
Drafting the manuscript:	B
Free text description of PhD student's contribution (mandatory) RT draftet the first version of the manuscript.	

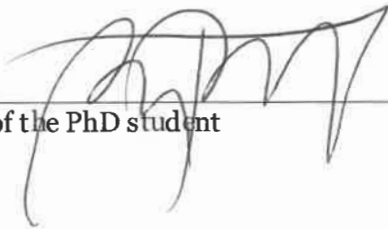*Free text description of PhD student's contribution (**mandatory**)*
RT has managed the submission process.

Signatures of first- and last author, and main supervisor

Date	Name	Signature
20/2-2023	Rikke Thorninger (first + corresponding author)	
20/2-2023	Jan Duedal Rölfing (last author + main supervisor)	

Date: 16.03.23

Signature of the PhD student

Declaration of co-authorship concerning <u>article for PhD dissertations</u>

Full name of the PhD student: Rikke Thorninger

This declaration concerns the following article/manuscript:

Title:	Posttraumatic arthritis and functional outcomes after nonoperatively treated distal radius fractures: A prospective study with a minimum 3-year follow-up
Authors:	Rikke Thorninger *, Karen Larsen Romme *, Daniel Wæver, Martin Bille Henriksen, Michael Tjørnild, Martin Lind, Jan Duedal Rölfing

The article/manuscript is: Published ☐ Accepted ☐ Submitted ☒ In preperation ☐

If published, state full reference:

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Please rate (A-F) your contribution to the elements of this article/manuscript, **and** elaborate on your rating in the free text section below.
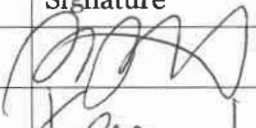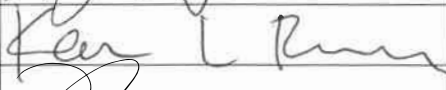
- A.   Has essentially done all the work (>90%)
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- C.   Has contributed considerably (34-66 %)
- D.   Has contributed (10-33 %)
- E.   No or little contribution (<10%)
- F.   N/A

Category of contribution	Extent (A-F)
The conception or design of the work:	A
Free text description of PhD student's contribution (mandatory) RT has concipated the study and applied for extension of the ethical approval.	
The acquisition, analysis, or interpretation of data:	B
Free text description of PhD student's contribution (mandatory) RT was granted approval to radiological examination and additional outpatient visit / followup. The latter was carried out by KLR. RT has significantly contributed to the analysis (radiographs), data and the interpretation.	
Drafting the manuscript:	B
Free text description of PhD student's contribution (mandatory) Shared first authorship. RT and KLR contributed equally to drafting the the manuscript.	

*Free text description of PhD student's contribution **(mandatory)***
RT has managed the submission process.

Signatures of first- and last author, and main supervisor

Date	Name	Signature
20/2-2023	Rikke Thorninger (shared first author)	
20/2-2023	Karen Larsen Romme (shared first author)	
20/2-2023	Jan D. Rölfing (last author + main supervisor)	

Date: 10.03.23

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Signature of the PhD student